Amyotrophic lateral sclerosis (ALS) is a progressive motor neuron disease with no effective treatment to cure, halt or reverse disease advancement. Also known as Lou Gehrig’s disease, ALS is characterized by the gradual loss of voluntary muscle movement. Depending on disease progression, a person with ALS (PALS) may lose their ability to speak, eat, move, and, eventually, breathe. The average life expectancy after diagnosis is 2-5 years.

Malnutrition in PALS is common, with studies varying its prevalence from 16% to 55%. Malnutrition, lower weight, and weight loss are associated with reduced survival time. However, many barriers exist to consuming adequate calories and protein. The objective of this review is to discuss the nutritional implications of ALS and supportive strategies.

OVERVIEW

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Etiology and Disease Trajectory

Most ALS cases (90-95%) are considered sporadic, occurring randomly. Familial ties account for the remaining 5-10% cases with roughly 25-40% of these cases caused by known gene mutations (most commonly, C9ORF72 and SOD1). Military veterans are twice as likely to develop ALS, regardless of service branch or time period.

Rate and trajectory of disease progression vary among individuals. Onset typically begins in one of two regions: limb or bulbar (or both). Limb onset ALS arises in the arms and legs, impacting manual dexterity and mobility. Bulbar onset ALS manifests in the face and neck area, altering swallowing function and speech. PALS with limb onset can later develop bulbar issues and vice versa. Less
commonly, onset can present as respiratory distress from weakness in the diaphragm/intercostal region. Disease progression can be quantified using a validated tool, the ALS Functional Rating Scale-Revised (ALSFRS-R). The ALSFRS-R measures 12 aspects of physical function categorized within 4 functional domains: bulbar, fine motor, gross motor, and respiratory. Each aspect of self-reported function is scored from 0 to 4, with the total score from all 12 domains ranging from 0 (no function) to 48 (highest function).

**Treatment**

There are currently two drugs approved for the treatment of ALS: riluzole (Rilutek®, Tiglutik®, Exservan®) and edaravone (Radicava®). Riluzole is a glutamate antagonist approved by the FDA in 1995 to extend life by 2-4 months for PALS. Edaravone, a free-radical scavenger, was approved by the FDA in 2017 to help prevent neuronal damage from oxidative stress. The efficacy of edaravone in PALS is controversial. While earlier trials showed edaravone slowed the progression of functional loss (as determined by ALSFRS-R) in patients with early-stage ALS, a later trial noted no significant differences in either disease progression or respiratory function. Unfortunately, neither riluzole nor edaravone reverse motor neuron death or treat the underlying cause of ALS.

Lack of treatment options lead many PALS to seek alternative therapies. Dietary supplement use is common though may result in drug-nutrient or nutrient-nutrient interactions. Providers and registered dietitians (RDs) should review supplement use routinely to ensure safe consumption. ALSUntangled (alsuntangled.com), a website created to educate on alternative and off-label treatments advertised for PALS, reviews many dietary supplements. Currently, clinical trials on the dietary supplements tauroursodeoxycholic acid and theracurmin are ongoing. Last, certain nutrient deficiencies (e.g., vitamin B12, copper, thiamine) may mimic ALS signs and symptoms and should be ruled out during diagnostic work-up.

**Malnutrition**

Malnutrition is a prognostic indicator for survival in PALS. Dardoitis et al. noted body mass index (BMI) at diagnosis to be significantly and inversely associated with ALS survival. Paganoni et al. noted an obesity paradox in PALS: a “U”-shaped association between BMI and mortality, with highest survival seen in the BMI range of 30–35 kg/m². Though not yet fully understood, decreased survival with BMI greater than 35 kg/m² may be due to weight-induced physical activity burden and respiratory distress.

Malnutrition in PALS is difficult to diagnose using typical malnutrition criteria. Muscle loss from nerve degeneration is characteristic of the disease. Weight loss may be a result of disease-related muscle loss. Edema due to immobility is common in the extremities. Handgrip strength measurement may not be plausible depending on manual dexterity and may signify disease progression instead of malnutrition. Oral intake may remain unchanged, but disease-related hypermetabolism may result in weight loss. The Subjective Global Assessment (SGA) and Global Leadership Initiative for Malnutrition (GLIM) should be considered when diagnosing malnutrition in PALS. Although these nutritional assessment tools incorporate some of the above criteria, malnutrition (as determined by SGA and GLIM) is noted to be an independent risk factor for reduced survival time.
Nutrition Needs

Early in the disease, PALS may lose weight despite no changes in dietary habits. Bouteloup et al. noted 50% of PALS are hypermetabolic.\textsuperscript{11} Mean measured resting energy expenditure was 19.7 +/- 6.4% higher than calculated by the Harris Benedict equation (HBE). Despite muscle loss with disease progression, the authors noted that 80% of PALS showed no change in metabolic status over time. Typically, energy requirements are estimated at 30-35 kcal/kg/day. Alternatively, the Kasarskis equation has been proposed to estimate energy requirements in PALS.\textsuperscript{12} The equation incorporates the HBE and 6 questions from the ALSFRS-R. A web-based calculator can be found here: mednet.mc.uky.edu/alscalculator

Protein needs in PALS are not well studied. While adequate calorie and protein intake is necessary to prevent malnutrition-related muscle loss, it is not known if increased protein intake mitigates disease-related muscle loss. In the absence of available data, registered dietitians use varying calculations for protein needs, most commonly 0.6-1.5 gm/kg/day.\textsuperscript{13}

Barriers to Adequate Nutrition Intake

Despite the emphasis on adequate energy intake, PALS on average only consume 84% of calorie requirements.\textsuperscript{14} Many barriers exist to consuming adequate calories. (Table 1)

Hypermetabolism

As mentioned previously, PALS can be hypermetabolic. High calorie foods and oral supplements are often prescribed to combat increased calorie requirements.

Dysphagia

Dysphagia from oral muscle spasticity and flaccid weakness impacts up to 85% of PALS.\textsuperscript{15} It is the result of degeneration of cortical motor neurons, corticobulbar tracts, and brainstem nuclei. Mechanically altered diets can help reduce chewing difficulty and aspiration risk.

Constipation

Constipation is one of the most frequent side effects of ALS, presumed to be caused by decreased activity, diminished diaphragmatic function, subconscious hesitation to move bowels related to ambulatory weakness, medication side effects, and inadequate fiber and fluid intake.\textsuperscript{16} Constipation can make eating uncomfortable, negatively impacting intake. Constipation is treated with lifestyle modifications (fiber [caution with use in decreased mobility as fiber can worsen constipation], fluid; exercise when appropriate) and bowel medications (stool softeners, laxatives, suppositories).\textsuperscript{16} Gut microbiota may be altered in PALS,\textsuperscript{17} and research on probiotic supplementation is ongoing.\textsuperscript{18}

Sialorrhea

Sialorrhea (excessive saliva) is not caused by saliva overproduction in PALS, but rather weakened oropharyngeal muscles and subsequent difficulty managing saliva. Untreated sialorrhea can result in drooling, choking on saliva, and difficulty speaking. Sialorrhea is often treated with glycopyrrolate, off-label medications (amitriptyline, scopolamine, atropine), or botulinum toxin injections into the parotid or submandibular gland. Attention to hydration is particularly important in PALS with sialorrhea.

Mood disorders, fatigue and frontotemporal dementia (FTD)

Mood disorders (e.g., depression) can result in
poor appetite. Counseling, support groups, and medications may help treat mood disorders. Fatigue often leads to skipped meals and is typically addressed with respiratory aid. FTD can inhibit adequate energy intake. FTD impacts up to 15% of PALS and causes alterations in behavior, personality and language skills.

A multidisciplinary team approach is optimal to identify and address nutrition barriers, with each team member having a unique role. (Table 2) In fact, multidisciplinary clinics have been shown to increase median survival rate by 6-10 months.19

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Nutritional Care of the Patient with Amyotrophic Lateral Sclerosis

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**Nutrition Support**
Inadequate oral intake compounds disease-related muscle mass loss. If in line with goals of care, gastrostomy tubes (G-tubes) and enteral nutrition (EN) are recommended for PALS unable to meet nutrition needs by mouth. G-tubes can provide safe and consistent delivery of nutrition, hydration, and medications. EN often begins as supplemental and is transitioned when needed to meet full nutrition needs as the disease progresses. Depending on the degree of aspiration risk, pleasure oral feeds may be allowed for quality of life (QoL) purposes.

Observational studies suggest a survival benefit with G-tubes,\(^{20,21}\) however, randomized control trials comparing the benefits of EN versus continuation of oral feeding are lacking. Indications for G-tube placement in PALS include:

- Insufficient nutrition or hydration (evidenced by weight loss, clinical signs, or serum laboratory values)
- Chewing or swallowing difficulty (food, hydration, and/or medications)
- Fatigue preventing adequate intake
- Prolonged mealtime (> 45 minutes)

Some have encouraged pursuit of G-tube placement while forced vital capacity (FVC) is ≥ 50% predicted normal value. FVC < 50% has been suggested to increase the risk of respiratory arrest during sedation/anesthesia as well as postoperative ventilator dependence. However, other studies challenge this FVC limit and suggest different risk stratifying tools.\(^ {22}\)

Physical limitations, caregiver availability and patient preferences must be considered when determining EN administration method. Table 3 lists pros and cons of each.

The benefit of G-tubes on QoL in PALS is debatable.\(^ {23}\) While some studies note a positive

<table>
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<th>Administration Method</th>
<th>Pros</th>
<th>Cons</th>
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<td><strong>Bolus</strong></td>
<td>• More physiological  &lt;br&gt; • Inexpensive (syringe)  &lt;br&gt; • Portable</td>
<td>• Require more manual dexterity</td>
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<tr>
<td>• Syringe  &lt;br&gt; • Feeding tube-EN product connectors (e.g., Figure 1)</td>
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<tr>
<td><strong>Intermittent</strong></td>
<td>• More physiological  &lt;br&gt; • Slower administration may improve tolerance  &lt;br&gt; • Certain bags (e.g., Bolee™ Bag) can be frozen with blenderized feeds for future use  &lt;br&gt; • Can free caregiver during mealtime</td>
<td>• Less portable  &lt;br&gt; • Requires bags, tubing, IV pole  &lt;br&gt; • More equipment waste</td>
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<td>• Gravity bag</td>
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<td><strong>Continuous or Cyclic</strong></td>
<td>• Slower administration may improve tolerance  &lt;br&gt; • Requires less frequent manipulation of feeds throughout day  &lt;br&gt; • Can free caregiver during mealtime</td>
<td>• Less portable  &lt;br&gt; • Requires bags, tubing, IV pole, pump  &lt;br&gt; • More equipment waste  &lt;br&gt; • Requires additional justification for insurance coverage</td>
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<tr>
<td>• Pump-assisted</td>
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Table 3. Pros and Cons of Different Enteral Nutrition Administration Methods
association between G-tubes and QoL, others note a negative association. Neurologists and palliative care physicians, along with registered dietitians, respiratory therapists, and speech language pathologists (SLP), play an integral role in aiding PALS in G-tube placement decision-making.

**SUMMARY**

ALS is a terrible, fatal disease. Nutrition plays a role in survival, yet many barriers exist to optimizing nutrition status. Together, the multidisciplinary team can offer supportive strategies to enhance nutrition status in PALS.

**References**