The accuracy of forced vital capacity for diagnosing restrictive allograft syndrome and mixed phenotype of chronic lung allograft dysfunction

Liran Levy[1,2], Ella Huszti[3], Gregory Berra[1], Benjamin Renaud-Picard[1], Mitsuaki Kawashima[1], Akihiro Takahagi[1], Sajad Moshkelgosha[1], Rasheed Ghany[1], Eyal Fuchs[1], Chung-Wai Chow[1], Shaf Keshavjee[1], Lianne G. Singer[1], Jussi Tikkanen[1,4] and Tereza Martinu[1,4]

[1]Toronto Lung Transplant Program, University Health Network, University of Toronto, Toronto, ON, Canada. [2]Institute of Pulmonary Medicine, Sheba Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel. [3]Biostatistics Research Unit, University Health Network, University of Toronto, Toronto, ON, Canada. [4]These authors have contributed equally to this work.

Liran Levy (liran.levy@sheba.gov.il)

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To the Editor:

Lung transplantation has become an invaluable approach for the treatment of end-stage respiratory diseases. However, survival after lung transplant remains limited due to chronic lung allograft dysfunction (CLAD), a fibrotic process affecting the airway and/or parenchymal compartments of the lung graft leading to a significant and persistent deterioration in lung function [1, 2]. With our accelerating understanding of CLAD, it has become evident that CLAD is a heterogeneous process comprised of multiple patterns of physiological and radiological features, which have strong implications for post-CLAD survival [3]. In a consensus document published by the International Society for Heart and Lung Transplantation (ISHLT) [2], CLAD remains defined as substantial and persistent decline (⩾20%) in forced expiratory volume in 1 s (FEV_1) from baseline, not explained by other conditions. There are four CLAD phenotypes defined by the presence or absence of obstruction (FEV_1/forced vital capacity (FVC) ⩽70%), restriction (total lung capacity (TLC) ⩽90% of baseline), and persistent pulmonary opacities on imaging (persistent parenchymal opacities and/or increasing pleural thickening consistent with a diagnosis of pulmonary and/or pleural fibrosis and likely to cause a restrictive physiology [2]). Bronchiolitis obliterans syndrome (BOS) is characterised by an obstructive ventilatory defect and no persistent pulmonary opacities; restrictive allograft syndrome (RAS) is characterised by a restrictive ventilatory defect with persistent pulmonary opacities; Mixed phenotype is characterised by a combination of obstructive and restrictive ventilatory defect, along with persistent opacities on chest imaging. Two “undefined” phenotypes, as outlined in the ISHLT consensus document, include 1) obstruction with persistent pulmonary opacities and no restriction; 2) a combined obstruction and restriction without persistent pulmonary opacities. Our group has previously shown that a subset of patients do not fit any of these combinations and remain unclassified [1] (patients

with a persistent decline in FEV_1 who do not meet criteria for obstruction or restriction or patients with a restrictive ventilatory defect without the presence of persistent pulmonary opacities).