Telomere Length In Chronic Hypersensitivity Pneumonitis Explant Lungs

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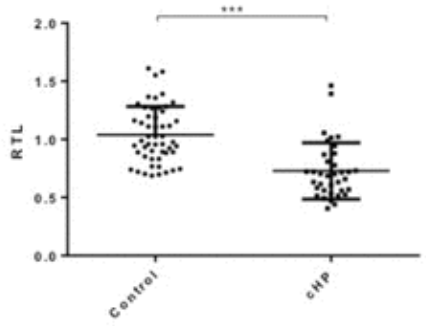
Rationale: Telomere length is believed to play an important role in the pathophysiology of interstitial lung diseases such as idiopathic pulmonary fibrosis, as a parameter of premature biological ageing. Chronic Hypersensitivity Pneumonitis (cHP) was associated with a lower telomere length in peripheral blood leukocytes. However, whether telomere length is also reduced in cHP lung tissue has not been studied. Furthermore, it is unknown whether telomere length is associated with fibrosis severity in cHP lungs.

Methods: We analyzed 9 cHP explant lungs and 9 matched unused donor lungs (controls). The lungs were air-inflated, fixed and systematically sampled. We analysed four 4 cores per lung (2 from upper lobe and 2 from lower lobe with varying degree of parenchymal fibrosis as assessed with microCT of the frozen lung sample (Skyscan 1172)). Afterwards the relative telomere length was measured using qPCR.

Results: Relative telomere length (RTL) in cHP lungs was statistically significantly reduced compared to donor lungs ($p<0.001$). There was a considerable heterogeneity within the samples derived from the same lung both in control and cHP lungs. The mean telomere length in the controls correlated with the age of the donor lungs ($p<0.001$). This demonstrates that lung telomere length is feasible and physiological relevant. However, no association between telomere length and surface density ($p=0.38$) or tissue% ($p=0.18$) was found, using a mixed effects model to correct for lung sample and age.

Conclusion: Similar to IPF, telomere length was reduced in cHP explant lungs compared to controls, providing further evidence for the pathophysiological role of biological ageing in fibrotic interstitial lung disease. However, there was no association with the degree of fibrosis. Hence, excessive biological ageing may represent an early risk factor for interstitial lung disease, possibly requiring another factor for progressive fibrosis.



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