

NUTRITIONAL ASPECTS OF NEUROMUSCULAR DISEASES

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Both rapidly progressive Duchenne muscular dystrophy (DMD) and the slowly progressive neuromuscular diseases (SP-NMDs) are associated with loss of skeletal muscle, gain of excess body fat, and changes in energy metabolism and physical activity over time. This article reviews several nutritional techniques and their adequacy in monitoring changes in the nutritional status of these individuals as the diseases progress. In addition, nutritional interventions that aim to counteract the effects of the disease process and increase the quality of life in individuals with DMD are reviewed. Finally, new research on physical activity and body composition, and the potential for development of secondary chronic diseases in SP-NMD are discussed.

DUCHENNE MUSCULAR DYSTROPHY

There is a high prevalence of obesity in DMD. Excess body weight in DMD subjects burdens already weakened muscles and makes breathing and mobility difficult. Older DMD patients tend to lose weight as the disease progresses and there is an acceleration in the breakdown of

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skeletal muscle. The progressive loss of lean tissue in DMD can be monitored through nutritional techniques. Nutritional interventions including weight loss and dietary supplementation have been evaluated for their effectiveness in increasing quality of life in DMD patients and attenuating the disease process. The following section will review studies on nutritional assessment and management of DMD.

Stature

Accurate measurement of stature of DMD patients is difficult because of the high incidence of spinal deformities and scoliosis in this population, particularly in the latter stages of the disease. Most cross-sectional data^{38, 47, 52} indicate that attained height in the first decade is similar to or slightly below the median height-for-age of the National Center for Health Statistics' reference,²⁵ but falls markedly below the fifth percentile during the second decade.³⁸ McDonald et al³⁸ found that this dramatic reduction in standing height relative to normal values occurred mainly in wheelchair users with contractures and scoliosis. These authors stated that although the *incidence* of scoliosis did not differ between boys in the lowest versus the highest quartile for stature, they could not rule out differences between quartiles in the *severity* of the scoliosis which potentially may have biased their results. However, longitudinal data from Eiholzer et al¹⁶ indicate slow linear growth in DMD patients beginning shortly after birth, before scoliosis occurs. Thus, the decreased linear growth seen in DMD subjects of all ages may not, in fact, be measurement artifact. McDonald and colleagues³⁸ point out that a lack of normal muscle tension or weight bearing on the skeleton may in theory contribute to decreased linear growth in this population, but this has not been evaluated by adequate techniques. The relatively short stature of individuals with DMD also may be due in part to undernourishment because they often do not consume enough protein and energy to meet their nutritional needs.^{38, 44} The hypothesis that skeletal development is reduced in DMD subjects is supported by their lower bone mineral density compared with age-matched controls.⁴⁶ Within the DMD group, there was a significant inverse relationship between bone mineral density and age; this relationship was not found for able-bodied controls.

Weight and Body Composition

The appropriateness of body weight in DMD patients has traditionally been evaluated against national standards of weight-for-age. It should be kept in mind, however, that weight-for-height may be a better index than weight-for-age for evaluating current nutritional status because weight-for-age does not take into account differences in height.¹⁴ A subject's weight may be appropriate for his or her age, but since DMD

subjects tend to be short for their age, using weight-for-age alone may underestimate the prevalence of overweight in this population. However, as stated in the previous section, accurate measurements of height often are difficult to obtain in individuals with DMD because of the presence of spinal abnormalities and contractures.

Overweight vs Underweight

Compared to the United States reference population, the prevalence of underweight (defined as weight-for-age <10th percentile) gradually increases with age, as shown in Figure 1A. Between the ages of 13 and 16.9, 40% of DMD subjects were underweight, and, over age 17, 65% of DMD subjects were underweight in McDonald et al's study.³⁸ This is much higher than the prevalence of underweight (10%) in the normal population. Overweight in DMD also is a problem. In the same sample

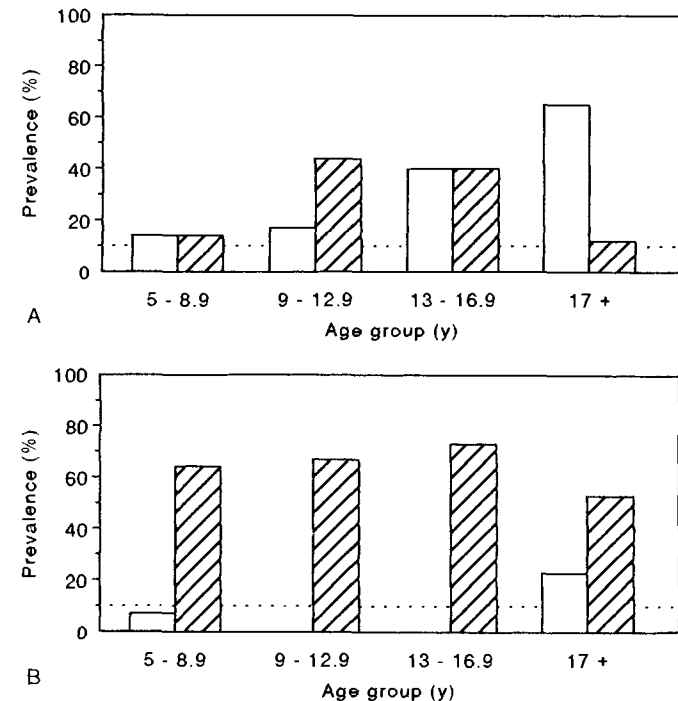


Figure 1. Percentage of Duchenne muscular dystrophy (DMD) subjects classified as underweight (weight-for-age <10th percentile) and overweight (weight-for-age >90th percentile) compared to the US reference population (Hamill et al) (A) and the DMD ideal weight chart (Griffiths and Edwards) (B). Dotted line = expected prevalence of overweight and underweight based on a normal distribution; Open bar = underweight; hatched bar = overweight. (Data from McDonald CM, Abresch RT, Carter GT, et al: Profiles of neuromuscular diseases: Duchenne Muscular Dystrophy. *Am J Phys Med Rehabil* 74:S70-92, 1995.)

of DMD subjects, between the ages of 9 and 16.9, about 40% were classified as overweight (defined as weight-for-age >90th percentile). These data indicate that in early adolescence there may be a divergence of weight in the DMD population such that many have either an extremely low or extremely high weight for their age, and that somewhere near late adolescence most individuals with DMD become underweight. Similar patterns of weight-for-age were reported by Willig et al,⁶⁵ who studied a sample of 252 DMD patients. They reported that 54% of their subjects were above the 90th percentile in weight-for-age by age 13, and 54% were below the 10th percentile by age 18. Scott et al⁵² link the development of obesity in DMD with loss of independent ambulation. However, McDonald et al³⁸ found no relationship between the presence of a high weight-for-age and either the age of wheelchair dependence, loss of strength, timed motor performance, functional grade status, pulmonary function, likelihood of ECG abnormalities, or age at death.

One limitation of simply using body weight as a standard is that the composition of the weight is unknown. Weight is made up of both fat and lean tissue, with skeletal muscle contained in the latter. Knowing the composition of the body allows us to gain insight into how much of the weight is excess body fat, or how much weight loss is due to loss in muscle mass from progression of the disease. Because the evolution of DMD is associated with progressive loss of skeletal muscle, at a given weight-for-age patients with DMD will have a lower lean mass than able-bodied subjects. Thus, an individual with DMD ideally should weigh less than an able-bodied individual for a given age, since loss of muscle mass over time is inevitable and excess body fat is undesirable.

In 1988, Griffiths and Edwards²⁴ proposed an ideal weight chart for DMD patients, which was meant to serve as a guideline for weight management in this population. This theoretical chart was constructed from previous observations and assumes a 4% decline in muscle mass per year.^{14, 15, 57} The effect of this new chart on weight classification is that at a given age, DMD patients are classified at a higher percentile than they would be on the standard chart. For example, a 10-year-old DMD patient who weighs 25 kg appears to be in the 10th percentile of weight-for-age based on the normal chart, but is actually at the 50th percentile on the DMD chart. This was illustrated in the study by McDonald et al,³⁸ who found that a much higher percentage of their subjects were classified as overweight when using the Griffiths and Edwards²⁴ chart than the standard weight chart (Fig. 1B). The Griffiths and Edwards²⁴ chart was tested for validity in 1993 by another set of investigators.⁶⁵ To evaluate the chart, Willig et al⁶⁵ compiled data from previous studies and also used their own data to produce a final sample size of 252 DMD subjects. They compared their weight-for-age data with the reference chart for French patients⁵³ and also the new DMD ideal weight chart proposed by Griffiths and Edwards.²⁴ These authors concluded that while the chart is a valid tool for monitoring weight in DMD patients, it may slightly underestimate the effect of the disease.

Whole-body Composition and Estimates of Skeletal Muscle Mass

Whole-body composition, and thus lean tissue mass, in DMD has been estimated with highly specialized techniques such as magnetic resonance imaging,⁵¹ computed tomography,⁴³ ultrasonography,²⁷ potassium-40 counting,^{4, 33} and potassium-40 dilution.¹⁴ In addition, estimates of muscle mass in DMD can be accomplished biochemically by 24-hour urinary creatinine, and skeletal muscle degradation can be estimated from 24-hour urinary 3-methylhistidine measurements.^{21-23, 44} However, these methods are either tedious or not readily available, and are not well suited to routine clinical use.

Two recent studies have used dual energy x-ray absorptiometry (DEXA) to assess whole-body composition in DMD.^{31, 46} Using this technique, the body mass can be divided into regional and total body bone mineral, fat tissue, and soft lean tissue masses. The major portion of the latter is skeletal muscle; thus, determination of lean soft tissue mass by DEXA provides a proxy measurement of skeletal muscle mass. DMD patients have been shown to have a higher body fat mass and a lower lean soft tissue mass than controls.^{31, 46} Palmieri et al⁴⁶ documented significant changes in body composition with increasing age in DMD. While the percentage of fat tissue mass increased with increasing age, the percentage of lean soft tissue mass decreased with increasing age. These relationships did not exist for control subjects. Further, these authors reported associations between the percentage of lean soft tissue mass and upper and lower extremity functional scores and manual muscle testing scores. Thus, DEXA may be useful for documenting changes in nutritional status with disease progression and responses to therapeutic interventions.

Use of Anthropometry in DMD

Upper Arm Muscle Area. In the absence of highly technical equipment such as DEXA, simple anthropometric techniques can be used to determine the upper arm muscle cross-sectional area (UAMA) using the following formula by Frisancho et al¹⁸:

$$UAMA = [(C - (\pi \times TSK))^2] / 4\pi$$

where C = mid-upper-arm circumference and TSK = triceps skinfold thickness. This equation has been found to overestimate mid-arm muscle area by 20% to 25%, and thus underestimates muscle atrophy.²⁸ However, expressing UAMA as a percentage of the median normal value negates this error, since the normal values also are overestimated by the same amount. In addition, the precision of estimates of UAMA by trained examiners is 7%; thus, it cannot be used to measure changes that are smaller than this. It must be emphasized that this equation only provides a rough estimate of UAMA. Caution also must be exercised when using this equation for individuals with DMD because of infiltra-

