Article published online: 2023-06-01

https://doi.org/10.1590/0004-282X20200105

ARTICLE

Simultaneous electrocardiogram during routine electroencephalogram: arrhythmia rates through the eyes of the cardiologist

Eletrocardiograma simultâneo durante eletroencefalograma de rotina: taxas de arritmia pelos olhos do cardiologista

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ABSTRACT

Background: The importance of simultaneous 2-lead electrocardiogram (ECG) recording during routine electroencephalogram (EEG) has been reported several times on clinical grounds. **Objective:** To investigate arrhythmia rates detected by simultaneous 2-lead ECG in our patient sample undergoing routine EEG. Remarkably, we sought to assess the possible expansion of results with a more experienced interpretation of simultaneous ECG. **Methods:** Simultaneous 2-lead ECG recordings during routine EEG, performed between January and March, 2016, have been retrospectively analyzed by a cardiology specialist. In addition, EEG reports were screened with the keywords 'arrhythmia, tachycardia, bradycardia, atrial fibrillation, extrasystole' to evaluate the neurologist interpretation. **Results:** Overall, 478 routine EEG recordings were scanned. The mean age of the patients was 42.8±19.8 (16–95), with a sex ratio of 264/214 (F/M). In 80 (17%) patients, findings compatible with arrhythmia were identified on simultaneous ECG after a cardiologist's evaluation. The detected arrhythmia subtypes were: ventricular extrasystole (n=27; 5.6%), supraventricular extrasystole (n=23; 4.8%), tachycardia (n=9; 1.8%), prolonged QRS duration (n=7; 8.7%), atrial fibrillation (n=6; 1.2%), and block (n=6; 1.2%). On the other hand, keywords related to arrhythmia were present in 45 (9.4%) of EEG reports. The reported statements were tachycardia (3.3%), arrhythmia (2.5%), bradycardia (2.1%), and extrasystole (1.5%). **Conclusions:** A considerably high rate of arrhythmia cases was determined on simultaneous ECG during routine EEG after being interpreted by a cardiologist. However, the screening results of EEG reports revealed relatively low arrhythmia rates. These results suggest that the detection rates of ECG abnormalities during routine EEG may be potentially improved.

Keywords: Electroencephalography'; Electrocardiography; Arrhythmia; Seizure; Association.

RESUMO

Introdução: A importância do registro simultâneo de eletrocardiograma (ECG) de duas derivações durante o eletroencefalograma (EEG) de rotina foi relatada várias vezes por motivos clínicos. **Objetivos:** Investigar as taxas de arritmias detectadas em ECG de duas derivações simultâneas em amostra de pacientes submetidos a EEG de rotina, para avaliar impacto nos resultados pela interpretação do ECG simultâneo por examinador experiente. **Métodos:** Registros simultâneos de ECG de duas derivações durante EEG de rotina realizados entre janeiro e março de 2016 foram analisados retrospectivamente por cardiologista. Adicionalmente, os relatórios de EEG foram selecionados com palavras-chave de 'arritmia, taquicardia, bradicardia, fibrilação atrial, extrassístole', para avaliar a interpretação dos neurologistas. **Resultados:** 478 registros de EEG de rotina foram digitalizados. A idade média dos pacientes foi de 42,8±19,8 [16–95] anos com uma proporção de sexo de 264/214 (F/M). Em 80 (17%) dos pacientes, achados compatíveis com arritmia no ECG simultâneo foram determinados após avaliação do cardiologista. Os subtipos de arritmia detectados foram extrassístole ventricular (n=27; 5,6%), extrassístole supraventricular (n=23; 4,8%), taquicardia (n=9; 1,8%), duração QRS prolongada (n=7; 8,7%), fibrilação atrial (n=6; 1,2%) e bloqueio (n=6; 1,2%), respectivamente. Por outro lado, palavras-chave relacionadas à arritmia foram citadas em 45 (9,4%) dos relatórios de EEG. As declarações relatadas foram taquicardia (3,3%), arritmia (2,5%), bradicardia (2,1%) e extrassístole (1,5%), respectivamente. **Conclusões:** Uma taxa consideravelmente alta de casos de arritmia foi determinada em ECG simultâneo durante EEG de rotina, após interpretação por cardiologista. No entanto, triagem dos relatórios de EEG revelaram taxas de arritmia relativamente baixas. Esses resultados sugerem que as taxas de detecção de anormalidades no ECG durante EEG de rotina podem ser melhoradas.

Palavras-chave: Eletroencefalografia de Rotina; Eletrocardiografia; Arritimias cardíacas; Convulsões; Associação.

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Conflict of interest: There is no conflict of interest to declare.

Authors' contributions: HO and SS: study design. VH: analyses of electrocardiogram (ECG) recordings during routine electroencephalogram (EEG). IT, SS and HO: reporting of routine EEG recordings. HO: data analysis. HO, IT, VK and SS: writing of the manuscript.

Received on February 26, 2020; Received in its final form on May 22, 2020; Accepted on June 18, 2020.

According to the definition of the International League Against Epilepsy in 2014, epilepsy is a brain disease determined by any of the following conditions:

(1) at least two unprovoked (or reflex) seizures occurring >24 h apart;

(2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years;

(3) diagnosis of an epilepsy syndrome[1]. It is one of the most common neurological disorders, with an incidence of 50/100,000[2]. However, a large number of seizures is triggered by other etiologies, and the differential diagnosis of epilepsy and these provoked attacks may be extremely difficult to handle among physicians[3]. A crucial report has revealed that 20% of followed patients diagnosed with epilepsy have been misdiagnosed[4]. Rates of misdiagnosed epilepsy have been described to be between 23 and 26%, with cardiac syncope standing out in these reports[5,6]. Thus, evaluating the cardiac condition might be critical for the differential diagnosis. On the other hand, another related topic of interest in this field may be the sudden unexpected death in epilepsy (SUDEP), which accounts for half of the causes of death related to seizures and has an annual frequency of 1.2/1000[7,8]. Although the exact mechanisms underlying SUDEP remain unknown, cardiac arrhythmia originating from central nervous system control constitutes the foreground hypothesis of focus[9,10]. Identifying epilepsy patients with high risk for SUDEP has become a significant subject of interest. As a result of their study, Nashef et al. have suggested investigating interictal cardiac abnormalities to determine SUDEP risk[7]. When taking these study results into account, we can understand the need to evaluate the cardiac status in epilepsy patients. In addition, by considering the arrhythmogenic effects of some particular antiepileptic drugs AEDs (phenytoin, carbamazepine, etc.), we can perceive that the cardiac status of patients with epilepsy should be kept in mind while making appropriate treatment regulations.

Up to now, a huge number of studies on cardiac monitoring has been published in the literature, addressing issues such as differential diagnosis between epilepsy and cardiac syncope; determination of patients at risk for SUDEP; and the association of arrhythmia subtypes with seizure onset sites. These studies have used several methods to evaluate cardiac status, including continuous electrocardiogram (ECG) monitoring[11,12], simultaneous ECG recording during video electroencephalogram monitoring (VEEGM)[13], implantable loop recorder,[9] and myocardial perfusion scintigraphy[14]. Moreover, studies addressing the results of ECG recordings performed concurrently with routine electroencephalogram (EEG) may provide crucial data, considering that EEG is a vital test in the evaluation process of patients with epilepsy, performed in all individuals prediagnosed with epilepsy. However, at present, only a limited number of studies have focused on this point[15,16,17]. In two of these studies[15,16], neurologists analyzed the ECG recordings, whereas evaluation by cardiologist was only conducted in a single report by Kendirli et al[17]. In the present study, we aimed to investigate the cardiac arrhythmia burden in patients undergoing EEG, based on a method that analyzes simultaneous ECG recordings in routine EEG by both cardiologist evaluations and EEG reports. Remarkably, we sought to draw attention to the potential usefulness of simultaneous ECG recordings during routine EEG with a more experienced interpretation of ECG. In addition, we will discuss the co-occurrence of cardiac arrhythmia in patients referred to the EEG laboratory.

METHODS

In our center, simultaneous ECG recording with two electrodes has been carried out in every routine EEG since 2007. In our practice, one electrode is placed over the precordium and the other over the left 3rd-4th intercostal space. One channel is used to evaluate ECG in the monitor. In this retrospective study, ECG recordings during routine EEG, which were performed between January 7 and March 2, 2016, have been analyzed by a cardiology specialist. Our laboratory performs a significant part of EEG monitoring analyses of out-patients (approximately 80–90%); however, a minor proportion belongs to in-patients. All records performed between the specified dates have been included in the study. To avoid overdiagnosis due to artifacts, evaluation processes have also been repeated (and confirmed) by the cardiology specialist under the supervision of a neurologist. Arrhythmia subtypes have been investigated. In addition, for patients with arrhythmia, data from the electronic patient record information system of the hospital related to demographic characteristics (age, gender), survival rates, and provisional diagnoses during EEG recordings were analyzed in the first week of April 2016. Among these patients, the subgroup of individuals who had been further investigated in our hospital as to their cardiac status (such as Holter monitoring, echocardiography) was identified by searching the hospital information system. EEG reports of the arrhythmia group were re-evaluated to detect epileptiform abnormalities, paroxysmal disorders, and slowing of background activity. AED use data were collected from EEG reports or the Hospital Nucleus Recording System. Patients with suspected long QT intervals were informed via telephone interview, and a 12-channel ECG was performed on those who were available.

In addition, EEG reports were scanned for the keywords 'arrhythmia, tachycardia, bradycardia, atrial fibrillation, extrasystole' to evaluate the interpretation of neurologists. The reports were investigated regarding diagnoses and preliminary diagnoses of the patients.

RESULTS

A total of 478 routine EEG recordings were scanned. All recordings were interictal. The mean age of the patients was 42.8±19.8 (16–95), with a gender ratio of 264/214 (F/M). In 80 (17%) patients, findings compatible with arrhythmia were identified on simultaneous ECG after a cardiologist's evaluation. Of note, 284 of the 478 patients undergoing routine EEG had a confirmed diagnosis of epilepsy. Among these patients, 44 (15.4%) presented arrhythmia, and arrhythmia rates showed no difference between the patient group with a confirmed diagnosis of epilepsy and other individuals (p=0.37).

The F/M ratio of the overall arrhythmia group (n=478) was 45/35 (56/44%), and the mean age was 51.8±23.3. The detected arrhythmia subtypes were: ventricular extrasystole (VES) (n=27; 5.6%), supraventricular extrasystole (SVES) (n=23; 4.8%), sinus tachycardia (n=9; 1.8%), prolonged QRS duration (n=7; 8.7%), atrial fibrillation (AF) (n=6; 1.2%), and first-degree atrioventricular block (n=6; 1.2%) (Table 1). Five records presented a long QT interval. Further investigation of the patients with suspected arrhythmia, based on the Hospital Nucleus Recording System, revealed that 28 of them had been examined by echocardiography or rhythm Holter monitoring, and 16 had abnormal results (hypokinetic segments, valve regurgitation, effusion, VES, bradycardia, etc.).

Table 1. Data on arrhythmia subtypes detected by cardiologist evaluation; diagnoses and pre-diagnoses of patients with arrhythmias; antiepileptic drug use by patients with arrhythmia according to cardiologist evaluation.

Arrhythmia subtypes detected by cardiologist evaluation		n (%) Total=80 (100)
Ventricular extrasystole		27 (5.6)
Supraventricular extrasystole		23 (4.8)
Sinus tachycardia		9 (1.8)
Prolonged QRS duration		7 (8.7)
Atrial fibrillation		6 (1.2)
First-degree atrioventricular block		6 (1.2)
Extrasystole		7 (1.5)
Diagnoses and preliminary diagnoses		
Epilepsy		40 (50.0)
Pre-diagnosis	Seizures	30 (37.5)
	Syncope	13 (16.2)
	Other	18 (22.5)
AED use	At least one AED	28 (35.0)
	No AED use	41 (51.2)
	Unknown	11 (13.7)

Other: impaired consciousness, psychogenic seizures, dementia, headache, etc.; AED: antiepileptic drug.

Four of the five patients with suspected long QT intervals were available. However, only two of them showed prolonged QT interval in the 12-channel ECG, which were evaluated as drug-induced prolonged QT. For further medication adjustments, a cardiologist was consulted. Moreover, when the EEG reports of patients with arrhythmia were scanned, they showed a slowing of background activity in 19 individuals, epileptiform abnormalities in 12, and paroxysmal disorders in 12 (Figure 1).

The detailed investigation of the preliminary diagnosis and the diagnosis of patients with suspected arrhythmia revealed that 40 (50%) of them were on follow-up with the diagnosis of epilepsy. Besides, seizure was the preliminary diagnosis in 30 (37.5%) patients and syncope in 13 (16.2%). EEG was requested for 18 (22.5%) patients with other preliminary diagnoses (impaired consciousness, dementia, psychogenic seizure, headache, etc. Some patients were referred to EEG laboratories with multiple preliminary diagnoses). Patient follow-up data revealed that 28 (35%) of them were taking at least one AED, while 41 (51%) were not on AED. Data on drug use could not be determined in 11 (14%) patients.

We found no difference as to gender in the group with suspected arrhythmia (F/M: 45/35; p=0.96). The mean age was higher in the arrhythmia group compared to the group without arrhythmia [A (+): 51.8±23.3; A (-): 38.8±16.0 (p=0.000; Student's *t*-test)]. The mean age of the subgroups of patients according to their arrhythmia subtype was 58.2±6.6 for SVES, 58.1±3.5 for VES, and 42.4±4.2 for tachycardia. The assessment of the survival rates of all patients revealed that seven individuals died, and, remarkably, six of them were in the group with suspected arrhythmia (Table 2). However, further investigation about the causes of death in these patients did not show any death etiology suggesting SUDEP. All patients who died during the follow-up were hospitalized patients. The cause of death was cardiac arrest following septic shock in all individuals (five of them were intubated during EEG). Finally, EEG reports were scanned for keywords related to arrhythmia to compare the interpretation of cardiologists and neurologists. We found keywords related to arrhythmia in 45 (9.4%) EEG reports. The reported statements were tachycardia (n=16; 3.3%), arrhythmia (n=12; 2.5%), bradycardia (n=10; 2.1%), and extrasystole (n=7; 1.5%) (Table 3). We noted that most of the assessments performed by the neurologists were confirmed by the cardiologist. Yet, a significant proportion of arrhythmia subtypes, consisting of VES, SVES, prolonged QRS duration, and AF, could not be reported by the neurologists.

The investigation of diagnoses and preliminary diagnoses showed that 16 (35.5%) patients were on follow-up with the diagnosis of epilepsy. Nevertheless, EEG was requested with a preliminary diagnosis of seizure for 11 patients and syncope for 5.

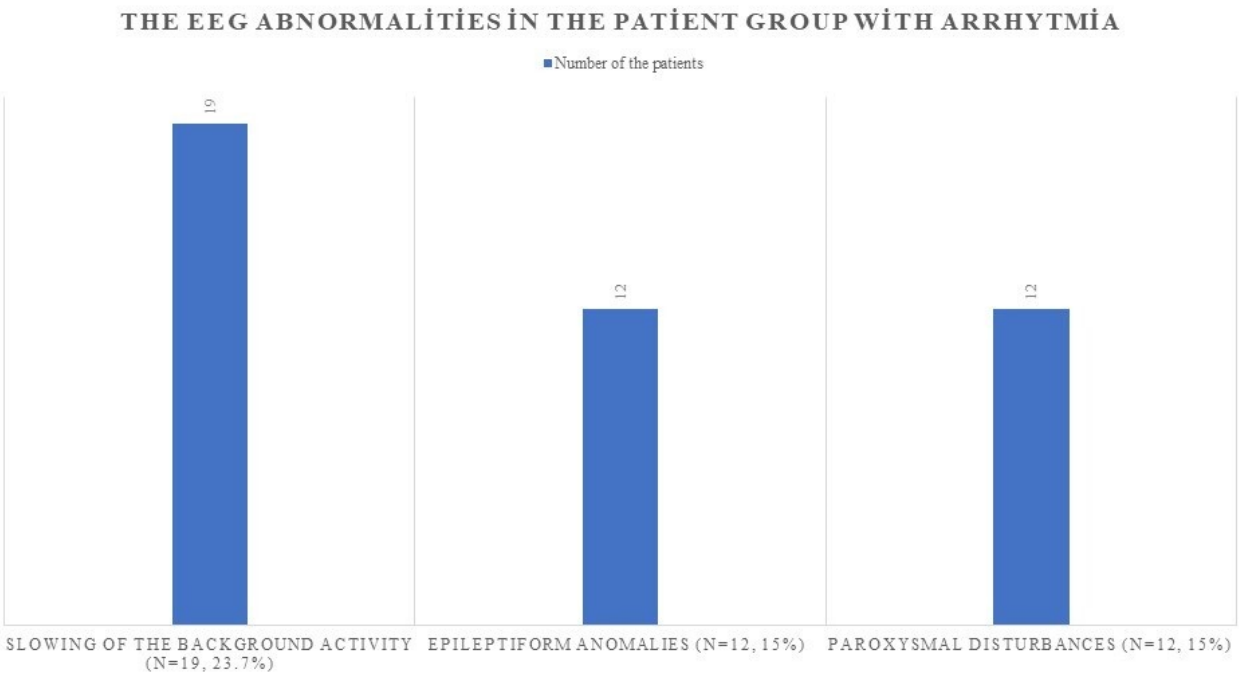

Figure 1. The figure shows the rates of electroencephalogram abnormalities in the patient group with arrhythmia detected by the cardiologist.

Table 2. Comparison of demographic data and death rates between patients with arrhythmia and those without arrhythmia.

	Patients with arrhythmia (n=80)	Patients without arrhythmia (n=398)	p-value
Age	51.8±23.3	38.8±16.0	0.000*, Student's *t*-test
Gender	45/35	221/179	0.096, chi-square test
Death rates	6/80 (7.5%)	1/398 (0.2%)	0.000*, chi-square test

*:<0.005.

Table 3. Arrhythmia results after scanning electroencephalogram reports for keywords.

Arrhythmia results after scanning EEG reports for keywords, n (%)	
Tachycardia	16 (3.3)
Arrhythmia	12 (2.5)
Bradycardia	10 (2.1)
Extrasystole	7 (1.5)

EEG: electroencephalogram.

DISCUSSION

This study revealed that 17% of EEG data presented findings compatible with arrhythmia on ECG following the cardiologist's evaluation. Remarkably, arrhythmia rates were similar in the subgroup of patients with a confirmed diagnosis of epilepsy. Among the limited number of previous reports, arrhythmia rates in routine EEG ranged from 2 to 18%[15,16,17]. In light of these study results, the arrhythmia rate in our study was considerably high. However, we believe that the method of interpreting EEG data (which was performed by a cardiologist) might be a crucial factor in these high rates. Accordingly, ECG abnormalities were detected at a similar rate of 18% in a previous unique report by Kendirli et al., in which the interpretations were also performed by a cardiologist[17]. We underline that other related reports had their evaluations carried out only by neurologists[15,16]. In this context, the scan of EEG reports for keywords revealed that results related to arrhythmia were present in only 9.4% of them.

The most common arrhythmia subtypes detected by the cardiologist were VES (5.6%), SVES (4.8%), tachycardia (1.8%), AF (1.2%), and block (1.2%). In the study by Kendirli et al., the ECG abnormalities identified were tachycardia, extrasystole, and bradycardia[17]. On the other hand, in a previous report from our center conducted retrospectively on 2,136 patients, the most common arrhythmia subtypes were extrasystole and tachycardia[16]. Of note, EEG reports were scanned for keywords, allowing us to measure the extent of the neurologists' interpretations. The most common arrhythmia subtype in our cohort, VES, has proven to be remarkably associated with cardiac syncope[18,19]. In the report by Kendirli et al., extrasystole was also a common arrhythmia subtype (13/376; 3.4%). Nonetheless, this report did not divide the subtypes into VES and SVES. Moreover, extrasystole was also the most common keyword in the previous report from our center[16]. Considering that cardiac

syncope is a crucial differential diagnosis of epilepsy[20,21], we believe that the identification of this finding, 'VES', in simultaneous ECG during routine EEG may potentially provide a crucial perspective to neurologists. In another aspect, some studies have reported that the use of carbamazepine may induce VES arrhythmia[22,23], which could also define VES as a potential critical sign in the clinical practice of neurologists.

We detected a prolonged QRS duration in 5% (n=6) of patients, which has also been previously associated with cardiac syncope[24]. Retrospective scanning revealed that 28 patients with suspected arrhythmia were examined by echocardiography or rhythm Holter monitoring, and 16 had abnormal results (hypokinetic segments, valve regurgitation, effusion, VES, bradycardia, etc.). However, due to the retrospective study design, we could not determine how many of these patients had a cardiology evaluation performed by the neurologist based on ECG data during routine EEG. Further follow-up of these patients was unavailable. Therefore, we cannot comment on the real significance and clinical impact of the evaluation of simultaneous ECG during routine EEG based on our study method. A significant result of our study was determining a high arrhythmia rate (17%) as a result of cardiologist evaluations, given that the detection rate was nearly half of this number (9.4%) in neurologist reports. Thus, the high arrhythmia results in our initial analyses may not reflect actual clinical values. Remarkably, a significant proportion of arrhythmia subtypes, consisting of VES, SVES, prolonged QRS duration, and AF, could not be reported by the neurologists. Indeed, no EEG report described long QRS duration or differentiated between extrasystole subtypes. Nevertheless, these results suggest that the efficacy of prolonged ECG monitoring during EEG may increase with a more ideal and experienced interpretation. We also draw attention to the need to raise awareness and expand ECG knowledge of arrhythmias among neurologists to avoid underdiagnosis (or insufficient cardiology consultation) for patients.

AF has been detected in 1.2% of the recordings. Similarly, AF showed a rate of 2% in the study by Kendirli and colleagues[17]. That being said, AF is the most common cardiac arrhythmia in the community, and its reported prevalence in Europe and North America ranges between 2 and 3%[25]. We found no increased co-incidence of AF in our group of patients with epilepsy or suspected epilepsy.

Besides, no significant difference was identified with respect to gender among arrhythmia patients. Yet, as expected, the mean age of patients with ECG abnormalities was higher than that of patients with normal ECG (p=0.00). This finding may be related to the increasing rate of cardiac comorbidities with aging. We did not include data on patient comorbidities due to the insufficient record-keeping system. On the other hand, we can hypothesize that longer duration of epilepsy, as well as AED use by aging, may also be associated with this increasing arrhythmia rate. Moreover, seven patients died in the overall group, and, remarkably, six of them were in the group with ECG abnormalities. However, further investigations about the causes of death among these patients did not show any death etiology suggesting SUDEP, and the mean age of the arrhythmia group was higher. Ergo, we believe that the increased death rates may be related to aging and a higher level of comorbidities. Finally, the most common EEG abnormality in the arrhythmia group was slowing of background activity (n=19; 24%).

Five patients with long QT syndrome were detected in the records. A 12-lead ECG was performed on the four available patients, and only two of them had long QT syndrome confirmed. Long QT syndrome in these patients was evaluated as drug-induced, and medical therapy was readjusted under the supervision of a cardiologist. Long QT syndrome is a disorder characterized by a prolonged QT interval in the ECG analysis and a propensity for ventricular tachyarrhythmias, which may lead to syncope, cardiac arrest, or sudden death[26]. Remarkably, a prolonged QT interval is usually present in epilepsy patients, and its significance and relationship with the risk of sudden cardiac death have been suggested as crucial topics for further discussions[27,28,29]. Nevertheless, its co-incidence with epilepsy is still controversial[27], as several studies found no increased incidence of prolonged QT in patients with epilepsy[30,31]. Lambert et al. hypothesized that the differences in epilepsy severity and drug use among the group of patients included in these studies might be responsible for these conflicting results[27]. In our study, patients with prolonged QT intervals did not differ as to epilepsy diagnosis and drug use compared to the overall patients (one of them was diagnosed with epilepsy and on monotherapy).

The usefulness of evaluating the QT interval in simultaneous ECG during routine EEG has been mentioned in a few previous reports[32,33]. In a study of pediatric patients, Jha et al. detected prolonged QT intervals in 2% of patients with seizures, whereas the incidence rate in patients diagnosed with syncope was 14%. In conclusion, they emphasized the importance of evaluating QT intervals in simultaneous ECG during routine EEG for neurologists[33]. In the previous study of our group, we detected 5 patients with prolonged QT interval (evaluated by a neurologist) in a large cohort of 2,136 patients[16]. Surprisingly, these studies did not confirm the long QT interval in these patients, which may represent a major limitation. Also, Kendirli et al. did not report patients with long QT syndrome in the evaluations performed by the cardiologist[17]. Thus, we believe that future prospective reports on a larger patient group may provide a substantial perspective on the usefulness of determining the suspicion of long QT interval in simultaneous ECG during routine EEG.

The main limitation of our study may be its retrospective design. We understand that prospective studies, including patient follow-up data with ECG abnormalities in routine EEG and 12-lead ECG data, as well as results of cardiology consultation in patient subgroups, may provide a significant contribution in this regard. The National Institute for

Health and Care Excellence (NICE) guidelines recommend performing 12-lead ECG in every individual with suspected epilepsy; however, the American Academy of Neurology (AAN) guidelines do not mention it[34,35]. Hence, further investigations addressing the association between epilepsy and arrhythmia, as well as evaluation procedures for these patients, are still necessary. A major concern may be that, although we have adopted a method of retrospective evaluation of long-term 2-lead ECG data by a cardiologist and held a committed discussion on the results, we cannot support that this method is practical and ideal for cardiac monitoring of patients undergoing EEG. Nevertheless, this method has provided a substantial contribution to the potentially greater usefulness of simultaneous ECG when evaluated in a more experienced manner, which was the main hypothesis of this study. Another limitation may the need for a larger group of patients for a more rational interpretation of this critical issue. However, considering that studies focusing on the importance of simultaneous ECG during routine EEG are extremely rare in the literature, we trust that the results of our study may provide a pivotal contribution.

In conclusion, we identified a considerably high arrhythmia rate in simultaneous ECG during routine EEG based on a cardiologist's interpretation. These results suggest that the efficacy of prolonged ECG monitoring during routine EEG may potentially increase with a more ideal and experienced interpretation. Besides, findings related to the significant arrhythmias rates in patients undergoing EEG can be interpreted as the high co-incidence rates of arrhythmia in patients with suspected epilepsy. Yet, these results cannot provide a detailed conclusion regarding the sub-items of arrhythmia rates in epilepsy patients, the high rates of cardiac syncope in the differential diagnosis of epilepsy, or the causal relationship between AEDs and arrhythmias. We believe that these subtopics need to be investigated separately in future prospective studies.

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