Accordant
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Clinical Practice Guidelines

Amyotrophic Lateral Sclerosis

Program Update: 05/31/2014

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INTRODUCTION

The AccordantCare™ program works with health plans to assess, monitor, and support those with certain complex, chronic conditions. The focus of the program is to improve health outcomes and prevent or limit disease-related complications. AccordantCare offers unique services at no additional charge to the patients, putting them in a strong position to adhere to their treatment plan.

There are several ways AccordantCare augments physicians' efforts. Through regular telephone contact, AccordantCare nurses:

- Keep patients informed about the disease process
- Coach patients in self-motivation and self-care skills
- Encourage patients to alert their physician when new symptoms arise
- Direct patients to resources that help pay for medication, transportation, home modifications, etc.
- Ensure preventive and screening measures are accomplished
- Provide emotional support to patients and caregivers
- Screen for depression
- Find local support groups

We invite physicians to make use of the services offered by AccordantCare and to suggest ways we can further patients' treatment goals. To offer feedback, get more information, ask questions or voice concerns; call toll-free1-800-948-2497 to speak with a program representative from 8 a.m. to 9 p.m., Monday through Thursday, and from 8 a.m. to 5 p.m. on Friday, Eastern Time. Messages left after hours will be returned the next business day.

Intent of Guidelines

The purpose of this Clinical Practice Guideline is to describe current patterns of practice where there is no fully established national guideline for diagnosis and management. It is not meant to dictate care of patients. Decisions about care are made by the physician and the patient based on the individual needs of that patient.

A patient's health plan may or may not pay for the all medicines, tests, equipment, or services mentioned in this document. Benefits should be checked with the individual's health plan to assure payment.

DISEASE OVERVIEW

Amyotrophic lateral sclerosis (ALS) is primarily a motor neuron disease that attacks the nerve cells responsible for controlling voluntary muscles. It affects both upper and lower motor neurons, is rapidly progressive, and is invariably fatal.[1]

ALS primarily causes the atrophy of voluntary muscles—including bulbar, limb, thoracic, and respiratory muscles[2]—and spares the involuntary muscles, such as those that control bowel, bladder, sexual function, heartbeat, and the gastrointestinal tract.[3]

ALS starts focally, either in the bulbar region with difficulties with speech and swallowing, or in the arms or the legs, and rarely initially with compromised breathing. ALS progresses within a region and to other regions. Individuals with ALS eventually die from respiratory failure over a median time of 2 to 4 years from the onset of symptoms.[1,3]

ALS should no longer be thought of as a disease restricted to the motor system. It is clear that up to 50% of patients have changes in behavior attributed to loss of neurons in the frontotemporal lobes, and a small percentage have sufficiently severe symptoms to warrant the diagnosis of frontotemporal lobe dementia. Even though extramotor cerebral pathology is not always clinically obvious, it is routinely observed on histopathological examination. If cognitive impairment occurs, it is typically seen early in the disease course. It often involves behavioral changes, and is generally associated with more rapidly progressive motor weakness.[4]

ALS only rarely affects the higher cortical functions or the individual's memory. More commonly it affects their ability to express themselves, (find the right words) and their decision-making ability. This type of dementia is called frontotemporal lobar dementia (FTLD). The special senses (sight, hearing, and sensory perceptions) are not affected. There may be other less obvious systems involved.

Individuals diagnosed with ALS rapidly lose their ability to use their arms, legs, and body.[1] Respiratory complications are the main causes of death in ALS, mostly due to diaphragm weakness, aspiration, and infection.[5] Median survival is two to four 4 years from the onset of symptoms.

Incidence

The incidence of ALS in the United States is about 2 per 100,000 population per year.[6] About 5,600 people in the United States are diagnosed with ALS every year.[7]

Prevalence[6]

The prevalence of ALS in the United States is about 6 to 8 per 100,000 people. About 22,600 Americans have ALS at any given time.

Costs of ALS

The expenses for treating ALS are considerable. Most DME and interventions are required during the second half of disease duration (about 15 months after symptom onset). One retrospective chart review of 78 patients estimates that,

following diagnosis, costs of equipment (e.g., motorized wheelchairs) and interventions (e.g., noninvasive ventilation) can exceed $36,000.[8] The ALS Association and the Muscular Dystrophy Association offer some advice and support for ALS families.

People with ALS, who have paid enough employment and Medicare taxes on their wages, can get full disability benefits through Social Security. Congress has eliminated the usual 24-month waiting period for Medicare benefits in cases of ALS. Cash benefits from Social Security and Medicare coverage begin at the same time (about five months after a person is deemed disabled).[9]

DIAGNOSIS OF DISEASE

There is no definitive test for diagnosing ALS. Typically, doctors gather the patient's medical history, conduct a clinical examination, perform neuroimaging studies, and conduct electrophysiological tests to rule out other diseases. Tests may be performed at regular intervals to confirm whether the symptoms are getting progressively worse.[1,10]

Tests for Diagnosing ALS[11]

- Electromyography (EMG)
- Nerve conduction studies (NCS)
- Serum protein electrophoresis
- Thyroid and parathyroid hormone levels
- 24-hour urine collection for heavy metals
- Spinal tap
- Myelogram of cervical spine
- Creatine kinase (CK)
- Magnetic resonance imaging (MRI) and/or computerized tomography (CT) scans

Genetic blood tests for SOD1, FUS, and TD-43 mutations are now available to help distinguish sporadic ALS (SALS) from family ALS (FALS). Voluntary genetic testing may be performed in first-degree adult blood relatives of patients with a known gene mutation. They should receive sufficient counseling and be in good mental and physical condition at the time of the test.[5]

APPROACH TO MANAGEMENT OF PRIMARY CONDITION

Treatment Goals

Since there is no cure for ALS, the goals of treatment include (a) enabling the patient to enjoy the maximum possible function and independence and (b) providing the greatest possible relief of symptoms.[12] These goals are best accomplished by a multidisciplinary team, including a neurologist who is expert in ALS care, a nurse specialist, a physical therapist, an occupational therapist, a speech pathologist, a pulmonologist, a gastroenterologist, an orthotist, and other

specialists as needed.[12] Both the ALS Association and the Muscular Dystrophy Association have certified multidisciplinary ALS Clinics throughout the country.

Principles of ALS Treatment

The American Academy of Neurology (AAN) recognizes that many evidence-based treatment recommendations for ALS are still underutilized. These gaps in care led the AAN to develop a new (2013) ALS quality measurement set to improve the quality of care for patients with ALS. The 11 measures in the set are evidence based and intended to be implemented in clinical practice for patients with ALS[13]:

1. Develop or update an ALS multidisciplinary care plan—percentage of patients for whom a multidisciplinary care plan is developed, if not done previously, or for whom the plan is updated at least once annually

2. Discuss disease-modifying pharmacotherapy—percentage of patients with whom the clinician discusses disease-modifying pharmacotherapy (riluzole) at least once annually

3. Screen for cognitive and behavioral impairment—percentage of patients who are screened at least once annually for cognitive impairment (e.g., frontotemporal dementia screening or ALS Cognitive Behavioral Screen [CBS]) and behavioral impairment (e.g., ALS CBS)

4. Offer symptomatic therapy—percentage of visits in which the patient is offered treatment for pseudobulbar affect, sialorrhea, and other ALS-related symptoms

5. Ask about respiratory insufficiency and refer for pulmonary function testing—percentage of patients who are queried about symptoms of respiratory insufficiency (awake or associated with sleep) and referred for pulmonary function testing (e.g., vital capacity, maximum inspiratory pressure, sniff nasal pressure, or peak cough expiratory flow), at least every three months

6. Discuss noninvasive ventilation treatment for respiratory insufficiency—percentage of patients with respiratory insufficiency with whom the clinician discusses at least once annually treatment options for noninvasive respiratory support (e.g., noninvasive ventilation, assisted cough)

7. Screen for dysphagia, weight loss, and impaired nutrition—percentage of patients who are screened at least every three months for dysphagia, weight loss, or impaired nutrition and the results of the screening are documented in the medical record

8. Offer nutritional support—percentage of patients with dysphagia, weight loss, or impaired nutrition who are offered at least once annually dietary or

enteral nutrition support via percutaneous endoscopic gastrostomy (PEG) or radiographic inserted gastrostomy (RIG)

9. Refer for communication support—percentage of dysarthric patients who are offered a referral at least once annually to a speech-language pathologist for an augmentative/alternative communication evaluation

10. Assist with end-of-life planning—percentage of patients who are offered at least once annually assistance in planning for end of life issues (e.g., advance directives, invasive ventilation, hospice)

11. Ask about falls—percentage of visits in which the patient is queried about falls within the past 12 months

Disease-Modifying Therapy for ALS

Riluzole (Rilutek®) is safe and effective for slowing disease progression to a modest degree.[14,15] It should be offered to ALS patients with:

- definite or probable ALS;
- symptoms for fewer than five years;
- forced vital capacity of greater than 60% predicted; and
- no tracheostomy.

Vitamins and Nutritional Supplements

Creatine is ineffective in slowing the rate of progression or in improving survival in ALS.[16] High-dose vitamin E (5,000 mg/day) has also been shown to be ineffective.[15]

Exercise

There is not enough evidence to conclude to what extent exercise is beneficial or whether it is harmful to ALS patients. However, the pooled results of two studies showed some benefit of an exercise program, and no adverse effects were reported.[17]

Treating the Symptoms of ALS

The goal of symptom management is to improve the quality of life of the patient, family, and care provider[18] and keep the patient as mobile and comfortable as possible.[1]

Pain[18]

- Physiotherapy[19]
- Anti-inflammatory drugs
- Antispasticity agents
- Nonnarcotic analgesic drugs
- Opioids (when nonnarcotics fail)

Cramps and Fasciculations[2,19]

- Magnesium
- Tegretol® (carbamazepine)
- Dilantin® (phenytoin)
- Isoptin®
- Verelan® (verapamil)
- Neurontin® (gabapentin)

Note that quinine sulphate, while still widely available on the internet, is not recommended by the FDA for leg cramps.[20]

PREVENTION AND MANAGEMENT OF COMPLICATIONS

Accordant helps patients prevent and manage complications by teaching early warning signs, encouraging adherence to treatment plans, offering supportive care, and recommending physician contact where needed. The list of goals and cooperative interventions below does not represent a comprehensive list of complications but reflects some of the more common clinical situations specific to ALS. General health topics (e.g., age-appropriate cancer screening) are beyond the scope of this document.

Goal: Minimize the impact of dysarthria, thick mucus secretions, and sialorrhea.
Cooperative interventions: Teach patients to:

- Use techniques and tools to help articulate and speak more loudly (e.g., emphasize the final sounds of each word, use a voice amplifier)[21];
- Apply for and use telephone assistive communication devices[21];
- Understand the benefits of voice banking;
- Access information and communication channels via the Internet[21];
- Understand the importance of clearing secretions using manually assisted coughing techniques, a cough machine, or a portable home suction device[22]; and
- Understand the treatment options for sialorrhea, like glycopyrrolate (Robinul®)[18] or botulinum toxin types A and B (medically refractory sialorrhea[22,23]).

Goal: Manage pseudobulbar affect.
Cooperative interventions:

- Inquire of patient or caregiver about episodes of inappropriate laughing or crying;
- Reassure patient or caregiver that these are not emotional disorders but part of the paththology of ALS;
- Educate patient or caregiver that in many cases treatment is not needed; and
- Educate patient or caregiver about the pharmaceutical options for pseudobulbar effect and their associated side effects/risks—e.g.,

amitriptyline (Elavil®), Nuedexta® [dextromethorphan/quinidine]), or Luvox® [fluvoxamine] [18,24].

Goal: Facilitate early recognition of cognitive impairment and dementia, including frontotemporal lobe dementia. Stress the importance of early decision-making about the care that will be required later.

Cooperative interventions:

- Ensure that patients are screened for cognitive and behavioral impairment[22];
- Help patients understand the symptoms of cognitive (e.g., difficulty making decisions) and behavioral (e.g., apathy) impairment[25];
- Request input from caregivers regarding the patient's cognitive abilities;
- Explain that impairment may interfere with decision making about feeding and respiratory assistance[25];
- Explain to patients and caregivers that impairment may cause patients to be less adherent to treatment like NIV;
- Involve the caretaker in assessing the patient's ability to make sound judgments about their care.[25] For example, patients with FTLD may make poor decisions about when to use equipment such as a walker or wheelchair[25];
- Instruct caregivers to supervise walking in patients with FTLD, as they may have poor judgment about where to walk, how far to walk, or when to use a walker;
- Teach caregivers that patient actions are part of the disease and not intentionally directed to them;
- Educate patients about the pharmaceutical options and their side effects/risks to moderate some of the behavioral changes associated with cognitive impairment and dementia, but warn they may be ineffective[25]; and
- Monitor patient behavior and decision making closely to measure the progress of dementia.

Goal: Promote an early diagnosis of depression and anxiety.

Cooperative interventions:

- Encourage patients and caregivers to speak openly about their fears, concerns, and emotions;
- Address patients' fears of choking, paralysis, etc;
- Attend to the emotional needs of the caregiver;
- Refer patients to community agencies, hospice, the ALS Association, the Muscular Dystrophy Association, and others, for support;
- Refer patients to a counselor, psychiatric nurse specialist, psychiatrist, or psychologist as needed[26];
- Provide information and education to convince patients that alternative methods of mobility, eating, and breathing exist and are used successfully by others with ALS[26];

- Teach patients to recognize the early signs of depression and the importance of reporting them to a doctor;
- Teach patients to report sleep disturbances or poor appetite to their doctor as soon as possible;
- Instruct patient and caregiver to report any suicidal ideation to their physician immediately;
- Educate patients about the medications used to treat depression and anxiety and the adverse side effects/risks associated; and
- Help patients understand the grieving process and accept changes in the stages of their grief.[26]

Goal: Minimize the impact of dysphagia and maintain adequate nutrition and hydration.

Cooperative interventions:

- Teach patients about feeding and swallowing techniques such as supraglottic swallowing, the Mendelsohn maneuver, and the chin tuck maneuver[2];
- Encourage patients to stay in an upright position for 30 minutes after eating;
- Instruct on how to modify the consistency of food to prevent choking (e.g., use a blender, add thickeners);
- Discuss benefits of working with a speech language pathologist for swallowing difficulties;
- Inquire of patient or caregiver about difficulty with eating (chewing and swallowing) which results in reduced food intake or elimination of certain types of food;
- Inquire about weight loss;
- Educate patient and caregiver on the benefits of maintaining weight with ALS[27];
- Explain to patients and caregivers that a nutritionist can teach them how to plan and cook numerous small meals throughout the day that provide enough calories, fiber, and fluids[1];
- Suggest dietary supplements that are high in protein and calories[2,28];
- Explain the benefits of nasogastric tube insertion for temporary treatment of eating problems[29];
- Explain the benefits of PEG (e.g., ensure adequate nutrition, spend less energy swallowing)[18];
- Explain how to clean and care for PEG site;
- Teach the importance of dental hygiene, encourage electric toothbrush; and
- Teach the importance of flu/pneumonia vaccines[30]

Goal: Make sure patient understands the treatment options for respiratory insufficiency before they are needed. Optimize patient comfort as this stage of the disease is reached.

Cooperative interventions:

- Initiate conversations with ALS patients and their families about all the treatment options, and about palliative care and advance directives, as soon as possible after diagnosis[31];
- Explain the need for routine tests of respiratory function soon after diagnosis of ALS;
- Educate about the symptoms of respiratory insufficiency, including sleep disturbance, dyspnea, and orthopnea, weak cough, marked fatigue, excessive daytime sleepiness, difficulty clearing secretions, apathy, poor appetite, poor concentration/memory, and morning headaches[5,18];
- Describe the types of tests for respiratory muscle strength (e.g., forced vital capacity, sniff nasal pressure, peak cough expiratory flow, nocturnal pulse oximetry);
- Encourage the flu and pneumonia vaccines to minimize the risk of respiratory infection;
- Explain that NIV improves the symptoms of hypoventilation, thereby improving their quality of life and increasing survival by 12 to 18 months[12,18];
- Help alleviate the side effects associated with NIV by encouraging patients to ask their doctor about[32]:
    - ❖ humidification of delivered gas
    - ❖ topical nasal steroids or ipratropium nasal spray;
    - ❖ trying different interfaces
- Explain that the NeuRx® diaphragm pacing system (DPS) may improve sleep and quality of life and also prolong survival, but its efficacy has not been firmly established[33-36]; members should understand that DPS is a temporary treatment that will not stop the progress of ALS respiratory complications;
- Realize that ALS eventually worsens to the point that NIV/DPS is unable to meet the patient's respiration needs[10];
- For those who want long-term ventilatory support[15], explain that invasive ventilation can increase survival for as long as 10 years, but with a high emotional and financial cost to the patient and the caregiver[31];
- Facilitate decision-making before tracheostomy and invasive ventilation to make sure it is clear what will trigger the removal of ventilator support[5];
- Avoid emergency invasive ventilation via tracheostomy[5]; and
- Provide information and opportunities to discuss advance directives and end-of-life decisions.[26]

Goal: Optimize patient comfort, mobility, and safety as muscle function declines
Cooperative interventions:

- Help reduce the frequency of cramps by encouraging the patient to stay well hydrated with water and high-mineral content drinks[37];
- Educate about the pharmaceutical options for cramps and fasciculations and their associated side effects/risks (e.g., Tegretol® [carbamazepine], Neurontin® [gabapentin])[8,15];
- Educate about the pharmaceutical options for spasticity and their associated side effects/risks including (baclofen, Zanaflex® [tizanidine], Namenda® [memantine])[2];
- Encourage patients to consider orthosis, ramps, walkers, braces, wheelchairs, and other devices as needed to maintain mobility[1];
- Encourage patients to maintain a doctor-approved exercise program to tone and strengthen unaffected muscles[26];
- Encourage patients to perform range-of-motion exercises to prevent contractures and joint pain[26]; and
- Encourage the use of tools and techniques to assist with activities of daily living and safety, including button hooks, shower chair, grab bars, etc.[38]

Goal: Minimize urinary urgency, discomfort, and skin breakdown
Cooperative interventions:

- Teach patients to manage urgency with a urinal, bedside commode, adult diapers, and/or condom catheter;
- Educate about the pharmaceutical options and their associated side effects/risks:
    - ❖ Ditropan® (oxybutynin)[39]
    - ❖ Detrol® (tolterodine)
    - ❖ Myrbetriq® (mirabegron)
    - ❖ Botox (for those who cannot use or do not adequately respond to anticholinergics[40]);
- Teach patients about the signs and symptoms of urinary tract infections[26] and to report them to their physician right away; and
- Teach patients to report skin irritations and sores to their physician.[26]

Goal: Promote appropriate assistance and emotional support for patients and caregivers through end-of-life care.
Cooperative interventions[18]:

- Counsel patients and caregivers in dealing with the emotional, social, and spiritual impact of the disease as part of their palliative care[41];
- Educate about the pharmaceutical options available to treat dyspnea, anxiety, and pain:
    - ❖ anti-inflammatory drugs
    - ❖ antispasticity agents
    - ❖ non-narcotic analgesic drugs
    - ❖ opioids (when non-narcotic agents fail)

  - ❖ benzodiazepines
  - ❖ chlorpromazine
  - ❖ opioids, benzodiazepines, and anticholinergic medications during withdrawl from ventilation[22]
- Describe the benefits of hospice to ALS patients in the terminal phase;
- Discuss advance directives well before the terminal phase and re-evaluate regularly;
- Make sure patient and caregiver know they have a right to refuse or legally withdraw life-sustaining interventions[42];
- Teach patient and caregiver that communication becomes difficult on full-time ventilation, and it is important to have a way to communicate (e.g., when he/she wants ventilation withdrawal)[42]; and
- Reassure patient and caregiver that ventilation withdrawal is made under deep sedation to ensure a peaceful passing in those with advanced stage ALS.[43]

PATIENT FOLLOW-UP

Provide close follow-up with a multidisciplinary team, including a neurologist who is expert in ALS care, a nurse specialist, a physical therapist, an occupational therapist, a speech pathologist, a pulmonologist, a gastroenterologist, an orthotist, and other specialists as needed.

A first follow-up visit can be scheduled one to two weeks following diagnosis. Afterwards, patients are typically seen every three months, or more frequently as needed.[44] Elements for follow-up include[44]:

- Motility problems
- Pain
- Mobility
- Respiratory function
- Sleep difficulties
- Dysphagia/nutrition/dehydration
- Sialorrhea
- Speech problems
- GI problems
- Physical function
- Personal care
- Psychosocial issues
- Neurologic function
- Patient education (mechanical ventilation, advance directives)

Monitor patients taking riluzole for liver function and side effects every month for the first three months; every three months thereafter.

Discuss advance directives well before the terminal phase and then re-evaluate at least every six months.[5,18]

PATIENT EDUCATION

The Accordant Health Communities Website at:
https://www.accordant.com offers resources for patients with ALS.

The ALS Association Website at:
http://www.alsa.org

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