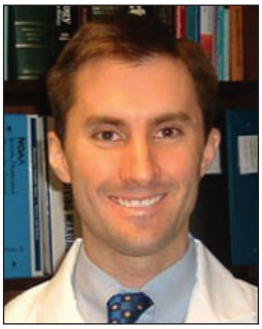
Carol Rees Parrish, R.D., M.S., Series Editor

Percutaneous Endoscopic Gastrostomy in the Patient with Amyotrophic Lateral Sclerosis: Risk vs Benefit?

Nicholas J. Procaccini



Edward C. Nemergut

Amyotrophic Lateral Sclerosis (ALS) is a progressive disease of unknown etiology characterized by the degeneration of motor neurons. Maintaining good nutritional status is a significant prognostic factor for survival in ALS, and many struggle in their efforts to achieve it. Given the association between nutritional status and survival, it is ideal to identify patients who might benefit from nutritional support earlier in their disease. Seventy percent of ALS patients develop difficulty chewing or swallowing as their disease progresses and thus may benefit from gastrostomy tube placement to provide consistent nutrition. Placement of a gastrostomy tube and the associated anesthesia/sedation may present additional risk to an ALS patient, especially those with advanced disease and compromised pulmonary status. Early placement of a gastrostomy tube, before it is "needed" to improve impaired nutritional status may provide ALS patients with the greatest benefit and least risk; we review the impact of nutrition on this patient population and the controversy surrounding the timing and placement of gastrostomy tubes.

Nicholas J. Procaccini, M.D., JD, Fellow in Gastroenterology, Digestive Health Center of Excellence, University of Virginia Health System, Charlottesville, Virginia. Edward C. Nemergut, M.D., Associate Professor of Anesthesiology and Neurological Surgery, Program Director, Department of Anesthesiology, University of Virginia Health System, Charlottesville, Virginia.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive disease resulting from the degeneration of motor neurons in the cerebral cortex, brainstem, spinal cord, and peripheral nervous system. The incidence is approximately two per 100,000 per year with an expected survival of three-to-five years after onset (1). Current therapy is primarily supportive. Drug therapy with Riluzole (Rilutek), a glutamate release inhibitor, extends survival by two-to-three months (2).

Malnutrition is known to be a significant problem in ALS patients for a variety of reasons (Table 1). Bulbar weakness with dysphagia and hypermetabolism are thought to be significant contributing factors. A recent prospective study examining resting energy expenditure in ALS patients with a mean disease duration of 24 months compared with a control group showed a 10% greater resting energy expenditure consistent with a hypermetabolic state (3). Potential causes of this hypermetabolic state have yet to be identified, but it appears clear that nutritional requirements are equal to, if not greater than, normal controls of similar body weight.

Failing nutritional status has been found to be a significant and independent prognostic factor for survival time in ALS patients (4). A body mass index (BMI) of <20 has been shown to be an independent predictor of life expectancy. In fact, relative risk for death is increased 7.7-fold over non-malnourished counterparts (4).

Table 1
Factors Contributing to Weight Loss and Malnutrition in Patients with ALS

- Dysphagia
- Coughing/choking with meals or medications
- Anxiety surrounding mealtime
- Length of time it takes to finish a meal
- Too fatigued to eat
- Unable to prepare meals
- Upper limb weakness and difficulty or inability to feed oneself
- Constipation
- Depression
- Withholding food or fluids to avoid the need to go to the bathroom
- Difficulty coordinating mealtimes with medications that require spacing of medications and meals/snacks
- Hypermetabolism.
  See January critique of recent article on this topic available at: http://www.healthsystem.virginia.edu/internet/dietitian/dh/journal/home.cfm

EARLY NUTRITIONAL INTERVENTION

Given the evidence demonstrating a direct relationship between survival and nutritional status, early nutrition intervention should be a standard component of care in the patient with ALS. Referral to a nutrition specialist soon after diagnosis facilitates careful monitoring of caloric intake and body mass (see Table 2 for nutrition assessment form used at the University of Virginia Health System's [UVAHS] ALS Clinic). Identifying subtle signs of nutritional decline, early in the disease process is vital. Appropriate intervention will depend upon the patient's wishes, along with the recognition by the interdisciplinary team that the patient's decision not to have a PEG tube should be respected.

Additional oral food recommendations for patients with dysphagia due to bulbar symptoms include utilizing foods that are soft, moist, and thickened (if necessary), depending on the patients swallowing capability. Table 3 includes a link to thickening agents/diets at one website. Maintaining proper posture by sitting upright and eating slower may also be of benefit. Some patients report that when they do require assistance at meals, although not intentional, family members may not appreciate the length of time they may need to chew, swallow, (and breathe), and will have a spoonful of food waiting before the preceding mouthful of food has been swallowed. This may make the patient feel rushed and anxious at mealtimes and result in the patient ending the meal before they might be actually satiated.

PROGRESSIVE DISEASE

Ultimately, due to disease progression and bulbar symptoms, approximately 70% of ALS patients develop difficulty with chewing or swallowing. Many of these patients, along with their physicians, will consider interventions such as nasogastric tubes (NGT) (short term only) or percutaneous endoscopic gastros-

(continued on page 28)

Table 2
UVAHS ALS Nutrition Assessment Form

ALS CLINIC NUTRITION ASSESSMENT FORM Patient Label _____

Male / Female Age _____ ALS dx: _____

PMH: DM HTN Chol/TG Liver Kidney ETOH: _____ Mobility: _____

PSH: _____

PEG / TF _____ ; Water flushes: _____

PERT MEDS: _____

Ht _____ Wt _____ UBW/date _____ IBW _____

Diet: _____ Diet restrictions imposed: _____

Appetite: _____ Dentition: _____

How many meals per day _____ Snacks _____ Time to finish a meal _____

Food allergies: nuts / shellfish / milk / other _____ Food Intolerances: lactose / other _____

PICA: clay / starch / dirt/ ice / other _____

Swallowing difficulties? _____ Oral Secretions: normal / thick / difficult _____

Nutritional Supplements: _____

Liquid: Ensure / + Boost / + Carnation Instant Breakfast Other: _____

Herbals: _____ Protein powders: _____ Probiotics _____

Creatine Vit C CoQ10 b carotene Vit E Glucosamine Fish oil Vit /Min

Other: _____

UOP: normal / avoids drinking at night UTI ± Bowel habits: q _____

Laxatives/ Fiber supplements _____

PEG info provided/discussed Y N

P/

_____ RD Date: _____

(continued from page 26)

Table 3
ALS Nutrition Resources

"So They're Telling You To Get A Feeding Tube," by Colin Portnuff, an ALS patient. The booklet addresses the questions people are most likely to ask and provides concrete answers. Topics range from the "what and whys" of feeding tubes, including topics such as:

- "Will it show?"
- "Can I still go in the swimming pool?"
- "Will you taste the food?"
- "What about acid reflux?"
- "What do you eat and how do you know how much to take?"

The following patient education materials were developed by the University of Virginia Health System ALS clinic nutritionists, Carol Parrish MS, RD & Coryn Commare MS, RD, CNSD and can be accessed at:

http://www.healthsystem.virginia.edu/internet/digestive-health/nutrition/patientedu.cfm

- What is a PEG?
- Medication delivery for feeding tubes for ALS patients
- What do you do if your tube clogs?
- Beverage thickening agents

http://www.temple.edu/instituteondisabilities/news/docs/PEG2007.pdf
Published by the Institute on Disabilities at Temple University:
http://disabilities.temple.edu

Table 4
Symptoms that Warrant Consideration of PEG Placement

1. Dysphagia with coughing
2. Choking during ingestion of food, fluid or medication
3. Sialorrhea (drooling or excessive salivation) (http://www.aafp.org/afp/20040601/2628.html)
4. Fatigue with eating
5. It takes too long to eat a meal and it's not fun any more
6. Significant anxiety with eating that creates too much of a burden for the patient (sometimes the caretaker's anxiety becomes the patient's anxiety as well)
7. Pills are too hard to swallow . . . literally! However, until such time that a PEG might be placed, many pills can be crushed and added to puddings, applesauce, etc.
8. Respiratory status has been declining and the ALS team is concerned that delay in PEG placement could make the procedure too risky in the future
9. Unhealthy, unintentional weight loss that alters strength and is concerning to patient enough to intervene

tomy (PEG) tube placement to allow them to maintain adequate nutrition and hydration. Enteral tube placement may improve overall quality of life by making it easier for patients to take their medications without having to take them orally.

There has been conflicting evidence regarding whether enteral nutrition support prolongs life in ALS patients. Many of the studies in this area are retrospective and plagued by poor methodology. Two prospective epidemiological studies did show a survival advantage in those patients who underwent PEG placement (4,5). Another parameter that deserves further scrutiny is whether PEG placement improves quality of life.

The overall consensus from prospective studies is that PEG tubes can be beneficial and are preferred over NGT's in maintaining nutritional status and potentially extending survival (4,5). In a randomized trial comparing nasogastric to PEG tubes, PEG tubes had significantly less failures, such as dislodgement or tube clogging, and patients were significantly more likely to receive their prescribed nutrition (6). However, the timing of PEG placement remains a significant issue for clinicians and patients. Some indications used to determine when it may be time to consider the patient for PEG tube placement include: coughing and choking during ingestion of food, difficulty with fluids or medications, lengthy mealtimes that exhaust the patient, etc. (see Table 4). A videofluoroscopic swallow evaluation performed by a speech pathologist is a very important tool in judging the extent of dysphagia and whether there is a component of silent aspiration. Based on the swallow evaluation, the speech pathologist can also provide the patient with compensatory strategy training and suggest safe or safer consisten-

cies, and regular reevaluation and monitoring.

Some patients become very anxious during mealtimes or when taking their medications and experience coughing and choking that escalate with further food/medication ingestion. PEG placement offers some relief due to the knowledge that their nutrition and fluid needs can be met should they be unable or disinclined to swallow food, fluids, or medications (personal experience of the series editor).

PEG placement provides immediate benefits of ensuring adequate nutrition intake, hydration, weight stabilization, and maintaining access for medications (4). If PEG placement is delayed until patients can absolutely not take oral nutrition and hydration they may already be at a significant disadvantage nutritionally including depletion of lean muscle mass. Evidence has shown better survival in patients who received a PEG at a higher BMI or for those who had not experienced significant weight loss prior to PEG placement (7). Finally, delaying PEG placement may result in additional risk due to further decline in pulmonary status.

COUNSELING PRIOR TO PEG PLACEMENT

While the medical decision to recommend PEG placement may be relatively straightforward, it can still be a difficult choice for patients and family members. Patients are often intimidated by the idea of the procedure, the presence of a foreign body in their stomach, and they may feel it is not consistent with their preferences. Discussing difficulties of swallowing and nutrition that commonly accompany disease progression early after initial diagnosis will better allow patients to consider their options and make decisions/plans before PEG placement becomes too risky.

In our view, counseling prior to PEG placement should ideally involve a multi-disciplinary approach including the patient's neurologist, as well as a gastroenterologist, nutritionist, and possibly a palliative care physician. The procedure should be well explained, as well as how the tube is cared for, and how tube feeds are given (see Table 3 for resources available).

Patients should be informed that placement of a PEG tube does not preclude one from eating or drinking orally for pleasure, or just supplemental oral nutrition if they are not at risk for aspiration, or even if they are, and they have decided on taking that risk for their overall quality of life. They should also be counseled on the limitations of the PEG tube, specifically, that a PEG does not prevent all aspiration events, but only those that occur during eating or drinking once a patient has been deemed an "aspiration risk for oral intake." See below for one patient's perspective.

> "A very important consideration for Chris was the PEG would NOT be used for sustaining life, only comfort. Also, that by having the PEG, it gave Chris more control for all the reasons you mentioned, not less control. You and others emphasized it did not have to be used, but was simply available when he decided he needed the PEG. By using the PEG when necessary he would be more comfortable and have more energy. It was very important to Chris we would not bypass his wishes. Most people have experience with "feeding tube" debates heard in the news, where people are tube fed unless a judge says "no." Also, you and the team made Chris aware that the option to have the PEG removed is always available. All those factors gave Chris the control he needed."

WHEN DOES IT BECOME TOO LATE?

The more controversial question is when is it too late to place a PEG tube due to risks of the procedure exceeding the potential benefits. The American Academy of Neurology's current guideline suggests PEG placement be made before the forced vital capacity (FVC) of patients falls to 50% of predicted (8). They point to data from studies showing that patients who underwent PEG tubes and had diminished vital capacities (FVC <60%) at the time of procedure had significantly shorter survival times than subjects that had greater FVC at the time of procedure (4,9). These results are not surprising as more diminished FVC is often a key prognostic indicator of worsening ALS, and hence, the patient would be expected to fair worse regardless of PEG placement. The question remains, "What level of FVC is safe from procedural standpoint and what procedural techniques might be used to minimize risks?"

Unfortunately, there is little evidence to support any specific approach other than the observation that patients with lower FVC tend to have more frequent

adverse events. General anesthesia in patients with ALS has been associated with exaggerated ventilatory depression and postoperative respiratory failure (10). Some patients may be exquisitely sensitive to the effects of non-depolarizing neuromuscular blockers and succinylcholine use may be associated with acute hyperkalemia. The risk of aspiration, especially in patients with significant bulbar symptoms, is thought to be high (10). Thus, the use of conscious sedation or alternative procedures to support ventilation without providing protection against aspiration may put the patient at increased risk.

Nevertheless, a recent case series described a technique for PEG placement using noninvasive positive pressure ventilation (NIPPV) for ventilatory support in a series of 33 patients with a FCV of <50% of predicted (11). Of the 33 patients reported by the authors, 29 PEG tubes were successfully placed endoscopically. Each patient received conscious sedation with ketamine (maximum dose = 25 mg) and propofol (maximum dose = 200 mg). Each received NIPPV and oxygen through nasal mask while continuous pulse oximetry was recorded. Of note, a dedicated anesthesiologist, rather than the gastroenterologist or surgeon, administered the sedation for the procedure. All patients were observed in the recovery room while NIPPV and pulse oximetry monitoring continued and were transferred to the floor when conscious with stable respiration. Pain medications were prescribed as needed. There was no in-hospital mortality or noteworthy morbidity, and there was no PEG tube related mortality.

As the authors did not report any adverse events related to PEG placement in their series, it is tempting to conclude that this technique is safe and effective in patients with ALS and FVC of less than 50%. Nevertheless, the small size of the study and its retrospective design does not allow this conclusion. Further, two patients (6%) perished secondary to severe respiratory insufficiency within 30 days of the procedure. It is thus unclear whether or not late gastrostomy tube placement provided an overall survival benefit in this subset of ALS patients. That said, nearly 90% of the patients survived more than 60 days and the FVC did not provide an accurate measure of predicting post-gastrostomy survival. As FVC <50% eventually is reached during the natural progression of ALS, it could be argued that the natural course of disease was the major cause of increased mortality in this population, not PEG tube placement.

The most logical conclusion is that in patients with a FVC of <50%, PEG placement should be very carefully considered with input from neurologist, gastroenterologist, anesthesiologist, and patient. Other variables such as patient age and functional status also merit consideration. If a decision is made to place a PEG tube, NIPPV may be a useful adjunct.

A possible alternative to PEG placement in those with compromised pulmonary function is percutaneous radiographic gastrostomy (PRG) tubes. These tubes can be placed under fluoroscopy without the use of sedation. A retrospective study comparing patients with impaired pulmonary function (FVC <50%) who had PRG tubes placed versus PEG tubes placed showed more favorable survival outcomes for the PRG group (12). Although PRG tubes are smaller in caliber and have a greater incidence of obstruction, they may prove to be an attractive option in patients with diminished vital capacity.

CONSTIPATION—A QUALITY OF LIFE ZAPPER

Constipation is a common secondary issue often seen in ALS patients that can appreciably alter quality of life (13). Patients often report it in the later stages of the disease process (experience of the series editor). Low dietary fiber intake, dehydration, inability to coordinate abdominal muscles, and a sedentary lifestyle are typical contributors to this problem in the general population. However, newer evidence reveals that ALS may also significantly affect motility and transit through the gastrointestinal tract (14). Several physiologic mechanisms play a role in GI motility including the autonomic nervous system (sympathetic and parasympathetic), neurotransmitters which play a regulating role, and the electric and contractile actions of smooth muscle (14). A study using radio-opaque markers to measure colonic transit time showed markedly delayed colonic transit time in ALS patients as compared to controls (15). It is important to determine what a patient's normal stool habits are at the time of diagno-

(continued on page 33)

(continued from page 30)

sis and reevaluate for any changes at every clinic visit.

Treatment is generally supportive, and close attention should be paid to medications commonly prescribed to these patients such as scopolamine (reduces excessive salivation), but may exacerbate constipation. Common dietary recommendations such as liberal hydration are often beneficial. Increasing fiber is a common recommendation for patients with constipation, but may meet with mixed results and should be used with caution in ALS patients, especially those confined to a wheelchair, or at the later stages of their illness. Fiber works to promote increased bowel movements by bulking stools. However, in patients with poor colonic transit, excessive bulking of stools may have the opposite effect of worsening constipation or increasing obstruction potential. Additionally, psyllium based supplements are degraded by colonic bacteria which can lead to a worsening of bloating and flatus. Stool softeners for preventive purposes are advisable at the first signs of constipation. Pharmacologic agents (such as Docusate sodium, Milk of Magnesia, magnesium citrate, polyethylene glycol (MiraLAX®), and enemas to facilitate bowel movements are appropriate (lactulose should be avoided in a slower gut as it may increase gas and cramping). A new option may be lubiprostone, a selective ClC-2 chloride channel activator, which leads to passive diffusion of sodium and water into the intestinal lumen and has been shown to be effective in relieving chronic constipation in a randomized placebo control trial (16). Lubiprostone has not been evaluated specifically in the ALS population, but so far appears to be a relatively safe and effective option in the general population.

Table 5
Important Points to Remember in the Nutritional Care of the ALS Patient

- Monitor weight closely, if overweight, some weight loss is acceptable if slow (1–2 lb per week only) and in the setting of well-balanced intake, to maximize ambulation potential
- Discussion of PEG placement should occur early in the disease process and involve a multidisciplinary approach to allow the patient time to ask questions and decide if this is right for them
- A PEG tube is not for everyone. The decision not to have one placed should be respected
- Evidence suggests early nutritional support may prolong life
- The patient may reach a point in the disease course where PEG placement is not advisable due to advanced respiratory decline
- When patients come in for PEG placement:
  - In the event of a long pre-procedure wait, offer a stretcher or recliner chair if that would make them more comfortable
  - Consider having them more upright during the procedure if possible—many patients are not comfortable lying flat due to excessive secretions in the oropharynx
- Finally, reevaluate the patients stool habits at every clinic visit—constipation is not something patients will often bring up on their own, but it is common and creates a tremendous amount of angst and discomfort—it is also very treatable

PEG PLACEMENT IS NOT FOR EVERYBODY . . .

The decision to have a PEG placed is a very personal one. Our practice is to introduce the option of PEG placement early after diagnosis to allow our patients time to consider it before dysphagia reaches a crisis stage. We are careful to offer it as an option, demonstrating how it works (if the patient or family members are interested). Occasionally, patients do not want to hear about PEG tubes in the early stages of ALS, although family members may wish to become informed. We offer private discussion for family members outside of the patient's presence when a patient is not prepared to participate in such a discussion.

A note from the editor (and one who follows patients in the University of Virginia Health System ALS Clinic):

If a patient with ALS chooses to proceed with PEG placement, ensure that there is a health care professional designated to see that a plan is in place for:

- Determining if insurance will cover enteral supplies
- Where the patient will obtain formula and supplies
- Education of the patient and caregiver how to use and care for the PEG.

More than one patient has come into our ALS clinic from around the state with a PEG already in

place and no idea how to use it, what and where to get tube feeding supplies, etc. Many of these patients are traveling with a 300–400 pound motorized wheelchair; so make the most of their clinic visits to avoid unnecessary trips."

CONCLUSION

The available information and clinical experience currently favors early PEG placement in receptive ALS patients. Further studies are needed in this area to determine if ALS is truly a hypermetabolic disease process, or whether calorie needs change over the course of disease progression. A decrease in ambulation and confinement to a wheelchair will precipitate an obligatory loss of lean body mass (and hence calorie needs actually decrease also), but whether there is also an underlying hypermetabolism present remains unclear. Toward endstage however, the work of breathing increases, hence calorie expenditure may also increase. Early placement obviates the higher risks associated with procedures in advanced disease and allows for early nutritional stabilization, hydration and ongoing delivery of medication via the enteral route. See Table 5 for suggested guidelines for the nutritional care of the patient with ALS. ■

References

1. Mitchell JD, Borasio GD. Amyotrophic lateral sclerosis. *Lancet*, 2007;369:2031-2041.
2. Miller RG, Mitchell JD, Lyon M, et al. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). *Cochrane Database Syst Rev,* 2007;24;(1): CD001447.
3. Desport JC, Preux PM, Magy, L, et al. Factors correlated with hypermetabolism in patients with amyotrophic lateral sclerosis. *Am J Clin Nutr,* 2001; 74: 328-334.
4. Mazzini L, Corra T, Zaccala M, et al. Percutaneous endoscopic gastrostomy and enteral nutrition in amyotrophic lateral sclerosis. *J Neurol,* 1995; 242: 695-698.
5. Chio A, Mora G, Leone M, et al. Early symptom progression rate is related to ALS outcome: a prospective population based study. *Neurology,* 2002; 59:99-103.
6. Park RHR, Allison MC, Lang J, et al. Randomised comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with persisting neurologic dysphagia. *Br Med J,* 1992; 304:1406-1409.
7. Chio A, Finnocchiaro E, Meineri P, et al. Safety and factors related to survival after percutaneous gastrostomy in ALS. ALS percutaneous endoscopic gastrostomy study group. *Neurology*, 1999; 53:1123-1125.
8. Miller RG, Rosenberg JA, Gelinas DF. Practice Parameter: the care of the patient with amyotrophic lateral sclerosis (an evidence based review): report of the Quality Standards Subcommittee of the American Academy of Neurology: ALS Practice Parameters Task Force. *Neurology*, 1999; 52:1311-1323.
9. Moser B, Lirk P, Lechner M, et al. General anesthesia in a patient with motor neuron disease. *Eur J Anaesthesiol,* 2004; 21(11):921-923.
10. Baur CP, Schara U, Schlecht R, et al. Anaesthesia in neuromuscular disorders. Part 2: specific disorders. *Anasthesiol Intensivmed Notfallmed Schmerzther,* 2002; 37: 125–137.
11. Gregory S, Siderowf A, Golaszewski AL, et al. Gastrostomy insertion in ALS patients with low vital capacity: respiratory support and survival. *Neurology*, 2002; 58:485-487.
12. Chiò A, Galletti R, Finocchiaro C, et al. Percutaneous radiological gastrostomy: a safe and effective method of nutritional tube placement in advanced ALS. *J Neurol Neurosurg Psychiatry,* 2004;74:645-647.
13. Mannino M, Cellura E, Grimaldi G, et al. Telephone follow-up for patients with amyotrophic lateral sclerosis. *Eur J Neurol,* 2007; 14:79-84.
14. Toepfer M, Folwaczny C, Klauser A, et al. Gastrointestinal dysfunction in amyotrophic lateral sclerosis. *ALS and other Motor Neuron Disorders,* 1999;1:15-19.
15. Toepfer M, Schroeder M, Klauser A., et al. Delayed colonic transit times in amyotrophic lateral sclerosis assessed with radioopaque markers. *Eur J Med Res,* 1997;2:473-476.
16. Johanson JF, Morton D, Geenan J, et al. Multicenter, 4-Week, Double-Blind, Randomized, Placebo-Controlled Trial of Lubiprostone, a Locally-Acting Type-2 Chloride Channel Activator, in Patients With Chronic Constipation. *Am J Gastro*, 2007;