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ORIGINAL ARTICLE

Factors affecting long-term prognosis in adult patients with psychogenic non-epileptic seizures

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Background and purpose – Among epileptic patients who are monitored using the video-electroencephalography monitoring (VEM) technique, in some patients a psychogenic non-epileptic seizure (PNES) can be identified as a definitive diagnosis. The long-term prognosis of these patients is not well known. In this study, we aimed to determine the factors that affect the prognosis of PNES.
Methods – Forty-one PNES patients diagnosed using VEM between 2012 and 2022 were questioned about their PNES frequencies in the last 12 months. According to their semiological characteristics, PNES types were divided into motor and non-motor seizures. The effects of clinical characteristics (e.g. age, gender, marital status, education level and PNES type) on the prognoses were identified.
Results – Twenty-one PNES patients (51.2%) had long-term seizure freedom after VEM. Thirteen of them (31.7%) entered the seizure-free period immediately after VEM, and the other eight (19.5%) continued suffering from PNES for several years and became seizure free in the last 12 months. In the poor-prognosis group, female cases showed worse prognoses than male cases. The prognoses of motor and non-motor PNES types did not show significant differences.
Conclusion – This study showed that 51.2% of the PNES patients examined had long-term seizure freedom and that female patients had worse prognoses than male patients.

Keywords: psychogenic non-epileptic seizures, long-term prognosis, video-EEG monitoring, epilepsy

A hosszú távú prognózist befolyásoló tényezők pszichogén nem epilepsziás rohamokkal küzdő felnőtt betegeknél

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Háttér és cél – Azon epilepsziás betegek közül, akiknek megfigyelését video-elektroencefalográfiás monitorozás (VEM) technikával végzik, egyes betegeknél definitív diagnózisként pszichogén nem epilepsziás roham (PNES) azonosítható. Ezen betegek esetében a hosszú távú prognózis nem ismert eléggé. Jelen tanulmány célja a PNES prognózisát meghatározó tényezők azonosítása.
Módszerek – A 2012 és 2022 közötti időszakban VEM által diagnosztizált 41 PNES-betegünket kérdeztük arról, hogy milyen gyakran tapasztaltak PNES-t az elmúlt 12 hónapban. Szemiológiai jellemzők szerint a PNES-típusokat motoros és nem motoros rohamokra osztottuk. Azonosítottuk a klinikai jellemzők (például életkor, nem, családi állapot, iskolai végzettség, PNES-típus) prognózisra gyakorolt hatását.
Eredmények – Huszonegy PNES-betegnél (51,2%) volt hosszú távú rohammentesség a VEM után. Közülük 13 (31,7%) közvetlenül a VEM után lépett be a rohammentes időszakba, a másik nyolc (19,5%) pedig több évig szenvedett PNES-ben, és az elmúlt 12 hónapban vált rohammentessé. A rossz prognózisú csoportban a nők rosszabb prognózist mutattak, mint a férfiak. A motoros és nem motoros PNES-típusok prognózisa nem különbözött szignifikáns mértékben.
Következtetés – Tanulmányunk a PNES-betegek 51,2%-a esetében mutatott hosszú távú rohammentességet; a nőbetegek prognózisa rosszabb volt, mint a férfiaké.

Kulcsszavak: pszichogén nem epilepsziás rohamok, hosszú távú prognózis, video-EEG-monitorozás, epilepszia

Psychogenic non-epileptic seizures (PNES) consist of paroxysmal motor, non-motor, or behavioural changes that resemble an epileptic seizure without electroencephalogram (EEG) correlates. This disorder is considered to reflect responses to distress or behavioural problems. According to the DSM–5, PNES is a sub-group of conversion disorders or, as indicated by the ICD–10, a dissociative disorder[1, 2]. Video-EEG monitoring (VEM) is the gold standard in the differential diagnosis of PNES versus epileptic seizures. Psychogenic non-epileptic seizure is diagnosed in 20–40% of patients hospitalised with drug-resistant epilepsy in tertiary VEM units, after which changes are made in the treatment of these patients[1]. The treatment of PNES consists of psychotherapy and medication for the accompanying psychiatric disorders[3, 4]. Long-term follow-up and treatment are required to achieve good results[5], but the prognosis of adult PNES is not very satisfactory and seizure freedom may be reached in only 40% of cases within five years after diagnosis[6].

Cultural differences (e.g. marital status, family support, and women's rights) may cause variations in the prognoses of PNES patients. Therefore, we aimed to determine the long-term prognoses of adult PNES patients in our population and the factors that affect their prognoses.

Materials and methods

The data of 470 adult patients (> 18 years old) who were admitted to the VEM unit of the Neurology Clinic between 2012 and 2022 were retrospectively analysed for the differential diagnosis of epilepsy or pre-surgical evaluation. Forty-one patients (8.7%) were diagnosed with PNES. The interictal and ictal EEG data of the PNES patients were found to be normal. Concurrent epilepsy and PNES were detected in 12 patients, but these cases were not included in the study because of their low numbers. Among the PNES cases, there was no case in which seizure freedom was achieved with a successful epilepsy surgery or medical treatment in the past. Seizures were evaluated by double peer reviews – one neurologist and one epileptologist. A recording of one habitual type of PNES was sufficient for diagnosis.

Data about age, gender, duration of illness before diagnosis, educational level, employment (fully or partially employed vs. unemployed), marital status (married or cohabiting vs. single), medications used, comorbid diseases, a history of head trauma and a family history of epilepsy were obtained from the hospital database. Patients who were using any psychiatric pharmacotherapy against depression or anxiety disorder were considered as having previous psychiatric treatment before VEM, and they were noted as cases with psychiatric comorbidities. After the diagnosis of PNES in VEM, all patients consulted with a psychiatrist. Deficits found in the neurological examination were noted. Brain tumours, parenchymal gliosis, mesial temporal sclerosis and cortical dysplasia found in magnetic resonance imaging (MRI) of the brain were recorded as abnormal MRI findings.

The frequencies of PNES before and during VEM was also recorded. According to the semiological characteristics of the PNES patients, seizure types were recorded as motor or non-motor. Motor PNES had prominent motor behaviours, whereas non-motor PNES had either no motor signs (e.g. long periods of motionlessness, and unresponsiveness, often accompanied by waxy flexibility) or only minor motor behaviours, such as low-amplitude, near-purposeful movements of the face or upper extremities, low-amplitude rhythmic/synchronous bilateral movements, crying, blinking and hyperventilation. Motor PNES was defined as brief four-extremity asynchronous (often violent) movements and long spells that included unusual behaviours (e.g. rocking, screaming and thrashing)[7].

Patients were questioned about their seizure frequencies in the last 12 months, either face to face at the outpatient clinic or by phone if meeting personally was not possible, to ascertain the prognoses. Cases who did not have seizures in the last 12 months were considered to have good prognoses, and those who continued to have seizures were considered to have poor prognoses.

Our study was approved by the local Scientific Research Ethics Committee on 8 April 2019 with decision number 07/04 and written informed consent about their inclusion in the study was obtained from all the participants. The study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

The results were expressed as means ± standard deviations or numbers (percentages). The compatibility of qualitative data with normal distribution was examined using the Shapiro–Wilk test. The Mann–Whitney U test was used to compare the numeric values of the PNES groups. Pearson's, Yates's or Fisher's chi-squared tests were used to compare categorical data between PNES groups. Statistical analyses were performed using SPSS 20.0 (License No: 10240642) package programme. A p value <0.05 was accepted as a statistically significant limit value.

Results

The mean age of the cases at PNES onset was 26.54 ± 12.06 years. The mean duration from the onset of the disease to the time of admission for VEM was 6.2 ± 6.3 years.

Comorbid diseases were present in 53.7% (22/41) of the patients. The most common comorbid diseases

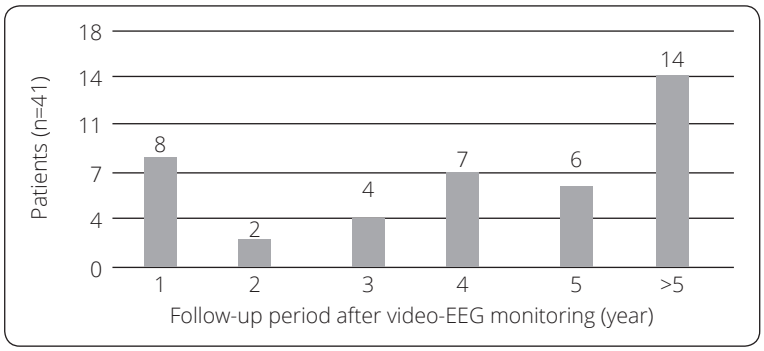

Figure 1. *Follow-up period after video-EEG monitoring*

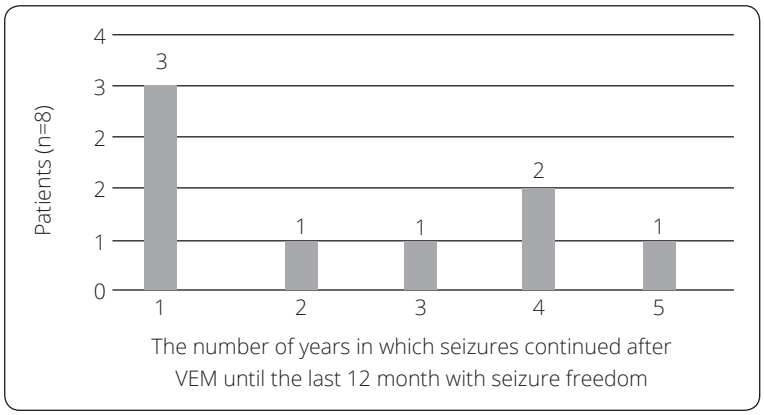

Figure 2. *Time interval between the PNES diagnosis and seizure freedom*

were headache, asthma and hypertension. Conversion disorder, depression and anxiety disorder were already diagnosed before VEM in seven, five and three patients, respectively. After their psychiatric consultations during VEM, 16 patients were additionally diagnosed as having psychiatric morbidities. No psychopathology was found in the remaining 10 patients. Eighty-five percent of patients were already using antiepileptic medications prior to VEM.

The average follow-up period of the PNES patients was 4.1 years (1–7 years). The years between the PNES diagnosis via VEM and the questioning of the prognosis are shown in **Figure 1**.

Twenty-one (51.2%) patients were found to be seizure free in the last 12 months. Thirteen of these cases (31.7%) entered a seizure free period immediately after VEM. The other eight (19.5%) continued suffering from PNES for several years, as shown in **Figure 2**, and became seizure free in the last 12 months before the onset of the study. We recorded 100 PNES in total, of which 39 (39%) were of the motor type and 61 (61%) were of the non-motor type. The prognoses of the two groups did not show significant differences.

The remaining 20 (48.8%) patients continued to have PNES and constituted the poor-prognosis group. Female cases had worse prognoses than male cases. The number of PNES before and during VEM was not different between the two prognosis groups. Education, work and marital status, previous psychiatric treatment history and its duration, a family history of epilepsy, use of anti-epileptic drugs, comorbid status, psychiatric treatment in the post-diagnosis period, presence of pathological findings in the neurological examination and cranial MRI, and duration of VEM were found to have no effects on prognosis. After VEM, 31 of 41 PNES patients (75.6%) were followed up by a psychiatrist and continued to receive pharmacotherapy **(Table 1)**.

Discussion

Our study showed that 51.2% of the patients with PNES achieved a long-term seizure freedom after VEM. The female patients showed poorer prognoses.

Various studies have reported remissions ranging from 17% to 55% in adult PNES patients[5, 8–16]. The identification of prognostic factors will undoubtedly contribute greatly to the regulation of PNES treatment and the follow-up of patients, but unfortunately, clinical studies to identify consistent risk factors are scarce in the literature[6, 14]. At the same time, the different methodologies used in these studies make it difficult to compare research results. Recovery (remission) was defined as a more than 50% reduction in seizures in some studies[17, 18], while in others[5, 9, 19–21], it was defined as complete seizure freedom. In addition, the duration of seizure-free periods varies greatly between studies, ranging from two weeks to 10 years[3, 5, 9, 15, 19, 22]. The patients in our study who did not have PNES in the last 12 months were considered in remission.

High good prognosis rates have been reported in studies with short follow-up periods. Two small-scale studies with a duration of 1–14 days after diagnosis of PNES with VEM showed very high seizure freedom rates of 69% and 81%, respectively[23, 24]. In a large study with 260 PNES patients who were followed up for a period of 6–12 months, the seizure freedom rate decreased to 38%[9]. The results of follow-up studies lasting more than one year were much less satisfactory. *Bodde* et al.[25] reported complete remission in 32% of patients in a four-to six-year follow-up. *Massot-Tarrús* et al.[18] found complete remission in only 26.8% of the patients in a mean follow-up study of 3.3 years. A good prognosis was associated with

Table 1. *Prognostic factors in PNES cases at the time of diagnosis*

	Good prognosis n = 21 (51.2%)	Poor prognosis n = 20 (48.8%)	p
Age	33.48±12.95	32.05±10.56	Ns
Gender (f/m)	10/11	19/1	<0.01
Age at the onset of PNES (year)	27.62±13.59	25.4±10.44	Ns
Time period till VEM (year)	5.85±4.60	6.65±7.88	Ns
Education (<8 year/>8 year)	11/10	7/13	Ns
Employment (yes/no)	16/5	15/5	Ns
Marital status (single/married)	11/10	7/13	Ns
Family history of epilepsy (yes/no)	3/18	7/13	Ns
Abnormal finding in neurological examination (yes/no)	2/19	2/18	Ns
Abnormality on MRI (yes/no)	3/18	5/15	Ns
Comorbid disease (yes/no)	11/10	11/9	Ns
Previous psychiatric treatment (yes/no)	10/11	5/15	Ns
Duration of psychiatric treatment before VEM (year)	1.57±2.35	0.90±1.83	Ns
Duration of AED treatment (year)	4.19±3.50	3.50±6.29	Ns
Number of AED's before VEM	1.52±0.92	1.75±1.07	Ns
Duration of VEM (day)	5.10±2,36	4.15±2.51	Ns
Number of PNES before VEM (n/year)	140.95±197.51	110.75±143.69	Ns
Number of PNES during VEM (n/day)	0.64±0.54	1.12±1.98	Ns
Psychiatric treatment in post-diagnosis period (yes/no)	17/4	14/6	Ns
Type of PNES			
Motor	22/55 (40%)	17/45 (38%)	Ns
Non-motor	33/55 (60%)	28/45 (62%)	Ns

Ns: not significant; AED: antiepileptic drug; VEM: video-EEG monitoring

an early diagnosis in both studies. In another study, which had a long follow-up[5], only 16% of the patients entered complete remission for 1–10 years after diagnosis with VEM, and PNES was still sustained in 71% of the patients. More recently, *Walther* et al.[10] reported that 37% of patients had no seizures in the last 12 months, with a follow-up of 1–16 years after the diagnosis of PNES. Late age at onset and high introversion were shown to be poor prognostic factors in these patients. Although not consistently found in all studies, an early diagnosis[5, 18], a young age of onset[5, 15], a short illness period[15], high education[5, 19], an independent lifestyle[22], good family relationships[19, 26], acceptance of the diagnosis by the patient[25], less dramatic seizures[5, 16, 21], and a low somatoform and dissociative score[5, 8, 9, 22, 27] were associated with good prognosis.

It has been reported that the diagnosis of patients with PNES is delayed by an average of 7.2 years and, in some case series, by 10–15 years[25, 28]. Some researchers have found that a delayed diagnosis affects the prognosis of PNES negatively[28, 29], while others have found limited[21] or no effects at all[5, 22]. Psychogenic non-epileptic seizures are most commonly present in the third decade of life, but they can affect all age groups, including children and the elderly[5, 22, 28, 30]. Studies have shown that children with PNES achieve 70–80% remission rate, and have better prognoses than adults[31, 32]. The prognosis of PNES is reported to be better in children than in adults, with a possible explanation that the causes are external to the child, easier to detect and more prone to immediate intervention[33]. In our study, the age of onset of PNES and the delayed diagnosis of PNES had no effects on the prognoses of the patients.

In our study, gender appeared to be the sole factor affecting long-term PNES prognosis. Nineteen of the 20 patients with poor prognoses were female, and one was male. The average number of seizures in patients with poor prognoses in the past 12 months was significantly higher in females than in males. Similar to our study, *McKenzie* et al.[9] reported lower long-term recovery rates in female PNES cases. However, several studies have also reported better prognoses in female PNES cases or same prognosis in both genders[16, 22, 34].

The prevalence of comorbid diseases in PNES is about 65.8%[35]. Their existence may facilitate the emergence of psychogenic seizures and may have negative effect on long-term prognosis[36]. Our findings did not support such an effect of comorbidities on prognosis. About half of our PNES cases (53.7%) had accompanying diseases, such as chronic headache, hypertension and asthma. Taking psychiatric treatment before or after VEM also did not affect the prognoses of our PNES patients. The prevalence of psychiatric comorbid conditions in PNES ranges

from 53% to 100%[37, 38]. Among the psychiatric conditions associated with PNES, depression, anxiety, somatisation disorder and conversion disorder were reported[21, 39, 40]. While a single comorbid psychiatric disease can occur in patients with PNES, sometimes more than one may exist simultaneously in the same patient[39]. Better prognosis of PNES was reported in patients with a single depressive episode and with low somatoform and dissociation score[41]. Those with continuing depressive episodes have poor prognosis[42].

Thirty-one percent of the cases diagnosed as PNES with VEM stopped having seizures immediately after their diagnoses. We assumed that the fact that the patients knew that seizures were evaluated in detail through camera recordings played a role in their acceptance of their diagnoses. Video-electroencephalography monitoring units are mostly located in tertiary health institutions or epilepsy centres. We supposed that a diagnosis by physicians specialising in epilepsy made it easier for the patients to accept their conditions. The rates of receiving psychiatric treatment after diagnosis did not differ statistically between patients with good and poor prognoses. Therefore, psychiatric drugs used after diagnosis were not analyzed in this study.

The limitations of our study are its retrospective nature and the different follow-up periods after VEM diagnosis. Our sample size was small relative to the large number of independent variables of interest. The number of gender groups was too small compare to the gender characteristics. Unfortunately, we had no clear data about some important prognostic factors, such as sexual abuse, trauma, IQ and social background, because the study was retrospective. Additionally, we did not ask about any occasions of sexual abuse during the questioning of the prognosis, as we were not certain that all patients would tell the truth. The types of psychotherapy and pharmacotherapy could not also be evaluated in our analysis, as most of our patients applied to the psychiatry outpatient clinic in another center. The positive aspect of our study is that diagnoses were made using the gold standard of VEM.

Overall, our study showed that 51.2% of the patients with PNES after VEM have long-term seizure freedom, but the prognosis is poor in female patients.

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