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First epileptic seizure and quality of life – A prospective study

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ABSTRACT

Objective: Impaired QoL and depression are common in patients with chronic epilepsies; however, data on the impact of a first seizure on QoL are sparse. According to the current ILAE-definition of epilepsy, patients may be diagnosed with epilepsy immediately after the first seizure, if EEG and/or imaging findings are abnormal. Patients with normal findings in imaging and EEG are not diagnosed as having epilepsy. We investigated QoL in patients after a first seizure with and without a consecutive diagnosis of epilepsy to detect differences between groups within the first year after seizure.

Methods: We examined patients ($n = 152$) after a first epileptic seizure and six and 12 months thereafter using demographic, clinical and QoL-related questionnaire data (Short Form-36 Health Survey (SF-36), Quality of Life in Epilepsy Inventory-31 (QOLIE-31), Beck's depression inventory II (BDI-II)).

Results: Patients diagnosed with epilepsy after the first seizure showed a tendency of reduced mental health-related QoL six ($p = .098$) and 12 months ($p = .092$) after the first seizure compared to patients who were not diagnosed with epilepsy, but were diagnosed as having had a single first seizure. There were no significant differences between the two groups in physical health-related QoL. Multiple regression analyses showed that especially depressive symptoms explained 22.0 – 48.7 % of the variance in mental health-related QoL six ($p < .001$) and 12 months ($p < .001$) after the first seizure. Physical health-related QoL was especially predicted by age ($p < .001$), group ($p = .002$) and recurrent seizures ($p = < 0.001$). In PWE, there was a statistical trend with improving QOLIE-31 overall scores from six to 12 months ($p = .086$).

Conclusion: Our results suggest that QoL may be impaired in patients diagnosed with epilepsy early, immediately after the onset of disease. Early follow-up monitoring from the beginning of patient career is important for possible interventions and to improve patients' daily life in the long term.

1. Introduction

Quality of life (QoL) is impaired in patients with epilepsy (PWE) [1,2,3]. This may be facilitated not only by antiseizure medication (ASM)[4] and seizure frequency[2], but also by associated limitations in daily life concerning driving, work and leisure activities. This issue was targeted early[5], unraveling QoL to be not vague but explicitly described by epilepsy patients, naming driving, employment and independence as the three most important aspects of daily living. The concept of health-related QoL can be divided into mental and physical components (see SF-36; [6]). In epilepsy patients, it is commonly assessed by epilepsy-specific QoL questionnaires, e.g. QOLIE-31[7,8]. Another important predictor of QoL is emotional wellbeing. With a prevalence of 25–50 %[9], psychiatric disorders, and depression in particular [10] are common in PWE. Apart from ASM and seizure frequency [1], depression appears to be one specific major predictor of QoL perception, not only in various population studies[11,12], but also in PWE. In addition, reduced QoL is associated with comorbid depression in PWE [3]. A recent study investigated predictors of QoL in a large multicenter, cross-sectional study in epilepsy patients[13]. Results showed that seizure frequency, tolerability of ASM and presence of depression, stigma and worry about seizure recurrence were associated with poorer QoL[13]. The authors suggested that apart from seizure control, psychosocial factors should be taken into account in the

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therapeutic process in order to support QoL in the context of a chronic disease. Impairments in QoL have further been found in various patient groups, including various epilepsy syndromes, gender and ethnicity [14,15,16]. Treatment options may comprise antidepressant drugs, an adjustment of anticonvulsant therapy or adjuvant psychotherapy [17].

While the interplay between QoL and depression has been extensively studied in PWE, few studies have looked at patients immediately after a first epileptic seizure. The experience of a seizure as a potentially life threatening event can be traumatic and is associated with perceived loss of control [18], eventually requiring therapeutic support in some cases. This is underlined by a recent study, which identified a comparable prevalence of mood disorders and suicidality in patients newly diagnosed with focal epilepsy[19] and patients with established epilepsy. Another recent study demonstrated an association between depression and a first seizure. It showed, that patients with a first seizure had increased depressive symptoms compared to a control group. This was particularly true for patients who had just received a diagnosis of epilepsy compared to patients diagnosed with a single seizure[20]. However, the study did not focus on QoL as a broader concept, possible confounding factors such as age [21,22], anti-seizure treatment or seizure frequency were not considered and there were no longitudinal data.

If a patient presents after a first unprovoked epileptic seizure, the diagnosis of epilepsy depends on the presence of epileptiform discharges in the EEG and /or the presence of a potential epileptogenic lesion identified by brain imaging (MRI or CT scan)[23,24]. If at least one of these pathologic findings is identified, the diagnosis of epilepsy is given and treatment with ASM is recommended. QoL and emotional wellbeing are of great importance for the patients' everyday life and up to date, little is known about their course in the early patients' careers, immediately following the first epileptic seizure. The current study investigated the presence of these mechanisms in a sample of patients immediately after a first epileptic seizure as well as during follow-up appointments at 6 and 12 months. We hypothesized that (1) there would be differences in health-related QoL between PWE and patients without a diagnosis of epilepsy (nPWE) within 12 months after the initial event. Within the PWE group, we further expected (2) the contribution of further seizures, depression and age on mental and physical health-related QoL.

2. Methods

2.1. Participants and design

Starting from February 2018, patients who presented with a first epileptic seizure at the University Hospital Marburg, Germany, were prospectively recruited to take part in the study. Assessment was performed at baseline (first visit), after six months and one year and involved questionnaires, demographic data and clinical data derived from the local clinical information system Orbis (Dedalus Healthcare Systems Group, 2020). The present sample comprises patients who completed the one year follow-up assessment. The study was approved by the local IRB of University Hospital Marburg (AZ 199/17) and all patients gave written informed consent. The study was conducted in accordance with the Declaration of Helsinki and the STROBE guidelines [25] were followed to minimize methodological bias (see supplemental material). This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

2.2. Measurements

At all time points, demographic data including age, gender, educational level and occupational status were collected. Clinical data comprised the date of first epileptic seizure, the clinical diagnosis of epilepsy, ASM administration and type, the presence of recurrent seizures and, if applicable, the seizure type. Questionnaires to examine QoL included the German versions of the SF-36 (Short-Form-36 Health Survey; [6]) and the QOLIE-31 (QoL in Epilepsy Inventory;[7]). Depressive symptoms were assessed with BDI-II (Becks Depression Inventory; [26]). All patients received the SF-36 and the BDI-II at all times of assessment. Patients who were diagnosed with epilepsy after their first seizure additionally filled in the QOLIE-31 upon all follow-up appointments.

2.3. Statistical analyses

Statistical analyses were performed using the statistic software SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp). Raw scores of SF-36 were transformed and standardized following the respective manual[6] to determine the mental (MCS) and physical component scores (PCS) and to compare levels of QoL to the normative population qualitatively. QOLIE-31 scores were calculated using a computer software. Mann-Whitney U tests were calculated to inspect group differences between PWE and nPWE at the three assessment time points respectively. Multiple regression analyses were calculated to examine an influence of BDI-II, age and seizure recurrence on MCS and PCS while considering group as factor at six months and one year respectively, resulting in four multiple regressions. Therefore, a Bonferroni correction for multiple testing was applied. Differences between six months and one year in QOLIE-31 overall score in epilepsy patients were examined using paired-samples *t*-test.

2.4. Data availability

Data can be obtained from the corresponding author upon reasonable request.

3. Results

3.1. Sample characteristics

The sample consisted of $n = 152$ patients (41.4 % female), $M_{age} = 58.60$, $SD = 20.02$, range 18 – 95 years. Fig. 1 demonstrates the dropout rates at each two follow up appointment.

Of all patients, 39.5 % ($n = 60$) were 65 years or older upon first seizure. Demographic and clinical data assessed at BL are presented in Table 1. Following the first seizure, 69.1 % ($n = 105$) of patients were diagnosed with epilepsy and received ASM; 10.5 % ($n = 16$) passed away in the course of the study, of which 75 % were 65 years or older and 50 % suffered from previously diagnosed brain tumors. According to close anamnesis upon enrolment in the study, $n = 21$ (13.8 %) patients stated that they might have suffered from a former seizure without noticing or recognizing an incident as such. The majority of those patients were consecutively diagnosed with epilepsy, while $n = 1$ patient remained in the nPWE group.

3.2. Group analyses

Table 2 summarizes the questionnaire scores given by the patients at the different appointments.

Using Mann-Whitney *U* test, we investigated possible group differences in physical health-related QoL (SF-36, PCS) at the three assessment time points. There was overall no significant difference in perceived physical health-related QoL neither at baseline (U (33, 56) = 836.00, $z = -0.75$, $p = .466$), nor six months after the first seizure (U (17, 42) = 293.00, $z = -1.07$, $p = .284$) or after one year (U (15, 35) = 216.00, $z = -0.98$, $p = .325$). There was no significant difference between PWE and nPWE in terms of physical health-related QoL within the first year after a first seizure. Applying the same approach for mental health-related QoL (SF-36, MCS), there was no significant difference between groups at baseline (U (33, 56) = 863.00, $z = -0.52$, $p = .604$). There was a statistical trend that PWE would differ from nPWE six months after a first seizure (U (17, 42) = 258.00, $z = -1.68$, $p = .098$), in which PWE

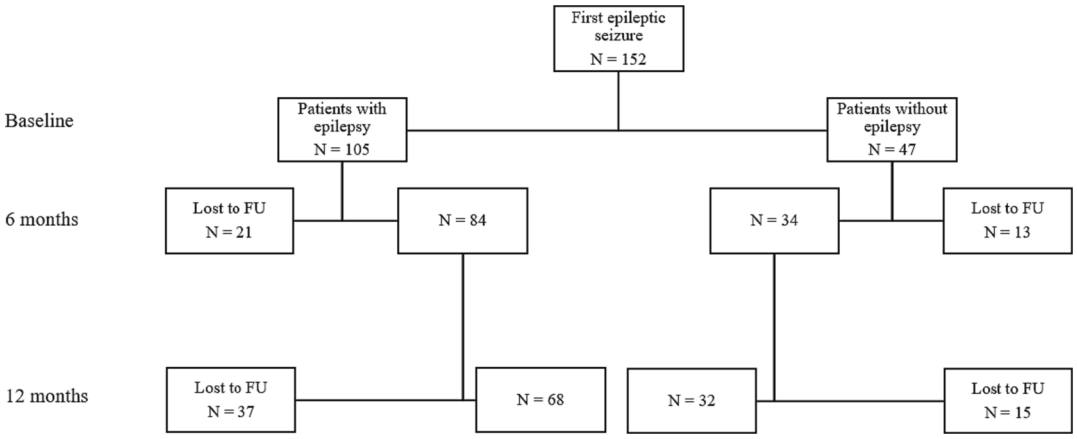

Fig. 1. Sample sizes and dropout rates at each measurement. FU = follow up.

Table 1
Demographic and clinical data at baseline (N = 152).

	Patients with epilepsy *N* = 105 (69.1 %)	**Patients without epilepsy** *N* = 47 (30.9 %)
Age[a]	62.58 ± 19.23	49.70 ± 19.04
Gender[b]		
Male	55 (52.4)	34 (72.3)
Female	50 (47.6)	13 (17.7)
Etiology[b]		
Generalized	11 (10.7)	–
Focal – structural	77 (74.8)	–
Focal – unspecified	15 (14.6)	–
Acute symptomatic	–	20 (42.6)
unspecified	–	27 (57.4)
Status epilepticus[b]	24 (23.8)	1 (2.2)
Seizure recurrence[b]		
After six months	35 (39.3)	2 (5.6)
After 12 months	12 (14.6)	1 (2.7)
Antiseizure medication[b]		
Administered in total	98 (93.3)	8 (17.0)
Levetiracetam	63 (60.0)	6 (12.8)
Lamotrigin	8 (7.6)	1 (2.1)
Lacosamid	18 (17.1)	1 (2.1)
other	9 (8.6)	–
Polytherapy BL	5 (4.8)	0 (0.0)
Polytherapy after six months	6 (6.9)	0 (0.0)
Polytherapy after 12 months	3 (4.3)	0 (0.0)
Premorbid depression[b]	6 (5.9)	4 (8.7)
Educational level[b]		
≤ 10 years	32 (68.1)	15 (60.0)
> 10 years	15 (31.9)	10 (40.0)
Currently employed[b]	26 (42.6)	23 (71.9)
Passed away[b]	14 (13.3)	2 (4.3)

Note. [a] = numbers displayed as means ± standard deviations. [b] = numbers displayed as total amount of patients (percentages).

Table 2
Questionnaire scores (SF-36, BDI-II, Qolie-31) per patient group.

	PWE BL	6 months	12 months	**nPWE** BL	6 months	12 months
SF-36 MCS[a]	-0.29 ± 0.93	-0.42 ± 0.89	-0.25 ± 1.06	-0.18 ± 0.93	-0.03 ± 0.79	0.16 ± 0.81
SF-36 PCS[a]	-0.61 ± 1.29	-0.34 ± 1.14	0.01 ± 1.01	-0.40 ± 1.11	-0.02 ± 0.79	-0.20 ± 0.99
BDI-II[a]	8.94 ± 8.19	9.07 ± 9.85	6.38 ± 7.74	5.84 ± 5.98	5.24 ± 6.54	3.60 ± 4.97
Unaffected[b]	28 (53.8)	24(58.8)	25(73.5)	24 (75.0)	12 (70.6)	14 (93.3)
Minimal[b]	12 (23.1)	5(12.2)	3(8.8)	4(12.5)	4(23.5)	–
Mild[b]	6(11.5)	6(14.6)	4(11.8)	3(9.4)	–	–
Moderate[b]	4(7.7)	4(9.8)	1(2.9)	1(3.1)	1(5.9)	1(6.7)
Severe[b]	2(3.8)	2(4.9)	1(2.9)	–	–	–
QOLIE-31[a]	–	61.03 ± 15.38	67.44 ± 13.37	–	–	–

Note. [a] = numbers displayed as means ± standard deviations. [b] = numbers displayed as total amount of patients (percentages). BL = baseline. PWE = patients with epilepsy. nPWE = patients with no epilepsy. MCS = mental component score. PCS = physical component score. BDI = Beck Depression Inventory. QOLIE = quality of life in epilepsy patients.

would display lower scores (Md = -0.42) compared to nPWE (Md = 0.29). Similar results were found comparing groups one year after a first seizure (U (15, 35) = 183.00, z = -1.68, p =.092); PWE showed again a tendency to score lower on MCS (Md = -0.11) than nPWE (Md = 0.40). Note that these are standardized mean scores. Yet, a higher score indicates better subjective well-being as measured by SF-36.

For multiple regression analyses, Bonferroni corrected p-values (p_c) were reported. A multiple regression investigated the influence of BDI scores, ongoing epileptic seizures, group and age on physical health-related QoL (PCS) six months after a first seizure. The total variance explained by the model was $R^2_{adj} = 0.28$, F (4, 52) = 6.34, $p_c < 0.001$. Age was the strongest significant predictor of PCS (beta = -0.47, t(152) = -3.83, $p_c < 0.001$), uniquely explaining 18.92 % of the variance in PCS. BDI was also a significant predictor of PCS (beta = -0.43, t(58) = -3.67, p_c 0.002) and uniquely explained 17.39 % of the variance in PCS. Group ($p_c = 0.950$) and further epileptic seizures were no significant predictors of PCS (p_c = 1.00). Using the same approach with respect to mental health-related QoL at six months (MCS), the model explained 27.2 % of the variance, F (4, 52) = 6.23, $p_c < 0.001$. As in PCS, BDI was a significant predictor of MCS and uniquely explained 22.00 % of the variance (beta = -0.49, t(58) = -4.11, $p_c < 0.001$). There was a significant effect of age, which uniquely explained 8.52 % of variance (beta = -0.31, t(152) = -2.56, $p_c = 0.03$), while ongoing seizures ($p_c = 0.710$) and group (p_c = 1.00) were again not significantly predictive of MCS. Thus, six months after the first seizure, age and depressive symptoms significantly predicted physical and mental health-related QoL in both patient groups (Fig. 2A).

The same analysis was applied on the data acquired one year after the first seizure. Using multiple regression, the whole model containing BDI scores, age, group and the presence of recurrent seizures explained 52.5 % of the variance in PCS, F (4, 42) = 13.70, $p_c < 0.001$. Age was the strongest predictor (beta = -0.55, t(152) = -5.16, $p_c < 0.001$) and uniquely explained 27.46 % of the variance in PCS. Recurrent seizures were also a significant predictor (beta = -0.48, t(119) = -4.62, $p_c <$ 0.001) and uniquely explained 22.00 % of the variance. The factor group

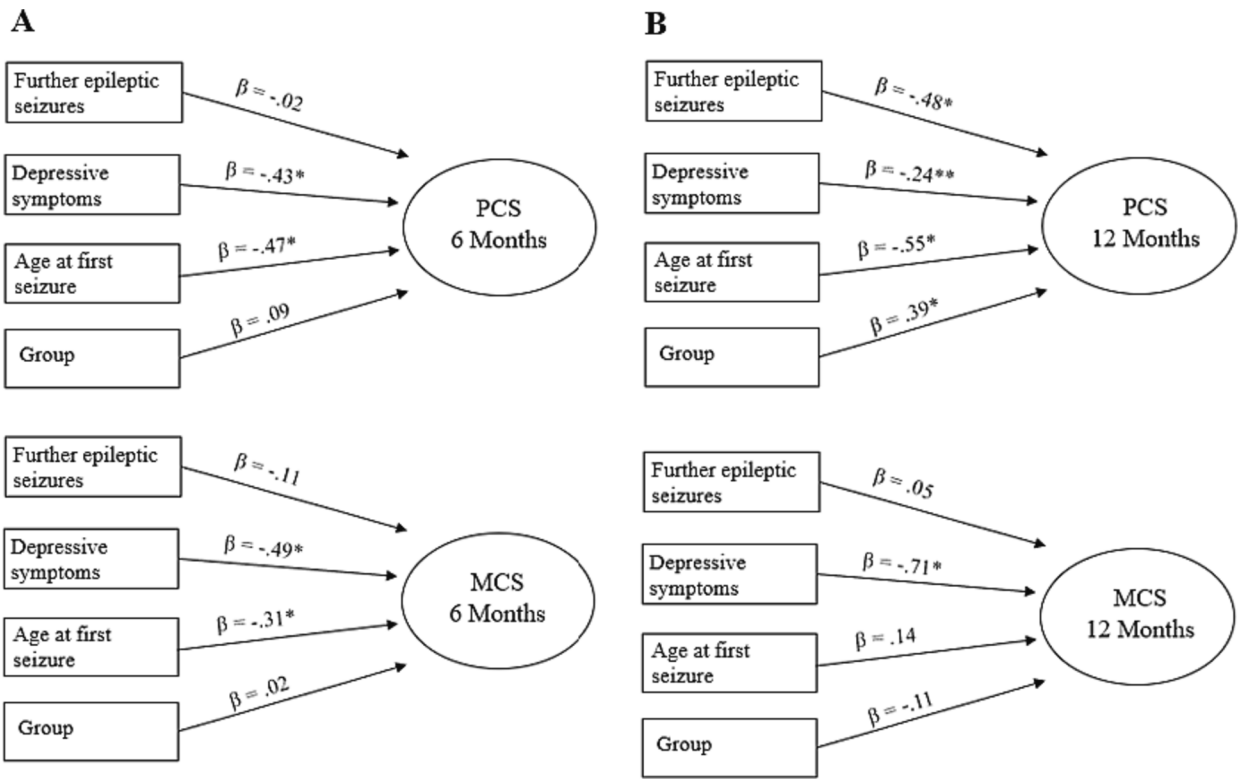

Fig. 2. Beta weights of respective predictors on dependent variables (PCS, MCS). * = significant at α = 0.05 after Bonferroni correction. ** Statistical trend (p =.054). PCS = physical component score. MCS = mental component score.

reached statistical significance (beta = 0.39, $t(152) = 3.54$, $p_c = 0.002$), uniquely explaining 13.00 % of the variance indicating an association between PWE group and lower PCS scores. There was a statistical trend that BDI-II scores contribute to the model (beta = -0.24, $t(49) = -2.30$, p_c = 0.054). With respect to MCS, the whole model explained 51.0 % of the variance, $F(4, 42) = 12.95$, $p_c < 0.001$. Here, the only significant predictor of mental health-related QoL after one year were the BDI scores (beta = -0.71, $t(49) = -6.77$, $p_c < 0.001$), which uniquely explained 48.86 % of the variance in MCS. In summary, physical health-related QoL was predicted by group, age and consecutive seizures, while mental health-related QoL was particularly predicted by depressive symptoms one year after the first seizure (Fig. 2B).

3.3. QoL in epilepsy patients

Using the respective manual of SF-36, we calculated z-scores to determine the relative differences in our sample to the German normative population ($n = 2914$) for both PWE and nPWE. Both patient groups indicated their perceived QoL as slightly lower than or similar to the normative group but did not exceed more than 1 SD on the mean level, which would generally speak for perceived QoL below average. Chi-square tests of independence investigating an association between groups and reduced/normal/above average categories revealed overall no significant results (all p >.05). Fig. 3 illustrates the frequencies of both patient groups scoring below average on an individual level.

To determine the differences in epilepsy-associated QoL, measured with QOLIE-31, six months versus one year after a first seizure, a paired samples t-test was calculated. There were was a statistical trend that there would be differences between the two time points, $t(23) = -1.79$, p =.086. Results indicate that there was a gradual improvement in epilepsy-associated QoL from 6 months after seizure ($M = 64.71$, SD = 12.97) to one year thereafter ($M = 69.31$, $SD = 12.57$) in patients who were diagnosed with epilepsy after a first seizure. T-transformed scores indicated an average QoL both six months (T = 49) and one year (T = 53) after the first epileptic seizure.

4. Discussion

In our study, we found that ongoing seizures, emotional well-being and age of patients contribute not only to QoL in a broader sense, but specifically to physical and mental components of this construct. Regarding physical health-related QoL, we found no significant differences between patients with or without immediate epilepsy diagnosis after a first seizure at either time point. Within one year after the first epileptic seizure, patients diagnosed with epilepsy immediately after the first seizure were more likely to report worse mental health-related QoL after six months and one year compared to patients not diagnosed with epilepsy. There was no significant difference between groups at baseline. Data from the MESS UK study showed lower perceived QoL in patients with epilepsy and ongoing seizures compared to patients with a single seizure only[27], which underscores the trends shown in the present study. However, the factor “group” only reached statistical significance in multiple regression analyses in PCS scores one year after the first seizure in the present study, questioning the validity of the trends identified by Mann-Whitney U tests. Most of these potential differences were primarily determined by depressed mood. This is in line with previous research showing that QoL is primarily predicted by emotional well-being (e.g.,[1]). Impairments in cognition[28] and emotional well-being (see [29] for review) have also been identified already early after seizure onset. Especially cognitive deficits were identified in up to 70 % of new-onset epilepsy patients (see [28] for review), however the authors state that due to the fact that most neuropsychological assessments take place in the course of epilepsy surgery evaluation, more research would be required. In our study, we did not examine cognitive impairment and the interaction between cognition and emotion as possible factor influencing mental health-related QoL, which would shed more light on the nature of these interactions. Yet, the former mentioned review underlines the importance of early-stage assessment of aspects

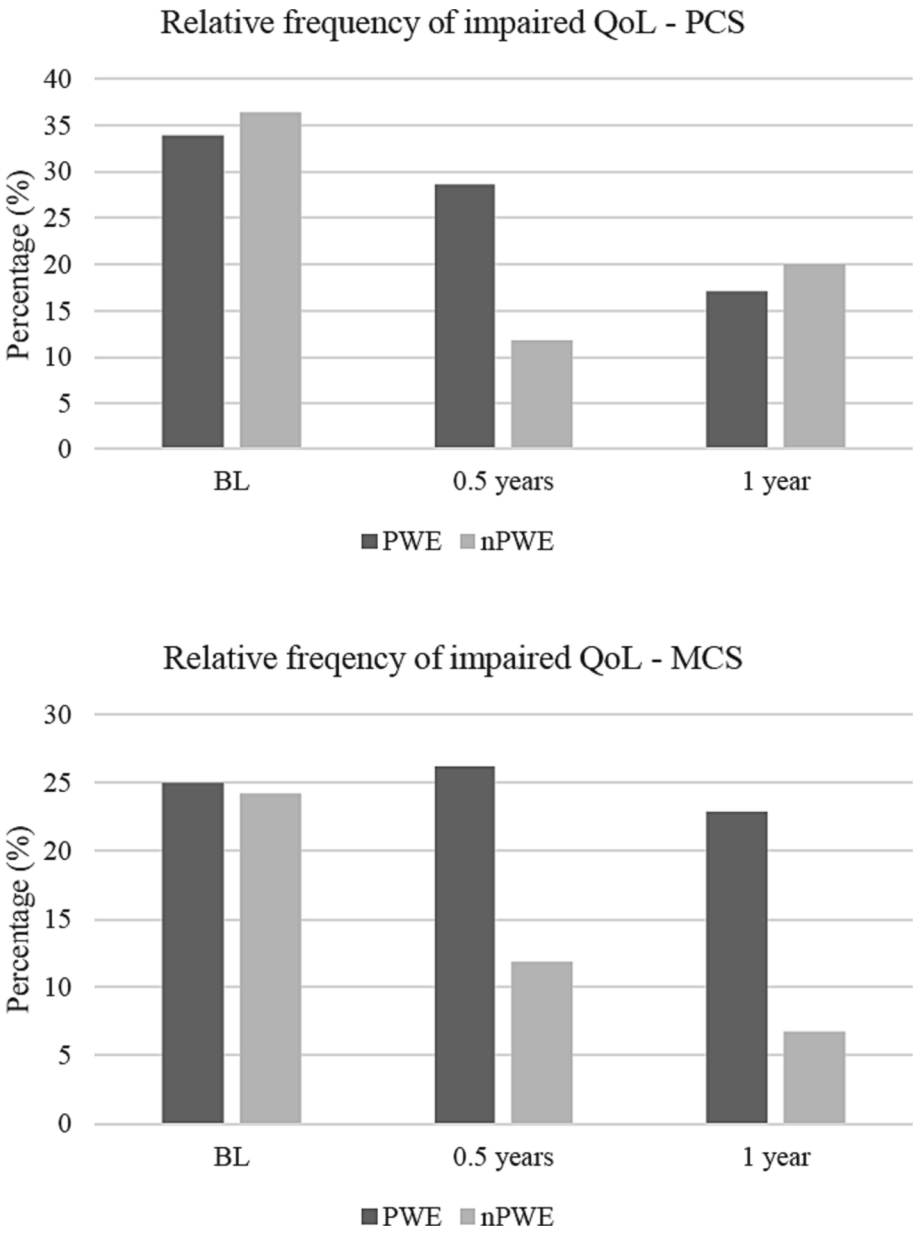

Fig. 3. Qualitative evaluation of QoL impairment measured by SF-36. QoL = Quality of life. BL = baseline. PCS = physical component score. MCS = mental component score. PWE = patients with epilepsy. nPWE = patients with no epilepsy. All p >.05 using chi-square tests of independence (Bonferroni-corrected).

relevant for QoL including emotional and cognitive states. In our study, while both patient groups did not display great impairments in QoL on a qualitative level when regarding mean values, impairments could be shown on an individual level in up to 34 % of PWE (see Fig. 2).

Within the epilepsy patient group, emotional well-being plays an outstanding role in one's perception of QoL. At both six months as well as one year after the first seizure, mental health-related QoL was most strongly predicted by depressed mood in patients diagnosed with epilepsy. In addition to this emotional factor, the presence of ongoing seizures and the patients' age strongly predicted physical health-related QoL. With increasing age, PWE rated the physical health-related QoL as more impaired, which might also be linked to a more general decline of physical functions associated with increased age. This could be underlined by the fact that we found no significant differences between PWE and nPWE.

The fact that age was not continuously significantly linked to mental health-related QoL in our data is supported by previous research demonstrating that older patients with epilepsy would not differ significantly from younger patients in terms of QoL, which is mainly predicted by BDI scores[30]. Depressed mood was associated with physical health-related QoL six months after the first seizure, but not after one year. This may reflect an adaption process in which there is stronger emotional impairment and disturbance in the first few months after a first seizure, which steadily decreases over the longer term and is eventually reflected in the mental component score. This is underlined by various studies on the relationship between depressed mood and physical health (e.g., [31,32]). Assuming that depressed mood occurs in response to the epileptic seizure, especially in the initial period after the seizure, this could be the reason for patients to not only perceive mental distress but also physical impairments, due to a raised body-awareness, which slowly declines over months. Investigating depression levels in our sample more closely, we found that premorbid clinically diagnosed depression was present merely in a minority of patients (Table 1), while there were also no significant differences regarding this comorbidity between PWE and nPWE (χ^2 (1) = 0.03, p =.870). This implies that presently reported depression levels can be predominantly attributed to

the acute clinical situation, rather than to premorbid depression.

QoL was investigated more specifically using the SF-36 to determine unique predictors more directly. In clinical practice, it is important to recognize that a patients' overall perception of QoL is determined by epilepsy-specific factors such as ongoing seizure activity, emotional well-being, and personal demographic characteristics. The knowledge of these three factors should be considered during comprehensive treatment to improve QoL: ASM can be prescribed to reduce recurrence risk; a screening for depressive symptoms early after the first seizure is useful to detect a possible depressive comorbidity or emotional disturbances secondary to the first epileptic seizure. In this case it would be important to a) choose an ASM which has minimal affective side-effects and to b) consider the need for further psychiatric diagnostic referral. A recent study pointed at this issue[33], showing reduced overall quality of life measured by QOLIE-31 in patients on ASM polytherapy compared to monotherapy and also a higher prevalence of psychiatric comorbidity in the polytherapy patient group, thereby underlining earlier research[34]. While the amount of patients treated with multiple ASM was not sufficient to allow statistical testing in our study (see Table 1), it would be valuable to investigate this patient subgroup across time more in depth. Early supportive care could help to improve QoL and emotional well-being, especially in patients who received a diagnosis of epilepsy. Elderly patients especially appear to be at risk for decreased QoL and should be monitored even more carefully, taking comorbidities into account. Dependent on these factors, early treatment, tailored to the individual patients' needs, may be initiated in patients with an initial diagnosis of epilepsy to not only reduce the recurrence risk for seizures itself, but also to allow for early adjustments in daily life routines and to thus maintain the greatest possible functionality.

Being diagnosed with epilepsy seems to have a substantial influence on patients' well-being. This might indicate that irrespective of ongoing seizures, mental health-related QoL is already impacted in patients by knowledge about having epilepsy. This might originate from e.g. culturally driven (fear of) stigmatization [35], impacting QoL of epilepsy patients[13]. Assuming this, it might lead patients to avoid contact to health systems, eventually impeding necessary medical interventions. Remaining untreated however increases the risk of further medical events such as hospitalization or emergency department visits [36]. Besides, being diagnosed with epilepsy often impacts the patient's social system, e.g. effecting caregivers QoL negatively (see [37] for review). Our findings therefore carry an important clinical implication and points to the need for comprehensive counselling and appropriate patient education programs, immediately at the onset of the disease, which could further facilitate an adaption process.

Finally, we detected a large gender difference in the nPWE group with a majority of male patients (Table 1). A closer inspection revealed that 90.0 % of patients diagnosed with an acute-symptomatic seizure were male, while the gender proportion in unclassified seizures was comparable (59.3 % male). This replicates a recent finding that acute-symptomatic seizures appear to be associated with male sex[38], also showing that the most common origin of acute-symptomatic seizures was alcohol withdrawal, while we did not explicitly investigate underlying etiologies of acute-symptomatic seizures in the present study.

4.1. Limitations

Depression, persistent seizures, and age have been identified as key factors contributing to mental and physical health-related QoL. However, given that across time points the PWE group was roughly 50 % larger than the non-PWE group, we have to interpret findings related to group comparisons with caution. Furthermore, our study did not reflect on additional possible influencing factors. For example, [4] described a substantial impact of ASM on QoL, which we did not consider in our study: In their study, medication adherence was found to have an effect, not only on seizure severity but also on QoL, while the ASM level itself was not found to be correlated with QoL. Given 93.3 % (n = 98) of PWE received ASM and only 17 % ($n = 8$) of nPWE in our study, we did not include this variable in regression analyses as such an imbalanced variable could have confounded our results severely. Furthermore, it might have contributed to multicollinearity, which would have led to difficulties interpreting our results. Future research should focus on the role of ASM and could investigate specific ASM and their impact on QoL. As mentioned above, it would also be interesting to include level of cognitive functioning as another factor that is not only related to QoL [39,40] but which has also been shown to be impaired early after seizure onset[28]. Further relevant variables in terms of QoL such as employment status or income were not included as this would have led to a reduced statistical power with respect to our sample size. In the course of the study, eight patients passed away who were diagnosed with brain tumors. While the size of this subsample impedes statistical inferences on QoL, it would be important to investigate possible influences of being diagnosed with not only epilepsy but with a potentially life threatening disease on QoL more in depth.

The absence of QOLIE-31 questionnaire data in the nPWE group obstructs statistical comparisons between the groups at follow-up appointments. However, multiple items of QOLIE-31 refer to epilepsy-specific daily living activities (working, driving restrictions) and ASM side effects, which does not match with patients experiencing a single seizure without being diagnosed with epilepsy. A valid evaluation of QOLIE-31 scores in the nPWE group would thus have been not possible.

With respect to group comparisons, the rather large differences in sample sizes might be one explanation for finding trends, but no sincere statistical differences between PWE and nPWE. Collecting more data in the nPWE group to fill this gap would be desirable to place stronger conclusions on these findings. The found trends should thus be interpreted with caution and future research is necessary to investigate those tendencies more in depth, especially to avoid overemphasizing of our results. With further respect to group comparisons, the collection of normative data of a matched healthy control group would improve the interpretation of the results. [20] showed significant differences in depression scores between patients and controls, but not that clearly between patient subgroups. In their study, patients were assessed only once between six and 12 months after the first seizure. Reduced mental health-related QoL, which is predominantly predicted by depressed mood, may have been an overall general reaction to a life-impairing event such as an epileptic seizure. Future studies would thus benefit from including level of cognitive functioning and matched healthy controls. Finally, the follow-up interval of one year after the first epileptic seizure might represent only part of patients' adjustment to the diagnosis, especially since recurrent seizures developed within one year in 36–37 % of patients and after two years in 43–45 % of patients [41].

4.2. Strengths

In our study, we were able to enroll and monitor not only patients consecutively diagnosed with epilepsy after a first seizure, but also patients with a single seizure across a 12-month trajectory. This enabled us to investigate clinical and QoL-related determinants from the very beginning of patients' careers. The longitudinal approach thereby adds to findings of other studies that only included one measurement (e.g., [20]), while further follow-up measurements would be desirable for a better understanding of the interplay of the factors contributing to QoL in the present study.

4.3. Conclusion

After a first epileptic seizure, QoL is influenced not only by demographic and emotional, but also by epilepsy-specific characteristics. There is a tendency in patients diagnosed with epilepsy showing reduced QoL immediately after the diagnosis as well as after 6 and 12 months compared to patients diagnosed with a first seizure, however future research is needed to substantiate these trends, which should be

interpreted with caution. Our findings stress the need for early and comprehensive monitoring of not only the medical, but also the affective and demographic characteristics of patients with epilepsy early in their careers. A better understanding of the interplay of these factors and their specific impact on different (physical or mental) aspects of a patient's QoL is important for an early tailored, personalized comprehensive treatment.

CRediT authorship contribution statement

Louise Linka: Conceptualization, Formal analysis, Writing – original draft. **Selina Nephuth:** Data curation, Investigation. **Iris Gorny:** Conceptualization, Writing – review & editing. **Kristina Krause:** Project administration. **Peter Michael Mross:** Writing – review & editing. **Panagiota-Eleni Tsalouchidou:** Writing – review & editing. **Felix Zahnert:** Writing – review & editing. **Sven Fuest:** Investigation, Writing – review & editing. **Katja Menzler:** Supervision, Writing – review & editing. **Susanne Knake:** Conceptualization, Project administration, Supervision, Writing – original draft. **Lena Habermehl:** Conceptualization, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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