Health-related quality of life in patients with poststroke epilepsy

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ABSTRACT

Background: Lesional epilepsy is an important long-term sequela of stroke. Data on health-related quality of life (HrQoL) in patients with poststroke epilepsy are limited. We investigated HrQoL in patients with epilepsy after ischemic stroke and identified independent HrQoL-determinants.

Methods and patients: All patients with acute ischemic stroke, who were permanent residents in the district Marburg-Biedenkopf (Hessia, Germany, reference population 240,000 inhabitants) were recruited within 12 months in the population-based Marburg Stroke Register (MARSTREG). Follow-up visits were performed after 6, 12, and 24 months, and patients who developed poststroke epilepsy were identified. Data on demographics, antiepileptic drugs (AEDs), stroke severity (National Institute of Heath Stroke Scale (NIHSS), Barthel-Index, modified Rankin Scale), depression (Geriatric Depression Scale), and HrQoL (EQ-5D and EQ VAS) were collected. A multiple regression analysis was performed to identify HrQoL-determinants.

Results: Among the study participants (n = 374), 23 (6.1%) developed poststroke epilepsy. The HrQoL of patients with poststroke epilepsy was reduced in comparison with patients without seizures (24-month follow-up: EuroQol Visual Analogue Scale (EuroQol-VAS): 55.3 ± 10.7 versus 64.2 ± 11.4, p = 0.03). Seizure frequency, depression, and functional impairment (Barthel-Index) were identified as independent determinants of HrQoL. The adjustment of AEDs between 6-month and 24-month follow-ups resulted in decrease of seizure frequency by 40% and reduction of complications (dizziness by 27.8%, nausea by 52.2%, fatigue by 84.2%).

Conclusion: Lesional epilepsy is associated with decreased HrQoL in patients with stroke. We identified HrQoL-determinants, which would improve the management of patients with poststroke epilepsy. These determinants include proper adjustment of AEDs with reduction of seizure frequency, treatment of depression, and focused rehabilitation programs for poststroke epilepsy.

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1. Introduction

Cerebrovascular disorders are among the most common causes of epilepsy in people beyond middle age [1]. New therapeutic approaches in stroke, such as thrombectomy, were introduced in the last years, improving the poststroke outcome and increasing the number of stroke survivors. Because of these developments, the management of long-term complications following stroke has become more important. Lesional epilepsy is an important long-term sequela of stroke. Although seizure control in poststroke epilepsy is not as challenging as in other forms of lesional epilepsy (e.g., hippocampal sclerosis), drug interactions and side effects of antiepileptic drugs (AEDs) are of major importance in patients with stroke. The treatment of patients with cerebrovascular diseases includes antihypertensive, lipid-lowering agents, antiaggregants or anticoagulants. In case of concomitant heart disorders, diverse cardiac pharmaceutical agents are applied. This medication can interact with certain AEDs, such as valproate, carbamazepine, or phenytoin. The knowledge of enzyme-inducing or -inhibiting properties of AEDs is important for the correct choice of antiepileptic therapy. In addition, poststroke depression can be attenuated by a number of AEDs, such as zonisamide or levetiracetam [2].

The persistent neurological deficits, concomitant affective disorders, and complex interactions between cardiovascular and antiepileptic medication with potential side effects are potential factors compromising the health-related quality of life (HrQoL) of patients with poststroke epilepsy. The HrQoL is an important aspect in the management of patients with chronic conditions. The goal of our study was to perform the assessment of HrQoL in patients with epilepsy following ischemic stroke and to identify independent HrQoL-influencing factors.

2. Methods and patients

2.1. Study design

A population-based stroke register recruiting all patients with acute ischemic stroke, who were permanent residents in the district Marburg-Biedenkopf (Hessia, Germany, reference population 240,000 inhabitants), was started in 2012. Within 12 months of recruitment, 440 patients with stroke were identified according to this criterion. Of these, 66 declined to participate in the register (dropout rate of 15%). Overall, 374 patients were included in the Marburg Stroke Register (MARSTREG). Dropouts did not differ significantly from participants according to age, gender, and stroke severity (p > 0.05).

The follow-up investigations were performed after 6, 12, and 24 months. Patients who developed poststroke epilepsy were identified. According to the International League Against Epilepsy (ILAE) practical definition, lesional epilepsy after stroke was diagnosed in patients with at least one late-unprovoked seizure (>7 days after stroke onset) [3]. Patients with early seizures (≤7 days after stroke onset), who developed late-unprovoked seizures in the course of their disease, were included in the analysis. Patients with only early seizures were not included. The following data were collected and documented on case report forms: demographics, stroke severity (NIH Stroke Scale, Barthel-Index, modified Rankin Scale), depression (Geriatric Depression Scale), and HrQoL. We also recorded data on drug treatment and analyzed the pattern of prescription of AEDs. The study received approval from the local ethic committee.

2.2. Evaluation of HrQoL

The EuroQol tool was applied for evaluation of European Quality of Life (EuroQol). This is a generic HrQoL-tool based of patients' self-reporting and proved to be valid for use in epilepsy [4,5]. The EuroQol consists of a five dimensional self-classifier (EQ-5D) and a visual analogue scale (EQ VAS). The EQ-5D describes three levels of severity (1 = no problems, 2 = moderate problems, 3 = severe problems) in five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and allows to generate 243 possible health states. Calculation of the EQ-5D index score was performed using a regression algorithm generated by Greiner et al. [6]. The EQ VAS is a vertical scale that varies from 0 to 100. A score of 0 represents the "worst…" and 100 the "best imaginable health state".

2.3. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics Version 23.0 (IBM Corp., Armonk, NY, USA). Data presentation is performed as mean with 95% confidence intervals (CI). We used the Kolmogorov–Smirnov test to prove for normal distributions. A t-test was applied for comparisons of normally distributed variables. If data were not normally distributed, the Mann–Whitney U-test (two independent groups), the Kruskal–Wallis test (more than two independent groups), or the Wilcoxon rank test (two dependent groups) were applied. In order to determine independent HrQoL-influencing factors, a multivariate regression analysis was performed. The variability accounted for by independent HrQoL-determinants was assessed using the R^2 method.

3. Results

Among study participants (n = 374), 23 (6.1%) developed poststroke epilepsy. The mean age of these patients was 67 ± 8.4 years. Thirteen (56.2%) of them were male and ten (43.8%) were female. There were no significant differences between patients with and without poststroke epilepsy according to age and gender (Table 1). The difference between these groups of patients was in functional impairment. Patients with poststroke epilepsy were more severely impaired at admission (NIHSS)

Table 1
Clinical parameters and HrQoL of patients with and without poststroke epilepsy.

	Patients with poststroke epilepsy	Patients without poststroke epilepsy	p-Value
n (%)	23 (6.1)	351 (93.9)	
Age, mean ± standard deviation (SD)	67 ± 8.4	69 ± 4.9	p = 0.88
Gender, n (%)			p = 0.72
Male	13 (56.2)	200 (57.0)	
Female	10 (43.8)	151 (43.0)	
Barthel-Index			
Discharge	68.30 ± 39.54	77.43 ± 42.56	p = 0.01
6 months	78.27 ± 25.64	86.63 ± 39.75	p = 0.02
12 months	72.83 ± 34.86	80.93 ± 30.11	p = 0.04
24 months	70.38 ± 21.28	79.18 ± 26.74	p = 0.03
NIHSS			
Admission	7.5 ± 8.3	5.9 ± 5.3	p = 0.02
6 months	3.8 ± 5.7	2.2 ± 4.5	p = 0.02
12 months	4.1 ± 8.2	3.1 ± 5.4	p = 0.03
24 months	4.2 ± 7.8	3.3 ± 6.8	p = 0.03
EQ-5D-Index			
Admission	0.55 ± 0.27	0.59 ± 0.29	p = 0.48
6 months	0.62 ± 0.36	0.69 ± 0.37	p = 0.04
12 months	0.51 ± 0.23	0.65 ± 0.19	p = 0.02
24 months	0.52 ± 0.31	0.66 ± 0.24	p = 0.02
EQ VAS			
Admission	51.84 ± 10.83	54.84 ± 17.93	p = 0.61
6 months	58.34 ± 27.49	67.42 ± 20.17	p = 0.04
12 months	56.38 ± 11.24	64.77 ± 14.51	p = 0.03
24 months	55.27 ± 10.74	64.24 ± 11.44	p = 0.03

and had a lower Barthel-Index at discharge from the hospital (Table 1). At all follow-ups, patients with poststroke epilepsy showed a worse functional outcome after stroke (Table 1). Approximately a half of all cases with poststroke epilepsy (47.8%) developed seizures within the first 6 months after stroke (Table 2). In the time span between 6 months and 12 months after stroke, the number of patients with poststroke epilepsy increased by 64%. At follow-up after 24 months, it increased by another 22%. The initial seizure frequency of 5 ± 3 within 6 months could be reduced by 60% (seizure frequency at follow-up 24 months: 3 ± 2) via adjustment of the AED therapy. The course of antiepileptic therapy and its complications are shown in Table 2 and Fig. 1. Approximately 61% of patients with poststroke epilepsy remained on monotherapy, whereas 30% of them required 2 AEDs and 9% had to be treated with 3 AEDs after 24 months. The most often drug-related side effects of AEDs were dizziness, fatigue, and nausea (Table 2). Status epilepticus occurred relatively rarely: in 3 patients (0.8% of all patients with stroke and 13% of patients with poststroke epilepsy).

There was a change in prescription pattern of AEDs at 24 months follow-up compared with 6 months follow-up (Fig. 1). At the 6 months follow-up, 53.8% of patients were treated with levetiracetam, 23.1% with valproate, 15.4% with carbamazepine, and 7.7% with gabapentin.

Table 2
Disease course in patients with poststroke epilepsy.

	6 months	12 months	24 months
Patients with poststroke epilepsy, n (%[a])	11 (2.9%)	18 (4.8%)	23 (6.1%)
Seizure frequency in 6 months	5 ± 3	4 ± 2	3 ± 2
AED therapy			
Monotherapy	9 (81.8%)	12 (66.7%)	15 (60.9%)
2 AEDs	2 (18.2%)	5 (27.8%)	6 (30.4%)
3 AEDs	0 (0%)	1 (5.5%)	2 (8.7%)
Complications of AED			
Dizziness	2 (18.2%)	3 (16.7%)	3 (13.0%)
Nausea	2 (18.2%)	2 (11.1%)	2 (8.7%)
Headache	1 (9.1%)	1 (5.6%)	1 (4.3%)
Fatigue	3 (27.3%)	2 (11.1%)	3 (4.3%)
Weight changes	1 (9.1%)	1 (5.6%)	1 (4.3%)
Increase of lever enzymes	0 (0%)	2 (11.1%)	2 (8.7)

[a] Percentage of the whole stroke population.