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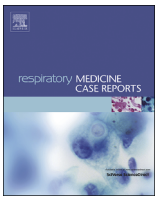

Case Report

Respiratory oscillometry with CT image analysis in idiopathic pulmonary fibrosis following single lung transplant

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ABSTRACT

Oscillometry is an emerging pulmonary function testing tool that is conducted during tidal breaths with minimal patient effort. It is highly sensitive to changes in lung mechanics. Oscillometry was recently shown to be highly associated with disease severity in idiopathic pulmonary fibrosis (IPF). The usefulness of oscillometry after single lung transplant in IPF patients is not well understood. Our study demonstrated that oscillometry can detect changes in the graft despite presence of a native fibrotic lung to provide useful information to complement spirometry.

1. Introduction

Idiopathic pulmonary fibrosis (**IPF**) is a common indication for single or bilateral lung transplantation (**LTx**). Graft monitoring with spirometry is the mainstay of post-LTx care. However, spirometry has only 57% sensitivity [1] and no specificity [2] for detecting acute rejection. It also requires maximal expiratory effort, a manoeuvre that is likely sub-optimal early post-LTx at a time when the risk of acute rejection is highest. By contrast, oscillometry measurements of respiratory mechanics are made during quiet breathing and require only minimal cooperation from patients. Oscillometry has been shown to be surrogate marker of graft injury after double LTx; it detected biopsy-proven but spirometrically-silent acute rejection [3] and was found to be associated with chronic lung allograft dysfunction, the major long-term cause of death after LTx [4]. Oscillometry is also useful in IPF, with the reactance metrics of **X5** and **Xel,** reactance at 5 Hz and end inspiration, respectively, being highly associated with disease severity [5].

The utility of post-transplant monitoring with oscillometry after single LTx is not known. We present pre- and post-transplant findings in an IPF patient who underwent single LTx and followed with paired oscillometry and spirometry.

2. Case details

A 66-year-old man with IPF, treated with nintedanib, underwent an uneventful single left LTx and was discharged home on day 20. At time of transplant, human leukocyte antigen crossmatch and donor-recipient cytomegalovirus IgG status were negative. Initial

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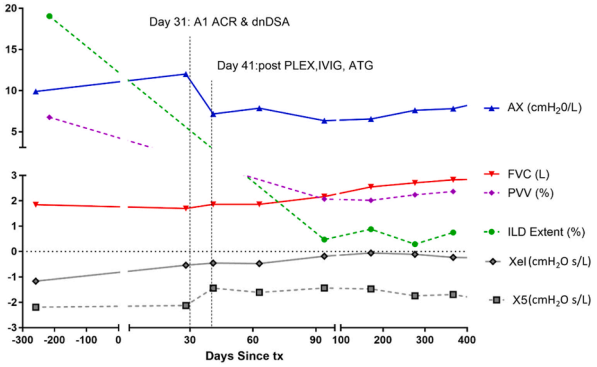

Fig. 1. Spirometry, Oscillometry and CT metrics before and after single LTx are shown. Measurements of ILD extent and PVV are for the transplanted lung.

oscillometry-spirometry on day 28 post-LTx were similar to pre-transplant except XeI which improved. Surveillance transbronchial biopsy and bloodwork on day 31 revealed grade A1 acute cellular rejection (ACR) and de novo donor-specific antibodies (dnDSA). He was admitted for plasmapheresis, intravenous immunoglobulin (IVIG) and thymoglobulin (ATG) therapy. On day 41, 10 days after starting augmented immunosuppression, X5 and AX, area of reactance (a robust metric that incorporates X5) had significantly improved whereas forced vital capacity (**FVC**) did not improve until day 94.

Pre- and post-LTx computed tomograph (**CT**) was analyzed using the automated Lung Texture Analysis. Based on the CALIPER technology, the analysis provides quantitative structural metrics of IPF severity that are expressed as a percentage of total lung volume: pulmonary vessel volume (**PVV**) and ILD extent, the sum of ground glass, reticular and honeycombing volumes. CT imaging at day 91 post-LTx showed no interstitial or airspace abnormalities but improved PVV and ILD extent in the transplanted lung whereas no change was seen in the native lung compared to pre-transplant (Fig. 1).

3. Discussion

The role of oscillometry for graft monitoring following single LTx is uncertain. Theoretically, measurement of respiratory mechanics in this scenario would be obscured by the significant abnormalities from the diseased native lung. Records of oscillometry testing prior to transplant allowed us to follow changes in the homogeneity of ventilation (X5 and AX) and respiratory elastance (X5 and XeI) post-transplant. XeI, is measured at zero flow at end-inspiration, and reflects the lung at its most stretched state during normal breathing. Both X5 and XeI improved (i.e. less negative) on day 41, reflecting improved respiratory stiffness post-transplant. ACR is characterized histologically by perivascular inflammation of lung parenchyma. The higher AX observed on day 31 likely reflect worsening of ventilatory homogeneity due to ACR. Oscillometry detected improved respiratory mechanics (higher X5 and XeI; lower AX) on day 41 following ACR treatment with augmented immunosuppression. In contrast, spirometry did not improve until day 94.

4. Conclusion

Oscillometry is sensitive to changes in lung mechanics after single lung transplant and can track changes associated with acute rejection and treatment. The current case demonstrates that oscillometry is feasible after single LTx and provides useful information about allograft function to complement spirometry.

Informed consent

Informed consent was obtained from patient prior to testing (REB # 19–5582).

CRediT authorship contribution statement

Joyce K.Y. Wu: Writing – original draft, Validation, Supervision, Project administration, Investigation, Formal analysis, Data curation. **Jessica Jia-Ni Xu:** Writing – review & editing, Formal analysis. **Anastasiia Vasileva:** Writing – review & editing, Data curation. **Cynthia Nohra:** Writing – review & editing, Data curation. **Matthew Binnie:** Writing – review & editing, Conceptualization. **Shane Shapera:** Writing – review & editing, Data curation. **Jolene H. Fisher:** Writing – review & editing. **Clodagh M. Ryan:** Writing – review & editing, Resources. **Micheal McInnis:** Writing – review & editing, Visualization, Formal analysis, Data curation. **Zoltán Hantos:** Writing – review & editing, Supervision, Formal analysis. **Chung-Wai Chow:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

CWC has received speaking fees from Thorasys Thoracic Medical Systems Inc. And AZ Canada, and has received consulting fees for Theravance Biopharma, Inc. CWC has received investigator-initiated research funding from Thoraysis Thoracic Medical Sys-

temic Inc. ZH has received consultation fees from Thorasys Thoracic Medical Systems Inc. On subjects unrelated to this study. JW has received consultation fees from Thorasys Thoracic Medical Systems Inc.

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