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Efficient diagnosis leads to better care: streamlining epilepsy diagnosis pathways

Added Value of Advanced Workup After the First Seizure: A 7-Year Cohort Study

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Objective: This study was undertaken to establish whether advanced workup including long-term electroencephalography (LT-EEG) and brain magnetic resonance imaging (MRI) provides an additional yield for the diagnosis of new-onset epilepsy (NOE) in patients presenting with a first seizure event (FSE). Methods: In this population-based study, all adult (≥ 16 years) patients presenting with FSE in the emergency department (ED) between March 1, 2010 and March 1, 2017 were assessed. Patients with obvious nonepileptic or acute symptomatic seizures were excluded. Routine EEG, LT-EEG, brain computed tomography (CT), and brain MRI were performed as part of the initial workup. These examinations' sensitivity and specificity were calculated on the basis of the final diagnosis after 2 years, along with the added value of advanced workup (MRI and LT-EEG) over routine workup (routine EEG and CT). Results: Of the 1010 patients presenting with FSE in the ED, a definite diagnosis of NOE was obtained for 501 patients (49.6%). The sensitivity of LT-EEG was higher than that of routine EEG (54.39% vs 25.5%, $P < .001$). Similarly, the sensitivity of MRI was higher than that of CT (67.98% vs 54.72%, $P = .009$). Brain MRI showed epileptogenic lesions in an additional 32% compared to brain CT. If only MRI and LT-EEG were considered, 5 would have been incorrectly diagnosed as nonepileptic (5/100, 5%) compared to patients with routine EEG and MRI (25/100, 25%, $P = .0001$). In patients with all 4 examinations, advanced workup provided an overall additional yield of 50% compared to routine workup. Significance: Our results demonstrate the remarkable added value of the advanced workup launched already in the ED for the diagnosis of NOE versus nonepileptic causes of seizure mimickers. Our findings suggest the benefit of first-seizure tracks or even units with overnight EEG, similar to stroke units, activated upon admission in the ED.

Commentary

The collective body of evidence strongly indicates that delay in diagnosing and treating epilepsy jeopardizes patient outcomes and quality of life.

For instance, a prospective community-based study revealed that following their second seizure, over 41% of children experienced a delay of more than a month in receiving a diagnosis of epilepsy. The delay was associated with notable developmental and intelligence quotient (IQ) deficits later in childhood.[1] Similarly, in adults, delays in diagnosis extending over a year or even decades were reported in ~ 15% of cases.[2]

Delays in diagnosis can occur at various points within the healthcare system, from patients/caretakers, their primary medical contact (such as primary care and emergency care providers), and at the neurology/specialist level. Patient-level delay is common and spans from patients and caretakers failing to recognize symptoms to challenges accessing appropriate medical care, particularly influenced by socioeconomic factors.[1,2] While addressing these broader issues is crucial, it is beyond the scope of this commentary.

This study by De Stefano and the team highlighted that the combined long-term electroencephalography (LT-EEG) and brain magnetic resonance imaging (MRI) produced the highest diagnostic yields for epilepsy compared to routine electroencephalography (rEEG) and brain computed tomography (CT).[3] Therefore, they propose establishing specialized first seizure units to promote prompt utilization of LT-EEG and MRI in the emergency setting. These units would expedite diagnostic testing and facilitate quick access to neurology specialists, thereby optimizing patient care. However, this proposal faces several challenges surrounding its feasibility in most healthcare environments.

The study assessed 1010 patients with a first seizure in the emergency room. Nearly half (49.6%) later had a diagnosis of epilepsy, and 25% of the epileptic patients had an interictal

epileptiform abnormality on an rEEG, especially when performed within 24 h after the presentation. Of those with normal or unspecific routine EEG findings, 46% had a subsequent LT-EEG showing interictal epileptiform abnormality leading to the diagnosis of epilepsy. For epileptic patients, CT showed an epileptogenic lesion in 48%. Demonstrating additional diagnostic value, 32% of epileptic patients with a normal CT had an epileptogenic lesion identified on their subsequent brain MRI. The authors outlined the higher sensitivity of LT-EEG over rEEG (54% vs 26%) and similarly with MRI over CT (68% vs 55%). Seventy-five patients had all 4 tests (rEEG, LT-EEG, CT, and MRI). A combination of LT-EEG and MRI had the highest diagnostic yield of 76%, higher than LT-EEG plus CT (64%). A combination of rEEG plus MRI had a diagnostic yield of 56%, while rEEG plus CT had the lowest yield of 37%.[3]

Considering these findings, I want to highlight the crucial role of the standardized MRI protocol for epilepsy diagnosis proposed by The International League Against Epilepsy (ILAE), which offers a uniform and high-quality approach across different care contexts and countries. The ILAE advocates for the Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS-MRI) protocol, which specifies isotropic, millimetric 3D T1 and FLAIR images, and high-resolution 2D submillimetric T2 images, available on most MR scanners, making this protocol widely applicable, irrespective of the clinical setting. Furthermore, the task force endorses artificial intelligence aid automated lesion detection techniques to enhance MRI diagnostic precision.[4] While technological advancements indicate scientific progress, the reality of healthcare delivery presents broader challenges. Immediate access to advanced testing (LT-EEG and MRI) and neurology specialists for all cases of first-time seizures in the emergency room may not be feasible in most current healthcare facilities. However, ensuring rapid access to specialists and streamlining subsequent timely diagnostic evaluations outside emergency rooms could represent a practical alternative. Incorporating EEG telemetry and telemedicine technologies could further expedite the process.[5,6] These innovations enable fast-track LT-EEG monitoring in the patient's own environment, remote consultations with specialists, removal of transportation barriers, and shifting tests to outpatient units, relieving pressure on emergency departments. Moreover, they may empower patients, fostering engagement and adherence to diagnostic and treatment plans.

It is crucial to have specific and up-to-date guidelines that encompass the latest evidence and recommendations to ensure optimal management of patients with seizures. There is evidence suggesting risks of seizure recurrence after the first unprovoked seizure, including an EEG with epileptiform abnormalities (Level A), a significant brain-imaging abnormality (Level B), prior brain insult, and nocturnal seizures.[7] Previously, the American Academy of Neurology (AAN) and the American Epilepsy Society (AES) issued a practice guideline for adults in 2007, which has since been retired. However, constrained by available evidence at the time, this guideline left substantial room for individual provider discretion. Its primary recommendation was to consider EEG and CT or MRI in the diagnostic process.[8] Similarly, a guideline for children experiencing their first nonfebrile seizure advised EEG for all cases and brain imaging only for specific circumstances.[9] The specific types of tests were not included in the guideline (rEEG vs LT-EEG and CT vs MRI). The lack of updated guidelines could lead to discrepancies in clinical practices among healthcare providers, potentially compromising the consistency and quality of care.

In conclusion, timely and accurate diagnosis is paramount in effectively managing epilepsy. Streamlined advanced diagnostic processes and rapid access to specialized care are essential for optimizing patient outcomes in emergency and nonemergency settings. Utilizing the latest technologies of remote EEG and specialist consultation along with updated scientific evidence and incorporating them in establishing practice guidelines can further enhance care quality.

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Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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