Evolution of the Amyotrophic Lateral Sclerosis Diagnostic Criteria towards the Gold Coast Criteria

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Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal, neurodegenerative disorder characterized by progressive degeneration of upper and lower motor neurons (LMNs). Careful history taking, neurological examination, and electromyography are used to confirm its clinical diagnosis. The El Escorial, revised El Escorial and Awaji criteria have proposed varying degrees of diagnostic probability for ALS. However, such categories may cause uncertainty among patients regarding the certainty of diagnosis. Cases labeled as “possible ALS” also risk exclusion from clinical trials. To clarify and simplify the diagnostic criteria of ALS, the previous diagnostic categories of possible, probable, and definite were abandoned in the newly suggested criteria, Gold Coast criteria. The simplified criteria offer practical utility for precise diagnosis of LMN-predominant ALS and clinical trial recruitment going forward.

Keywords: Amyotrophic lateral sclerosis; Electromyography; Motor neuron disease

Changes in ALS Criteria from Past to Present

The Lambert criteria, initially proposed in 1957, confirmed the value of electrodiagnosis in evaluating ALS [9]. These criteria include normal sensory nerve conduction studies, relatively

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preserved motor conduction velocities, and the presence of widespread fibrillation potentials, fasciculation potentials, a reduction in the number of motor unit potentials, and enlargement of motor unit potentials as observed on needle electromyography (EMG) [10].

The Lambert criteria, which depend on extensive denervation for diagnosis, continue to be valuable for confirming cases of advanced ALS [11]. Nevertheless, these criteria have been deemed too stringent, as they are typically only met by patients with advanced stages of the disease [12].

The El Escorial criteria, established in 1990, introduced a category for “clinically suspected ALS,” which included not only sporadic ALS but also associated conditions such as ALS plus syndromes, LMN-predominant ALS, and familial ALS [3]. This broadened the range of potential diagnoses, but it also heightened the risk of incorrectly diagnosing conditions such as neuropathies, myopathies, and LMN syndromes as ALS [13].

Another key change in the El Escorial criteria was the acceptance of electrophysiological evidence as proof of LMN signs [14]. This shift was probably influenced by the earlier Lambert criteria and was notable for not requiring clinical manifestations. However, the El Escorial criteria diverged by not recognizing fasciculations, even though they were acknowledged in the Lambert criteria [11].

The revised El Escorial criteria, proposed in 1998, aimed to improve the limited sensitivity of the original criteria [15]. Significant modifications included the elimination of the “clinically suspected ALS” category to reduce the risk of misdiagnosis [13]. In its place, a new category, “clinically probable ALS with laboratory support,” was introduced. This category reclassified individuals who met the EMG criteria from “clinically possible ALS” to a status more aligned with probable ALS [16].

The EMG criteria were also simplified; they now accept either active denervation or chronic reinnervation alone as sufficient evidence [17]. Furthermore, the criteria have been expanded to include patient-reported symptoms during history taking as part of the diagnostic process [18]. In light of discoveries confirming genetic underpinnings of ALS, such as the superoxide dismutase 1 (SOD1) gene [19], a “genetically-determined ALS” category also replaced the former ambiguous “familial ALS” designation.

Through these changes, the revised El Escorial criteria improved specificity regarding ALS-mimicking LMN syndromes but possibly increased false negatives in LMN-predominant presentations [20].

The Awaji criteria, proposed in 2008, further revised the El Escorial criteria [14]. A central aspect of these criteria was the recognition of fasciculation potentials observed on EMG as indicative of LMN involvement, on par with fibrillation potentials or positive sharp waves [21]. This made it possible to interpret all electrophysiological evidence as a demonstration of LMN signs. Consequently, the “clinically probable ALS with laboratory support” category used in the revised criteria was eliminated [22].

By recognizing fasciculation potentials, the Awaji criteria have enhanced diagnostic sensitivity compared to earlier criteria in patients who exhibit fasciculations but lack adequate evidence of LMN involvement [11].

Gold Coast Criteria: New Diagnostic Criteria Complementing Conventional ALS Diagnosis

While numerous criteria have been proposed over the years to standardize the diagnosis of ALS, they have consistently fallen short in terms of sensitivity, reproducibility, and practical utility [23]. The complex diagnostic framework has shown a poor correlation with the actual progression of the disease, leading to confusion among patients about the certainty of their diagnosis [13]. Additionally, there has been considerable variability in interrater agreement when applying the existing criteria [23].

Moreover, criteria demonstrated suboptimal sensitivity in capturing the heterogeneous presentations of ALS, such as bulbar-onset and LMN-dominant forms [24]. Consequently, these cases often do not meet the traditional criteria, leading to exclusion from trials [25]. These persistent issues have prompted a re-assessment of the diagnostic process.

In September 2019, an international group of neurologists gathered in Gold Coast, Australia to deconstruct and simplify the diagnostic process for ALS [26]. Prior to defining the Gold Coast criteria, a collective understanding of ALS was established based on several key tenets:

1. ALS is a progressive disorder of the motor system.
   1. It typically has a focal onset, but a generalized onset is also recognized.
   2. UMN signs are not always clinically evident, since they may be obscured by muscle wasting.
   3. Evidence of LMN involvement can be derived from clinical examination and/or EMG.
   4. Evidence of UMN dysfunction is currently mostly derived from clinical examination.
   5. Supportive evidence of UMN or LMN dysfunction can be provided by other modalities such as neuroimaging and biofluids, but they are not necessary for diagnosis.

2. ALS may have associated cognitive, behavioral and/or psychiatric abnormalities, although these are not mandatory for di-
agnosis.

Based on these discussions, new simplified criteria for the diagnosis of ALS, known as the Gold Coast criteria, were proposed (Table 1). The traditional framework categorizing ALS as possible, probable, or definite was discarded. The new criteria were designed to more accurately identify LMN syndromes such as PMA, while excluding certain cases of primary lateral sclerosis that were previously classified as possible ALS.

The key features of the proposed criteria are: (1) the presence of only two diagnostic categories, "ALS" and "not ALS"; (2) the inclusion of motor neuron disease (MND) with pure LMN dysfunction in two or more regions as a form of ALS; and (3) the exclusion of MND with pure UMN signs as a form of ALS.

Recent studies have evaluated the diagnostic performance of the Gold Coast criteria for ALS. Hannaford et al. [22] analyzed data from 506 patients, which included 350 with ALS and 156 with non-ALS neuromuscular disorders. The overall sensitivity of the Gold Coast criteria was 92%, which is comparable to 90.3% for the Awaji criteria and 88.6% for the revised El Escorial criteria when including possible ALS cases. For bulbar-onset ALS, the Gold Coast criteria demonstrated a higher sensitivity of 90.9% compared to previous criteria. Additionally, the specificity of the Gold Coast criteria remained high, although it was slightly lower than that of the Awaji and revised El Escorial criteria. However, this reduced specificity would not negatively affect patient recruitment into clinical trials, due to the mandatory exclusion of mimicking disorders through appropriate investigations.

Similarly, Shen et al. [27] assessed 1,185 Chinese patients with ALS. The Gold Coast criteria demonstrated a greater sensitivity of 96.6%, compared to 85.1% for the revised El Escorial criteria and 85.3% for the Awaji criteria. This increase in sensitivity was most pronounced in patients with limb-onset ALS. However, the specificity of the Gold Coast criteria was lower, at 17.4%, versus over 30% for the conventional criteria. This lower specificity is likely attributable to the study's inclusion of patients who were highly suspected of having ALS, leading to an increased risk of false-positive ALS diagnoses with the Gold Coast criteria due to its less stringent diagnostic requirements.

In summary, the Gold Coast criteria enhance diagnostic sensitivity, though they may exhibit reduced specificity when compared to previous iterations. Nevertheless, with proper investigations, the potential decrease in specificity can be offset by the mandatory exclusion of disorders that mimic the condition in question.

**Conclusion**

Various diagnostic criteria have been proposed over the past decades to standardize the diagnosis of ALS in research and clinical practice (Table 2). Although revised versions such as the Awaji criteria have addressed the sensitivity limitations of previous criteria, issues related to complexity, reproducibility, and correlation with disease progression have persisted. These challenges have driven the development of a simplified, comprehensive diagnostic framework.

In September 2019, an international consortium of ALS experts convened to distill the key tenets of ALS and to formulate new criteria that reflect recent advances and clinical experience. The resulting Gold Coast criteria exhibit higher sensitivity across various disease stages and phenotypic spectra compared to pre-

**Table 1. Gold Coast Criteria for ALS Diagnosis (2020)**

1. Progressive motor impairment documented by history or repeated clinical assessment, preceded by normal motor function, and
2. Presence of upper* and lower† motor neuron dysfunction in at least 1 body region‡, (with upper and lower motor neuron dysfunction noted in the same body region if only one body region is involved) or lower motor neuron dysfunction in at least 2 body regions, and
3. Investigations§ excluding other disease processes

**Table 2. Sensitivity and Specificity of Various Diagnostic Criteria for ALS Diagnosis**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
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<tbody>
<tr>
<td>Awaji</td>
<td>90.3</td>
<td>30.1</td>
</tr>
<tr>
<td>Revised El Escorial</td>
<td>88.6</td>
<td>30.0</td>
</tr>
<tr>
<td>Gold Coast</td>
<td>96.6</td>
<td>17.4</td>
</tr>
</tbody>
</table>

*Upper motor neuron dysfunction implies at least one of the following: (1) Increased deep tendon reflexes, including the presence of a reflex in a clinically weak and wasted muscle, or spread to adjacent muscles; (2) Presence of pathological reflexes, including Hoffman sign, Babinski sign, crossed adductor reflex, or snout reflex; (3) Increase in velocity-dependent tone (spasticity); (4) Slowed, poorly coordinated voluntary movement, not attributable to weakness of lower motor neuron origin or Parkinsonian features.

†Lower motor neuron dysfunction in a given muscle requires either: Clinical examination evidence of muscle weakness, and muscle wasting or electromyography (EMG) abnormalities that must include: Both evidence of chronic neurogenic change, defined by large motor unit potentials of increased duration and/or increased amplitude, with polyphasia and motor unit instability regarded as supportive but not obligatory evidence. And evidence of ongoing denervation including fibrillation potentials or positive sharp waves, or fasciculation potentials.

‡Body regions are defined as bulbar, cervical, thoracic and lumbosacral. To be classified as an involved region with respect to lower motor neuron involvement, there must be abnormalities in two limb muscles innervated by different roots and nerves, or one bulbar muscle, or one thoracic muscle either by clinical examination or by EMG.

§The appropriate investigations depend on the clinical presentation, and may include nerve conduction studies and needle EMG, magnetic resonance imaging or other imaging, fluid studies of blood or cerebrospinal fluid, or other modalities as clinically necessary.
### Table 2. Summary of Changes in ALS Criteria from Past to Present

<table>
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<tbody>
<tr>
<td></td>
<td>Including suspected ALS</td>
<td>Excluding suspected ALS</td>
<td>Excluding suspected ALS&amp; probable ALS: laboratory-supported</td>
<td>(Abolished)</td>
</tr>
<tr>
<td><strong>Definite ALS</strong></td>
<td>UMN and LMN signs in three spinal regions, OR Bulbar region and two spinal regions</td>
<td></td>
<td>Progressive motor impairment documented by history or repeated clinical assessment, preceded by normal motor function, AND Presence of UMN and LMN dysfunction in at least one body region, OR LMN dysfunction in at least two body regions, AND Investigations excluding other disease processes</td>
<td></td>
</tr>
<tr>
<td><strong>Probable ALS</strong></td>
<td>UMN and LMN signs in at least two regions With some UMN signs necessarily rostral to (above) the LMN signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Probable ALS: laboratory-supported</strong></td>
<td>None</td>
<td>UMN and LMN dysfunction in only one region, OR UMN signs alone in one region, AND LMN signs defined by EMG criteria present in at least two regions</td>
<td>(Abolished)</td>
<td></td>
</tr>
<tr>
<td><strong>Possible ALS</strong></td>
<td>UMN and LMN signs in one region, OR UMN signs in two or more regions; OR LMN signs are found rostral to UMN signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Suspected ALS</strong></td>
<td>Only LMN signs in 2 or more regions</td>
<td>(Abolished)</td>
<td>(Abolished)</td>
<td></td>
</tr>
<tr>
<td><strong>Electrophysiology</strong></td>
<td>Definite: Fibrillation + large MUAP + reduced recruitment Acute + chronic denervation required</td>
<td>Fasciculation = Fibs/PSW Acute + chronic denervation required including fasciculation potentials</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neuroimaging</strong></td>
<td>Exclusionary</td>
<td>Exclusionary</td>
<td>Inclusionary</td>
<td></td>
</tr>
</tbody>
</table>

ALS, amyotrophic lateral sclerosis; UMN, upper motor neuron; LMN, lower motor neuron; EMG, electromyography; MUAP, motor unit action potential; Fib, fibrillation; PSW, positive sharp wave.

previous iterations. However, further validation is needed to determine their specificity. Overall, the Gold Coast criteria provide practical utility in capturing the heterogeneity of ALS with fewer categories and a greater focus on clinical fundamentals. This simplified framework may facilitate earlier diagnosis and trial recruitment in the future.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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**References**


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