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Title: Reference values for vastus lateralis fiber size and type in healthy subjects over 40 years old. A systematic review and meta-analysis

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Body: Skeletal muscle atrophy is a major systemic impairment in chronic diseases. Yet its determinants have been hard to identify because a clear research definition has not been agreed upon. The reduction in muscle fiber cross-sectional area (CSA) is a marker of muscle atrophy, but no reference values for the muscle fiber CSA at the age of the onset of chronic diseases have ever been published. Thus, we aimed to systematically review the studies providing data on the fiber CSA and fiber type proportion in the vastus lateralis of the quadriceps of healthy subjects (age >40 yrs) and then to pool and analyze the data from the selected studies in order to provide reference values for fiber CSA. Following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), we identified 19 studies, including 423 subjects, that matched the inclusion criteria. Based on fiber type and gender, the mean fiber CSA and the lower limits of normal (LLNs) were (%type I*60)+1743µm² and (%type I*60)-718µm², respectively, for males; and (%type I*70)+139µm² and (%type I*70)-1485µm², respectively, for females. The pooled type I fiber proportion was 50.3% (LLN=32.9%). In multivariate analysis, fiber CSA was significantly correlated with peakVO_2 (r=190.92; p=0.03), and type I fiber proportion was correlated with age (r=-0.024; p=0.005), BMI (r=0.096; p=0.005), and peakVO_2 (r=-0.053; p=0.005). Our meta-analysis of a homogeneous set of studies is the first to provide valuable LLNs for fiber CSA according to fiber type and gender. This analysis will be improved by prospective assessment in well-characterized healthy subjects.