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Title: Mid-thigh intramuscular fat is associated with physical inactivity and quadriceps fibre type profile in patients with COPD

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Body: Introduction: Quadriceps muscle dysfunction is an important complication of COPD occurring in mild and more advanced disease. It is largely driven by physical inactivity and is characterised by atrophy and a shift towards a less aerobic phenotype, with reduced Type I fibre proportions and oxidative enzymes. We hypothesised that physical inactivity and fibre type shift would be associated with intramuscular fat and that this could be a non-invasive and non-volitional marker of muscle quality. Methods: Mid-thigh cross-sectional area (MT_{CSA}) and percentage intramuscular fat were assessed using computed tomography (CT) image analysis. Tissues were differentiated using standard attenuation ranges; fat -190 to -30 and skeletal muscle -29 to 150 Hounsfield Units. Daily step count and physical activity level (PAL) were recorded using an armband accelerometer (SenseWear, Bodymedia). Type I and II fibre proportions were determined from vastus lateralis samples using immunohistochemistry. Associations were determined using multivariate regression models incorporating MT_{CSA} and age. Results: CT data were available for 102 patients (61 male, mean (SD) age 65(8) years, FEV_1 41(20)% predicted) and 10 age-matched healthy controls. Accelerometer and biopsy data were obtained in 69 and 58 participants respectively. Percentage intramuscular fat was higher in the patient group (6.7(3.5) vs 4.3(1.2)%, $p<0.01$) and was independently associated with PAL ($r=-0.33$, $p=0.02$) and Type I fibre proportion ($r=-0.33$, $p<0.01$). Conclusion: Intramuscular fat assessed using CT reflects multiple aspects of muscle dysfunction in patients with COPD and may provide a valuable biomarker in this group.