

Benefits of Timely Diagnosis

A Forward-Looking Statement for General Neurologists

The Problem:

Many people living with ALS are diagnosed after the disease has already taken significant hold.(1) This delay can mean functional loss, access to disability benefits, and missed opportunity for interventions that can improve outcomes. While there is no definitive diagnostic tool, there are diagnostic guides based on clinical symptomatology and thorough examination findings to reduce the time to diagnosis. This statement provides an overview of the importance of timely diagnosis.

Published evidence suggests that in the U.S., the average time from first symptom to confirmation of ALS diagnosis continues to range between from 11.5 months and 15 months, during which a patient has an average of three to four consultations with various health professionals prior to seeing an ALS specialist (Paganoni et al., 2014). This is undeniably a prolonged delay in obtaining a confirmatory diagnosis of ALS for many patients.

ALS diagnosis is complex and may mimic other neurological conditions, especially in the earlier stages. It is primarily based on a detailed history, a thorough neuromuscular examination for upper and lower motor neuron signs, taking into account the progression pattern of clinical symptoms, ruling out other diagnoses, and using supportive laboratory data.(2) Because people with ALS present first symptoms and progress in varied ways, this adds to the diagnosis complexity. For example, people with faster progression (change in functional ability over days or weeks) are generally easier to diagnose as symptom changes are more evaluable, versus someone with slower progression (functional ability changes over months to years) where symptoms present and change over a longer period (Galvin et al., 2017).

In retrospect, it is noted that along the diagnosis journey, patients often undergo redundant, unnecessary, and sometimes painful diagnostic tests. Patients may erroneously receive alternative neurological, orthopedic, or ear nose and throat (ENT) diagnoses that could lead to non-beneficial invasive treatments, such as spine surgeries, carpal tunnel releases, immunotherapies, etc. Unnecessary procedures, plus the uncertainty and frustration from the lack of a clear reason for their symptoms can cause significant stress and anxiety in people with ALS and their families (Paganoni et al., 2014).

Benefits of Timely Diagnosis:

Reducing diagnostic delays, from the patient's initial clinical interaction to confirmed diagnosis of ALS in an ALS clinic, is critical for early initiation of multidisciplinary care, supportive treatments, and standard of care therapies (Matharan et al., 2020). Drawing from the examples of tremendous therapeutic advances seen in stroke neurology (Fonarow et al., 2011) and multiple sclerosis (Waubant, 2012) over the past two decades (where shortening time to diagnosis and the time to initiating treatments have led to accelerated therapeutic discovery and improved outcomes) decreased diagnostic timelines may have similar direct impact in the field of ALS. There is emerging evidence that ALS is characterized by a prolonged pre-symptomatic prodromal period(3) where neuronal loss and compensatory reinnervation changes have already started, which later continues to spread and perpetuate until end stages of the disease. Therefore, identifying ALS patients at an early stage of disease when more motor neuron reserve pool is available in the brain and spinal cord provides more time to potentially modify disease course with clinically beneficial treatments and promising experimental drugs (Benatar et al., 2019). This in turn could help retain function longer and allows for more options to further understanding of the underlying causes of ALS. Finally, timely diagnosis reduces expense, stress, frustration, and burden on people with ALS and their families.

Timely diagnosis can help to ensure that patients can begin treatment with appropriate approved therapies as soon as possible. A prompt referral to the nearest multidisciplinary ALS center/clinic at the earliest suspicion for ALS by the patient's general neurologist or primary care physician, without waiting for ALS diagnosis confirmation is usually appropriate (Miller et al., 2009). ALS clinics have standard practices in place for diagnostic work up, diagnosis delivery, and psychosocial support around the time of diagnosis. Evidence suggests patients who receive multidisciplinary ALS care can have improved outcomes and enhanced quality of life, so it is important to help patients access this care as soon as possible (Matharan et al., 2020). [See resources listed below on how to contact an ALS specialist.]

In addition, earlier diagnosis expands patients' options for participation in clinical trials, many of which are statistically modeled to detect treatment effect within shorter trial durations in patients with early disease. Currently, there are more than 100 pharmaceutical companies actively engaged in drug development for ALS. With an expanding pipeline of novel experimental agents in late-stage therapeutic development and potential commercialization in the near term, this opportunity to have early access to potentially beneficial experimental therapies will continue to be important for people with ALS. Furthermore, researchers have identified a growing number of genes discovered as causative for ALS. There is also a rapidly growing number of clinical trials with gene therapy targets for certain forms of ALS, which require early suspicion for genetic underpinnings of a patient's ALS and expeditious genetic testing to access experimental gene therapies (Kiernan et al., 2020)

Addressing Concerns About Early Diagnosis:

It is important to address the fatalistic thinking that some patients, health care providers, and families have about an ALS diagnosis. They may think nothing that can be done to improve outcomes for people diagnosed ALS, which has no cure. Many physicians may believe that if they spare a patient and their family from having a definitive ALS diagnosis for a few months, they will be providing them with respite from a death sentence (Richards et al., 2020).

However, for many patients and their families, this extended period of uncertainty is not a blessing, but instead a type of ‘distraught purgatory.’ Timely diagnosis allows patients and families time to prepare to fight the disease in any way possible and to prepare for the extraordinary familial, financial, and emotional trauma that ALS inflicts (Paganoni et al., 2014). At the same time, because access to specialists, disease modifying treatments, experimental clinical trials and multidisciplinary care can make a meaningful difference for patients today, it is important not to allow fatalism to derail the chance for the earliest possible diagnosis, even while recognizing how difficult it can be to give and receive an ALS diagnosis.

Resources to Contact an ALS Specialist:

- Northeast ALS Consortium contact an ALS specialist search:
<https://www.neals.org/for-people-with-als-caregivers/contact-an-als-specialist/>
- ALS Association multidisciplinary clinic search:
<https://www.als.org/local-support/certified-centers-clinics>

Citations:

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Footnotes:

(1) According to two published studies, the average ALSFRS-R at diagnosis is around 38 out of 48 points (Kollewe K, et al, 2008 and Kaufmann et al., 2005).

(2) Laboratory data includes electrodiagnostic features of anterior horn cell dysfunction and absence of imaging findings supportive of other treatable conditions.

(3) Prodromal stage begins with possible symptoms/signs and ends with the emergence of definite symptoms/signs that reflect unequivocal development of symptomatic disease.