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SPECIAL REPORT

Minimum standards for inpatient long-term video-electroencephalographic monitoring: A clinical practice guideline of the International League Against Epilepsy and International Federation of Clinical Neurophysiology

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Summary

The objective of this clinical practice guideline is to provide recommendations on the indications and minimum standards for inpatient long-term video-electroencephalographic monitoring (LTVEM). The Working Group of the International League Against Epilepsy and the International Federation of Clinical Neurophysiology develop guidelines aligned with the Epilepsy Guidelines Task Force. We reviewed published evidence using the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) statement. We found limited high-level evidence aimed at specific aspects of diagnosis for LTVEM performed to evaluate patients with seizures and nonepileptic events. For classification of evidence, we used the Clinical Practice Guideline Process Manual of the American Academy of Neurology. We formulated recommendations for the indications, technical requirements, and essential practice elements of LTVEM to derive minimum standards used in the evaluation of patients with suspected epilepsy using GRADE (Grading of Recommendations Assessment, Development, and Evaluation). Further research is needed to obtain evidence about long-term outcome effects of LTVEM and to establish its clinical utility.

KEYWORDS

diagnosis, nonepileptic, seizures, surgery, video-EEG

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1 | INTRODUCTION

Long-term video-electroencephalographic monitoring (LTVEM) provides an objective means to evaluate selected people with seizures[1] from a cohort of more than 65 million active cases of epilepsy in the world each year.[2–4] Seizures impair normal neurological function and impart safety risk,[5] affecting people of all ages, genders, ethnic backgrounds, and cultures.[2,4] One-third of people with epilepsy are uncontrolled by antiseizure medication (ASM).[6,7] Practice guidelines and quality measures are available to provide national and international standards for diagnosis and treatment of patients.[8–10] Because the manifestations of epilepsy are brief and intermittent, a standard 20–30-min electroencephalogram (EEG) often fails to show epileptiform activity. Inpatient LTVEM is the reference standard to provide a definitive diagnosis when standard EEG in conjunction with a clinical approach to diagnosis and management is unrevealing[5,11–20] Position papers and standards,[16] services,[21] and guidelines[11,14,22–25] exist for specific indications and certain aspects of LTVEM, although an international guideline to identify minimum performance standards is needed. In this clinical practice guideline (CPG), we address the current minimum standards for performing LTVEM as they apply to recording seizures and events for the purposes of differential diagnosis, classification, quantification, and characterization for presurgical evaluation. This adds to the International League Against Epilepsy (ILAE) and the International Federation of Clinical Neurophysiology (IFCN) guidelines on neurophysiological methods in people with epilepsy. The target audience for this CPG are clinicians and allied health care personnel. LTVEM is increasingly being performed in the home or ambulatory setting, although for this CPG, we refer to traditional inpatient use. Our objective is to provide evidence-based recommendations for performing inpatient LTVEM.

Key Points

1. This clinical practice guideline identified standards with recommendations summarized in Table S1
2. Limited high-level evidence addressing standards for LTVEM exist, and further research is needed
3. Selected topics for utility of LTVEM exist, although comprehensive criteria addressing minimum standards for performance are needed
4. Clinicians, hospital administrators, and insurers benefit from establishing standards for inpatient video-EEG monitoring applied to patient management

2 | STUDY METHODS

We extracted, reviewed, and evaluated published evidence on standards in LTVEM using the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) statement.[26] For the purposes of this study, we defined LTVEM as inpatient video-EEG monitoring lasting more than 24 h (usually days to 1–2 weeks). Data sources included PubMed and Embase supplemented with articles from Ovid Medline, CINAHL (Cumulative Index of Nursing and Allied Health Literature), and Cochrane databases including conference proceedings. All articles involving human subjects were included in the search, without language restrictions. The search strategy included broad search terms ("epilepsy AND seizures AND video-EEG") and synonyms ("epilepsy AND seizures AND telemetry") pertaining to LTVEM and subtopics evaluated (i.e., "epilepsy AND standards/guidelines"). Article search took place before October 16, 2019, and relevant articles were supplemented thereafter, with high-level evidence identified (Figure 1). Studies on neonates and continuous EEG monitoring during critical illness were excluded. Two independent reviewers screened titles and abstracts, and full text articles were examined for eligibility.

Due to the large heterogeneity in study design and the use of different LTVEM outcomes, quantitative synthesis (meta-analysis) was not possible. Therefore, we conducted a qualitative synthesis of high-level studies (Table 1). We posed questions to address patient populations, interventions, comparators, and measured outcome (Table 2) and aimed at answering the following questions: (1) What are the indications for LTVEM that influence management? (2) What are the technical requirements for LTVEM? and (3) What are the essential practice elements for performing LTVEM?

Individual studies were rated using predefined published criteria[11] to evaluate the evidence assessing the risk of bias given the paucity of high-level evidence.[27,28] The most relevant articles were identified, rated, and linked to recommendations predicated on Category I and II rated studies. Preexisting guidelines, consensus/position statements, and task force proposals were incorporated when applicable. Studies had to specify key outcome metrics (diagnosis and management) according to the STARD (Standards for Reporting Diagnostic Accuracy Studies) criteria.[29,30] High-level evidence was classified, rated, and subjected to a second rating. We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to formulate recommendations.

We developed this CPG as an evidence-based and consensus-driven document modeled after the Epilepsy Guidelines Working Group.[31] The ILAE Commission on Diagnostic Methods and the Executive Committee of the IFCN each appointed members of the Working Group. Two face-to-face meetings were held to review objectives and progress. Where relevant high-level evidence was absent, we used the Delphi

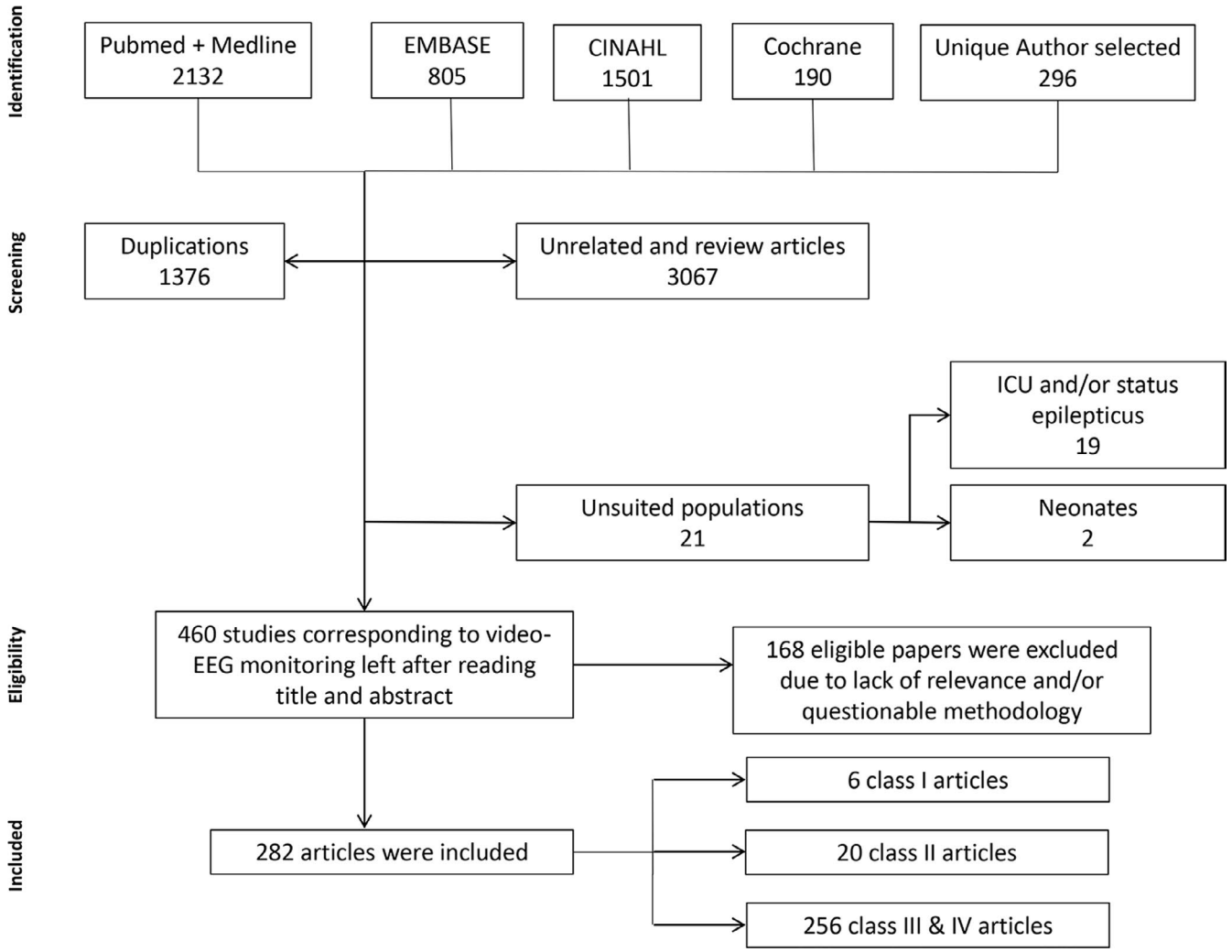

FIGURE 1 PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) evaluation of evidence using search terms to identify minimum standards of long-term video-electroencephalographic monitoring. CINAHL, Cumulative Index of Nursing and Allied Health Literature; EEG, electroencephalographic; ICU, intensive care unit

method[32] to obtain blind consensus when a majority agreed.[23] Additional information about the methods can be found in the Appendix, online in the Supporting Information.

3 | INDICATIONS

Epilepsy and neurology communities have produced 11 references to LTVEM in the form of guidelines and position papers, although comprehensive assessment of practices outside individual topics involved in LTVEM is limited in adults and children.[14,16,22,25,33]

3.1 | Differential diagnosis

LTVEM is most used for differential diagnosis of epileptic and nonepileptic attacks, with compelling evidence from 143 LTVEM papers (no Category I, six Category II) for clinical usefulness to distinguish between them.[17,34–38] One Category II study involved 22 epileptologists performing a blinded review of a sample of video and EEG extracted from LTVEM. Classifying events into epileptic, nonepileptic psychogenic, and nonepileptic physiologic categories demonstrated good interrater reliability for epilepsy, but only moderate reliability for psychogenic nonepileptic attacks (PNEA), and only fair interrater reliability for physiologic nonepileptic events.[39,40] Overall, most evaluable studies involved adult patients. Some studies support a misdiagnosis rate of epilepsy in 20%–30% of patients admitted for LTVEM,[35,37] whereas others note a wider prevalence between 5% and 50%.[41,42] Misinterpretation of an interictal EEG reporting epileptiform activity was one reason for misdiagnosis prior to LTVEM.[41–46] A meta-analysis of 135 LTVEM studies found 60% of referrals were for diagnostic reasons.[47] Most epilepsy mimics demonstrate generalized motor activity,[48] and to correctly interpret them

TABLE 1 High-level evidence involving standards in LTVEM ($n = 26$)

Authors and year	Class	Aspect of LTVEM	Patients, *n* (M vs. F)	Age range (years) and mean	Prospective/ retrospective	Control	Randomization	Comparison arm	Single vs. multicenter	Type of seizures
Dwivedi et al. 2017	1	Diagnosis	116 (57 vs. 59)	0.8–17 (9.0; 10.0)	Prospective	Yes	Yes	Yes	Single	Focal and generalized
Engel et al. 2012	1	Diagnosis	23	Not specified (34.3)	Prospective	Yes	Yes	Yes	Multicenter	Focal (TLE)
Wiebe et al. 2001	1	Diagnosis	80 (40 vs. 40)	Not specified (34.4; 35.5)	Prospective	Yes	Yes	No	Single	Focal (TLE)
Jonas et al. 2011	1	Hyperventilation	80 (39 vs. 41)	7–77 (32)	Prospective	No	No	Yes	Single	Focal and generalized
Kumar et al. 2018	1	Withdrawal of ASM	140 (88 vs. 52)	2–80 (20.3)	Prospective	Yes	Yes	No	Single	Focal and generalized
Lancman et al. 1994	1	Activation	93	6–53 (26.7)	Prospective	Yes	No	Yes	Single	PNEA
Koutroumanidis et al. 2008	2	Classification	33 (15 vs. 18)	7–44 (20); 13–56 (24.3)	Prospective	No	No	No	Single	Generalized
Kandler et al. 2013	2	Safety	Not specified	Not specified	Prospective	No	No	No	Multicenter	Focal and generalized
Hedegard et al. 2014	2	Complications	Not specified	2–58 (26)	Prospective	No	No	Yes	Single	Not specified
De Marchi et al. 2017	2	Safety and efficacy	113 (35 vs. 78)	10–70 (24.9)	Prospective	No	No	No	Single	Generalized
Craciun et al. 2017	2	Safety	976 (428 vs. 528)	1–80 (24.57)	Prospective	No	No	No	Single	Not specified
Guaranha et al. 2009	2	Activation	76 (35 vs. 41)	12–53 (24.3)	Prospective	No	No	No	Single	Generalized
McGonigal et al. 2002	2	Yield of VEM	30 (8 vs. 22)	>16	Prospective	Yes	Yes	No	Single	PNEA
Walczak et al. 1994	2	Utility and reliability	68	Not specifed	Prospective	No	No	Yes	Single	PNEA
Chen et al. 2011 (295)	2	Induction	51 (42 vs. 9)	No range (12.56; 11.26; 17.78)	Prospective	No	No	Yes	Single	PNEA
Rizvi et al. 2014	2	Safety	158 (83 vs. 75)	Not specified (37.2)	Prospective	No	No	No	Single	Focal and generalized
Furbass et al. 2015	2	Automatic detection	205	Not specifed	Prospective	No	No	Yes	Multicenter	Not specified
Salinsky et al. 1997	2	Automatic detection	72	11–56 (32.4)	Prospective	No	No	No	Single	Not specified
Benbadis et al. 2001	2	Classification	78	Not specified	Prospective	No	No	Yes	Multicenter	Focal and generalized

TABLE 1 (Continued)

Authors and year	Class	Aspect of LTVEM	Patients, *n* (M vs. F)	Age range (years) and mean	Prospective/ retrospective	Control	Randomization	Comparison arm	Single vs. multicenter	Type of seizures
Lee et al. 2009	2	Diagnosis and management	129 (72 vs. 57)	7–89 (38.3)	Prospective	No	No	Yes	Single	Epileptic and PNEA
Goyal et al. 2014	2	Induction	190 (73 vs. 117)	No range (21.38; 21.08)	Prospective	Yes	No	Yes	Single	Epileptic and PNEA
Baheti et al. 2011	2	Utility and reliability	148	No range (51.3)	Prospective	No	No	No	Single	Epileptic and PNEA
Kane et al. 2014	2	Hyperventilation	3170	.25–97 (33.1)	Prospective	No	No	Yes	Multicenter	Epileptic and PNEA
Yogarajah et al. 2009	2	Duration	612	No range (36)	Retrospective	No	No	Yes	Single	Epileptic and PNEA
Jedrzejczak et al. 1999	2	Diagnosis	1083	Not specified	Retrospective	Yes	No	Yes	Single	Epileptic and PNEA
Alving et al. 2009	2	Diagnosis and duration	234	.6–80 (30)	Retrospective	No	No	Yes	Single	Epileptic and PNEA

Abbreviations: ASM, antiseizure medication; EEG, electroencephalographic; F, female; LTVEM, long-term video-EEG monitoring; M, male; PNEA, psychogenic nonepileptic attacks; TLE, temporal lobe epilepsy; VEM, video-EEG monitoring.

based on clinical grounds alone is challenging.[49] In an evaluation of 181 consecutive patient LTVEM records, useful information was obtained in 72% and the clinical diagnostic question was answered in 67%.[50] In older adults (mean age = 51 years), LTVEM was most useful in 93.5% of 31 patients with pure PNEA.[34] Standards for diagnosis of PNEA including use of LTVEM have been developed by an international consensus group of clinician-researchers.[51] A diagnostic LTVEM outcome study in 230 people resulted in a change in diagnosis in 133 (58%) and refinement of a diagnosis in 29 (13%) to provide overall diagnostic value in 71% of patients and was particularly useful to differentiate frontal lobe seizures from generalized seizures and nonepileptic attacks.[36] Similarly, another diagnostic LTVEM outcome study found 58% of 131 patients had their diagnosis altered by LTVEM, with the greatest change being an increase from 7% to 31% of patients with nonepileptic attacks.[17] Following LTVEM, the diagnosis was reversed in 29 (24%) of 121 patients and four diagnoses changed from nonepileptic to epileptic seizures.[37] Overall, patients with pure PNEA are more common than those with a dual diagnosis[38,52] and those with physiological nonepileptic events identified by LTVEM.[19] In one Category II controlled study of 1083 patients diagnosed with epilepsy, 85 (7.8%) were clinically diagnosed with PNEA, 48 were believed to manifest only PNEA, and 37 patients were suspected of both PNEA and epileptic seizures.[38] When LTVEM was subsequently performed, 55 of 70 (79%) cases had PNEA only and only nine of 230 (3.9%) with PNEA also had epileptic seizures, demonstrating the pitfalls for dual diagnoses based on clinical grounds alone. One retrospective study in 49 patients with PNEA identified 18.2% with pseudostatus compared with 5.2% of 154 patients with epileptic status epilepticus.[53]

In a systematic review of diagnostic procedures, 33 papers comprising a range of procedures including seizure induction, Minnesota Multiphasic Personality Inventory, prolactin levels, single photon emission computed tomography (SPECT), and clinical metrics (i.e., preictal pseudosleep, ictal, and postictal characteristics) found no procedure attained reliability equivalent to video-EEG monitoring (VEM),[54] with none of the tests investigated demonstrating both high sensitivity and high specificity. In one pediatric retrospective diagnostic accuracy study (Category IV), chart review found superior sensitivity of 54% and comparable specificity of 88% with LTVEM compared to standard EEG even in the absence of ictal recording.[55]

In a group of 221 patients undergoing LTVEM, sessions were significantly shorter in the diagnostic group (mean = 2.4 days) than in a group admitted for presurgical evaluation (3.5 days).[37] With respect to management following LTVEM, one study of 148 consecutive patients over approximately 3 years noted a significant reduction in ASM usage in people with epilepsy and PNEA.[34] When PNEA are misdiagnosed

Questions	Outcome
Population	Children and adults with seizures with intensive need for diagnosis, for classification/quantification, or to characterize refractory seizures for surgery
Intervention	Video-EEG monitoring lasting for more than 24 h
Comparator	Historical diagnosis and site of surgery
Outcome	Event cessation in nonepileptic attacks, seizure reduction or seizure freedom, usefulness

TABLE 2 Population, intervention, comparator, and outcome targeted questions for guideline focus

Abbreviation: EEG, electroencephalographic.

as epilepsy, potential adverse consequences of unnecessary ASM and invasive procedures may be averted by LTVEM.[56]

The highest level studies in this area included six Level II studies, which are downgraded due to unexplainable inconsistencies between these studies but upgraded due to the magnitude of effects. The overall confidence in evidence for these studies is therefore moderate for LTVEM to provide differential diagnostic utility in differentiating epileptic from nonepileptic events.

Recommendation: LTVEM monitoring should be used to differentiate between epileptic and nonepileptic events, in patients where the diagnosis is in question (strong recommendation).

3.2 | Classification

Classification of seizures and epilepsy syndromes is essential for appropriate selection of ASM.[43,57,58] LTVEM studies reporting seizure and epilepsy classification are Category III and IV for specific purposes of classifying some patients with epilepsy. A minority will remain unclassified despite LTVEM until more information becomes available. One retrospective diagnostic study of 230 patients changed diagnosis in 133 patients, and in this group of patients LTVEM proved useful in differentiating focal from generalized epilepsy in 47 of 133 (35%),[36] in compliance with the International Classification of Epileptic Seizures that divides seizure types into focal, generalized, and unknown.[59] LTVEM provides a definitive diagnosis and supports a continuum of disease[11,58,60–62] by identifying a spectrum of clinical seizure types and neurophysiologic patterns on EEG.[13,19,24,59,63,64] A prospective study of inpatient LTVEM (minimum = 3 h) clarified the epilepsy syndrome in 93% of 143 epilepsy patients (7% remained unclassified), with one-third eligible for epilepsy surgery.[65]

Alternative classification systems based purely on semiology have been proposed.[66] A prospective comparison (Category II) between ILAE and semiological seizure classification systems in 78 consecutive patients found seizure classification changed significantly between pre- and post-LTVEM, using ILAE more than semiological classification.[40] Another adult semiology study (Category IV) of 90 patients found some seizure types (e.g., myoclonic and hypermotor seizures) had excellent consistency between historical description and an LTVEM-confirmed diagnosis, although focal seizures were less reliable.[67] In a large study (Category IV) of 323 children (mean age = 7 years) with episodes of staring, myoclonic jerking, and abnormal eye movements and posturing, 53% of epileptic patients were correctly classified for seizure type or epilepsy syndrome by new information derived from LTVEM.[68] Other retrospective (Category IV) studies involving patients with juvenile myoclonic epilepsy reported focal clinical and EEG features in about one-half of patients, complicating clinical diagnosis.[69,70]

A large retrospective LTVEM-based surgical series classified patients by EEG, with a focal EEG found in two-thirds, generalized abnormalities in 22%, lateralized features in 4%, and 6% mislocalized or mislateralized.[71] Sleep-related events can be diagnosed and correctly classified (focal vs. generalized) with overnight LTVEM.[72,73] Despite a small number of patients, one retrospective (Category IV) study found the percentage of patients with a diagnosis of generalized epilepsy more than doubled after LTVEM.[17] In genetic generalized epilepsies (GGE), gene defects do not lend themselves to reliable classification.[74] EEGs with interictal epileptiform discharges (IEDs) noted during LTVEM are not specific for seizure type(s) or for epilepsy syndromes.[75,76] However, LTVEM may classify and subclassify GGE,[77] and reclassify seizures to guide ASM selection.[43]

The practical usefulness of LTVEM for classifying epilepsy is axiomatic, as ILAE classification is based on data extracted from LTVEM to serve as the standard, with a consistent effect across subjects. Therefore, the group issues a strong recommendation despite the presence of weak evidence.

Recommendation: LTVEM helps classify patients with epilepsy in whom the seizure type or epilepsy syndrome is undetermined (strong recommendation).

3.3 | Seizure quantification

Thirty articles (Categories III and IV) addressed seizure quantification and LTVEM. On average, fewer than 50% of

seizures (47%–63%) are correctly documented by patients prior to diagnosis established by LTVEM, with reporting accuracy that varies over time.[78] One (Category IV) questionnaire study that focused on patient awareness noted 44.2% of LTVEM-proven seizures went unnoticed.[79] Self-reporting seizures are essential for appropriate management.[80] Ambulatory EEG and LTVEM studies reveal 20%–25% of patients are always unaware of seizures.[81–85] Patients with temporal lobe epilepsy (TLE),[79,82,84] cognitive decline,[86–89] and transient epileptic amnesia are at risk for underreporting seizures that may be clarified during LTVEM.[90,91] In a (Category III) LTVEM study evaluating 327 consecutive TLE patients, subclinical seizures were detected in 8.3%, and 1% had only subclinical seizures recorded (all of which were detected within the first 24 h).[92] One LTVEM study used postictal surveys and found awareness present in patients with convulsions associated with GGE, but those with focal to bilateral tonic–clonic seizures had incomplete awareness.[81]

Patients with generalized epilepsies, severe epilepsies, and frequent seizures are candidates for seizure quantification by LTVEM, and more pediatric studies are represented in this section. Convulsions are readily identifiable[93]; however, subtle nonconvulsive seizures and frequent IEDs (i.e., electrical status epilepticus in sleep), subclinical seizures, and nocturnal seizures may evade clinical detection. Failure to recognize nocturnal seizures may occur in up to 86% of patients.[94] Irrespective of semiology, LTVEM can quantify seizure burden and identify clinical phenomenology to yield more favorable response to treatment[95] and improved patient outcome.[84]

Most available literature consists of lower-class studies that were inconsistent, and the overall confidence in evidence for utility of LTVEM to quantify seizures is low, depending upon duration.

Recommendation: The usefulness of LTVEM to quantify seizures in patients with epilepsy is unknown (confidence in effect estimates is so low that a recommendation would be speculative).

3.4 | Seizure characterization for surgical management

Three prospective longitudinal cohort studies evaluating patients with epilepsy managed with ASMs over 30 years failed to show a meaningful decline in the number of people with drug-resistant epilepsy,[96] and despite new advances,[97] risks exist for patients when seizures are uncontrolled.[98–101] Three Category I randomized controlled clinical trials including one in children, and multiple Category III and IV studies support the effectiveness of epilepsy surgery compared with best medical practice following LTVEM.[98–100] Adult studies focus on TLE,[98–100] whereas proportionally more extratemporal resections have been performed in children, reflecting site and pathology specificity.[98–100] Position statements recommend a presurgical evaluation be considered incorporating LTVEM when patients are resistant to ASMs to confirm an epilepsy diagnosis and seek concordance with other evaluations (i.e., history, magnetic resonance imaging, positron emission tomography).[101] Surgery remains greatly underutilized,[102–105] with multiple reports of efficacy.[47,106]

Scalp-based VEM and invasive EEG (iEEG) during LTVEM are standard neurophysiological techniques to characterize the seizure onset zone for surgery.[11,47] Modern high-resolution video is an essential adjunct to EEG during LTVEM to corroborate semiology and localization of the seizure onset zone (see Section 5.2). Few studies characterize seizure onset patterns denoted by EEG relative to outcome, and whereas some patterns are localizing, others are not.[107–109] In a retrospective Category III study involving 3057 seizures in 75 consecutive patients with drug-resistant focal epilepsies, individualized scalp and iEEG LTVEM sessions were compared following successful epilepsy surgery.[106] A localized scalp EEG during LTVEM at seizure onset (independent of location) predicted a favorable outcome after surgery, whereas multilobar and widespread seizure onset predicted unfavorable surgical outcomes.[106,110] Other retrospective Category III studies involving combined scalp and iEEG during LTVEM demonstrate moderate to favorable sensitivity and specificity for scalp ictal EEG patterns predicting localization in patients with TLE.[111,112] In a prior report analyzing 61 patients with lesional drug-resistant focal epilepsies, 71 paired seizure onset patterns matched between scalp EEG and iEEG found some scalp seizure onset patterns were highly associated with a specific intracerebral pattern, specific pathologies, and depth localized seizure onset.[105] Single-center retrospective (Category IV) studies demonstrate that focal temporal[113] and extratemporal scalp patterns predicted a seizure-free outcome.[109] Other reports, in contrast, note that dissimilar cerebral generators may produce similar ictal patterns on scalp recording,[114,115] and that presurgical tools including LTVEM did not provide unambiguous long-term outcome predictions for TLE surgery.[113] A consortium funded by the European Union performed a systematic review and meta-analysis and found LTVEM had substantial heterogeneity across studies associated with moderate sensitivity and low specificity for identification of the epileptogenic zone, with higher sensitivity in lesional TLE compared to lesional extratemporal lobe epilepsy (ETLE).[116] As a result, LTVEM guidelines were implemented across Europe based upon the diagnostic accuracy of LTVEM in identifying the epileptogenic zone in epilepsy surgery candidates.[116] Due to lack of evidence for the utility of LTVEM in children, a modified Delphi process was used among pediatric epilepsy experts to develop consensus-based guidelines

for LTVEM in the presurgical evaluation of children with epilepsy in the United Kingdom.[23]

There is high confidence in evidence that LTVEM should be used as part of the presurgical evaluation for TLE patients. For ETLE, there is heterogeneity and low confidence in evidence for or against LTVEM for seizure characterization in the presurgical evaluation. The evidence basis for LTVEM monitoring and ETLE is weak due to smaller number of cases (vs. TLE), heterogeneous semiology, and poorly localized scalp ictal EEG. Unfortunately, there is not a better way to evaluate patients, and therefore the group issues a strong recommendation for ETLE too.

Recommendation: LTVEM must be used in the presurgical evaluation of patients with drug-resistant epilepsies (strong recommendation).

4 | YIELD OF INPATIENT LTVEM

The overall diagnostic yield of LTVEM from Category III and IV studies varies widely (19%–75%) due to differences in endpoints, definitions, methodology, and patient cohort evaluated[11,13,17,35,37,50] independent of the hospital course.[117] A systematic review found most of the literature on LTVEM focused on noninvasive and invasive presurgical evaluation prior to epilepsy surgery.[47] A large, prospective study demonstrated LTVEM was useful to clarify the clinical diagnosis in 56.3% of patients,[118] and meta-analysis found the preadmission diagnosis changed in 35.6% of patients following LTVEM, implicating change in management.[47] Successful LTVEM sessions are significantly longer in a presurgical group of patients than in a diagnostic group.[35] No difference in diagnostic yield has been identified with respect to age,[19,119–121] patients with neurological impairment,[122] or reason LTVEM was performed.[35] One retrospective study did not find a correlation between the preadmission frequency of seizures and the yield for recording events during LTVEM.[123] Despite undergoing thorough evaluation including repeat EEGs obtaining sleep recording and short-term video-EEG in patients with daily spells, and in other patients evaluated with ambulatory EEG,[119] LTVEM was found to be useful in nearly one-half of cases.[35] In a prospective comparative study (Category II) of 129 patients with 10-month follow-up, after LTVEM, the diagnostic categories were changed from preadmission in 41.1% of the patients, and 40.3% had revisions in management.[124]

Pitfalls in diagnosis without LTVEM compromise yield if semiology alone is used and result in misdiagnosis as PNEA.[11,125,126] There is a small risk that provocation by suggestion may lead to false-positive results in patients with PNEA.[127] Results from Category IV LTVEM studies and expert opinion support that overinterpretation of EEG may be a reason for epilepsy misdiagnosis in patients with PNEA.[43,128] During LTVEM, approximately 20%–30% of patients never have a seizure or event.[41,129,130] In patients with epilepsy, LTVEM may not reveal IEDs in EEG or be devoid of a detectable scalp ictal rhythm during some focal seizures,[131,132] falsely leading to a nonepileptic diagnosis.[133] Furthermore, patients with PNEA can generate rhythmic movement artifacts that falsely mimic an electrographic seizure[134] or obscure the ictal EEG during hyperkinetic epileptic seizures to limit identification of the seizure onset zone.[135] Scalp ictal EEG may falsely localize and lateralize focal seizures,[136] especially those arising from mesial and posterior quadrant neocortices[127,137] but may be potentially localized when iEEG is recorded.[138,139]

Overall, one Class II study provides low confidence in evidence that more than one-third of patients will experience a change in management after undergoing VEM.

Recommendation: LTVEM may result in a change in management in some patients (weak recommendation).

5 | TECHNICAL STANDARDS

Minimal technical standards are required to ensure high-quality recording, adequate storage, optimal review, and web-based remote exchange of information.[126,140] With the advent of digital technology and increasing computer sophistication, instrumentation has transformed the practice of LTVEM.[141,142] Signal processing, adjunctive software and analytics, high-speed electronic transfer, and larger storage capacity facilitate widespread use.[14,143,144] High-level evidence-based standards evaluating equipment and instrumentation are lacking, with heterogeneity in clinical practices in epilepsy monitoring units (EMUs).[145] We assessed technical parameters for LTVEM using the modified Delphi method[32] to supplement prior published information.[11,140–144]

5.1 | Electrode array and EEG recording

LTVEM allows acquisition and analysis of signals from the brain that can be configured based on clinical need. Standard configurations apply the 10–20 system in common bipolar and referential montages for clinical EEG,[146] but in some cases, alternative arrays such as high-density EEG may be used to improve detection.[147,148] A minimum of 16 channels for diagnostic LTVEM and 32 for presurgical evaluation is recommended by the American Clinical Neurophysiology Society (ACNS).[14,22] Majority consensus was achieved for technical features and personnel-based issues (Tables 3A,B). Consensus was reached to endorse using more than the 21 electrodes of the International 10–20 system of electrode placement (Table 3A). Specifically, our results support IFCN recommendations to use 25 electrodes in children and adults during scalp-based LTVEM.[25] Dense EEG arrays

TABLE 3A Results using the Delphi method of consensus for the selected aspects involving technical features in long-term VEM where high-level evidence was absent

VEM technical feature	Majority response
Disc electrodes applied individually for diagnostic scalp-based VEM	Yes
Intracranial monitoring electrodes	Yes
Basal temporal additional electrodes	Yes
Nasopharyngeal or sphenoidal additional electrodes	No
10–10 system application	Yes
Source localization software recommended (surgical VEM)	Yes
Minimal number of electrodes for VEM	>21
Use of electrocardiogram	Yes
Use of oximetry, extraoculography, polygraphy	Optional

Abbreviation: VEM, video-electroencephalographic monitoring.

TABLE 3B Results using the Delphi method of consensus for the selected aspects involving personnel-based issues in long-term VEM where high-level evidence was absent

Personnel	Majority response
Board certification for physicians performing VEM	Yes
Epileptologist preferred	Yes
Use of a dedicated hospital area for VEM	Yes
Designated EMU	Yes
Solo NP/PA patient care	No
Solo resident patient care	No
Registered technologists performing VEM	Yes
Electrodes require measuring and marking (scalp EEG)	Yes
VEM physician coverage	24 h/day
Optimal number of technologists per patient	2:1
Archiving: segments selected by technologists/residents	Yes
Review entire VEM file before EEG report is finalized	Yes
Review selected video clips before EEG report is finalized	Yes

Abbreviations: EEG, electroencephalography; EMU, epilepsy monitoring unit; NP/PA, nurse practitioner/physician assistant; VEM, video-EEG monitoring.

during LTVEM and higher sampling rates can improve electrical source localization.[25,149–151] Routine use of basal temporal electrodes (but not sphenoidal, nasopharyngeal, or nasoethmoidal electrodes) is recommended. No consensus was reached regarding use of diagnostic electrode caps. Nor was consensus reached to recommend maximal allowable scalp electrode impedance, although values less than 5 kΩ have previously been recommended for standard EEG.[25,140] Consensus was reached for EMUs performing LTVEM to have the optional technical capability of using invasive electrodes. Polygraphy incorporating eye and limb movement, oximetry, autonomic metrics, and direct current channels usage is an acceptable option during LTVEM and tailored to the specific condition being investigated.[152–155] All raters agreed that electrocardiographic recording was necessary during LTVEM.

LTVEM storage servers require hard drive memory capability to acquire at least 200 GB of data per week per LTVEM recording unit in clinical operation.[156] Solid-state multichannel amplifiers need to include an isolation amplifier stage and follow the technical criteria established for minimum standards of recording clinical EEG.[11,140] Consensus was reached for analogue to digital converters to use 12 bits or more and sample rates of 256 samples/s or higher. Many commercial systems use at least 16-bit resolution and sample at 512 Hz to minimize aliasing and optimize signal resolution to improve localization. High-pass (low-frequency) filter settings of .5 Hz or less and low-pass (high-frequency) filter settings of 70 Hz or greater should initially be applied during LTVEM EEG review. Following acquisition, EEG signals should be stored in a central server with long-term archiving performed by a technologist or physician. Consensus supported maintaining all video and EEG files until LTVEM reporting was finalized. A recent retrospective 15-year study (Category III) involving 1025 cases showed a trend toward normal VEM patient results, minimizing the need for detailed archiving,[157] with polygraphic recordings supplementing EEG in select cases when informative.[158–160] Despite the similar localizing ability of noninvasive dense EEG arrays to iEEG in patients with focal seizures,[161,162] only low-level evidence and expert consensus exist to support the use of iEEG in complex patients during presurgical evaluation.[163,164]

5.2 | Video

Video recording is routine during LTVEM[165–167] in concert with EEG in expanding numbers of EMUs.[118,168,169] One camera is standard for LTVEM; however, some centers use two to provide different viewpoints. Prospective multirater studies (Categories II and III) have shown that compared with LTVEM, video alone may be useful when evaluating the clinical description of patients with observed seizures,[126,170] with similar sensitivity (Category III) compared with EEG[171] in various patient populations.[172] Implementing video recording added to EEG increases the diagnostic yield over EEG alone[173,174] and details seizure semiology.[66] However, no uniform nomenclature and consistent classification system differentiates patients with PNEA from epilepsy by video alone,[175] although semiologies[42] allow hierarchical clustering.[176–178] Based on video data alone, a prospective

LTVEM study involving five epilepsy experts found seven of 23 (30%) cases by all raters correctly classified epileptic seizures and PNEA.[179] A prospective study analyzing 120 seizures from 35 consecutive subjects found that of 45 signs demonstrated on video, only three for epileptic seizures and three for PNEA were useful in categorizing seizures, and no single clinical feature was sensitive and specific for either event.[180] The sequence of seizure phenomenology recorded on video during LTVEM identifies patterns that localize and lateralize signs.[181] When scalp ictal EEG onset follows clinical onset, a deep or distant generator, often extratemporal in origin, is suggested.[106,111]

Standard digital audio–video data are acquired by standard industry codecs. Precise specification for time synchronization between video and EEG has been standardized in the DICOM format and MED format, although they are not in broad clinical use.[182] Split screen synchronized video and dual screen review may be useful to evaluate paroxysmal neurological events.[183] Digital video (and audio) are typically encoded into MPEG, MPEG2, or MPEG4 formats differing in the degree of resolution and compression algorithms used and synchronized with EEG by use of a time marker, but other audio–video formats can be used successfully. Twenty-four-hour LTVEM requires up to 30 GB of memory and varies depending upon video resolution, degree of coloration, number of frames/s, and machine data compression algorithm employed. For archiving, relevant LTVEM clips involving events of interest are selected to minimize long-term data storage requirements.

There were 4 Class II studies (two without EEG and two with EEG) that consistently showed benefit with the use of video. Confidence in the evidence of using video with EEG monitoring is moderate.

Recommendation: Video should be combined with EEG during LTVEM (strong recommendation).

5.3 | Safety

The potential for dangerous consequences exists during LTVEM because patients' seizures are induced.[8] Convulsions and seizure emergencies such as falls, injury, and postictal psychosis, among others, are possible safety risks.[33,168] Standardized protocols are recommended for use to ensure basic patient safety.[145,184] Safety and quality data from a meta-analysis of 181,823 patients reporting on 34 different safety variables demonstrate a great deal of variation in reporting safety and quality measures in EMUs.[47] No validated protocols are universally available and utilized, and substantial variation in practice for essential aspects of LTVEM exist for performing optimal patient observation, tapering ASMs, and ASM rescue protocols.[185–187] Therefore, variation in quality and safety measure may exist during LTVEM, with a pooled proportion of adverse events in 5%–9% present in a meta-analysis.[47] In addition, practice variability performing LTVEM was found among 32 epilepsy centers in the United Kingdom, likely reflecting variance in usage for different patient populations.[168]

5.3.1 | Clinical safety

Overall, LTVEM is an acceptably safe procedure with appropriate precautions in adults and children.[25,188–190] Safety issues are more frequently encountered during LTVEM in patients with focal epilepsy undergoing presurgical evaluation than for those with GGE undergoing diagnostic evaluations.[191] Seizure provocation poses potential safety risks to patients represented by Category III and IV studies.[185,192,193] For children, and patients with intellectual, cognitive, and behavioral challenges, patient companions during the night are recommended both for safety and for documenting events, assessing awareness, ensuring video integrity, and alerting staff at seizure onset. Immediate family members are more helpful than nonfamily members and always necessary for children less than 5 years of age.[25] Even patients with PNEA are prone to adverse events, usually falls, at a significant rate,[185] often while in the bathroom.[194] A large Category III study of 976 patients found only 1.9% of patients fell (without injury) despite being freely mobile, a similar finding reported in other centers practicing restricted mobility.[195] One comparative study (Category III) found alert patients fell in the bathroom within the first 3 days of LTVEM compared to patients hospitalized for mental status changes where falls occurred after 3 days in their rooms.[196] Novel lift systems, patient education, frequent nursing rounds, use of bed alarms, and assistance when out of bed may limit fall risk.[194] A Category IV study reviewing records from an Epilepsy Foundation database identified two of 733 patients with aspiration following a generalized tonic–clonic seizure, and shoulder dislocation in eight of 806 during seizures, for an overall risk of less than 1%.[197] Rarely, serious medical consequences associated with seizures may occur, such as malignant cardiac arrhythmias, bony fractures, and pneumonia.[189,193] Prospective comparative studies (Category III) show patients with PNEA have increases in heart rate and systolic blood pressure during the ictal phase, potentially predisposing to complications when attacks are prolonged.[198] Ictal asystole has been reported in 0.22%–0.4% of patients undergoing LTVEM, and a systematic review of 157 cases found females with preexisting heart conditions and males with autonomic dysregulation were predisposed.[199] Sudden unexpected death in epilepsy during LTVEM has been noted in retrospective series (Category IV) from 160 EMUs throughout the world.[200,201]

Current practice recommendations reached consensus that informed consent should be obtained before VEM,

with continuous observation of patients by nursing and professional staff over the monitoring duration as a minimum standard, supplemented with alarm systems and video monitors.[168] A multicenter Category II survey study of epilepsy centers in the United Kingdom involving 198 adults and 78 children recommended the nurse-to-patient ratio in an EMU should not exceed 4:1 to ensure patient safety.[168,202] In a United Kingdom pediatric consensus statement, a ratio of 2:1 for scalp EEG was recommended and 1:1 during iEEG.[25] Complications involving iEEG electrodes in a prospective population-based observational Category II study were associated with intracranial hemorrhage in a significant minority of epilepsy patients during LTVEM.[203]

Safety studies involving nurse-to-patient ratio during LTVEM and risk of intracranial hemorrhage with iEEG electrodes provide low confidence in the evidence.

Recommendation: The safe, maximal nurse-to-patient ratio to provide constant supervision of patients during LTVEM may be 4:1 (weak recommendation).

5.3.2 | Electrical safety

Category IV clinical reports reflect essential safety features during LTVEM (Table 4).[204–208] Electrical safety rules and governance are unique to individual countries and established by the International Electrotechnical Commission.

TABLE 4 Recommendations for basic electrical safety during performance of long-term video-electroencephalographic monitoring[a]

VEM	Recommendations
Power source	• Use approved three-pronged plugs, receptacles, and power cords for electrical devices. • Patients should be connected in each EMU room to a single cluster of power receptacles. • Banks of electrical receptacles should be located together near the head of the bed.
Patient room	• Move dual-wired devices away from patients and avoid metal contact with the bed. • Educate EMU and nursing staff to avoid connections between the patient and ground. • Do not touch metal objects and the patient at the same time to avoid electrical connection.
Grounding	• Do not connect the patient to earth ground. • Only use equipment with an isoground connection to the patient. • Periodically test electrical equipment for current leakage (cable current should be <10 mA).
Electrical equipment	• Turn equipment on before patient connection/disconnect before turning equipment off. • Do not use extension cords. • Employ battery-operated equipment where possible.
Patient	• Recording electrodes should not be connected to building ground, only through isoground.
Stimulation	• The cardiac area should not be within the stimulating field. • For electrical stimulation studies, do not exceed intensity or duration recommendations. • The stimulus delivery subsystem should be entirely isolated from the building ground.
Equipment testing	• Equipment should be checked for compliance with hospital safety standards and biomedical services. • A sticker should be placed to attest equipment safety (and date). • Testing at regular intervals by biomedical engineering should determine electrical safety and include visual inspection of power cords, plugs and grounds, wiring, and room wall receptacles. • Measurements of ground pin contact tension should not be >10 oz, chassis leakage current should normally be <100 mA, and leakage current from each terminal should be <20 mA.

Abbreviation: EMU, epilepsy monitoring unit.

[a]Extracted from Burgess RC. Electrical safety. In: Handbook of clinical neurology. New York, NY: Elsevier; 2019. p. 67–81.

Electrical injury is possible when current passes through a patient from an electrical source or electrode contacts.[209,210] Any mains-powered electrical device may "leak" current and enter the patient through direct contact of a nearby metal object or indirectly by capacitive coupling inside an electrical device from nearby wiring conducted from the transformer to the case. Electrical shocks usually result from chassis leakage current from LTVEM equipment powered by 120-V, 60-Hz alternating current (AC) in the United States and 230-V, 50-Hz AC in Europe. Safe current limits are set for both normal conditions and for single fault conditions (i.e., a disconnected earth ground). LTVEM safety guidelines exist for individual components of equipment. Biomedical engineering services should check equipment for safe use according to safety standards.[211]

Microshock is of greatest concern to patients undergoing LTVEM with scalp electrodes, created by a low-resistance pathway to the body.[211] Susceptibility is maximal when electrical frequency reaches 60 Hz and is especially concerning when patients have an intravenous (IV) cannula, because it provides a very low-resistance pathway to the heart.[211] Currents of 5–10 A can induce ventricular fibrillation[209] as a function of body habitus, current intensity, duration, and pathway.[210,212,213] Similarly, when patients undergo LTVEM and have cardiac pacemakers, the leads create a potential for electrically induced arrhythmia. Ground loops are critical to avoid during LTVEM. Current flowing from one ground to another on separate parts of a patient's body produce magnetic fields through inductive coupling of nearby power-line wiring and may pose potential electrical safety risk to patients.

There is no evidence for or against methods to ensure electrical safety in patients undergoing LTVEM. Ethical constraints prevent studies of this nature from being performed.

5.4 | Practice and personnel

Despite the use of LTVEM as a gold standard for seizure diagnoses, limited appreciation of this technique is held by some general neurologists, psychiatrists, hospital administrators, and insurance carriers managing people with paroxysmal neurological disorders (Table 5).[16] The current practice of LTVEM has been outlined in a European multicenter web-based survey study.[33]

5.4.1 | Seizure monitoring

Considerable variation in the practice and organization of EMUs was found in a web-based survey study involving 25 centers across 22 European countries, and authors subsequently recommended development and implementation of evidence-based LTVEM practices.[33] Delayed response to seizure alarms may occur due to high false-positive rates of detection.[214] A retrospective multicenter study found the average response time from caregivers was twice as fast as the response by EMU-based personnel. In addition, staff uncovering patients during seizures to evaluate semiology found 40% of patients were fully or partially obscured for more than 30 s during the event, compromising visualization.[215] Hence, presence of a parent or caregiver is encouraged, especially at night, while monitoring young children, and patients with intellectual and developmental disabilities. Encouraging observers to report and describe seizures in a log is useful. Implementing standardized protocol for testing patients during seizures can potentially improve the quality of the data recorded during LTVEM. A task force appointed by the ILAE Commission on European Affairs and the European Epilepsy Monitoring Unit Association prospectively studied (Category II) testing paradigms during seizures in 152 consecutive patients (250 seizures) at 10 epilepsy centers; interictal, ictal, and postictal testing adaptive paradigms during seizures were successfully implemented in 93% of patients, limited only by seizures of short duration.[216] A European survey showed 91% of EMUs performed ictal or postictal testing; however, there was no standardization of the procedure, and many EMUs lacked institutional guidelines for testing patients during seizure monitoring.[145] Retrospective comparative assessment of seizures in 33 adult or pediatric patients captured during VEM found behavioral testing during seizures could be performed in only 50% of patients, whereas automated video-recorded behavioral tasks activated by computer-based seizure detection provided reliable behavioral assessment.[217] Overall, the one Category II study was unable to demonstrate superiority of a particular testing paradigm during LTVEM. Confidence in evidence is therefore low. Testing during seizures in patients with cognitive and behavioral disorders is highly variable and individualized.

Recommendation: A written, standardized protocol may be used in each LTVEM unit for managing and testing patients during seizures (weak recommendation).

5.4.2 | Services

Guidelines for facilities, personnel, and essential LTVEM services are established by experts at referral hospitals to comply with national and international standards.[218] Partnerships between epilepsy specialists at full-service epilepsy centers performing LTVEM and referring clinicians should exist to form care networks ensuring continued best practices and follow-up patient management.[16,219]

TABLE 5 Synthesis of high-level evidence for the utility of LTVEM

Intervention	Outcome	Highest level studies	Precision	Consistency	Directness	Plausible	Magnitude of effect	Dose response	Confidence in evidence	Strength of recommendation
LTVEM	Differentiating epileptic from nonepileptic	6 Category II	-	D	-	-	U	-	Moderate	Strong
LTVEM	Classifying epilepsy	1 Category II	-	-	-	-	-	-	Low	Weak
LTVEM	Quantifying numbers of seizures	Multiple Category III	-	D	-	-	-	-	Very low	None
LTVEM	Evaluation of presurgical temporal lobe epilepsy	3 Category I	-	-	-	-	U	-	High	Strong
LTVEM	Evaluation of presurgical extratemporal lobe epilepsy	Multiple Category IV	-	-	-	-	-	-	Very low	None
LTVEM with video	Diagnostic yield	4 Category II	-	-	-	-	-	-	Moderate	Strong
Nurse:patient ratio	Patient safety	1 Category II	-	-	-	-	U	-	Moderate	Strong
Standardized protocol	Evaluation of seizures	1 Category II	-	-	-	-	-	-	Low	Weak
LTVEM length	Type of seizures, localization of seizure onset	2 Category III	-	-	-	-	-	-	Low	Weak
Activation	Eliciting seizures	1 Category I	-	-	-	-	-	-	Moderate	Strong
Medication reduction	Eliciting seizures without status	1 Category I	-	-	-	-	-	-	Moderate	Strong
Automated detection	Spikes and seizures	2 Category III	-	-	-	-	-	-	Low	Weak

Abbreviations: -, no influence of bias; D, downgraded studies; LTVEM, long-term video-electroencephalographic monitoring; U, upgraded studies.

5.4.3 | LTVEM personnel

Patients undergoing LTVEM are subject to various personnel and staffing models.[117,219,220] Available standards applied to personnel and their role caring for a variety of complex patients during LTVEM are resource dependent, with significant variability throughout the world. We obtained consensus for some aspects of personnel working in LTVEM units (Table 3B). Staffing models for an LTVEM laboratory[22] and American standards for individual qualifications and responsibilities for personnel performing neurodiagnostic procedures have previously been outlined.[221] Monitoring personnel should be comprised of dedicated staff with expertise in performing LTVEM, with expertise in seizure management, rescue medication, and behavioral testing. One retrospective Category III study found implementing peri-ictal nursing intervention shortened the duration of postictal generalized EEG suppression,[222] but oxygen supplementation did not. Ictal SPECT requires multidisciplinary personnel to be successful. A survey study in the United States found 68.8% of participants provided continuous patient observation during LTVEM.[193] A European survey study reported 80% of participants provided continuous observation, with 10% only during daytime hours of operation and 10% performing observation intermittently in conjunction with automated seizure and spike detection algorithms.[145] Despite limited evidence, continuous EEG monitoring is recommended to be performed by appropriately trained, certified, and supervised neurodiagnostic technologists in the EMU and intensive care unit.[223]

5.4.4 | Duration of recording

Wide variability exists among epilepsy centers regarding the duration of LTVEM, which is dependent upon the reason for admission.[224,225] One Category III diagnostic LTVEM study of 226 patients found most patients undiagnosed following outpatient EEG were diagnosed in the first day.[204] Other prospective studies (Category III) required a second day of LTVEM,[205] and other Category IV studies were split between 1 and 2 days.[76] In contrast, a Category IV study of 439 LTVEM cases found 3 days was necessary to record at least one seizure in 90% of patients with epilepsy (2 days with PNEA).[123] By 5 days of LTVEM, a retrospective study (Category IV) reported a 98% recovery rate for the targeted clinical event.[76]

In patients diagnosed with PNEA, Category III and IV studies suggest LTVEM could be averted by diagnostic outpatient short-term VEM.[130,206–208] However, one single-center Category III study of 865 patients noted a higher readmission rate when short-duration VEM was initially performed.[226]

A minimum of 72 h of LTVEM is therefore necessary for patients with drug-resistant epilepsy, whereas those with PNEA are typically diagnosed in the first 1–2 days.[227] A longer duration of monitoring is required for epilepsy patients to ensure appropriate seizure recording, supported by a retrospective Category III review of 596 admissions.[225] Accurate identification of the seizure onset zone through iEEG LTVEM requires an extended period of time.[228] For surgery, at least three seizures are sought as representative in uncomplicated cases. In complicated cases with more than one seizure onset zone, the average duration to record the first electrographic seizure from a second focus can be more than 1 month (Category III).[229] In pediatric patients, a retrospective (Category III) LTVEM study of 1000 children (mean age = 7 years) usually monitored for 1.5 days investigators found longer sessions had higher rates of epilepsy using ILAE classification, and fewer inconclusive session in adolescents. This resulted in recommendations for LTVEM durations of more than 3 days when events were less than daily.[230] Because the duration of LTVEM depends on the indication and the seizure frequency, a standard duration is variable.

Recommendation: The duration of LTVEM will vary relative to the indication for performance and number of seizures and events captured (conditional recommendation).

5.4.5 | Activation

Activation protocols provide relative degrees of usefulness in patients with epilepsy.[231] Two prospective multicenter studies (Category II) support safety and efficacy of activation procedures.[232,233] General methods of activation including hyperventilation, photic stimulation, and sleep deprivation are recommended in guidelines to elicit abnormalities.[140,144,234] In addition, exercise, stress, and dietary influences may precipitate seizures in some patients with epilepsy.[235,236] A random sample of 1000 standard EEGs in the United Kingdom verified the additive effect of activation to routine EEG in 11% of cases.[237] In patients with epilepsy, standard EEG from Category II and III studies demonstrates sleep as a potent form of activation to trigger seizures and IEDs.[170,238] Sleep deprivation during LTVEM has previously demonstrated diagnostic value in activating IEDs[239,240] as an acceptable practice in the United States and Europe[140,241] to increase the yield.[242,243] In contrast, a Class III study of acute whole night sleep deprivation every day during LTVEM found no change in precipitating focal to bilateral tonic–clonic seizures.[244] Similarly, a recent systematic review found no effect from sleep deprivation, suggesting usage may be overrated during LTVEM.[245] The ACNS, ILAE, and National Institute for Health and Care

Excellence recommend that hyperventilation is performed as part of a standard EEG.[241,242] Hyperventilation with breath counting and intermittent photic stimulation are most useful in patients with GGE, to clarify specific epilepsy syndromes.[62] A prospective study (Category I) of 52 seizures recorded over 247 days of LTVEM demonstrated that the rate of activated seizures was nine times higher than the rate of control seizures and demonstrated the value of instituting repeated hyperventilation as an activation technique combined with ASM withdrawal.[246] One Category II study found hyperventilation useful in activating temporal lobe seizures in 25% of patients during LTVEM.[247] A Category III study in focal epilepsies found the rate of activated seizures was nine times higher with hyperventilation.[248] Unique methods of activation during LTVEM may provoke seizures in some patients with reflex epilepsies using individualized stimuli (e.g., reading, writing, eating, performing arithmetic, and somatosensory stimulation).[238,249]

In the diagnosis of PNEA, activation techniques had a marked methodological heterogeneity and low level of evidence in a systematic review including 11 prospective studies.[250] Standard EEG and short-term outpatient video-EEG studies[130,141,232,233] have performed activation to achieve a diagnosis of PNEA using techniques that are similar to those used during LTVEM, either alone[232,233] or in combination with photic stimulation,[130] to provide evidence of suggestibility.[251] Temple compression and tuning fork application were found in one retrospective (Category IV) study to be most effective.[252] However, controversy exists regarding ethical use.[39,253–255] Nonetheless, sensitivity ranges from 77% to 84%[256–259] and specificity approaches 100%[256] for diagnosis. In older comparative trials (Categories III and IV), using placebo (e.g., saline injection, application of color patches, alcohol patches, or tuning fork) elicited PNEA in most patients.[257] Atypical events or epileptic seizures occur in a minority of patients and result in an incorrect diagnosis.[256] Provocation without placebo such as combined hyperventilation and photic stimulation has demonstrated comparable sensitivity to placebo without the disadvantages of deception, given its routine use in standard EEG[253] demonstrating noninferiority.[255] Provocation methods potentially reduce costs by shortening the duration of LTVEM and expedite diagnosis for patients with infrequent events.[256]

There is moderate confidence in evidence that hyperventilation was successful in conjunction with ASM withdrawal as an activating procedure to provoke seizures in patients. Expert opinion-based recommendations suggest patient-specific provocation methods be performed in patients with reflex epilepsies.

Recommendation: Patients should undergo hyperventilation in conjunction with ASM withdrawal as an effective activating procedure (strong recommendation).

5.4.6 | Drug reduction

ASM is routinely reduced during LTVEM to increase the likelihood of event capture. A judicious speed of reduction should be balanced against ineffective or prolonged hospitalization.[123] Current practices of ASM reduction are highly variable, and studies provide a wide range of evidence across epilepsy centers performing LTVEM. Rapid withdrawal may potentially obscure localizing information at seizure onset in the EEG during LTVEM.[33,260] Introducing a scheduled taper of ASM according to a preprescribed protocol facilitates a standardized approach to safe seizure provocation.[184] However, no standardized protocols for reduction of ASM during LTVEM exist[261] and current practices are highly variable across centers.[186] Overly aggressive ASM taper may result in capturing nonhabitual seizure semiology, obscure localizing information on ictal EEG, or produce seizure clustering and status epilepticus. Formal protocols focused on ASM taper were shown to have fewer seizure clusters during LTVEM.[262] Various study methodologies and small sample sizes have limited reliable conclusions regarding the optimal rate of ASM taper during VEM.[263] In a comparative study (Level II), ictal EEG localization did not change during ASM withdrawal during reduction of lamotrigine and carbamazepine during LTVEM performed during presurgical evaluation.[264] Two prospective studies have provided high-level evidence for the withdrawal of ASM during LTVEM.[265,266] One randomized controlled (Category I) trial, using open-label treatment but blinded outcome, assessed ASM reduction in two arms of 70 patients each, comparing fast taper by 30%–50% (fast) and slow taper by 15%–30%, in patients without a prior history of status epilepticus or frequent daily seizures and concluded that fast taper of ASMs was safe and effective aside from an increase in 4-h seizure clusters.[265] A second prospective study of 158 patients with no control arm (Category II) found that rapid taper of ASM combined with sleep deprivation during LTVEM was safe and effective in adults relative to time of first seizure, resulting in reduced time spent in the EMU.[266] This compares favorably with other retrospective, single-center, observational studies.[267] In contrast, rapid ASM tapering within 1 day was associated with longer EMU admissions and greater seizure frequency during LTVEM.[123] Rapid ASM taper in a Category III study did not produce a significant adverse effect on electrocardiogram or heart rate variability.[268] Tapering carbamazepine was found to influence ictal semiology, intensifying seizure frequency and severity compared to valproate in a Category III study.[269] In Category IV studies involving barbiturates and benzodiazepines, taper triggered seizures in some people without epilepsy.[270] Patients completely discontinued from ASM appear more likely to experience focal to bilateral tonic–clonic seizures than those in whom ASM was partly discontinued.[271] Slowly tapering ASM at home prior to inpatient LTVEM

starting 1 week or more prior to admission has been reported to be safe in a retrospective observational cohort of 273 patients (Category III) without complications.[272]

In patients without a prior history of status epilepticus or frequent daily seizures, ASM taper by 30–50% (fast) and slow taper by 15%–30% were safe.

Recommendation: In patients without a history of status epilepticus or frequent daily seizures, a fast taper of 30%–50% daily should be considered (strong recommendation).

5.4.7 | Automated analyses

Automated analyses are used to identify IEDs and electrographic seizures in an attempt to condense large volumes of data requiring physician review for time-efficient interpretation.[273] Relying solely on automation alone is not recommended. Commercially available automated software is used to detect and validate epileptiform activity, and to classify and quantify EEG abnormalities.[274] Software systems available for seizure detection have been tested in a prospective multicenter study[275] and retrospectively.[275–277] Algorithms for automated seizure detection during scalp LTVEM have a greater sensitivity than IED detection. These may exceed 75.0% detection with low false-positive rates,[278] thus supplementing patient- and witness-identified seizures. In a study of 159 patients with TLE, 794 seizures were analyzed, with a sensitivity of 87.3% and .22 false detections per hour.[279] However, this has not been confirmed in extratemporal seizures or generalized seizures of a short duration. In a recent study, 14 seizure detection algorithms from 120 patients found performance of the system was comparable to three human experts, with a sensitivity of 78% and false-positive rate of one per day.[277] Most commercially available systems will only detect seizures when the ictal EEG has a duration of 12 s or longer. Employing computer-based automated analyses for seizure detection is estimated to save 1.3 hospital days per patient admission, based on the percentage of seizure detections captured solely by the computer.[280] Better algorithms with greater sensitivity and specificity and a lower number of false-positive detections are evolving.

Recommendation: Automated algorithms for spike and seizure detection may provide complementary aid to expert assessment (weak recommendation).

5.4.8 | Rescue medication

Fortunately, seizure emergencies rarely occur during LTVEM,[281] and consequences are reduced when slow reduction of ASM is combined with a benzodiazepine rescue protocol.[16,282] In children and adults, Class I evidence included in an evidence-based guideline demonstrates both IV lorazepam and IV diazepam as efficacious initial therapy in convulsive status epilepticus, although ASM usage and new routes of administration have proven efficacy.[283,284] A retrospective LTVEM study (Category III) reported different seizure durations guided the use of rescue medication for patients with focal and generalized seizures.[285] No universal approach or standardized protocol exists for use of rescue medications.[286] The National Association of Epilepsy Centers recommends standing orders for both IV and non-IV emergency ASM to be used for seizures lasting more than 5 min.[287]

5.5 | Reporting

The LTVEM report has traditionally been a qualitative description of waveform interpretation using a free text format.[288,289] LTVEM interpretative reports, like standard EEG, are becoming increasingly automated.[290] Providing graphic display of EEG samples[28] enhances reproducibility of interictal and ictal EEG portions of the LTVEM report to facilitate patient management and clinical research.[288] Updated terminology[59,175] and newer classification systems[104] provide a current framework for the report. Despite established American guidelines[289] and European consensus,[290] significant variation in LTVEM reporting exists. Moderate interobserver variability plagues EEG interpretation, which may be in part due to inconsistencies and lack of standardization for reporting style and terminology utilized.[288–291] In 2017, the second international version of SCORE (Standardized Computer-Based Organized Reporting of EEG), initially published as a European consensus, established a template for automated LTVEM reporting.[290] It was endorsed as a guideline by the IFCN in a subsequent version adapting IFCN, ILAE, and ACNS classification systems and glossary of terms to enhance the initial European version.[290] Instituting electronic databases with a list of pre-established terms may result in higher interrater agreement of EEG features.[290,292,293] Both semiology and ictal EEG reporting should follow a chronological order using standardized terminology (IFCN glossary for EEG; ILAE glossary for semiology).

6 | CONCLUSIONS

This CPG provides a comprehensive synthesis of the currently available evidence for performing inpatient LTVEM. In addition to the level of evidence, practical implementation of LTVEM recommendations such as the wise use of resources, preferences of the patients/health care personnel, and potential outcome benefit for patients will modify practical usage. There is strong evidence that LTVEM should be used to differentiate between epileptic and nonepileptic

events in adults and children when seizures remain uncontrolled despite appropriate treatment. LTVEM is a standard to help classify patients with epilepsy. The ability to quantify seizures in patients with epilepsy is possible for patients with sufficient seizure frequency to be captured during monitoring (1–2 weeks). There is strong evidence that LTVEM should be used as part of the presurgical evaluation for TLE patients, although for extratemporal epilepsies, low confidence in evidence exists to support LTVEM in the presurgical evaluation, but this does not obviate the current standards of practice. Video should be combined with EEG during LTVEM for greater yield. Activating procedures should be used in conjunction with ASM withdrawal in concert with local practice dictating adaptive testing paradigms during LTVEM. In patients without a history of status epilepticus or frequent daily seizures, tapering ASM by 30%–50% daily should be considered. As a new era in EEG monitoring unfolds, home video recordings and subscalp devices for ultra-long-term recording could be an alternative for patients less amenable to LTVEM, but their efficacy still needs to be determined.[294]

We found limited high-level evidence exists across published international studies, although this does not preclude the numerous reports, national and international guidelines, and position statements from providing guidance to perform inpatient LTVEM. Significant gaps in knowledge exist due to substantial study heterogeneity and narrow spectrum conclusions involving selected features of LTVEM, and therefore further research is needed. Formal CPG (strong and weak) recommendations are not intended to replace sound clinical judgment, and must be adapted for use in limited resource settings. It remains to be proven whether the standards of performance have a direct relationship to meaningful use and outcome. This CPG will require revision as technology, science, and evidence evolve. Nevertheless, experience gained from selective aspects of LTVEM provides insight into current uses and emphasizes the need for conducting comprehensive high-level studies in areas with limited information to further clinical and research development. A table summarising the recommendations is available online, in the Supporting Information section.

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CONFLICT OF INTEREST

S.B. has been an invited lecturer for Natus Medical Incorporated. D.G. is an evidence-based medicine consultant. J.J.H. serves as a consultant for Takeda Pharmaceuticals and SK Life Sciences. W.O.T. has received personal compensation as a stipend from Elsevier as Editor-in-Chief of *Epilepsy Behavior Reports*. He serves as a consultant for BioSerenity and Medtronics, and holds patents/patents pending for intraoperative monitoring sensor devices (#62527896; #62770362). Royalties from publications include Demos Publishers and Springer Publishing. Honoraria for speaking engagements include American Academy of Neurology, American Epilepsy Society, and American Clinical Neurophysiology Society. He has received research support from Mayo Clinic, the Martin Family Foundation, the McKelvey Foundation, and the Epilepsy Foundation for data collected during intracranial monitoring, and Xenon, Esai, Engage, Cerevel, and LivaNova. None of the other authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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