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Letter to the Editor

Before Concluding that Muscle Fat Increases in DMD/BMD Carriers Over a Period of 6.5 Years, All Influencing Factors must be Included in the Analysis

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Letter to the Editor

We read with interest the article by Lyu *et al.* on a cross-sectional study of changes in muscle structure and function over a period of 6.5y in 31 female Duchenne/Becker muscular dystrophy (DMD/BMD) carriers ^[1]. The muscle-fat ratio in the lower back, thighs, and calves increased by 2% over a period of 6.5y, with a maximum increase of 31% ^[1]. At the same time, muscle strength decreased more in DMD-carriers than in BMD-carriers ^[1]. The study is interesting, but some points need clarification.

The first point is that no interobserver variability was calculated between the researcher who drew the initial muscle contours and the second researcher who checked them for accuracy ^[1]. How many measurements did the two observers disagree on, and how large was the deviation in the measurements of both observers? If the two observers disagreed on the determination of muscle boundaries, how was this disagreement handled? Since individual muscle boundaries are not always easy to identify on cross-sectional areas of a limb, especially when intramuscular and extramuscular fat has increased, it is very likely that there was disagreement on several muscles.

The second point is that DMD/BMD-carriers not only manifest phenotypically in skeletal muscles, but also in the myocardium, cardiac conduction system, brain, and smooth muscle cells, since dystrophin is expressed not only in myocytes, but also in cardiomyocytes, certain neurons, glial cells, and smooth muscle cells ^[2]. This may have a secondary effect on muscle performance. Furthermore, muscle involvement may not always be the first clinical symptom in DMD/BMD-carriers; in some of these women, the disease may initially manifest itself in the myocardium or other tissues ^[3]. For example, dilated cardiomyopathy may be the first manifestation of a DMD-carrier ^[4]. Accordingly, it is conceivable that the exertional dyspnea in patient 20 was due to cardiac involvement, as FVC was normal, ruling out respiratory muscle involvement ^[1].

The third point is that muscle strength and muscle-fat mass depend not only on the underlying dystrophin mutation, but also on daily or weekly physical activity. Since daily activities, occupation, extent of physical therapy, and extent of sports activities were not included in the analysis, the results may be unreliable. The inclusion of physical activity in the analysis is crucial, as it affects muscle composition, strength, and function ^[5].

The fourth point is that the ratio of fat to muscle may also depend on the diet of the patients examined. Patients with a high-fat, high-calorie diet may have an increased risk of muscle adiposity compared to patients who consume little fat. Therefore, the composition of the diet must be included in the analysis.

The fifth point relates to the occurrence of symptoms in childhood in four BMD-carriers (patients 21, 22, 25, 26) ^[1]. Initial clinical symptoms in childhood in BMD-carriers are rather unusual. We should know whether the sons of these women also showed their first symptoms in childhood.

Finally, it is not clear why 34 patients were included in the analysis, even though only 31 completed the follow-up examination using MRI.

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