

The Emergency Department Evaluation of the Adult Patient Who Presents with a First-Time Seizure

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KEYWORDS

• Seizures • Evaluation • Discharge • Diagnostic testing

The emergency physician faces many challenges in evaluating a patient after a seizure, as the differential diagnosis is broad and many conditions can mimic a seizure. A detailed history from the patient and witnesses is paramount, as well as a thorough physical examination focusing on vital signs and neurologic findings. Adult patients visiting the emergency department (ED) with first-time seizures fall into 2 groups. Patients in the first group include those with altered mental status, focal neurologic abnormalities, signs of infection or significant medical disorder that requires an extensive work-up. Patients in the second group, which is the focus of this article, are the adults who return to a normal baseline mental status after a first-time seizure. In the past, the extent of diagnostic testing required for the second group was controversial because most studies comprised diverse populations of varying ages and causes of the seizure (**Box 1**).¹⁻⁸

In approximately 45% of patients with a first-time seizure no cause is identified, and less than 10% have a metabolic or toxicologic cause.⁶⁻⁸ Other causes of first-time seizures include stroke, tumor, trauma, and infection, including human immunodeficiency virus (HIV). The history and physical examination provides the basis for risk stratifying patients with new-onset seizures and for formulating the diagnostic evaluation required in the ED.

DIAGNOSTIC TESTING

Laboratory Testing

Various studies have examined the usefulness of blood tests in evaluating a first-time seizure. The literature suggests the yield from laboratory tests is low, and their routine

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Box 1**Practice guidelines for management of unprovoked seizures in the emergency department (ED)**

In an adult presenting with an apparently unprovoked first seizure, should an electroencephalogram (EEG) be ordered routinely?

Recommendation 1 (level B): for an adult with an apparent unprovoked first seizure, the EEG should be considered as part of the neurodiagnostic evaluation, because it has a substantial yield

Recommendation 2 (level B): for an adult with an apparent unprovoked first seizure, the EEG should be considered as part of the neurodiagnostic evaluation because it has value in determining risk of seizure recurrence

For an adult presenting with an apparent unprovoked first seizure, should a brain imaging study (computed tomography [CT], magnetic resonance imaging [MRI]) be ordered routinely?

Recommendation 3 (level B): for an adult presenting with an apparent unprovoked first seizure, brain imaging studies using CT or MRI should be considered as part of the neurodiagnostic evaluation

For an adult presenting with an apparent unprovoked first seizure, should blood counts, blood glucose, and electrolyte panels be routinely ordered?

Recommendation 4 (level B): there are insufficient data to support or refute routine recommendation of laboratory tests such as blood glucose, blood counts, and electrolyte panels for an adult presenting with an apparent unprovoked first seizure, although they may be helpful in specific clinical circumstances

For an adult presenting with an apparent unprovoked first seizure, should lumbar puncture be routinely performed?

Recommendation 5 (level B): there are insufficient data to support or refute recommending routine lumbar puncture in the adult initially presenting with an apparent unprovoked first seizure; however, in special clinical circumstances (eg, febrile patients), it may be helpful

In an adult presenting with an apparent unprovoked first seizure, should toxicologic screening be routinely ordered?

Recommendation 6 (level B): there are insufficient data to support or refute a routine recommendation for toxicology screening; however, it may be helpful in specific clinical circumstances

What laboratory tests are indicated in the otherwise healthy adult patient with a new-onset seizure who has returned to a baseline normal neurologic status?

Recommendation 1 (level B): determine serum glucose and sodium levels on patients with a first-time seizure with no comorbidities who have returned to their baseline

Recommendation 2 (level B): obtain a pregnancy test if a woman is of child-bearing age

Recommendation 3 (level B): perform a lumbar puncture, after a head CT scan, either in the ED or after admission, on patients who are immunocompromised

Which new-onset seizure patients who have returned to a normal baseline require a head CT scan in the ED?

Recommendation 4 (level B): when feasible, perform neuroimaging of the brain in the ED on patients with a first-time seizure

Recommendation 5 (level B): deferred outpatient neuroimaging may be used when reliable follow-up is available

Which new-onset seizure patients who have returned to normal baseline need to be admitted to the hospital and/or started on an antiepileptic drug?

Recommendation 6 (level C): patients with a normal neurologic examination can be discharged from the ED with outpatient follow-up

Recommendation 7 (level C): patients with a normal neurologic examination, no comorbidities, and no known structural brain disease do not need to be started on an antiepileptic drug in the ED

Data from American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures [systematic review]. Ann Emerg Med 2004;43:605–25.

use is not recommended. The history and physical examination will normally predict most metabolic disturbances, with glucose abnormalities and hyponatremia being the most commonly identified.^{1,2,5,6} A retrospective chart review by Henneman and colleagues,⁷ which excluded patients with trauma, drug ingestion, or diabetes, identified 333 adult patients with new-onset seizures in a 5-year period. Seven patients were found to have hyponatremia and 2 had hypocalcemia. However, it is unclear if the abnormalities were predicted or if they were the cause of the seizure. In a prospective study of 136 patients, Turnbull and colleagues⁵ found 4 cases of hypoglycemia and 4 cases of hyperglycemia. Two of the cases of hypoglycemia were not suspected based on the history and physical examination. Tardy and colleagues⁸ found 1 case in 247 patients of unsuspected hypoglycemia, and 4 cases of hyponatremia, of which only 1 was not suspected from the history. In a prospectively studied cohort of 98 patients with first-time seizure, Sempere and colleagues⁶ found 1 case of unsuspected hyponatremia in a patient with psychogenic water ingestion. There are no prospective data to support extensive metabolic testing (eg, calcium, magnesium, phosphate) beyond a sodium and glucose determination in patients who are otherwise healthy and who have returned to baseline mentation. Patients with predisposing factors to metabolic derangements (eg, renal failure, malignancy, malnutrition, or those on diuretics) should, in general, receive a comprehensive metabolic evaluation, although there are inconclusive data to direct laboratory testing. Turnbull and colleagues⁵ found 2 patients with hypocalcemia in a prospective study of 136 patients with new-onset seizure (1 with cancer and 1 with renal failure). Tardy and colleagues⁸ reported 1 case of hypocalcemia but clinical correlation was not provided.

Based on a systematic review of the literature, the American College of Emergency Physicians' (ACEP) Clinical Policy on the initial approach to patients presenting with a chief complaint of new-onset seizure does not recommend extensive metabolic testing in patients who return to normal baseline.⁹ This conclusion has also been reached in a practice parameter published by the American Academy of Neurology on the evaluation of first-time seizures in children.¹⁰

All women of reproductive age require a pregnancy test.¹¹ Pregnancy causes significant physiologic stress and can thus theoretically lower the seizure threshold in patients with an underlying focus. In 1 study of 59 patients with new-onset seizures in pregnancy, 14 patients were diagnosed with gestational epilepsy, a seizure disorder that occurs only during pregnancy.¹¹ Determination of pregnancy status may affect disposition, initiation of therapy, and management. Noneclamptic pregnant patients with new-onset seizures and no comorbidities, such as recreational drug use or HIV, still require a neuroimaging study and an electroencephalogram (EEG). If these tests are normal, it is reasonable to observe the patient without initiating pharmacologic therapy.

A drugs-of-abuse screen and alcohol level are considerations in patients with a first-time seizure, although there is no evidence that such testing changes outcome.^{12–14} These tests are indicated when a patient has a seizure associated with a toxidrome or with altered mental status. However, a positive drugs-of-abuse screen does not necessarily prove causality for new-onset seizure and the patient still requires

a neuroimaging study in the ED to direct management. Pesola and Westfal¹⁴ reported 4 cases of cocaine-related seizures in 120 patients studied, although not all patients received the same tests and a direct correlation was not demonstrated. Seizure caused by alcohol intoxication or withdrawal is a diagnosis of exclusion, as alcoholics are at increased risk for electrolyte abnormalities and traumatic injuries.¹⁵ Routine testing for drugs of abuse and alcohol is of unknown benefit, but may suggest a cause of new-onset seizures and help with future medical and psychiatric management.

Neuroimaging

The necessity and timing of neuroimaging for patients with new-onset seizure remain controversial for emergency physicians. Noncontrast head CT scans reveal abnormalities ranging from 3% to 40% in patients with first-time seizure, which includes two-thirds with focal lesions and one-third with diffuse cerebral atrophy.^{7,8,16} The incidence of finding an abnormality is increased if the patient has a focal neurologic finding, focal onset of the seizure, history of malignancy, or HIV.¹⁷ In 1 study of 247 patients with a first-time seizure, 117 CT scans were normal, and 130 were abnormal.⁸ Of the abnormal CT scans, 85 showed focal lesions (eg, stroke or tumor), and 45 showed diffuse atrophy. Twenty percent of patients with a nonfocal examination and a first-time seizure had an abnormality identified on CT.^{6,8}

Alcoholics, patients with head trauma, patients with HIV, and the elderly deserve special mention. A 1988 Denver study reported that of 259 alcohol-related new-onset seizures, 58% had abnormal head CT. A clinically significant lesion was present in 16 (6.2%), 7 of whom were alert and had nonfocal neurologic examinations and no history of trauma. Ten (3.9%) had a lesion that led to a change in clinical management.¹⁸ This study emphasizes the importance of avoiding labeling alcoholics with a first-time seizure as having an alcohol-withdrawal seizure; it also emphasizes that alcohol is a comorbidity that drives the need for ED neuroimaging. Seizure related to mild traumatic brain injury is rare, but when it occurs it has been associated with a 47% increased incidence of intracranial bleeding.¹⁹ Pesola and Westfal¹⁴ reported that 6 of 26 HIV patients with a first-time seizure had an acute lesion found on CT, 2 of which were not otherwise suspected based on physical examination. The elderly are at risk for both stroke and malignancy, thus head emergent CT is required when presenting with a new-onset seizure in the ED.⁸

The question remains whether identifying the abnormality in patients with nonfocal neurologic examinations who are evaluated in the ED has an effect on patient outcome. This depends on the outcome measure used; identifying a lesion may direct disposition and argues in favor of neuroimaging in the ED. In 2007, the American Academy of Neurology updated previous guidelines on neuroimaging in patients with first-time seizure.¹⁷ A multidisciplinary group with topic expertise conducted a literature review from 1966 to 2004. Based on the best available evidence the Task Force could only generate weak recommendations that included obtaining a CT in the ED in patients with a history or physical examination suggestive of a focal lesion, or a focal seizure with or without generalization: for all other patients, the Task Force concluded that acute neuroimaging is probably beneficial, but not mandatory and may be deferred if scanning is not immediately available.

Magnetic resonance imaging (MRI) is more sensitive than CT in detecting subtle alterations of brain structures and is often preferred by neurologists for evaluating first-time seizure. However, CT is better than MRI for detecting acute hemorrhage, which is a critical determination when evaluating new-onset seizure in the ED. In addition, CT is more widely and rapidly available in many EDs. There are currently no ED-based studies that have investigated the use of MRI. The joint practice guideline discussed earlier deferred recommendations on emergent MRI pending further study.

EEG is useful in determining the cause of seizure and quantifying recurrence risk. Emergent EEG recording is important in patients with persistent altered mental status and in those who may be difficult to diagnosis clinically, such as those in nonconvulsive status epilepticus (SE), pharmacologically induced coma, or in patients who have received a paralytic agent. Although EEG may be helpful and can facilitate antiepileptic drug (AED) treatment to terminate a seizure, no studies to date have shown that rapid EEG may improve outcome in patients with nonconvulsive SE. Access to EEG is limited in many EDs, and there are insufficient data to make definitive recommendations for its use in the acute setting. A practice parameter by the American Academy of Neurology reported that for adults presenting with a first seizure, a routine EEG revealed epileptiform abnormalities in approximately 23% of patients, and these were predictive of seizure recurrence. They recommend that EEG should be considered as part of the routine neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure.²⁰

Lumbar Puncture

A lumbar puncture (LP) is indicated in the work-up of first-time seizure in cases of suspected central nervous system (CNS) infection or suspected subarachnoid hemorrhage. In particular, patients with new-onset seizure who present with fever, severe headache, immunocompromised state, or persistently altered mental status should undergo an LP.^{7,8,14,21} A retrospective cohort of 100 consecutive HIV-positive patients identified 14 cases of CNS infections on LP, however, clinical correlation was not provided.²² In a prospective cohort, Sempere and colleagues⁶ reported on 8 HIV-positive patients found to have a CNS infection as a cause of their seizure, 2 of whom were afebrile without meningial signs.

A review of the literature found no cases of occult bacterial CNS infection manifesting as an isolated seizure, without fever or abnormal neurologic findings. An exception may occur in cases of partially treated meningitis. Although there are no adult studies, it has been reported that in the pediatric population, those who have been taking antibiotics and present with a complaint of seizure may have meningitis even if afebrile; LP should be seriously considered in these cases.²³ One retrospective study reported 4 cases of meningitis in seizure patients with normal physical examinations, but none had a bacterial cause. Most patients in this study did not receive an LP and indications for LP were not clear.⁷

HOSPITAL ADMISSION

The need for hospital admission is obvious in the critically ill patient. The dilemma arises when establishing disposition for the patient who has fully recovered without persistent neurologic symptoms in the setting of a first-time seizure. To determine which of these patients require hospitalization, it is necessary to identify a valid outcome measure that assesses the correctness of the decision. Useful measures would include seizure recurrence, morbidity, or mortality within a defined period.

The recurrence risk of unprovoked (eg, epileptic) seizures has been studied rigorously, but is generally reported in 1-year and 5-year recurrence rates.^{24–28} These studies also generally excluded patients who had an identifiable cause of their seizure. The cause of the seizure and EEG findings are the best predictors of recurrence. Recurrence rates are lowest when no cause is identified and the EEG is normal.²⁶ Patients who have structural lesions on head CT or those with focal seizures that generalize secondarily have a 1-year recurrence risk of up to 65%. Those patients will most likely benefit from initiating AED therapy.²⁶

Unfortunately, this information is not easily applicable in the ED setting where results of EEG and high-quality neuroimaging studies are often not available. In addition, the 1-year

recurrence rate is not the most appropriate outcome measure from the standpoint of disposition from the ED. A more salient outcome is the short-term risk of recurrence, and in this respect, there is a paucity of data. One study compared adult patients presenting with first-ever seizures comprising multiple seizures within 24 hours versus first-time single seizure and it was found that those presenting with multiple seizures were no more likely to have seizure recurrence, irrespective of cause or treatment.²⁹ Only 1 study investigated the incidence of seizure recurrence within 24 hours of ED presentation.⁸ This was a retrospective review of all adult patients admitted to the hospital with a first-time seizure during a 2-year period. The investigators reported a 19% seizure recurrence rate within 24 hours of ED presentation, decreasing to 9% if those patients with alcohol-related events or focal lesions on CT were excluded. However, the applicability of these results is limited because those patients with recurrent seizures were not well described, thus making it impossible to assess whether recurrence could have been predicted based on physical findings or comorbid factors. ED-based studies have reported rates of hospital admission, but the decision to admit was not standardized, and the ability of admission to improve outcomes was not studied.^{8,30}

In summary, the most rational approach to admitting patients with first-time seizure should be based on the physician's risk assessment of the patient's overall condition, taking into account other symptoms, medical problems, and social factors, including the patient's access to follow-up care (Fig. 1). Patients with comorbidities including age more than 60 years, known cardiovascular disease, history of cancer, or history of being immunocompromised should be considered for hospital admission. At present, there is insufficient evidence to support a recommendation to admit or discharge the awake, alert, and stable patient who has returned to baseline mental status after a new-onset seizure.

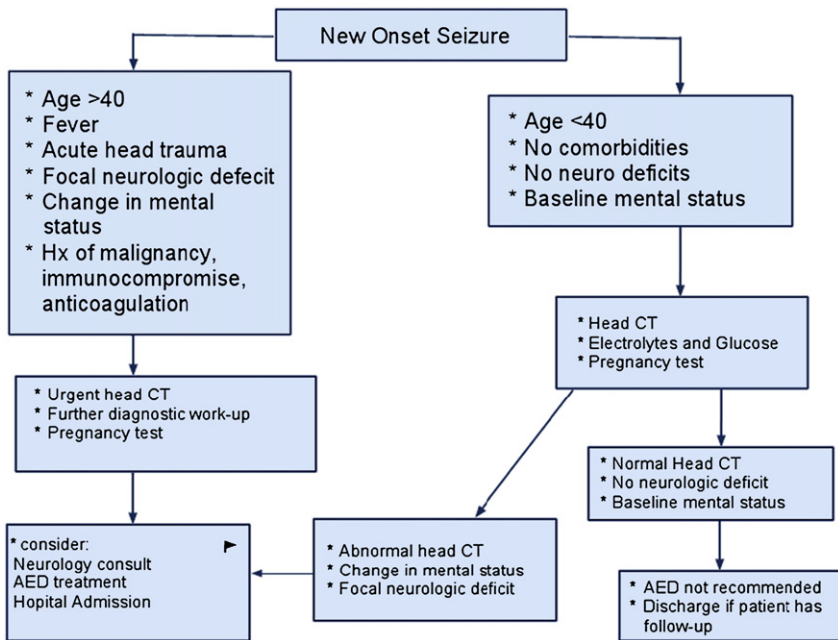


Fig. 1. Algorithmic approach to first time seizure. (Data from American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures [systematic review]. *Ann Emerg Med* 2004;43:605–25.)

INITIATION OF AED THERAPY

Preventing a seizure recurrence is the rationale behind starting an AED in the ED. Patients who have structural lesions on CT or patients with focal seizures that generalize secondarily have high risk (65%) of recurrence within 1 year, and are the group of patients that probably benefit from initiating AED therapy. However, identification of this subgroup requires laboratory testing, neuroimaging studies, and EEG, all of which are rarely immediately available in the ED. Moreover, AED treatment does not necessarily lower the risk of recurrence in all subsets of patients who have had a seizure. An uncontrolled study with a high rate of noncompliance reported a benefit for early initiation of AED treatment,²⁷ whereas an extended follow-up study of seizure recurrence by Hauser and colleagues²⁵ found that AED treatment was actually associated with an increased risk of recurrence. A study of patients with a history of traumatic brain injury has shown that phenytoin does not decrease the incidence of seizure recurrence.^{31–33} There is no clear evidence-based data regarding initiation of AED treatment in adult ED patients with first-time seizures and this decision is best made in conjunction with the physician who will be providing long-term care for the patient.

SUMMARY

In the evaluation of a first seizure, determination of serum glucose and electrolytes is recommended, as is a pregnancy test in women of child-bearing age. A head CT should be obtained in the ED whenever feasible, but when reliable follow-up is available, it is acceptable to discharge the stable patient with no comorbidities for deferred outpatient evaluation. The decision to initiate anticonvulsant therapy is based on the patient's risk of recurrence, which is highest among patients with structural lesions on CT or focal seizure, which secondarily generalize. Because all AEDs have associated side effects, the risks and benefits of initiating pharmacologic therapy must be carefully weighed and discussed with the patient. Anticonvulsants are not recommended for patients with normal neurologic findings who lack comorbidities or known structural brain abnormalities. In this group, it is appropriate to withhold AED therapy pending the results of a complete diagnostic evaluation.

KEY CONCEPTS

- A serum glucose and electrolyte determination is indicated in adult patients with a first-time seizure who have no comorbidities and who have returned to their baseline. A pregnancy test should be obtained in women of child-bearing age.
- Ideally, neuroimaging of the brain in the ED should be obtained on all adults with a first-time seizure. If a head CT is not available in the ED, options include discussion of the risk of recurrence with the patient and with the patient's primary physician, and either admit the patient to the hospital or make arrangements for an outpatient evaluation versus deferred outpatient neuroimaging if reliable follow-up can be arranged.
- Patients with a first-time seizure do not require an LP unless they are immunocompromised, or have a fever, severe headache, or persistently altered mental status.
- Patients with a first-time seizure who have no known structural brain pathology, normal serum glucose and sodium levels, and a normal neurologic examination can be discharged from the ED with appropriate outpatient follow-up.
- Patients with a first-time seizure who have a normal neurologic examination and no known structural abnormality of the brain do not need to be started on an AED in the ED.

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