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Reference values for vastus lateralis fiber type proportions and fiber size

Harry R. Gosker and Annemie M. W. J. Schols
Department of Respiratory Medicine, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center+, Maastricht, The Netherlands

TO THE EDITOR: Recently Gouzi et al. (3) reported reference values and lower limits of normal (LLNs) for vastus lateralis fiber size and type in healthy subjects over 40 years old. LLNs are useful to distinguish pathology from physiological variation in high-risk patient groups such as chronic obstructive pulmonary disease (COPD). The authors report a LLN for fiber type I of 33% and claim this value is more valid than the one (27%) we reported previously (2) because the latter would not have resulted from a systematic review. We would like to rectify this statement because our reference value also resulted from a systematic review. Although we reported the same average fiber type I proportion (51%) in healthy subjects, the pooling of SDs was done using different approaches, which could have caused the differences in LLNs. Regardless, a substantial subgroup of COPD patients has a fiber type I proportion below either LLN, indicating that abnormally low fiber type I proportions indeed occur in this disease. Interestingly, this loss of type I fibers is frequently attributed to reduced physical activity, whereas this review clearly contradicts this assumption as physical activity was not a determinant of fiber type I proportion, which is in line with our recent findings (4).

Gouzi et al. also provide prediction formulas and LLN values for fiber size [expressed as cross-sectional area (CSA)], based on sex and fiber type I proportion. We appreciate that sex should be considered in any fiber CSA analysis as elegantly illustrated in the paper, but we seriously doubt the usefulness of the presented prediction formulas. We correlated the actual fiber CSAs with the proposed predicted normal values of 53 healthy controls (36 men and 17 women, average age 63 yr) derived from two previously published studies (Refs. 1, 4, and additional unpublished data). Albeit statistically significant, we found a rather weak correlation ($r = 0.561, P < 0.001$), with 68.5% unexplained variation. Furthermore, applying the LLN prediction formula to determine whether muscle fiber size is abnormally low in COPD appears impractical. Of 44 patients with COPD (1, 4) none had a fiber CSA below the calculated LLN, in contrast to consistently reported reduced values compared with healthy age- and sex-matched controls (1, 5).

Moreover, for 10 of the 15 patients with advanced COPD (1), the LLN value was $<338 \mu m^2$ (being the smallest average LLN for fiber CSA regardless of fiber type or sex, as reported by Gouzi et al.), and for five the LLN even was $<0 \mu m^2$. The average LLN was $134 \mu m^2$, which is unrealistically low. Even for patients with less advanced COPD (4) we calculated negative LLNs. The patients with LLNs close to or below zero are characterized by abnormally low fiber type I proportions, indicating that the prediction formulas do not apply in case of fiber type redistribution. The review by Gouzi et al. reveals two important insights. First, the traditionally presumed contribution of physical inactivity to the loss of type I fibers is likely overrated. Second, sex should be considered when analyzing fiber sizes. The presented formulas for normal and LLN CSA values however, are of limited utility, especially when applied in situations of changed fiber type distribution.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
Author contributions: H.R.G. drafted manuscript; A.M.S. edited and revised manuscript; A.M.S. approved final version of manuscript.

REFERENCES

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