Clinical Characteristics of Lymphangioleiomyomatosis and Application of a Novel Automated Cyst Burden Score

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Rationale: Lymphangioleiomyomatosis (LAM) is a rare cystic lung disease affecting women and usually presents during reproductive years with an estimated prevalence of 3-8 cases/million women. Serum vascular endothelial growth factor-D (VEGF-D) is a robust diagnostic biomarker and has been shown to predict progression but is normal in 30% of cases. With effective therapy available, it is increasingly important to determine biomarkers that predict progression. Methods: Clinical demographics for all patients with LAM attending the Rare Lung Disease Clinic (RLDC) which was established in 2019, were collated; this included age, menopausal status, presence of tuberous sclerosis complex, histology, VEGF-D levels, history of pneumothorax or chylous effusion, presence of renal angiomyolipomas (AMLs), pulmonary function tests and CT cyst-burden scores. Fully automated CT derived clustered volumetric analyses was performed on HRCT images using commercially available software. Clustering of low attenuation cysts by volume was quantified to determine percentage of total lung involvement and distribution of cyst size. Cyst scores were calculated for a range of Hounsfield units (HU) from -900HU to -950HU. Cyst scores were correlated with DLCO, FEV1 and VEGF-D. Results: Twenty-one female patients with LAM were included; mean age 51.24 years (range=27-84). Seven patients had a history of pneumothorax, three had chylothorax, and nine had AML. Mean VEGF-D level was 702.69 (SD+/-228.1). Mean DLCO was 66.92% predicted (SD+/-17.2). There was a negative correlation between VEGF-D and DLCO (n=13; R²=0.458; p=0.0111) and VEGF-D with FEV1 (n=14; R²=0.2741; p=0.0547). Cyst scores calculated at -940HU positively correlated with VEGF-D levels (n=6; R²=0.8847; p=0.0052) and cyst scores utilising a cut-off of -900HU (n=6, R²=0.7957; p=0.0169). DLCO There was an inverse correlation between DLCO and cyst burden scores at -940HU (R²=0.8239; p=0.0124) and -900HU (R²=0.749; p=0.0259). Conclusion LAM is a rare progressive lung disease; however, it is likely that the prevalence is underestimated. The identification of 21 women with LAM in a one year period highlights this; the female population of Ireland is 2.4 million, hence the prevalence is at least 8.75 per million; which is likely higher as all cases are not identified or accounted for in this initial national study. Future studies are needed to determine the true prevalence of LAM in Ireland, which is feasible given the limited geography and population. Such data may inform the prevalence worldwide. Finally, this widely available automated cyst-burden score will be a useful biomarker in LAM and we aim to further validate this prospectively.