Nutritional and Gastrointestinal Management of the Patient With Duchenne Muscular Dystrophy

David Brumbaugh, MD, MSCS, Laura Watne, MS, RD, Frederic Gottrand, MD, Ann Gulyas, MA, CCC-SLP, BCS-S, Ajay Kaul, MD, Jacqueline Larson, MS, RDN, Jean Tomezsko, PhD, MPH

Advances in treatment and multidisciplinary management have resulted in improved survival of individuals with Duchenne muscular dystrophy (DMD). Updated DMD treatment recommendations as found in the 2018 DMD Care Considerations are aimed to assist multidisciplinary care teams in providing standardized care to their patients, including attention to nutritional and gastrointestinal health. Challenges remain for care teams in accurately estimating height and nutritional status for individuals with DMD. It can be difficult for patients to maintain a healthy weight. Risk factors for obesity include glucocorticoid therapy and loss of ambulation. In contrast, in the later stages of the disease, swallowing dysfunction can lead to poor nutrition and consideration for gastrostomy tube placement. Constipation is highly prevalent, underrecognized, and undertreated in DMD. With this article, we address the assessment and management of gastrointestinal and nutritional issues, as well as clinical controversies.

The multidisciplinary team caring for patients with Duchenne muscular dystrophy (DMD) will be familiar with the most commonly anticipated gastrointestinal and nutritional hurdles that occur during the life course (weight gain with the initiation of glucocorticoid therapy and at loss of ambulation, weight loss with progression of dysphagia, and struggles with gastrointestinal motility, specifically constipation). Unanswered questions faced by the DMD care team in...
**Assessment and decision-making** are shared with other progressive neuromuscular diseases, including accurate assessment of nutritional adequacy in the face of deteriorating lean body mass and optimal timing to initiate supplemental nutrition. With this review, we present key nutritional and gastrointestinal recommendations that emerged from the 2018 DMD Care Considerations sponsored by the Centers for Disease Control and Prevention (CDC). For an overview of those recommendations, see Fig 1. This article is also focused on areas of clinical controversy that are encountered in the management of patients with DMD.

### NUTRITION

#### Critical Role for the Nutrition Team in Management

The goal of nutritional management is to prevent overweight or obesity and undernutrition or malnutrition through regularly evaluating growth and weight and promoting a healthy, balanced diet. Toward that goal, a critical recommendation from the 2018 DMD Care Considerations is the inclusion of a registered dietitian nutritionist (RDN) as an essential member of the multidisciplinary DMD care team. Acknowledged in this recommendation are the ongoing nutritional needs of patients with DMD beginning at diagnosis and the importance of reassessment throughout life. At every neuromuscular team visit, the RDN may assist with and/or review anthropometric measurements, assess the nutritional status of the patient, and create a specific nutritional plan. Anthropometric measurements should be obtained by a trained care team member according to standardized procedures. Assessment should consist of the following: interpretation of anthropometric measurements; medical history with laboratory results; diet history, including food and fluid intake; vitamin, mineral, and/or herbal intake; estimated energy, protein, and/or micronutrient as well as fluid needs; medications; food allergies and intolerances; gastrointestinal symptoms; chewing and swallowing function; ambulatory status; and psychosocial issues. A nutritional plan includes recommendations regarding increasing, decreasing, or maintaining caloric intake; macronutrient and micronutrient composition of the diet; hydration goals; and alterations in food textures to aid in safe and comfortable chewing and swallowing. Nutrition education materials should be offered along with patient and family counseling. Most nutrition recommendations are based on those for the general population because strong, evidence-based nutrition research for DMD is not available at this time. The promotion of a healthy,
balanced diet for both the patient with DMD and the family is based on the 2015–2020 Dietary Guidelines for Americans.2

Transition Periods That Predictably Affect Nutritional Status

The life course of DMD frequently presents care teams with the successive opposite challenges of managing patients who are overweight earlier in life followed by the struggle to maintain adequate weight as the patients reach adulthood. Patients treated with glucocorticoid therapy gain more weight compared with untreated children with DMD.3 Steroids can increase appetite, caloric intake, and sodium and/or fluid retention. A small study in which researchers studied steroid-treated and steroid-naive children for 2 years suggested that the weight gain experienced in the treatment group was driven by increases in fat-free mass rather than fat mass.4 The more potent driver of increased fat mass in early life may be at loss of ambulation, when children experience a significant decrease in energy expenditure at a time when swallowing function is intact and caloric intake remains high relative to activity. Families should be prepared for these anticipated impacts, and management plans should be focused on providing a healthy, balanced diet as well as achieving appropriate levels of exercise, adapted as needed by an experienced physical therapist. Later in life, as dysphagia progresses, caloric intake will decrease and unintentional, sometimes severe, weight loss is typical. Malnutrition can also result when patients lose the ability to self-feed, such as when they experience progressive upper extremity weakness or as a postoperative complication after spinal fusion surgery.5 For details on assistive technology for arm support and robotics, see the specialty article in this supplement, “Rehabilitation Management of the Patient With Duchenne Muscular Dystrophy.”6

Clinical Controversy: Growth Charts for Assessing Nutritional Adequacy

A fundamental component of pediatric nutritional assessment is anthropometric measurement and comparison of these measures to validated, age-appropriate growth references such as the World Health Organization growth charts for children ages 0 to 2 years7 and the CDC Clinical Growth Charts for children ages 2 to 18 years.8 Clinicians wishing to use these growth charts for patients with DMD face the following 2 major obstacles: (1) obtaining accurate estimates of height becomes difficult once patients lose ambulation, and (2) the loss of lean body mass over time makes it impossible to compare weight in DMD to reference data compiled from unaffected children.

DMD-specific growth charts have been reported in the literature. Edwards et al9 used 24-hour urine creatinine excretion to estimate the total muscle mass in a group of 26 patients with DMD, finding a decline of muscle mass of ~4% per year. By adding these data to “0 muscle mass charts,” the authors constructed a weight-for-age curve for DMD, in which the appropriate centile would be found by first identifying the centile on a standard height centile chart.10 Subsequent research has revealed that urine creatinine excretion is poorly predictive of skeletal muscle mass in DMD, calling into question the original approach to deriving this growth chart.11 West et al12 constructed DMD-specific growth curves using repeated growth measures in a cohort of 513 patients with DMD ages 2 to 12 years from the Muscular Dystrophy Surveillance, Tracking, and Research Network surveillance system. These curves revealed that male patients with DMD were shorter than unaffected male individuals measured on CDC clinical growth charts and tended toward extremes in weight. Because weight and height measures were excluded after loss of ambulation, their sample sizes dropped off dramatically after age 10 years, making these growth curves most useful for the preadolescent population. The accuracy of the height measures were questioned by the authors because of a failure to use a standard method for measurement in the setting of loss of ambulation and body posture in their subjects. Their data set did not include any patients on glucocorticoid therapy, thereby limiting applicability. However, this same group returned to interrogate the Muscular Dystrophy Surveillance, Tracking, and Research Network cohort, recently reporting growth data in a cohort of 324 amulatory patients on glucocorticoid therapy for at least 6 months.3 Compared with untreated patients, this cohort had shorter stature, increased weight, and greater BMI. Because the mean age of steroid initiation in this cohort was 6 1/2 years, data were more limited for the preschool-aged children, but growth charts conducted from this cohort represent the best reference available for preadolescent patients with DMD.

Clinical Controversy: Estimating Height in DMD

An accurate standing height measure is necessary for all ambulatory patients. Measuring standing height in ambulatory patients with DMD can be problematic because of their characteristic toe walking and difficulty with placing their feet flat on the floor. Because an accurate standing height measure is often impossible in nonambulatory patients with DMD, the clinician should use another method for estimating height. Although many methods are available for estimating height of nonambulatory patients,
including patients with cerebral palsy, no specific method has been studied for use in DMD. Potential methods include segmentally measured recumbent length, arm span, ulnar length, knee height, and tibia length. Because each of these techniques requires either special equipment or operator skill, the recommendation from the 2018 DMD Care Considerations is for centers to choose 1 method and gain experience with that method. Clinical studies are needed to validate the use of 1 or more of these techniques by comparing them to standing height in patients with DMD before a complete loss of ambulation.

Clinical Controversy: BMI and Body Composition Assessment in DMD
The most commonly used clinical tool for estimating body fat in children is BMI, which is calculated as weight in kilograms divided by height in meters. When compared with population-based norms, BMI is used to categorize a person as underweight, normal weight, overweight, or obese. As an assessment of “normal weight,” BMI is used to assume a relationship between muscle mass and fat mass that is reasonable for the general population. At extremes of muscle mass and/or fat mass distribution, such as in the case of bodybuilders or patients with muscular disease, BMI cannot be compared with whole population references to assess nutritional adequacy. In DMD, the use of population-based BMI norms inappropriately characterizes patients as underweight who have normal or increasing fat mass. Additionally, by incorporating the exponent of height in calculating BMI, inaccuracies in height estimation in nonambulatory patients will substantially affect the reliability of BMI. Despite these shortcomings, BMI charts can be helpful for tracking individual patient’s growth trends over time, assuming height is estimated correctly. When height is unable to be accurately measured, the clinical team may be limited to longitudinal tracking of weight-for-age percentiles on CDC clinical growth charts, noting that consistent growth within the 10th to 85th percentile is generally considered good for children in the general population.

Accurate, readily available methods of estimating body composition in DMD are needed for ongoing nutritional assessment. Dual-energy x-ray absorptiometry (DXA) is a reference standard for the measurement of body composition, against which other techniques are frequently assessed. The expense of DXA and fact that this approach involves patient exposure to ionizing radiation, albeit a small amount, has made DXA unavailable for the routine longitudinal assessment of body composition. Bioelectrical impedance analysis (BIA) is an indirect estimate of fat mass and is used to measure the resistance to electrical current in tissue that is proportional to total body water, from which estimates of fat-free mass and then fat mass are derived. A strength of BIA is that it is easily obtained in a clinic setting. Several investigators have studied the use of BIA for body composition assessment in DMD. Unfortunately, the researchers of these studies used different equations to calculate fat-free mass, calling into question the external validity of this approach. Like BMI, a major drawback to BIA is that height is a required variable; therefore, inaccuracy in height measurement in nonambulatory patients adds substantial error to the prediction of fat mass.

Triceps skinfold (TSF) and mid-upper arm circumference measurements are used to provide information about body composition, and these measurements can be taken in clinic by a trained RDN. TSF is an estimation of body fat, and mid-arm muscle area can be calculated from TSF and mid-upper arm circumference measurements. As with population-based norms for growth and BMI, comparing the arm anthropometrics of patients with DMD to population-based norms has limitations, although they can be useful anthropometrics to track over time. The most important concern regarding anthropometric measurements such as skinfolds is reliability. However, studies revealing acceptable intraobserver precision for TSF can be used to support the ideal scenario of having an experienced RDN perform skinfold measurements in a cohort of patients over time. Clinical studies are needed to further evaluate the use of arm anthropometrics to track body composition in patients with DMD.

Clinical Controversy: Vitamin, Mineral, Amino Acid, and Herbal Supplements
The 2018 DMD Care Considerations recommend that dietary calcium and serum 25-hydroxy vitamin D be assessed each year as part of routine bone health management. Supplementation with calcium and vitamin D may be recommended if the patient’s dietary intake of calcium is less than the Recommended Dietary Allowance for age or if serum 25-hydroxy vitamin D is <30 ng/mL (see the “Bone Health and Osteoporosis Care of the Patient With Duchenne Muscular Dystrophy” article in this supplement). A multivitamin and/or mineral supplement may be recommended if the patient’s energy intake or food variety is low. Beyond assessing bone health, authors of few studies have assessed the impact of micronutrient, amino acid, and herbal supplements on the nutritional status in patients with DMD; yet, the use of these products occurs in up to 65% of patients with DMD.
Evidence for the use of coenzyme Q10, green tea extract, resveratrol, glutamine and/or amino acids, creatine, and Protandim to improve muscle cell function is limited, so it is difficult to provide meaningful recommendations for individual patients.24 It is best to discuss nutritional supplementation on a case-by-case basis with patients, and the RDN can help determine safe and appropriate doses of individual nutrients.

Clinical Controversy: Role of Gastrostomy Tube Placement in DMD Management

Evidence clearly indicates that gastrostomy tubes can be helpful for nutrition support in the management of undernourished patients with DMD.25,26 The 2018 DMD Care Considerations urge care teams to provide anticipatory guidance for patients and families on the topic of gastrostomy tube feedings. The goal of early, proactive discussion is to familiarize families with the device and its indications for placement, thereby reducing the likelihood patients and families view placement as a surprise or care team failure. Consideration of anesthesia risks for patients with advanced disease would also be used to argue for earlier discussion and decision-making. Reports of the use of noninvasive ventilation during percutaneous endoscopic placement of a gastrostomy tube in patients with a forced vital capacity <1 L suggest that in a care setting with experienced anesthesia and pulmonary support, gastrostomy tube placement is feasible even in patients with advanced DMD.27,28

Shared decision-making around the timing of this procedure will require the involvement of the patient, family, and several members of the care team, including the pulmonologist and cardiologist, to establish anesthesia risk. Clinicians may choose to place a gastrostomy tube when patients are underweight or malnourished or have experienced significant weight loss, when they have moderate to severe dysphagia resulting in aspiration, and/or when they are unable to maintain adequate energy, protein, or hydration intake by mouth.

SWALLOWING

Beginning usually in the teenage years, swallowing dysfunction (dysphagia) is universal and progressive in patients with DMD.29 Patients also have difficulties with chewing, slow oral food bolus transit, and pharyngeal residue after swallowing.30 The first symptom may be prolonged duration of mealtimes, advancing to fear of or actual choking events, and difficulty swallowing solid foods.31 When severe, dysphagia can place patients at risk for weight loss, dehydration, choking, and aspiration events. Hence, the care team must be vigilant at every visit to identify clinically significant dysphagia and to institute appropriate interventions and a referral to a feeding therapist, typically a speech-language pathologist. Although authors of few studies have assessed the efficacy of swallowing strategies in the DMD population, the following strategies have been shown to provide clinical value in other populations: altering diet texture (soft, chopped, or puree foods); use of half teaspoon amounts, administered slowly; a swallow-hard strategy; and a cough-and-swallow strategy.

Interestingly, worsening of swallowing function may be associated with declining respiratory status. Authors of 1 study assessed swallows per bolus and bolus swallowing time in a cohort of patients with advanced DMD who were mechanically ventilated noninvasively and who then underwent tracheostomy, finding significant improvements in swallowing after the tracheostomy.32

CLINICAL CONTOVERSY: ASSESSMENT OF SWALLOWING DYSFUNCTION IN CLINICAL PRACTICE

The modified barium swallow study (MBS) and/or the fiberoptic evaluation of swallowing (FEES) are 2 instrumentation procedures that can be used to visualize swallowing movement and provide essential information on how the food moves safely through the swallowing mechanism. These studies are also used to provide necessary information on how the patient with DMD protects his or her airway to deflect aspirated material. MBS-detected dysphagia is nearly ubiquitous in patients with DMD.33 Thus, some authors have questioned whether MBS adds additional benefit beyond that achieved by taking a feeding history and observing feeding.30 Because no studies have been used to assess the impact of using MBS or FEES procedures on clinical outcomes in DMD, the 2018 Care Considerations suggest visualizing the swallowing mechanism with either an MBS or FEES when clinical swallowing symptoms are significant and aspiration is apparent. Consulting a speech-language pathologist who typically performs all 3 assessments (clinical, MBS, and FEES) is necessary to determine the extent of dysphagia.

It is important for the DMD care team to be aware of the early signs of dysphagia and proactively ask patients about difficulty chewing and swallowing, fear of choking, coughing or gagging with eating or drinking, and prolonged meal times. Although early signs of difficulty swallowing can be assessed through a clinical assessment, the presence of moderate to severe dysphagia, suspected aspiration events, or significant weight loss should prompt
an instrumentation procedure to definitively assess swallowing motility as well as the extent of potential aspiration.

**CONSTITUTION**

In a recent study in which a widely adopted criteria for defining constipation was used, Kraus et al\(^\text{34}\) reported the prevalence of constipation in a large single-institution cohort of DMD patients to be 47%. With this finding, it is suggested that constipation is more common than previously suspected in DMD and far more prevalent than in unaffected children and adults.\(^\text{31}\) Constipation was underreported by patients with DMD, and typical symptoms such as hard stools and infrequent defecation were relatively uncommon in this cohort. A more detailed inquiry of constipation-related symptoms, such as pain with defecation and stool caliber, was necessary for the identification of constipated patients. Because the problem was underrecognized, less than half of DMD patients with constipation in this cohort received any treatment at all. With Table 1, we provide an overview of constipation screening, assessment, and management.

Multiple potential risk factors can contribute to the development of constipation in DMD, including a lack of mobility, dehydration due to swallowing dysfunction, lack of dietary fiber, and underlying motility dysfunction. However, in their study, Kraus et al\(^\text{34}\) did not find that any patient-specific characteristic, including age or functional status, could be used to predict the presence of constipation. This argues for targeted, expanded questioning of all patients with DMD for signs and symptoms of constipation.

Treatment strategies include increasing water and fiber intake and using osmotic laxatives. Examples of osmotic laxatives include Polyethylene Glycol 3350, the milk of magnesia, and lactulose. Emphasis must be placed on providing proper hydration to prevent constipation and renal insufficiency.\(^\text{35}\) The desired goal of treatment is to achieve soft, nonpainful stooling that does not interfere with activities of daily living.

Clinical studies measuring intestinal motility in DMD patients are limited, but researchers of 1 case series documented delays in colonic transit time in a pediatric cohort.\(^\text{36}\) Both smooth muscle and enteric neurons express the dystrophin gene, and slow intestinal transit has been documented in the dystrophic (mdx) mouse model.\(^\text{37,38}\) Associated strongly with a history of constipation, chronic intestinal pseudo-obstruction (CIPO) is a problem that can severely affect quality of life in DMD. CIPO is characterized by abdominal pain and distension associated with the inability to defecate. Vomiting may be present, mimicking a mechanical partial obstruction. During acute episodes, radiologic findings of distended bowel loops and air-fluid levels in the upright position are typical. Between acute episodes, patients with CIPO almost invariably complain of chronic, severe constipation. The diagnosis of CIPO is mainly clinical, supported by radiographic findings. Decompressive maneuvers (ie, placing nasogastric and/or rectal tubes) are the mainstay of acute management, whereas long-term treatments remain elusive.\(^\text{39}\) Although sigmoid volvulus is more common in adults and rarely seen in children, it has been described in children with muscle disease.\(^\text{40}\) Sigmoid volvulus, which is hypothesized to result from long-term constipation that results in severe sigmoid colon dilatation, can

| Table 1 Overview of Constipation Screening, Assessment, and Management |
| --- | --- | --- |
| Constipation | The pediatric and adult versions of the Rome III Questionnaire can be used in the outpatient clinic setting for the diagnosis of functional constipation (Kraus et al\(^\text{34}\)) | Delay or difficulty in defecation, present for 2 or more wk | Ensure adequate hydration Increase fiber intake Maintenance of osmotic laxatives to maintain soft stools (Polyethylene Glycol 3350, milk of magnesia, lactulose) If stools are soft but the patient still has difficulty with defecation, an addition of stimulant laxatives to enhance colonic motility (oral sennosides, bisacodyl and/or rectal bisacodyl, glycerin) should be provided Disimpaction is required before maintenance therapy will be successful Strategies for disimpaction include oral, rectal, or combination of both approaches Oral approach: high doses of Polyethylene Glycol 3350 or magnesium citrate are the most common approach Rectal approach: phosphate soda or saline enemas |
| Fecal impaction | Physical examination of the abdomen and consideration of digital rectal examination | History of constipation and hard mass palpated in lower abdomen and/or dilated rectum containing excessive stool on digital rectal examination | Strategies for disimpaction include oral, rectal, or combination of both approaches Oral approach: high doses of Polyethylene Glycol 3350 or magnesium citrate are the most common approach Rectal approach: phosphate soda or saline enemas |
also be a complication of chronic colonic dysmotility. Symptoms can mimic an acute presentation of CIPO with abdominal pain, distension, and vomiting. Abdominal radiographs will reveal dilated sigmoid loops and air-fluid levels, but diagnosis is often missed or delayed. Endoscopic reduction by exsufflation is successful in most of the patients, but recurrence occurs in >50% of the patients, and thus, sigmoidectomy is often required to prevent recurrence.

**Gastroesophageal Reflux and Gastric Emptying**

The prevalence of gastroesophageal reflux in DMD is incompletely understood. In a cohort of 118 adolescents and adults, only 5 reported reflux requiring pharmacologic treatment, although nearly half reported occasional heartburn. Heartburn was significantly more often described in nonambulatory patients with DMD than in ambulatory patients. Potential additional risk factors for the development of gastroesophageal reflux in DMD include the presence of scoliosis and obesity. Evidence suggests that the use of positive-pressure ventilation may protect against gastroesophageal reflux events.

Slowed gastric emptying has been reported in children with DMD and may worsen over time. This problem can mimic gastroesophageal reflux symptoms, leading to postprandial abdominal pain, early satiety, nausea, and vomiting. Gastric emptying time can be measured with a nuclear medicine study. If gastric emptying is significantly delayed, appropriate interventions include dietary modification, such as beginning a low-fat diet; feeding frequent small meals; offering prokinetic pharmacologic therapy; and in severe cases, providing postpyloric feedings through a gastro-jejunal feeding tube.

**Clinical Controversy: Use of Proton Pump Inhibitors**

No studies have been used to assess the impact of acid suppression therapy on upper gastrointestinal symptoms in DMD. Acid suppression therapy options include the use of histamine-2 receptor antagonists and proton pump inhibitors (PPIs), and significant increases in PPI use have been observed in recent years. Although the PPI class of medications is typically well tolerated, data detailing adverse effects associated with long-term use have been accumulating. Although the mechanism is not understood, an association between PPI use and an increased risk of bone fractures has been reported. This relationship is troubling for the DMD population, which is already at an increased risk of osteoporosis and fracture. Additional reported associations with PPI use include hypomagnesemia, increased risk of *Clostridium difficile* infection, and pneumonia.

For upper gastrointestinal symptoms, care teams should also consider the possibility that gastric emptying delay, rather than gastroesophageal reflux, is the cause of symptoms. Symptom relief provided by long-term use of PPI must be considered along with any potential adverse events.

**CONCLUSIONS**

Careful attention to the common nutritional and gastrointestinal problems experienced by patients with DMD is essential to health and quality of life. Beginning at diagnosis, anticipatory guidance can help prepare patients and caregivers for the years ahead and should address themes of weight fluctuation, dysphagia, future needs for supplemental nutrition, constipation, gastroesophageal reflex, and delayed gastric emptying.

**REFERENCES**


**ABBREVIATIONS**

BIA: bioelectrical impedance analysis
CDC: Centers for Disease Control and Prevention
CIPO: chronic intestinal pseudo-obstruction
DMD: Duchenne muscular dystrophy
DXA: dual-energy x-ray absorptiometry
FEES: fiberoptic evaluation of swallowing
MBS: modified barium swallow studies
PPI: proton pump inhibitor
RDN: registered dietitian nutritionist
TSF: triceps skinfold


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