Original article

Epileptic Disord 2019; 21 (4): 337-46

Comparison of clinical and electrophysiological characteristics between ictal and cardiac asystole encountered during video-EEG monitoring

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Received February 28, 2019; Accepted July 01, 2019

ABSTRACT – *Aims*. Differentiation between syncope secondary to epileptic seizures and cardiac disease in patients displaying transient loss of consciousness associated with convulsive movements is a diagnostic challenge both for neurologists and cardiologists. In such patients, prolonged video-EEG monitoring not only helps in identifying asystole as the cause of syncope, but also in categorizing asystole as primarily cardiac in origin (cardiac asystole) and secondary to epileptic seizures (ictal asystole). We carried out this study to ascertain the prevalence of asystole in an epilepsy monitoring unit, and to contrast the clinical and electrophysiological characteristics between ictal asystole and cardiac asystole.

Methods. Through a retrospective search, we identified patients who were shown to have had asystole using a database of patients who underwent prolonged video-EEG monitoring during a 68-month period. We compared the data of 18 consecutive patients; five with ictal asystole and 13 with cardiac asystole, with 121 and 64 events recorded from them, respectively.

Results. Of the 10,096 patients who underwent prolonged video-EEG monitoring during the study period, we identified 18 (0.17%) patients with asystole. Cardiac asystole was 2.6 times more frequent than ictal asystole. Older age at onset, heralding symptoms of presyncope, occurrence during wakefulness, and brief duration of the events supported the diagnosis of

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doi:10.1684/epd.2019.1085

cardiac asystole. Ictal asystole events were more protracted, and prolonged asystole more frequently occurred in patients with extratemporal seizures compared to temporal lobe seizures. Asystole occurred in only half of the recorded seizures.
Conclusions. The accurate categorization of asystole as seizure-related or heart disease-related has huge implications for management strategy and outcome. The necessity of permanent pacemaker implantation is more frequent and urgent in patients with cardiac asystole because of the greater risk of sudden death. Hence, in patients with an ominous diagnosis of cardiac asystole, a thorough cardiac evaluation should surpass neurological evaluation.

Key words: cardiac syncope, epilepsy, ictal syncope, syncope, transient loss of consciousness, SUDEP

Epileptic seizures are frequently associated with changes in heart rate, but clinically significant arrhythmias are rare, and are often spotted as an incidental finding during prolonged video-EEG monitoring (VEM) (van der Lende *et al.,* 2016; Shmuely *et al.,* 2017). In addition, arrhythmias observed during VEM may point to a diagnosis of primary cardiac disease in patients who are otherwise assumed to have epilepsy. Among the clinically significant arrhythmias noticed during VEM, the best characterized is asystole secondary to epileptic seizure (ictal asystole [IA]) (Rocamora *et al.,* 2003; Tényi *et al.,* 2017). In epilepsy monitoring units (EMU), IA is encountered infrequently, in less than 0.5% of patients (Rocamora *et al.,* 2003; van der Lende *et al.,* 2016). In contrast, studies undertaken with long-term electrocardiographic (ECG) implantable loop recorders (ILR) in people with drug-resistant epilepsy (DRE), have reported a much greater prevalence of IA (Rugg-Gunn *et al.,* 2004; Nei *et al.,* 2012). Although IA was assumed to typically occur in the context of drug-resistant left temporal lobe epilepsy (van der Lende *et al.,* 2016; Tényi *et al.,* 2017), the lateralizing and localizing value of IA and its association with duration of epilepsy and drug resistance have recently been doubted (Britton *et al.,* 2006; Schuele *et al.,* 2007; Nguyen-Michel *et al.,* 2014; Bestawros *et al.,* 2015; Tényi *et al.,* 2017).

Transient loss of consciousness (TLOC) is a common clinical scenario in which the neurologist may come across in a patient with asystole. While TLOC in the setting of primary cardiac asystole (CA) may be associated with convulsive movements (Zaidi *et al.,* 2000; Petkar *et al.,* 2012), IA may display atonic falls (Ghearing *et al.,* 2007; Schuele *et al.,* 2007; Nguyen-Michel *et al.,* 2014), directing to an erroneous diagnosis in either situation. Epidemiological studies have shown that people with epilepsy have a higher prevalence of structural cardiac disease than those without epilepsy (Shmuely *et al.,* 2017). The neurologist's opinion is sought to rule out epilepsy even in those with a background history of cardiac disease, as the initial cardiac evaluation may be negative for arrhythmias. VEM offers a distinctive advantage in such clinical situations as both ECG and EEG are simultaneously monitored.

While the available studies deliberate on IA, often taking CA as an exclusion criterion (Rocamora *et al.,* 2003; Britton *et al.,* 2006; Schuele *et al.,* 2007; Nguyen-Michel *et al.,* 2014; Bestawros *et al.,* 2015; van der Lende *et al.,* 2016; Tényi *et al.,* 2017), comparative studies between IA and CA are scant. With this background, we undertook the present study to establish the clinical and electrophysiological profiles of patients with asystole encountered during prolonged VEM, and to contrast between IA and CA patients.

Patients and methods

Study setting

This study was conducted at the EMU of Amrita Institute of Medical Sciences, Kochi, Kerala, India. Patients are referred to the EMU either for diagnostic purposes (to distinguish between epileptic and non-epileptic paroxysmal events or for categorization of the seizure types and epilepsy syndromes), or for presurgical evaluation. This retrospective study was approved by the Institutional Review Board with a waiver of consent.

Study definitions

We defined *prolonged VEM* as continuous VEM for eight hours or more. We defined *asystole* as R-R interval in the ECG of more than three seconds (van der Lende *et al.,* 2016; Tényi *et al.,* 2017). The *duration of asystole* was calculated from the beginning of asystole until the resumption of sinus beat. We defined *prolonged asystole* as asystole lasting for more than six seconds (Bestawros *et al.,* 2015), and *very prolonged asystole* as asystole lasting for more than 30 seconds (Tényi *et al.,* 2017). For the study purpose, we grouped the patients into *cardiac asystole (CA)*

(those with asystole secondary to cardiac disease) and *ictal asystole (IA) (those with asystole secondary to epileptic seizure)*. The EEG of IA patients was analysed in three phases: pre-ictal, ictal and post-ictal. We defined the pre- and post-ictal periods as 10 epochs preceding and 10 epochs after the termination of the ictal EEG activity, respectively. The epochs, where the R-R interval could not be defined because of artefacts, were excluded from analysis. For CA patients, the *onset of asystole* was taken as first detected change in baseline ECG rhythm in relation to cardiac asystole, and for IA patients this was the first perceived EEG change from the baseline in relation to clinical seizure. *Latency of IA* was computed as time lapse between EEG ictal onset and ECG asystole onset (*figure 1*). Duration *of the seizure* was considered as time duration between ictal EEG onset and offset. We defined *atonia* as loss of muscle tone leading onto head drop or collapse shortly following the asystole. *Drug resistant epilepsy (DRE)* was defined according to recent ILAE definition (Kwan *et al.,* 2010).

Technical considerations

VEM was performed by using 32- or 40-channel digital video-EEG systems (Nicvue Version 2.9.1, VIASYS Healthcare and Natus Database Xltek Version 7.1.0) with scalp disc electrodes placed according to the International 10/20 system. Additional anterior temporal and sub-temporal electrodes were used regularly. At least 18 channels of EEG and one channel of ECG were concurrently displayed. Patients who were on AEDs had their drugs decreased. The monitoring was continued non-stop until a sufficient number of events was recorded.

Study subjects and data collection

We retrospectively identified patients who were reported to have had asystole from the database of patients who underwent prolonged VEM during January, 2013 through August, 2018 (68 months). Utilizing a structured proforma, we collected the demographic and clinical characteristics of these patients. Their interictal EEG, event semiology, and ictal EEG were reviewed by one of the epilepsy fellows (PM or MS) under the supervision of one of the consultant epileptologists (SG or KR) involved in the study. Patients identified as having CA were comprehensively evaluated by the consultant cardiologist (NM), who also reviewed their continuous ECG recordings obtained during the VEM. We further categorized IA patients into temporal and extra-temporal seizure onset subgroups based on a consensus established following a thorough discussion of their history as well as VEM and neuroimaging findings at the multidisciplinary patient management conference.

Statistical analysis

We expressed the data dispersion as means, medians, standard deviations, and percentages. To assess the statistical significance of the difference between the IA and CA groups of patients, we carried out univariate analysis using the Pearson Chi-Square Test, Fisher's Exact Test, and Mann-Whitney U Test, as appropriate. We considered a p value of ≤ 0.05 as significant.

Results

Characteristics of the whole cohort

Of the 10,096 patients who underwent prolonged VEM during the study period, we identified 18 (0.17%) patients with asystole (10 males and eight females); age ranged from 16 to 86 years (median: 44.5 years). Five patients (27.8%) had IA and the remaining 13 (72.2%) had CA.

Characteristics of patients with ictal asystole

The median age of five patients (two males and three females) with IA was 36 years, and the median age at onset of their epilepsy was 18 years. All of them had DRE and underwent VEM as a part of presurgical evaluation and were on multiple AEDs. Except one, all of them were right-handed. During VEM, one patient had secondary generalized seizures; the rest only had focal seizures. Three out of five patients (60%) with IA had seizure onset from the left hemisphere. An MRI-identified epileptogenic lesion was detected in three IA patients (focal gliosis in the left parietal lobe, bilateral parieto-occipital gliosis, and focal cortical dysplasia in the left postcentral gyrus, in each patient, respectively). Two patients had mesial temporal lobe onset of seizures, while three patients had extra-temporal onset of their seizures (two parietal and one occipital). None of the patients with IA had a pre-existing cardiac disease. The characteristics of individual IA patients are detailed in *supplementary table 1*.

Characteristics of patients with cardiac asystole

Out of the 13 patients with CA (eight males and five females; median age: 49 years), only four (30.8%) had a history of pre-existing heart disease. Eight (61.5%) CA patients were receiving AEDs at the time of VEM. The most common AED in use was levetiracetam, followed by valproate and oxcarbazepine. Two patients received phenytoin and one lacosamide. The detailed

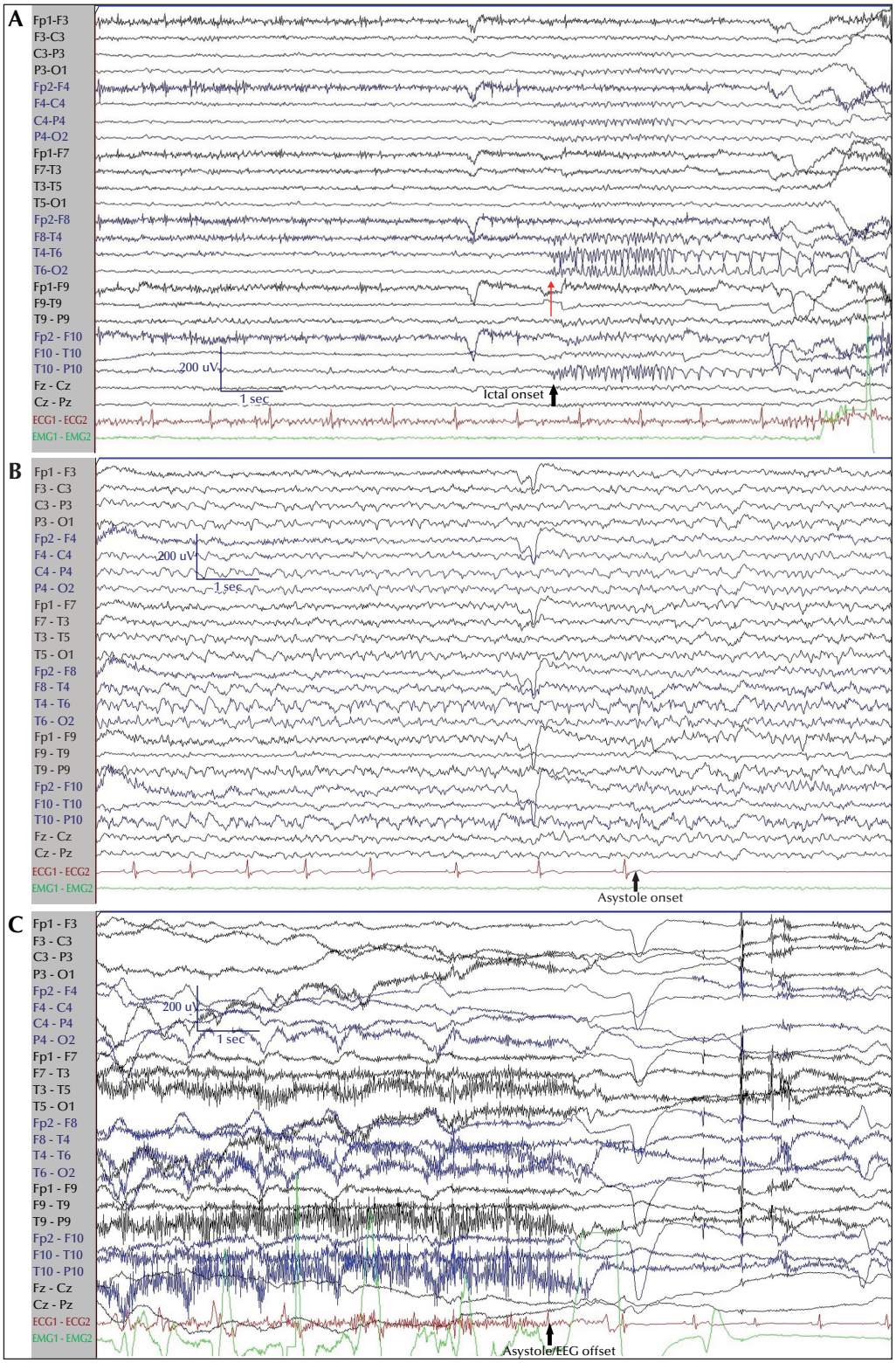

Figure 1. VEM findings of Patient 3 (*see supplementary table 1*) (24-channel EEG with one channel of simultaneous ECG recorded with high frequency filter = 70 Hz, low frequency filter = 0.5 Hz, sensitivity = 10 μV/mm, and display speed = 30 mm/sec): (A) ictal onset characterized by a burst of multiple spikes followed by rhythmic spikes over the right posterior temporal region with phase reversal at T6, as illustrated by the red arrow; (B) onset of asystole after a latency of 24.1 seconds following the ictal EEG onset; and (C) diffuse slowing with attenuation of activity and asystole offset.

individual characteristics of CA patients are provided in *supplementary table 2*.

Comparison of the clinical characteristics of IA and CA patients

We have compared the clinical features of IA and CA groups of patients in *table 1*. The mean age at onset of events was significantly lower for IA patients in contrast to CA patients (group mean ± standard deviation [SD]: 18.00 ± 16.09 *vs*. 41.67 ± 24.10 years, $p = 0.03$). A significantly greater number of CA events occurred during wakefulness when compared to IA events (83% *vs*. 57%, $p = 0.0004$). The mean duration of VEM was significantly briefer in the CA group when compared to the IA group (1.83 ± 2.97 *vs*. 3.20 ± 0.84 days, $p = 0.01$). While 10 patients (77%) with CA complained of symptoms of pre-syncope such as light headedness, dizziness, and blurring of vision, none with IA had such a sequence of symptoms. There was no significant difference in gender distribution, mean duration of illness, presence of aura, atonic falls or limb jerking during atonic falls between the IA and CA groups of patients.

Comparison of the electrophysiological characteristics of IA and CA patients

A comparison of the EEG and ECG findings between IA and CA groups of patients is presented in *table 1*. A total of 207 epileptic seizures were recorded during the monitoring period from IA patients; among them, 86 seizures were excluded due to either absence of asystole during the seizures or inability to interpret them due to artefacts. Finally, 121 events were analysed for the clinical and electrophysiological features of IA. The number of recorded seizures from IA patients was inflated due to one patient, who had postoperative focal status epilepticus. Out of 121, 108 seizures were from this patient (outlier). Overall, the median number of seizures recorded in the IA group of patients was six and median number of asystole was four. After excluding the outlier, the median number of seizures was five and median number of asystole was three. Out of the 207 seizures recorded from our IA patients, only 121 (58.5%) were associated with asystole. Thirteen patients with CA had a total of 64 episodes of asystole and all of them could be included in the final analysis. While 96 out of 121 (79.3%) IA events were prolonged, 26 out of 64 (40.6%) CA events were prolonged ($p = <0.0001$). While 12 out of 121 IA events (9.9%) were very prolonged, three out of 64 (3.1%) CA events were very prolonged ($p = 0.09$) (*table 1*). Eleven out of 12 prolonged ictal asystole events (92%) occurred among the subgroup of patients with extratemporal seizure onset. None of the prolonged IA and CA events progressed to a generalized tonic-clonic seizure. The latency of ictal asystole (36.52 ± 11.3 *vs*. 22.28 ± 9.09 seconds, $p = <0.0001$) and duration of epileptic seizures (75.62 ± 29.74 *vs*. 58.14 ± 18.13 seconds, $p = 0.02$) were more prolonged in the temporal lobe seizure onset sub-group when compared to the extratemporal seizure onset sub-group of patients (*table 2*). There was no significant difference in the mean duration of asystole, pre-asystole bradycardia, or diffuse delta slowing in the EEG during asystole between the IA and CA groups of patients (*table 1*).

Follow-up data

Three IA patients underwent resective epilepsy surgery; only one of them has remained completely seizure-free during a follow-up period of seven months. One IA patient with a left parietal lobe focal cortical dysplasia (Patient 5) (*supplementary table 1*) developed focal status epilepticus immediately following resective surgery with frequent and prolonged asystoles that necessitated emergency permanent cardiac pacemaker implantation. This patient during the subsequent 30 months of follow-up continued to have frequent seizures, but none of them resulted in asystole. All the 13 patients with CA underwent detailed cardiac electrophysiological studies. One of them was diagnosed with cough syncope and was managed conservatively with antitussive and bronchodilator medications. Another patient with CA, with an inducible polymorphic ventricular tachycardia after provocation with flecainide, was suspected to have Brugada syndrome that necessitated an implantable cardioverter-defibrillator. Five CA were diagnosed with sick sinus syndrome and six with AV block. Seven out of 13 (54%) CA patients had already undergone permanent cardiac pacemaker implantation, while four of them were waiting for this procedure. For further information on the management and outcome of individual CA patients, refer to *supplementary table 2*.

Discussion

Several studies containing a small number of patients and reviews have provided, in recent years, a wealth of information with respect to the electroclinical characteristics (Schuele *et al.*, 2007; Nguyen-Michel *et al.*, 2014; van der Lende *et al.*, 2016; Tényi *et al.*, 2017), clinical implications (Britton and Benarroch, 2006; Ghearing *et al.*, 2007), and management of IA (Schuele *et al.*, 2008; Moseley *et al.*, 2011; Strzelczyk *et al.*, 2011; Bartlam and Mohanraj, 2016; Morita and Cendes, 2017). First, IA is a rare incident in patients undergoing prolonged VEM (Rocamora *et al.*, 2003; van

Table 1. Comparison of the characteristics of ictal asystole and cardiac asystole patients by univariate analysis.

Characteristic	Ictal asystole (*n*=5)	Cardiac asystole (*n*=13)	Statistical analysis (*p* value)
Gender, male, *n* (%)	2 (40)	8 (61.5)	0.62
Age at presentation, years (mean ± SD)	33.4 (10.9)	51.83 (21.7)	0.09
Age at onset of symptoms, years (mean ± SD)	18.0 (16.1)	41.67 (24.1)	0.03
Duration of VEM, days (mean ± SD)	3.20 ± 0.8	1.83 ± 3.0	0.01
Number of asystole events during VEM	121	64	NA
Duration of asystole, seconds (mean ± SD)	15.49 (9.2)	10.61 (7.0)	0.29
Asystole events during wakefulness, n (%)	69 (57)	53 (83)	0.0004
Aura, n (%)	73 (60)	49 (77)	0.48
Atonia during asystole, *n* (%)	48 (40)	21 (33)	1.0
Limb jerking during asystole, *n* (%)	73 (60)	32 (50)	1.0
Pre-asystole bradycardia, *n* (%)	97 (80)	43 (66.7)	1.0
Diffuse delta activity in EEG during asystole, *n* (%)	97 (80)	53 (83.3)	1.0
Prolonged asystole (>6 sec), *n* (%)	96 (79)	26 (41)	<0.0001
Very prolonged asystole (>30 sec), *n* (%)	12/121 (9.9)	3/64 (3.1)	0.09

NA: not applicable; SD: standard deviation; VEM: video-EEG monitoring

Table 2. Comparison of the characteristics of asystole during seizures of temporal lobe and extratemporal lobe origin by univariate analysis.

Characteristic	Temporal lobe seizures (*n*=8)	Extratemporal lobe seizures (*n*=113)	Significance (*p* value)
Duration of ictal EEG, seconds (mean ± SD)	75.6 ± 29.7	58.1 ± 18.1	0.02
Latency of asystole*, sec (mean ± SD)	36.5 ± 11.3	22.3 ± 9.1	<0.0001
Duration of asystole*, sec (mean ± SD)	17.2 ± 11.1	14.8 ± 9.8	0.52
Prolonged asystole (>6 sec), *n* (%)	6/96 (6.3%)	90/96 (93.7%)	<0.0001
Very prolonged asystole (>30 sec), *n* (%)	1/12 (7%)	11/12 (93%)	<0.0001

SD: standard deviation. *See text for definitions

der Lende *et al.*, 2016). Second, although IA is more often associated with chronic DRE, it may occur in the setting of drug-responsive new-onset epilepsy (Tényi *et al.*, 2017). Third, in patients with IA, the seizure onset zone is more often lateralized to the left and localized to the temporal lobe (van der Lende *et al.*, 2016; Tényi *et al.*, 2017). However, prolonged IA is more often encountered with secondary generalized and extratemporal-onset seizures (Britton *et al.*, 2006; Nguyen-Michel *et al.*, 2014; Tényi *et al.*, 2017). Fourth, although brain regions such as the insula, anterior cingulate cortex, amygdala, and orbitofrontal cortex are implicated in the pathogenesis of IA, intracranial EEG recordings have shown that IA often appeared when the ictal activity has become bilateral (Rugg-Gunn *et al.*, 2004; Britton and Benarroch, 2006; Catenoix *et al.*, 2013). Last, compared to postictal asystole, IA is often a self-limiting condition (Schuele *et al.*, 2008; van der Lende

et al., 2016). Although it can result in syncope-related falls and injuries (Moseley *et al.,* 2011; Bartlam and Mohanraj, 2016), control of seizures by AEDs or surgery prevents these morbidities in the majority; only in a minority of patients does cardiac pacemaker implantation become necessary (Schuele *et al.,* 2008; Bartlam and Mohanraj, 2016).

In this study, based on a large number of patients who underwent prolonged VEM in an EMU, we ascertained five patients with IA and 13 patients with CA, with 121 IA events and 64 CA events recorded from the patients, respectively, and compared and contrasted their electro-clinical characteristics. We wish to elaborate on the clinical relevance of our results.

Prevalence of asystole

We came across asystole in only 0.17% of over 10,000 patients who underwent prolonged VEM during a period of five and a half years. In our EMU set-up, the prevalence of CA was two and a half times that of IA (0.13% *vs.* 0.05%). Others have endorsed the very rare occurrence of IA in the EMU (Rocamora *et al.,* 2003; Schuele *et al.,* 2007; Nguyen-Michel *et al.,* 2014; Bestawros *et al.,* 2015). van der Lende *et al.* (2016) undertook a systematic review of 65 articles published up to July 2013 that reported cardiac arrhythmias during VEM and computed a mean prevalence of IA of 0.18%. The prevalence of CA and IA would be influenced by the referral patterns of patients undergoing prolonged VEM (whether for event characterization or for presurgical evaluation), which differs between EMUs.

Since IA does not recur with every seizure in an individual patient, the prevalence would be influenced by the number of seizures recorded per patient during VEM. One of our patients graphically exemplifies this point. In this patient with MRI-negative right posterior cortex epilepsy, while all the four scalp-recorded seizures were associated with IA, IA did not occur in any of the 11 seizures recorded by stereo-EEG (*see supplementary material*). Based on a systematic review of 80 published patients with 182 IA in 537 seizures, Hampel *et al.* (2017) estimated an IA recurrence risk of 40%. Among our patients, IA occurred in 58% of the recorded seizures. Therefore, recording one or two seizures during VEM in patients with suspected IA may be inadequate to rule it out. Furthermore, in patients with higher risk of IA, physicians would be less inclined to record more seizures, instead would prefer to refer them for cardiac evaluation. Based on long-term ILR undertaken in highly selected patients with drug-resistant epilepsy, a much higher prevalence of IA has been reported, varying from 5% to 21% (Rugg-Gunn *et al.,* 2004; Nei *et al.,* 2012).

Differentiation between IA and CA

In our study, the mean age at onset of events was significantly lower for IA patients (18 years) in comparison to CA patients (42 years). When compared to the mean age at onset of 41 years based on a systematic analysis of 157 IA patients (Tényi *et al.,* 2017), our patients were younger. A significantly greater number of CA events occurred during wakefulness and within a shorter monitoring period. Two thirds of our patients with CA were receiving one or more AEDs for several years before VEM because of the mistaken diagnosis of epilepsy. Only one third of them had a prior diagnosis of cardiac disease. All of our patients with IA had DRE. In our small number of IA patients, the presumed or proven ictal onset zone was evenly lateralized between the right and left hemispheres and localized between temporal lobe and extratemporal regions. Among our patients, while three quarters of CA patients complained about symptoms such as light headedness, dizziness, and blurring of vision prior to TOLC, none of the IA patients had these pre-syncope symptoms. We did not find any significant difference in gender distribution, mean duration of illness, presence of aura, atonic falls, or limb jerking during atonic falls between the IA and CA groups of patients.

Clinical implications

It is estimated that nearly a third of patients on long-term follow-up in tertiary referral centre-based epilepsy clinics do not have epilepsy and are being treated unnecessarily with AEDs (Benbadis *et al.,* 2004; Xu *et al.,* 2016). In these patients, cardiovascular syncope is the most commonly misdiagnosed condition (Chowdhury *et al.,* 2008; Xu *et al.,* 2016). In a study that reported 74 patients who were diagnosed with epilepsy, but required elaborate neurological and cardiac evaluations because of the lack of response to AEDs or uncertainty about the diagnosis of epilepsy, an alternate diagnosis was derived in 31 (42%) patients (Zaidi *et al.,* 2000). While the head-up tilt test confirmed the diagnosis of vasovagal syncope in 19 (25.7%) patients, carotid sinus massage precipitated CA lasting for more than three seconds in seven (9.5%) patients (Zaidi *et al.,* 2000). Long-term unnecessary treatment with AEDs (especially with sodium channel blockers such as phenytoin, carbamazepine and lacosamide) in patients with cardiovascular syncope, in addition to drug side effects and the psycho-social implications, may have a potentially adverse influence on the cardiac conduction system.

Differentiation between ictal syncope and cardiac syncope in patients presenting with TLOC associated with convulsive movements is a diagnostic challenge both

for neurologists and cardiologists. The routine neurological and cardiac evaluations including EEG, ECG, and echocardiography often fail to provide any useful information. A head-up tilt test is positive in only a third of patients with unexplained syncope, and is nonspecific because susceptibility to orthostatic stress occurs in a variety of conditions (Flevari *et al.,* 2009). The most sensitive and specific test for the diagnosis of ictal syncope is prolonged VEM (Schuele *et al.,* 2007; Nguyen-Michel *et al.,* 2014; Bestawros *et al.,* 2015; Tényi *et al.,* 2017) and for cardiac syncope is ILR (Solbiati *et al.,* 2016; Padmanabhan *et al.,* 2019). The recent European Society of Cardiology guidelines for evaluation and management of syncope recommends ILR in the early phase of evaluation of people with unexplained recurrent syncope (Brignole *et al.,* 2018) However, VEM and ILR may not be widely available, especially in developing countries, and many patients may not be able to afford the cost. In patients with rare events, in spite of recording for several days, VEM and ILR may fail to capture the habitual events. As ILR is only a continuous ECG recording devise, in the absence of simultaneous EEG recording, it may not be possible to establish whether a documented asystole is due to IA or CA using ILR. Hence, VEM is strongly recommended in a patient diagnosed with CA based on ILR, when there is recurrence of TLOC despite insertion of a cardiac pacemaker, to make sure that IA has not been overlooked.

Are there any clinical clues that can guide the physician to optimally utilize the above investigations? Among our patients, symptoms of presyncope prior to TLOC occurred exclusively in CA patients. Although we did not find any significant difference in the phenomenology of convulsive limb movements after a fall between the IA and CA groups of patients, others who have methodically characterized them have uncovered clinically useful information. Shmuely *et al.* (2018) compared video-EEG-recorded motor phenomena of 65 tilt-induced syncope episodes with those of 50 convulsive seizures. Although postures occurred in two thirds and jerks occurred in half of the syncopal episodes, fewer than 10 jerks occurred in syncope, while the jerks were rhythmic and more than 20 occurred in epileptic seizures. The authors even suggested a "10/20 rule" to distinguish between syncope and seizures. Atonia occurred exclusively in syncope (Shmuely *et al.,* 2018). Although history obtained from an eye witness of the event is less likely to reliably reveal these distinguishing characteristics, review of events captured by home or mobile phone video will enhance the yield.

Based on our results and literature review, we wish to advocate the following cost-effective dichotomized diagnostic approach for patients presenting with TLOC with or without convulsive movements. Prodromal symptoms such as light headedness, dizziness and blurring of vision, atonic falls, and few, irregular jerks after the fall would strongly favour a cardiovascular syncope. Patients with these characteristics should initially be evaluated by a cardiologist to ascertain the cause of syncope. Very few of them might require ILR to settle the diagnosis of potentially life-threatening cardiac arrhythmias. Slow evolution of the symptoms with behavioural arrest and automatisms progressing on to fall and convulsive jerks lasting for several seconds or few minutes denote an epileptic seizure-related TLOC. Patients with these characteristics should be evaluated by a neurologist. Few of them may require prolonged VEM (along with simultaneous ECG) to settle the very rare diagnosis of seizure-induced asystole as the cause of TLOC.

Study limitations

We acknowledge the following limitations of our retrospective study. Although we included all patients in whom asystole was reported, we could have missed patients in whom asystole was present but was not identified. However, in view of the systematic way in which VEM data is read and reported in our EMU, we believe that the number of missed cases is unlikely to be significant. Because of the small sample size, and sampling and referral biases inherent to retrospective studies, generalizability of our findings is limited. The video data of many patients were either pruned or were deleted for want of storage space. Hence, we could not reliably ascertain and analyse the differential phenomenological features of seizures with and without asystole. The number of seizures with IA is probably under-reported in our study as we could not analyse the ictal EEG of some of the events because of artefacts. We also could not reliably assess the influence of postures such as standing/sitting *versus* supine on the occurrence of TLOC. Because of the retrospective design, the dependability of our recommendations on the best management options is limited and needs verification through prospective studies.

Conclusions

The accurate categorization of asystole as seizure-related (IA) or heart disease-related (CA) has huge implications on the management strategy and outcome. The necessity of permanent pacemaker implantation is more often and urgently required in patients with CA than IA, because of greater risk of sudden cardiac death in this subset of patients. As clinical characteristics, such as relatively older age at onset, heralding symptoms of presyncope, occurrence during wakefulness, and brief duration of the events,

favour the ominous diagnosis of CA, in patients with these attributes a thorough cardiac evaluation should surpass neurological evaluation. □

Supplementary data.
Summary didactic slides and supplementary materials are available on the www.epilepticdisorders.com website.

Disclosures.
None of the authors have any conflict of interest to declare.

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TEST YOURSELF

(1) In patients presenting with recurrent transient loss of consciousness, what clinical cues aid in distinguishing between cardiovascular syncope and ictal syncope?

(2) Is there an indisputable and consistent association between ictal asystole and chronic drug-resistant left temporal lobe epilepsy?

(3) Does detection of ictal asystole warrant urgent cardiac pacemaker implantation?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".