A checklist to support the diagnosis of Lennox-Gastaut syndrome

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Overview

QUESTION

Can a checklist based on International League Against Epilepsy (ILAE) mandatory criteria for Lennox-Gastaut syndrome (LGS) provide a reliable, simple-to-use resource to aid diagnosis for non-specialists in clinical practice?

INVESTIGATION

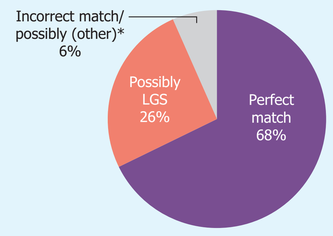
- Ten experts formulated seven questions for the checklist, based on ILAE criteria for classification and definition of LGS, through an iterative process.
- Checklist had four outcomes based on a scoring system: likely LGS, possibly LGS, unlikely LGS, and insufficient data.
- Accuracy of the checklist was tested by each expert on LGS and non-LGS cases from their records; original diagnosis and answers to checklist questions were provided to an independent third party for assessment.

RESULTS

Checklist accuracy

A total of 120 cases were assessed, including 64 LGS cases, and 56 non-LGS. The outcome was correct for 94% (n=113) of cases; either a perfect match with original diagnosis or 'possibly LGS' outcome with matching original LGS diagnosis (see **Figure**).

Breakdown of checklist outcomes



LGS, Lennox-Gastaut syndrome.
*'Possibly (other)' were those cases matching a checklist outcome of 'possible diagnosis of LGS' with an original diagnosis of non-LGS.

Complexities of diagnosis

Incorrect matches resulted from absence of characteristic electroencephalogram (EEG) features and lack of cognitive/behavioural impairment, highlighting that mandatory ILAE diagnostic features are not always initially present and may evolve over time.

CONCLUSIONS

The checklist offers a simple-to-use resource to support LGS diagnosis, using the ILAE criteria as the framework.

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Background

- Diagnosing Lennox-Gastaut syndrome (LGS) is challenging because it is characterised by a widespread variation in clinical presentation and evolution of symptoms (1)
- The International League Against Epilepsy (ILAE) has defined LGS based on a 'triad' of key features: (a) multiple and drug-resistant seizure types, of which tonic seizures are a hallmark; (b) abnormal electroencephalogram (EEG), namely diffuse, slow spike-and-wave (SSW) complexes, and generalised paroxysmal fast activity during sleep; (c) mild to severe cognitive and behavioural impairments, which may develop after seizure onset (2)
  - Based on this triad of symptoms, the ILAE identified mandatory criteria which must be present for an LGS diagnosis, exclusionary criteria which must be absent, and alerts (features seen rarely but are absent in the vast majority of cases) (2)
- An early and accurate diagnosis is essential to ensure timely interventions and potentially improve the prognosis of people with LGS (3)
- Despite the guidance provided by the ILAE, treating physicians may struggle with recognition of LGS, resulting in delayed diagnosis, misdiagnosis or overdiagnosis (3)

Objective

- To develop and test a simple-to-use checklist for non-specialists to support LGS diagnosis

Methods

- A panel of ten paediatric and adult epileptologists from seven countries formulated seven questions for the checklist, based on ILAE criteria for classification and definition of LGS, through an iterative process
- A scoring system was developed whereby each question was assigned a score of 1 point (for a total of 7 points). Each point was allocated a colour based on the alignment with the ILAE criteria:
  - Green - if the answer was in line with the mandatory ILAE criteria for an LGS diagnosis
  - Amber - if the answer was unknown or not available
  - Red - if the answer was not in line with the mandatory ILAE criteria for an LGS diagnosis
- The total number of green, amber, and red points was calculated and four possible outcomes determined based on the total score: likely LGS, possibly LGS, unlikely LGS, and insufficient data (**Figure 1**)

Figure 1. LGS decision-making checklist

LGS diagnostic checklist and scoring system
(Select a single response for each question)

Q1. What was the patient's age at the first seizure?
- <8 years
- 8–17 years old
- ≥18 years

Q2. Are there cognitive or cognitive plus behavioural impairments present?
- Yes
- Patient too young
- No

Q3. Has the patient ever experienced tonic seizures?
- Yes
- Unknown
- No

Q4. Has the patient experienced other seizure types? Atonic, myoclonic, focal, generalised tonic-clonic, nonconvulsive status epilepticus, epileptic spasms
- Yes
- Unknown seizure type
- No additional seizure types

Q5. Are the seizures resistant to antiseizure medications?
- Yes
- No

Q6. Has the EEG of the patient ever shown generalised, bifrontal or bilateral slow spike-and-wave complexes (<2.5 Hz)?
- Yes
- Unknown/ insufficient data
- No, never

Q7. Has the EEG of the patient ever shown generalised paroxysmal fast activity in sleep (>10 Hz or greater)?
- Yes
- Unknown/ insufficient data
- No, never

Score
(Count and insert the total number of responses for each column below)
- Green
- Amber
- Red

Score interpretation
- 7 Green = Likely diagnosis of LGS
- 1–2 Amber = Possible diagnosis of LGS; 3–4 Amber = Insufficient data (Can include any number of green but **no** red responses)
- ≥1 Red = Unlikely diagnosis of LGS (Regardless of the number of green or amber responses)

Result
- Likely diagnosis of LGS
- Possible diagnosis of LGS
- Insufficient data — Repeat checklist if new symptoms present, or every 6 months
- Unlikely diagnosis of LGS

EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome.

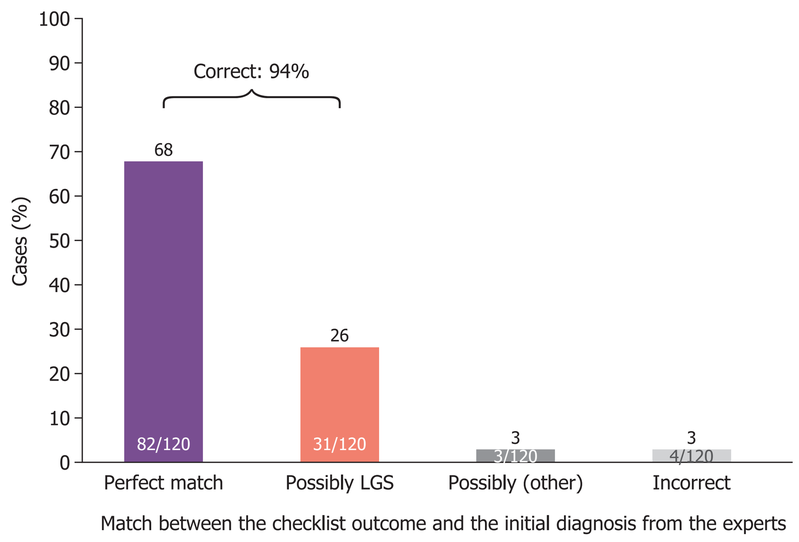
- Accuracy of the checklist was tested in a two-step process:
  - Firstly, each expert re-evaluated some LGS and non-LGS cases from their records using the checklist and for each case provided the original diagnosis and answers to the checklist questions to an independent third party for assessment of accuracy. The experts re-convened to assess findings and refine the checklist questions/outcomes
  - Secondly, all cases were re-evaluated using the updated checklist and results collected as previously
- Correct outcomes were defined as a perfect match with the original diagnosis (both LGS and non-LGS cases) or a 'possibly LGS' outcome matching an original LGS diagnosis
- Incorrect matches were those that had a different outcome from the original diagnosis provided by the expert: either an original diagnosis of LGS matching a checklist outcome of 'unlikely LGS'; or an original non-LGS diagnosis matching a checklist outcome of 'likely LGS'
- 'Possibly (other)' classification was a checklist outcome of 'possibly LGS' with an original diagnosis of non-LGS

Results

Of the 120 cases assessed, 64 were LGS and 56 non-LGS

- The checklist outcome was correct for 94% (n=113) of cases tested (**Figure 2**)
  - 68% (n=82) were a perfect match with the original diagnosis
  - 26% (n=31) were 'possibly LGS' matching an original LGS diagnosis
- The checklist outcomes were incorrect for only 3% (n=4) of cases tested (**Figure 2**)
- Incorrect outcomes, where the checklist outcome did not match the original LGS diagnosis, resulted from absence of documented characteristic EEG features and lack of cognitive/behavioural impairment, highlighting that mandatory ILAE diagnostic features are not always initially present and may evolve over time (**Table 1**)
- The outcome was 'possibly (other)' for 3% (n=3) of cases (**Figure 2**)
  - For these cases, key information on the EEG was unknown or had insufficient data, making a diagnosis of LGS still possible based on the amount and type of information available at diagnosis

Figure 2. Checklist outcomes versus original diagnosis of cases



LGS, Lennox-Gastaut syndrome.

Conclusions

- The overall accuracy of the checklist was 94% which is promising given the complexities of LGS and that only a limited number of questions were included
- The findings also highlight the relevance of EEG findings for an LGS diagnosis and the need to re-evaluate patients during follow-up
- The checklist offers a simple-to-use resource for treating physicians to support LGS diagnosis, using the ILAE criteria as the framework

Table 1. Incorrect matches where the checklist outcome did not match the original LGS diagnosis.

	What was the patient's age at the first seizure?	Are there cognitive or cognitive plus behavioural impairments present?	Has the patient ever experienced tonic seizures?	Has the patient experienced other seizure types?	Are the seizures resistant to antiseizure medications?	Has the EEG of the patient ever shown generalised, bifrontal or bilateral slow spike-and-wave complexes (<2.5 Hz)?	Has the EEG of the patient ever shown generalised paroxysmal fast activity in sleep (>10 Hz or greater)?	Checklist outcome	Original diagnosis	Does diagnosis match checklist outcome?
Case #1	<8 years old	Patient too young	Yes	Yes	Yes	Yes	No/Never	UNLIKELY LGS	LGS	No
Case #2	<8 years old	Yes	Yes	Yes	Yes	Yes	No/Never	UNLIKELY LGS	LGS	No
Case #3	<8 years old	No	Yes	Yes	Yes	No, Never	Yes	UNLIKELY LGS	Probable LGS	No
Case #4	<8 years old	Yes	Yes	Yes	Yes	No, Never	Yes	UNLIKELY LGS	LGS	No

EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome.

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