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Cardiac stress after electroconvulsive therapy and spontaneous generalized convulsive seizures: A prospective echocardiographic and blood biomarker study

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ABSTRACT

Aim: Knowledge about cardiac stress related to seizures in electroconvulsive therapy (ECT) and spontaneously occurring generalized convulsive seizures (GCS) is limited. The aim of the present study was to analyze cardiac function and circulating markers of cardiac stress in the early postictal period after ECT and GCS.
Methods: Patients undergoing ECT in the Department of Psychiatry, Psychotherapy and Psychosomatics and patients undergoing diagnostic video-EEG monitoring (VEM) in the Department of Neurology were prospectively enrolled between November 2017 and November 2018. Cardiac function was examined twice using transthoracic echocardiography within 60 min and >4 h after ECT or GCS. Established blood markers (troponin T high-sensitive, *N*-terminal pro brain natriuretic peptide) of cardiac stress or injury were collected within 30 min, 4 to 6 h, and 24 h after ECT or GCS. In the ECT group, the troponin T values were also correlated with periprocedural heart rate and blood pressure values. Because of organizational or technical reasons, the measurement was not performed in all patients.
Results: Twenty patients undergoing ECT and 6 patients with epilepsy with a GCS during VEM were included. Postictal echocardiography showed no wall motion disorders and no change in left ventricular and right ventricular functions. Four of 17 patients displayed a transient increase in high-sensitive cardiac troponin T 4–6 h after the seizure (3 patients with ECT-induced seizure). None of these 4 patients had signs of an acute cardiac event, and periprocedural blood pressure or heart rate peaks during ECT did not significantly differ in patients with and without troponin T elevation.
Conclusions: Signs of mild cardiac stress can occur in some patients following ECT or GCS without clinical complications, probably related to excessive catecholamine release during the seizure.

1. Introduction

Epileptic seizures are commonly associated with mostly benign cardiovascular dysfunctions [1–3]. However, cases of malignant cardiac arrhythmias have also been described [4–6]. In addition, it is well known that epileptic seizures can trigger a Takotsubo syndrome (TTS, [7–9]). In most cases, such cardiac complications are associated with spontaneous generalized convulsive seizures (GCS), but there are also case reports of TTS in electroconvulsive therapy-triggered seizures (ECT-triggered seizure, [10–14]).

Patients with TTS display acute chest pain and dyspnea, and may develop severe acute heart failure. An ECG pattern similar to an acute coronary syndrome may arise. An increase in cardiac laboratory markers and transient echocardiographic changes can also be detected [15–16].

Apart from of these clinically fulminant events, the incidence and severity of transient subclinical cardiac dysfunction following epileptic seizures and ECT-triggered seizures have not been studied in depth. A difference between these two types of seizure is that GCS are usually

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the result of an underlying cerebral disease process, which is not the case in ECT-induced seizures.

In addition, spontaneous GCS differ in clinical manifestation compared with ECT-induced seizures in that GCS are associated with hypoxia, increased muscle activity, and consequent transient metabolic acidosis [17].

Regarding cardiac function, it is unclear whether pathological changes are direct cerebral effects following seizure activity or indirect 'peripheral' effects.

The aim of the present study was to investigate whether and how cardiac features change after epileptic seizures. To that end, we used transthoracic echocardiography to evaluate cardiac function, and we measured laboratory cardiac markers after two different types of convulsive seizures, namely spontaneously occurring GCS and ECT-triggered seizures (which happen under controlled conditions with no or only minor contractions and continuous oxygenation) compared with spontaneously occurring GCS to ascertain the effect of generalized convulsive seizure activity on the heart. In order to compare the different metabolic situations after the two types of seizures, we additionally compared serum lactate, bicarbonate, and pH levels within 30 min after seizure.

2. Materials and methods

2.1. Patient groups

The patients of this prospective clinical study were selected, on the one hand, from a sample of psychiatric patients, who had an ECT-induced seizure for therapeutic reasons, and on the other hand, from a sample of patients with epilepsy, who had a generalized convulsive seizure during monitoring in an epilepsy unit. The study was conducted in the period from November 2017 to November 2018 in the Department of Psychiatry, Psychotherapy and Psychosomatics and the Department of Neurology of the University Hospital RWTH Aachen. We enrolled adult patients (≥18 years of age) who had (1) an ECT-triggered seizure or (2) a GCS in the epilepsy unit. Therefore, EEG monitoring data was available for all seizures included in the study. Overall, a much larger number of patients with epilepsy undergoing diagnostic video-EEG monitoring (VEM) were screened for eligibility than later included in the study. The reason for this was that most patients did not have a seizure during the study period.

Our study was approved by the Ethics Committee of University Hospital RWTH Aachen. Informed consent was obtained from all individual participants included in the study.

2.2. Electroconvulsive therapy (ECT)

Electroconvulsive therapy was carried out in the University Hospital RWTH Aachen by the Department of Psychiatry, Psychotherapy and Psychosomatics and Anaesthesiology in a standardized procedure, using a Thymatron IV device (Somatics, LLC., Lake Bluff, IL, USA). All patients received short-term anesthesia in ECT, routinely composed of etomidate as an anesthetic, remifentanil as analgesic, rocuronium bromide as nondepolarizing muscle relaxant, and suxamethonium chloride as depolarizing muscle relaxant. In two cases, patients received ketamine instead of etomidate.

Electroconvulsive therapy is an established procedure in the Psychiatric Clinic of the University Hospital RWTH Aachen. Every year, about 70 patients receive ECT treatment here.

2.3. Transthoracic echocardiography

After informing and including the patients, transthoracic echocardiography was used to measure cardiac function at two different points in time: within 60 min after seizure and >4 h after seizure. Left ventricular systolic function was assessed by evaluation of left ventricular ejection fraction (EF). In addition to visual assessment, quantitative evaluation was made by measuring the end-diastolic and end-systolic volumes. According to the recommendations of the American Society of Echocardiography (ASE) and the European Association of Echocardiography (EAE), the EF was calculated biplanar from the apical four- and two-chamber views. The determination of the volumes was carried out using Simpson's method of discs [18]. The wall movement was judged by visual assessment in the apical 2-, 3-, and 4-chamber views. The diastolic function was evaluated with the aid of PW-Doppler parameters E/A, E′, E/E′ and the deceleration time of the E-wave. The classification of the diastolic function was carried out according to Khouri et al. [19]. The assessment of right ventricular function was performed visually and by determining the TAPSE (TAPSE = tricuspid annular plane systolic excursion, [20]).

All ultrasound examinations were performed and interpreted by two trained vascular examiners (O.M., J.L.) with several years of experience in conducting and interpreting echocardiography.

A Vivid S6© ultrasonic device (General Electric Company, Fairfield, USA) with a 2 MHz phased array (cardiac) transducer was used for B-mode and color coded echocardiography.

2.4. Circulating cardiac biomarkers

In patients undergoing ECT, cardiac markers (troponin T high-sensitive [cTnT-hs], *N*-terminal pro brain natriuretic peptide [NT-proBNP]) were measured at three different time points: within 30 min after seizure, 4 to 6 h after ECT, and about 24 h after seizure. The detection limit for cTnT-hs is 3 pg/ml. A cTnT-hs ≥ 14 pg/ml (>99th percentile of a healthy reference population) is defined as elevated indicative of pathology. In case of increased cTnT-hs values, the patient was reevaluated using ECG, and further cTnT-hs determinations were carried out according to the ECS Guidelines for the management of acute coronary syndromes [21–22], where applicable. The default value for NT-proBNP is age-dependent. Both parameters are routinely measured in the laboratory of the Aachen University Hospital.

2.5. Metabolic biomarkers

Serum levels of lactate, bicarbonate, and pH were determined using blood gas analysis (BGA) as a point-of-care test (POCT). The measurements were made within 30 min after seizure.

2.6. Definition of outcome measures and statistics

2.6.1. Primary endpoints

The primary endpoints of the study were the measurements of cardiac function (LV/RV function, LV diastolic function, assessment of wall motion) using transthoracic echocardiography after ECT-induced seizures and GCS.

2.6.2. Secondary endpoints

Secondary endpoints include measurements of cardiac and metabolic markers.

The echocardiographic examination was performed at two time points. We compared the continuous parameters (EF, TAPSE) in the GCS and ECT group with the paired t-test. For the comparison of dichotomous variables, we used the McNemar test. In addition, the two-factorial ANOVA was used to analyze the evolution of the two continuous parameters (EF, TAPSE) across time with regard to the group factor (GCS group, ECT group) and the repeated measures factor time points.

The cardiac markers cTnT-hs and NT-proBNP were determined at three measurement times. Because of the age dependence of NT-proBNP and the lower detection limit of <3 for cTnT-hs, the

statistical tests for continuous parameters could not be carried out for these two parameters.

Therefore, we used Cochran's Q test for the comparison of dichotomous variables for the three time points of assessment.

In addition, we investigated whether the presence of elevated cTnT-hs levels in patients correlated with changes in vital signs such as heart rate and blood pressure. For this purpose, a comparison of the maximum systolic blood pressure values and the maximum heart rate was carried out at ECT.

This was not possible with the patients with GCS as blood pressure is not continuously measured during the VEM.

A hypertensive episode was defined as periprocedural peak systolic blood pressure ≥ 180 mm Hg, and tachycardia was defined as a peak heart rate ≥ 100 beats per minute.

The statistical analysis was carried out with the t-test.

The comparison of the metabolic markers (serum lactate, bicarbonate, and pH) was also carried out by t-test.

Statistical analysis was performed using SPSS 24 Software (SPSS Inc., Chicago, IL, USA).

3. Results

In total, 153 patients were screened for eligibility. We included 20 patients undergoing ECT and 6 patients with GCS in the study (Fig. 1). Their characteristics are shown in Tables 1 and 2. The complete measurements could not be obtained in all patients. Reasons for this were, on the one hand, that some patients were scheduled to be discharged immediately after ECT treatment and repeated measurements would have prolonged hospitalization and, on the other hand, that some echocardiographic parameters could not be determined because of technical causes.

The 127 excluded patients were all monitored in the epilepsy unit, but none had a generalized epileptic seizure during the surveillance period. The number of 20 patients undergoing ECT was determined before the study started. The choice of patients undergoing ECT was random. None of the 20 patients undergoing ECT had history of epilepsy or epileptic seizures.

Cardiovascular risk factors in the ECT group included arterial hypertension in 5 cases, obesity in 3 cases, diabetes mellitus in one case, and hyperlipidemia in two cases. None of the patients in the GCS group had cardiovascular risk factors.

3.1. Primary outcome measures

3.1.1. Patients undergoing ECT

In 16 out of 20 patients, the EF could be calculated at the first two points in time. In the case of two patients, unfavorable examination conditions enabled only a visual estimate. The EFs were normal in these two patients and did not differ substantially in the two measurements. The other two patients were discharged before the second echocardiography. In the remaining 16 patients, no significant difference between first and second measurements ($t\ (15) = 0.398$, $p = 0.696$) was detected.

We did not detect wall movement disorders at any time in any patient.

In the McNemar test, the diastolic function at the two time points did not differ significantly between the assessments directly after seizure and >4 h after seizure ($p = 0.5$, $n = 17$). Two patients showed diastolic dysfunction immediately after seizure, which was not detectable in the examination 4 h later. However, all patients undergoing ECT also had echocardiography before treatment. In those two patients, there was diastolic dysfunction also in the preexamination. Thus, the differences in diastolic function in these two patients are most likely to be considered preexisting and not associated with the ECT.

To assess the right ventricular function, the TAPSE was determined, which was normal in all patients. As mentioned above, the second examination was not possible in two patients. There were no significant differences between the two measurements ($t\ (17) = 0.379$, $p = 0.709$).

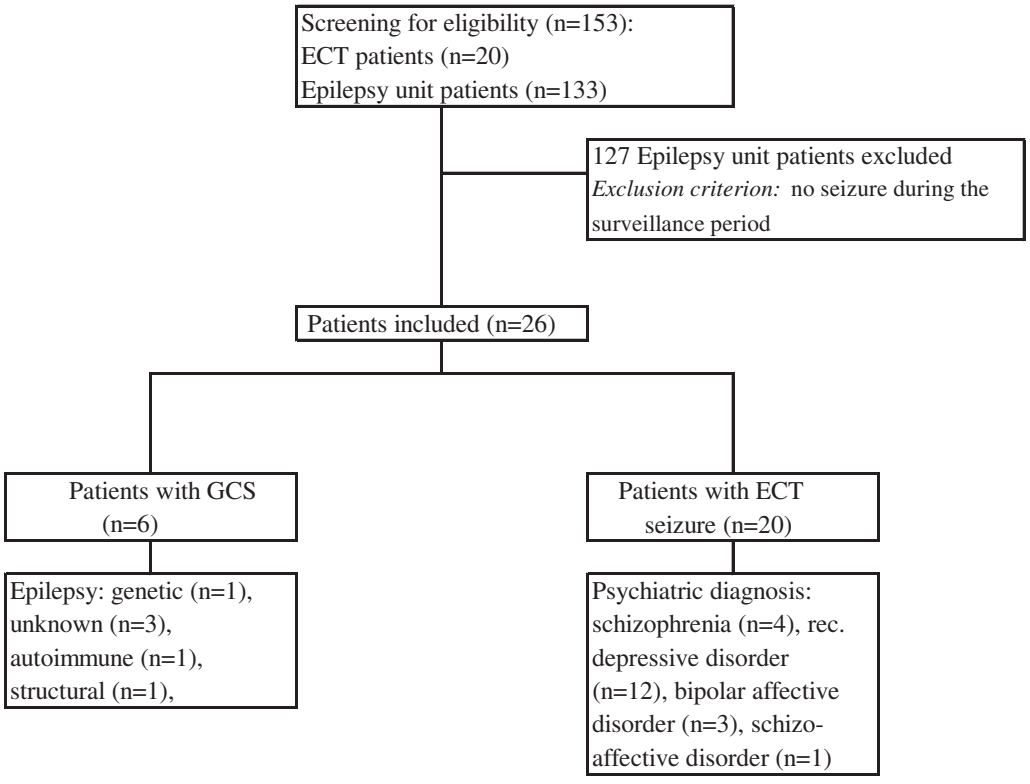

Fig. 1. Study flow chart of patient selection.

Table 1
Individual patient characteristics of the GCS group.

Patient	Sex	Age (years)	Epilepsy etiology	Seizure type	Epilepsy type	Cardiovascular diseases/risk factors	Other diseases	EF[2] < 30 min (%)	EF > 4 h (%)	TAPSE[3] < 30 min (mm)	TAPSE > 4 h (mm)	Diastolic dysfunction < 30 min	Diastolic dysfunction > 4 h	Wall motion disorders	Pathological cTnT-hs	Pathological NT-proBNP
Patient 1	Male	20	Unknown	GCS[1]	Focal to bilateral	No	No	60	59	22	22	No	No	No	No	No
Patient 2	Female	29	Genetic	GCS	Generalized	No	No	73	59	21	20	Yes	No	No	Not measured	Not measured
Patient 3	Male	26	Unknown	GCS	Generalized	No	No	68	58	22	20	Yes	Yes	No	No	No
Patient 4	Male	20	Structural	GCS	Focal to bilateral	No	No	60	63	21	22	No	No	No	Not measured	Not measured
Patient 5	Female	47	Autoimmune	GCS	Focal to bilateral	No	No	61	66	29	27	No	No	No	No	No
Patient 6	Male	26	Unknown	GCS	Focal to bilateral	No	No	76	70	30	24	No	No	No	Yes	No
Mean ± SD/ distribution	4/6 (66.6%) male	28.0 ± 9.98						66.33 ± 7.06	62.5 ± 4.76	24.17 ± 4.17	22.5 ± 2.66	2/6 (33.33%)	1/6 (16.66%)	0/6 (0%)	1/6 (16.66%)	0/6 (0%)

[1] Generalized convulsive seizure.
[2] Left ventricular ejection fraction.
[3] Tricuspid annular plane systolic excursion.

3.1.2. GCS group

The EF was normal in all patients at both times without significant mean differences (t (5) = 1.257, p = 0.264). We detected no wall movement disorders in the GCS group. Diastolic dysfunction was present in the GCS group in two patients immediately after seizure, in the follow-up only in one patient. The difference in the probability of diastolic dysfunction between the two measurement times was not significant (p = 1.0, n = 6) in the McNemar test. The determination of the TAPSE showed values in the standard range in all patients. There was no significant difference between both measurements (t (5) = 1.685, p = 0.153).

3.1.3. GCS group vs. ECT group

The two-factorial ANOVA for the continuous parameters (EF, TAPSE) revealed that there were no significant group effects (EF: $F(1.20)$ = 0.537, p = 0.472, partial η^2 = 0.026; TAPSE: $F(1,22)$ = 0.558, p = 0.463, partial η^2 = 0.025) or time (EF: $F(1.20)$ = 2.799, p = 0.110, partial η^2 = 0.123; TAPSE: $F(1.22)$ = 2.627, p = 0.119, partial η^2 = 0.107) as well as no interaction between them (EF: $F(1.20)$ = 1.769, p = 0.198, partial η^2 = 0.081; TAPSE: ($F(1.22)$ = 1.536, p = 0.228, partial η^2 = 0.065).

3.2. Secondary outcome measures

3.2.1. Patients undergoing ECT

We obtained cardiac blood markers in 13 patients. Values for cTnT-hs in the first measurement after seizure were normal in all patients. Pathologically elevated cTnT-hs levels were detected in 3/13 patients 4 to 6 h after seizure (23.1%, patient 1 [age 45 years]: 50 pg/ml, patient 2 [age 48 years]: 21 pg/ml, patient 3 [age 65 years]: 24 pg/ml). In these cases, follow-up values were obtained after further 3–6 h, which showed elevated but already decreasing values (patient 1: 20 pg/ml, patient 2: 17 pg/ml, patient 3: 19 pg/ml). The cTnT-hs values were within the normal range after 24 h in all three patients (patient 1: 7 pg/ml, patient 2: 8 pg/ml, patient 3: 10 pg/ml). None of these three patients showed clinical or electrocardiographic signs of myocardial infarction. Because of an elevated cardiovascular risk profile, we carried out further diagnostics (myocardial SPECT) in the second and third patients (patient 2: obesity; patient 3: arterial hypertension, obesity, age). There was no evidence of coronary heart disease (CHD) in either examination.

Overall, there was a tendency toward significant difference in probability of a pathological cTnT-hs (Cochran's Q: $\chi^2(2) = 6$, p = 0.05, n = 13) in the comparison of the three measurements after seizure. The probability of a pathological cTnT-hs test was not significant in comparison between the measurement times 1 and 2 (p = 0.25), nor between measurement times 2 and 3 (p = 0.25) in the McNemar test.

In the case of NT-proBNP, there was no significant difference (Cochran's Q: $\chi^2(2) = 2$, p = 0.368, n = 13) between the three measurements after seizure. Two patients had increased NT-proBNP levels after seizure, though preexisting bloodwork showed previously elevated NT-proBNP. The three patients with elevated cTnT-hs levels had normal NT-proBNP values.

Regarding vital signs, there was a periprocedural hypertensive episode (RRsys ≥ 180 mm Hg) in 16 out of 20 patients undergoing ECT (maximum systolic blood pressure [mean (mm Hg) ± standard deviation, range] 191.35 ± 30.64, 117–253). Tachycardia (>100 bpm) occurred in 19 of 20 patients undergoing ECT (maximum heart rate [mean (bpm) ± standard deviation, range] 130.6 ± 26.18, 54–161). One patient showed sinus bradycardia as low as 25 bpm after the administration of anesthesia, which increased to a maximum of 54/min in ECT. When comparing patients with elevated vs. normal cTnT-hs levels, there was no significant difference in the comparison of maximum systolic blood pressure (t (17) = 1.816, p = 0.087) and heart rate (t (17) = 0.477, p = 0.64). However, cTnT-hs positive patients tended to have higher systolic blood pressures (maximum systolic

Table 2
Individual patient characteristics of the ECT group.

Patient	Sex	Age (years)	Psychiatric diagnosis/ECT[1] indication	Cardiovascular diseases/risk factors	Other diseases	EF[2] < 30 min (%)	EF > 4 h (%)	TAPSE[3] < 30 min (mm)	TAPSE >4 h (mm)	Diastolic dysfunction <30 min	Diastolic dysfunction >4 h	Wall motion disorders	Pathological cTnT-hs	Pathological NT-proBNP	Max. RR sys[4] (mm Hg)	Max. Heart rate (bpm)
Patient 1	Male	51	Schizophrenia	No	No	61	60	23	23	No	No	No	No	No	180	114
Patient 2	Female	48	Rec. depressive disorder	Obesity	No	Not measured	Not measured	25	25	Yes	Yes	No	Yes	No	212	135
Patient 3	Male	79	Rec. depressive disorder	Arterial hypertension	Prostatic hyperplasia	68	67	22	20	No	No	No	Not measured	Not measured	213	147
Patient 4	Female	45	Bipolar affective disorder	No	Hypothyroidism	75	65	20	22	No	No	No	Yes	No	191	153
Patient 5	Female	61	Rec. Depressive disorder	Diabetes mellitus	Hypothyroidism	Not measured	Not measured	19	22	Not measured	Not measured	No	Not measured	Not measured	194	160
Patient 6	Female	65	Rec. Depressive disorder	Obesity, hyperlipidemia	Hypothyroidism	75	70	25	25	Yes	No	No	Yes	No	253	131
Patient 7	Female	49	Rec. Depressive disorder	Arterial hypertension	Breast cancer	63	60	25	26	No	No	No	Not measured	Not measured	195	130
Patient 8	Male	37	Schizophrenia	No	Benzodiazepine addiction, cannabis addiction	70	65	23	24	No	No	No	No	No	187	115
Patient 9	Male	69	Bipolar affective disorder	Arterial hypertension	No	71	71	25	25	Yes	Yes	No	No	No	117	54
Patient 10	Male	34	Schizophrenia	No	No	65	63	25	25	Yes	No	No	No	No	155	130
Patient 11	Female	71	Bipolar affective disorder	Hyperlipidemia	OSAS, chronic venous Insufficiency	62	Not measured	19	Not measured	Yes	Not measured	No	Not measured	Not measured	189	134
Patient 12	Female	62	Schizoaffective disorder	Arterial hypertension	Breast cancer	61	67	21	21	Yes	Yes	No	Not measured	Not measured	211	160
Patient 13	Male	58	Rec. Depressive disorder	No	No	68	70	26	27	No	No	No	Not measured	Not measured	220	161
Patient 14	Female	78	Rec. Depressive disorder	Arterial hypertension	Hypothyroidism, brain tumor	65	Not measured	25	Not measured	Yes	Not measured	No	Not measured	Not measured	185	113
Patient 15	Female	23	Rec. Depressive disorder	Obesity	Chronic pain syndrome	64	68	23	27	No	No	No	No	Yes	187	152
Patient 16	Female	49	Rec. Depressive disorder	No	No	72	69	29	30	No	No	No	No	No	192	157
Patient 17	Female	47	Rec. Depressive disorder	No	No	64	69	30	28	No	No	No	No	Yes	235	140
Patient 18	Male	37	Schizophrenia	No	No	60	58	24	18	No	No	No	No	No	162	100
Patient 19	Male	56	Rec. Depressive disorder	No	No	61	64	26	24	No	No	No	No	No	202	107
Patient 20	Male	23	Rec. Depressive disorder	No	Autoimmune thyroiditis	60	65	29	24	No	No	No	No	No	147	119
Mean ± SD/ distribution	9/20 (40%) male	52.1 ± 16.26				65.83 ± 5.02	65.69 ± 3.93	24.2 ± 3.09	24.2 ± 2.94	7/19 (36.84%)	3/17 (17.65%)	0/20 (0%)	3/13 (23.08%)	2/13 (15.38%)	191.35 ± 30.64	130.6 ± 26.18

[1] Electroconvulsive therapy.
[2] Left ventricular ejection fraction.
[3] Tricuspid annular plane systolic excursion.
[4] Maximum systolic blood pressure.

blood pressure [mm Hg]: 218.67 ± 31.53 vs. 190.88 ± 23.2) and heart rates (maximum heart rate [bpm]: 139.67 ± 11.72 vs. 133.69 ± 20.79). The patient with anesthesia-induced sinus bradycardia was excluded from the evaluation. Otherwise, no relevant cardiac arrhythmias were observed in patients undergoing ECT. As a limitation, it should be mentioned that the period of monitoring after ECT was primarily dependent on the subsequent anesthesia-related waking time of the patient and thus, in some cases, relatively short. The occurrence of arrhythmias after the monitoring period cannot be ruled out.

Since there was no continuous circulatory monitoring of the patients with GCS in the epilepsy unit, no comparison could be made.

3.2.2. GCS group

The values of NT-proBNP and cTnT-hs were measured in four patients at three time points. In all measurements, NT-proBNP was normal. One patient with GCS showed an increased cTnT-hs value in the 4–6 h follow-up (14 pg /ml). Because of the patient's young age (26 years) and the lack of clinical signs for myocardial ischemia, no further diagnostics were carried out.

3.3. Metabolic biomarkers: GCS group vs. ECT group

Compared with the patients undergoing ECT (n = 20), the patients with GCS (n = 4) showed significantly elevated serum lactate values (t (3012) = 4871, p = 0.016) and significantly reduced serum bicarbonates (t (22) = 3.388, p = 0.002). By contrast, the difference was not significant when comparing the pH values (t (3067) = 1585, p = 0.209, Table 3).

4. Discussion

The principal aim of this study was to investigate cardiac function and signs of cardiac stress after ECT-triggered seizures and to compare these findings to those after spontaneous GCS. Overall, no significant echocardiographic changes were observed in the study group in both seizure types. However, signs of cardiac stress without apparent clinical symptoms were detected, as transiently elevated cTnT-hs values were found in 4 (23.5%) of 17 patients. We could not determine a significant correlation with drastic increase in blood pressure or heart rate, at least in the ECT group.

Supratentorial and cortical brain areas such as the insula, amygdala, hippocampus, thalamus, and cingulate gyrus are closely involved in the control of cardiovascular and respiratory functions [17,23]. Therefore, it is unsurprising that spontaneously occurring and electrically induced seizures are associated with prominent alterations of autonomic function. However, it remains unclear to what extent the autonomic dysfunction is due to direct cerebral effects following seizure activity, or due to indirect 'peripheral' effects. For instance, spontaneously occurring generalized convulsive seizures (GCS, i.e., focal to bilateral tonic–clonic seizures and generalized onset tonic–clonic seizures) are commonly associated with sustained and unphysiologic contractions of a large number of skeletal muscles along with pronounced tachycardia and respiratory arrest, leading to considerable metabolic stress including acidosis, hypercapnia, and hypoxemia [17]. Furthermore, in people with chronic epilepsy, the cardiorespiratory and metabolic responses to epileptic seizures may be exaggerated, because of long-standing epilepsy-related alterations of the autonomic nervous system [1–24].

The marked metabolic changes in GCS compared with those in ECT-induced seizures were also shown in the comparison of venous blood gas parameters between the two groups of our study. As a sign of metabolic acidosis and hypoxia, patients with GCS showed significantly increased serum lactate levels and significantly reduced serum bicarbonate levels after seizure. The insignificant difference in pH values is probably due only to the small GCS group size.

The fact that the transient cTnT-hs elevations were detected in three cases after ECT suggests that cardiac stress after seizure is not a peripheral effect because of hypoxia or metabolic derailment.

Given the circumstances, it is probable that cardiac stress was induced by an excessive release of catecholamines during the seizures [25], which may be directly cerebrally triggered. Analogously, high-sensitivity assays for troponin have shown striking values following extreme exercise. It has been suggested that troponin release can occur without cardiomyocyte necrosis [26].

It should also be noted that the patient with GCS with elevated cTnT-hs values was significantly younger than the three patients undergoing ECT with elevated cTnT-hs values.

This could possibly indicate that different pathophysiological mechanisms are responsible for the troponin elevation when comparing both types of seizures. The number of cases in our study does not allow us to draw statistically significant consequences in this regard.

Although this is only speculation, because of the lack of determination of catecholamine levels, the present data may be interpreted as a mild subclinical phenotype of a TTS. Takotsubo syndrome is a sudden-onset disease that is clinically similar to acute coronary syndrome. In addition to ECG changes akin to myocardial infarction, echocardiographic transient disorders of cardiac function with wall motion disorders can also be found. Trigger factors can be both mental and physical stressors. These also include diseases of the central nervous system, such as subarachnoid hemorrhage or epileptic seizures [27]. As a pathophysiological mechanism, excessive catecholamine release is discussed. Furthermore, vasospasms and microcirculation disturbances are likely to be present [15].

There are also case reports of TTS after ECT treatment, in which the excessive catecholamine release was also discussed as the cause [10–14]. None of the patients had a lethal course. On the contrary, ECT has been proven as a safe treatment in more than 80 years [28].

Regarding the occurrence of TTS leading to sudden unexpected death in epilepsy (SUDEP) in spontaneous epileptic seizures, there are a number of case reports and reviews. In a review by Stöllberger et al., 36 cases with two fatal courses could be found. In most cases, generalized seizures were present [7]. In another review, 74 cases of TTS were found, of which 3% were fatal [9]. The descriptions show that TTS is an occasional seizure-associated complication, but rarely results in SUDEP. Stöllberger et al. were also able to demonstrate that many patients lack typical symptoms such as chest pain [7]. It can therefore be assumed that, on the whole, there are more likely to be mild subclinical courses of TTS. This is confirmed by the data of the present work with the result of elevated cTnT-hs values in 23.5% of the cases. These are similar to the results of other studies that found troponin elevations in 6.5–28.6% of patients with epilepsy [29–33]. In ECT studies, increases in troponin were also found in 8–11.5% of patients [34–35]. A recent prospective study under video-EEG-controlled conditions revealed that elevations of cardiac troponin and of cTnT-hs occurs in 10% and 26% of the patients following GCS [25], confirming that the use of cTnT-hs improves the detection rate of cardiac stress.

There are only few data on echocardiographic changes after seizures. A case report described a pronounced TTS with markedly reduced EF and apical wall disorders after ECT treatment [10]. In addition, three studies found a transient decrease in left ventricular dysfunction shortly after ECT, with one study even describing wall movement disorders in

Table 3
Compared venous BGA values among GCS and ECT group.

Seizure type	Number of patients	Lactate (mmol/l) (mean ± SD, range)	Bicarbonate (mmol/l) (mean ± SD, range)	pH (mean ± SD, range)
GCS	4	11.33 ± 4.17 7.9–17	15.58 ± 2.24 13.5–18.7	7.25 ± 0.13 7.08–7.38
ECT	20	1.15 ± 0.42 0.5–1.8	25.07 ± 1.49 22.2–28.4	7.35 ± 0.03 7.3–7.39

the sense of hypokinesia [36–38]. In the present study, collective wall movement disturbances or a decrease of the LV or RV function was not detected.

4.1. Implications of the study

Transient cTnT-hs elevations occurred in some patients of our study after spontaneous and ECT-induced seizures. This is in good accordance with the literature, reflects the high sensitivity of the method, and probably reflects the stress due to the temporary increase in blood pressure and catecholamines. At the same time, the postictal echocardiography did not show any pathological changes and neither did the clinical course. Therefore, our measurements can presently not be associated with an increased clinical risk.

4.2. Limitations of the study design

One of the main limitations of the study is the relatively small sample size, particularly of patients with epilepsy with GCS, and the resulting imbalance in group sizes. Further limitations exist because of the examiner dependence of the echocardiography method and the fact that not all measurements and bloodwork (cTnT-hs and BNP values) could be obtained from all patients.

4.3. Conclusion

Signs of mild cardiac stress are not uncommon after ECT-induced seizures and GCS, which are likely due to seizure-related excessive catecholamine release and increases in blood pressure in patients without cardiac disease. The treating clinicians should be aware of these laboratory findings. The clinical significance is unclear to date. Larger longitudinal studies are needed to evaluate the clinical relevance of these findings.

Declaration of competing interest

Rainer Surges has received fees as speaker or consultant from Bial, Cyberonics, Desitin, Eisai, LivaNova, Novartis, and UCB Pharma. The other authors declare that they have no potential conflict of interest.

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