

Predictive factors of quality of life in temporal and extratemporal lobe epilepsy: association with affective temperament profiles and psychiatric comorbidities

Factores predictivos de la calidad de vida en la epilepsia del lóbulo temporal y extratemporal: asociación con perfiles de temperamento afectivo y comorbilidades psiquiátricas

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ABSTRACT

Background: Investigating predictive factors of reduced quality of life (QOL) of patients and their association with focal epilepsy can improve management and treatment strategies. **Objective:** This study aimed to investigate the relationship between affective temperaments, depression, anxiety, disease characteristics, and QOL and to explore the predictors of QOL in patients with temporal lobe epilepsy (TLE) and extratemporal lobe epilepsy (ETLE). **Methods:** A total of 50 patients with TLE, 51 patients with ETLE, and 70 controls were enrolled. Affective temperaments were evaluated using the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Autoquestionnaire (TEMPS-A). QOL was assessed by the Short-Form Health Survey (SF-36). Beck Depression Inventory and Beck Anxiety Inventory were used to explore depression and anxiety severity, respectively. **Results:** Compared with the controls, patients with TLE and ETLE had significantly higher scores on all TEMPS-A scales, except on hyperthymic temperament. All the SF-36 subscale scores were lower in the TLE and ETLE groups. Linear regression analysis revealed that depressive symptoms, anxiety, depressive and irritable temperament, and seizure frequency were significant predictors of QOL in TLE. Patients with ETLE with temperamental disturbances, depressive symptoms, and polytherapy had a poorer QOL. **Conclusions:** Affective temperaments, psychiatric disorders, and clinical factors may predict impaired QOL in patients with TLE and ETLE. Further studies are needed to identify predictors of QOL in various epilepsy subtypes.

Keywords: Epilepsy; Temperaments; Quality of Life; Temporal Lobe; Epilepsy, Temporal Lobe.



RESUMEN

Antecedentes: Explorar los factores asociados y predictivos que reducen la calidad de vida en la epilepsia focal produce un efecto beneficioso en las estrategias de gestión y tratamiento. **Objetivo:** Investigar la relación entre temperamentos afectivos, depresión, ansiedad, características de la enfermedad y calidad de vida (QOL) y explorar los predictores de QOL en pacientes con epilepsia del lóbulo temporal (TLE) y epilepsia del lóbulo extratemporal (ETLE). **Métodos:** Se inscribieron un total de 50 pacientes con TLE, 51 pacientes con ETLE y 70 controles. Los temperamentos afectivos se evaluaron mediante el cuestionario de autoevaluación de Temperamento de Memphis, Pisa, París y San Diego (TEMPS-A). La calidad de vida se evaluó mediante la encuesta de salud de formato corto (SF-36). También se realizó a todos los participantes el Inventario de Depresión de Beck (BDI) y el Inventario de Ansiedad de Beck (BAI). **Resultados:** Los pacientes con TLE y ETLE tuvieron puntuaciones significativamente más altas en todas las escalas TEMPS-A que los controles, excepto la hipertimia. En la comparación de las puntuaciones del SF-36 dentro de cada grupo, todas las subescalas fueron más bajas en los pacientes con TLE y ETLE. El análisis de regresión lineal reveló que la depresión y la ansiedad, el temperamento depresivo e irritable y la frecuencia de las convulsiones fueron predictores significativos de la calidad de vida en el TLE. Además, los pacientes con ETLE con desequilibrios de temperamento afectivo, depresión comórbida y politerapia tenían una peor calidad de vida. **Conclusiones:** Los temperamentos afectivos, los trastornos psiquiátricos y los factores clínicos pueden predecir el deterioro de la calidad de vida en pacientes con TLE y ETLE. Se necesitan más estudios para descubrir los predictores de la calidad de vida en varios subtipos de epilepsia.

Palabras clave: Epilepsia; Temperamentos; Calidad de Vida; Lóbulo Temporal; Epilepsia del Lóbulo Temporal.

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INTRODUCTION

Epilepsy is a chronic neurological disorder of the brain characterized by recurrent seizures that affects individuals of all ages¹. Epidemiological studies have revealed that patients with epilepsy (PWE) have a higher incidence of psychiatric comorbidities than the general population². Although there is no clear evidence, pathogenic mechanisms underlying neurobiological, iatrogenic, and psychosocial factors may cause mood disorders (MDs) in the course of epilepsy³.

Depending on the chronic and episodic nature of epilepsy, occurrence of unexpected seizures and adverse effects of antiseizure medicines (ASMs) negatively influence quality of life (QOL). In addition, stigmatization, low self-esteem, and social isolation are potential factors for poorer QOL⁴. Although decreased QOL in PWE is well established, its association with MDs in this group is often overlooked⁵. Previous studies have suggested that patients with temporal lobe epilepsy (TLE) are more likely to develop psychiatric disorders due to the role of the limbic system in regulating mood and behavior^{6,7}. On the contrary, several authors failed to demonstrate the superiority of the temporal corticosubcortical network in the development of psychiatric comorbidities^{4,8}. Thus, the predominance of psychiatric symptoms in TLE remains controversial.

Temperament is defined as an automatic emotional response to events based on the underlying biological and genetic tendencies of personality⁹. Akiskal et al. described five temperaments that can be measured by the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Autoquestionnaire (TEMPS-A). According to this tool, affective temperaments can provide clues to the subclinical manifestations of MDs¹⁰.

To date, two studies have assessed affective temperaments in a population with mixed types of epilepsy using TEMPS-A^{11,12}. Therefore, this study aimed to evaluate 1) affective temperaments, 2) the relationship between temperaments, depressive symptoms, anxiety, disease characteristics, and QOL, and 3) possible predictors of QOL in patients with TLE and extratemporal lobe epilepsy (ETLE).

METHODS

Participants

We screened 101 adult patients with a diagnosis of focal epilepsy and follow-up duration of at least 2 years in our epilepsy outpatient clinic. Patients were evaluated by their medical records including seizure semiology, video electroencephalography (EEG) and/or ictal and interictal EEG analysis, and high-resolution 1.5 Tesla cranial magnetic resonance imaging (MRI). Patients with TLE and ETLE were classified according to the anatomical origin (epileptogenic focus originated from temporal or outside the temporal lobe, respectively), based on semiologic, electroencephalographic, and neuroimaging findings with the International League Against Epilepsy classification

of focal epilepsies (1989)¹³. All the valid and reliable scales were applied by an experienced psychiatrist. Patients with high psychopathological scores were referred to the liaison psychiatry unit of our hospital.

The control group consisted of seventy age- and sex-matched healthy volunteers. Individuals with a known psychiatric comorbidity, cognitive disorder and acute/chronic medical disease that could affect test performance were excluded.

This study was approved by Ethics Committee of Canakkale University (2011-KAEK-27/2018E.1800148473).

Questionnaires

Sociodemographic and clinical data were collected by face to face interview. TEMPS-A, Short Form Health Survey (SF-36), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were applied to all participants.

TEMPS-A

Affective temperaments were evaluated by the TEMPS-A questionnaire: a self-administered, Likert-type scale consisting of 110 items that measures five subdimensions as suggested by Akiskal et al.: depressive, cyclothymic, hyperthymic, irritable, and anxious temperaments¹⁰.

BDI

BDI is a 21-item self-report instrument that assesses the presence and severity of depressive symptoms in the past two weeks. Each item is rated on a 4-point Likert-type scale ranging from 0 to 3. The total score ranges from 0 to 63; subjects with ≥ 16 points are considered to have depression¹⁴.

BAI

BAI is used to assess anxiety levels and consists of 21 questions with a Likert scale ranging from 0 to 3 and raw scores ranging from 0 to 63¹⁵. Scores are categorized as minimal (0 to 7), mild (8 to 15), moderate (16 to 25), and severe anxiety (30 to 63).

SF-36

SF-36 consists of 8 subscales that assess QOL: physical functioning (PF), role limitation due to physical problems (RP), mental health (MH), role limitation due to emotional problems (RE), social functioning (SF), general health (GH), vitality (VT), and bodily pain (BP). All scores range from 0 to 100 and higher scores reflect better QOL¹⁶.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive analysis was presented using mean \pm standard deviation or percentages and numbers. Categorical data were analyzed using the chi-square test. Clinical data were compared between groups using the independent sample t-test and Mann-Whitney U test for normally and non-normally

distributed variables, respectively. All scores were compared among the three groups with one-way analysis of variance. For non-normally distributed data, Spearman correlation analysis was used to assess the relationship between TEMPS-A, BDI, BAI, clinical variables, and SF-36 subscales. Multiple linear regression analysis was performed to explore the predictive effect of temperaments, depressive symptoms, anxiety, and clinical variables on QOL. A p value less than 0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics

There were no statistical difference between sociodemographic parameters among patients and controls. ETLE patients had significantly fewer seizures than TLE ($p=0.028$) (Table 1).

Comparison of TEMPS-A, BDI, BAI, and SF-36 scores

Patients with TLE and ETLE had no significant differences in TEMPS-A categories. Depressive, cyclothymic, anxious, and irritable scores in TLE and ETLE were statistically higher than

controls ($p<0.001$). However, there were no significant difference in hyperthymic scores among the groups ($p=0.628$).

Compared to the control group, PWE had significantly higher BDI and BAI scores. No differences were found in BDI and BAI scores between the two patient groups. In addition, SF-36 subscales in TLE and ETLE patients were significantly lower than controls. There were no significant differences in SF-36 subscales among patient groups (Table 2).

Correlations between SF-36 subscales, clinical variables, affective temperaments, BDI and BAI

Correlation analysis of patients with TLE

SF-36 subscales scores, except for MH, were negatively correlated with seizure frequency in TLE patients. Number of ASMs was negatively correlated with GH. Depressive, cyclothymic, and anxious temperament and BDI and BAI scores were negatively correlated with all SF-36 subscales. There was a positive correlation with hyperthymic temperament and PF, GH, and RE. Irritable temperament was negatively correlated with all subscales except SF (Table 3).

Table 1. Demographic and clinic characteristics of patients with TLE, ETLE and controls.

		TLE (n=50)	ETLE (n=51)	Controls (n=70)	p
Age (years)		39.02±10.53	40.05±16.35	36.91±9.88	0.359
Sex (male,%)		25 (50.0)	29 (56.9)	31 (44.3)	0.393
Education (years)		8.66±4.11	8.21±3.33	9.31±3.79	0.274
Occupational status	Unemployed	7 (14.0)	6 (11.8)	2 (2.9)	0.183
	Employed	33 (66.0)	38 (74.5)	56 (80.0)	
	Retired	10 (20.0)	7 (13.7)	12 (17.1)	
Marital status	Single	10 (20.0)	12 (23.5)	23 (32.9)	0.264
	Married	39 (78.0)	39 (76.5)	45 (64.2)	
	Separated/divorced	1 (2.0)	0 (0.0)	2 (2.9)	
Age of epilepsy onset (years)		20.40±13.67	24.39±17.50		0.205
Disease duration (years)		18.72±12.95	15.76±12.49		0.246
Seizure frequency (past 3 months)		3.52±3.12	2.35±2.84		0.028
Seizure type (n,%)	Simple focal	2 (3.9)	1 (1.9)		0.781
	Complex focal	39 (76.5)	42 (82.4)		
	Secondarily generalized	9 (19.6)	8 (15.7)		
Seizure lateralization	Left/ right	20/15	13/21		
	Bilateral	3	1		
	Undetermined	12	16		
MRI	Normal	23	20		
	Abnormal	27	31		
Number of ASMs (n,%)	Monotherapy	28 (56.0)	28 (54.9)		0.691
	Bitherapy	19 (38.0)	17 (33.3)		
	Polytherapy	3 (6.0)	5 (9.8)		
	Without therapy	0 (0.0)	1 (2.0)		

TLE: Temporal Lobe Epilepsy; ETLE: Extratemporal Lobe Epilepsy; ASMs: Antiseizure Medicines; MRI: Magnetic Resonance Imaging.

Table 2. Comparison of TEMPS-A, SF-36, BDI and BAI scores among patients with TLE, ETLE and controls.

		TLE (n=50)	ETLE (n=51)	Controls (n=70)	p
TEMPS-A Scales	Depressive	10.74±5.37†	8.88±4.13‡	3.87±2.32	<0.0001
	Cyclothymic	11.14±4.99†	9.50±5.08‡	4.32±2.90	<0.0001
	Anxious	11.54±7.16†	8.50±6.38‡	2.57±2.65	<0.0001
	Hyperthymic	7.40±4.79	7.70±4.33	6.98±3.81	0.628
	Irritable	6.24±4.17†	5.39±3.27‡	2.18±2.26	<0.0001
SF-36	PF	61.20±31.35†	68.52±27.35‡	90.50±14.52	<0.0001
	RP	44.00±41.20†	49.50±42.57‡	89.64±20.18	<0.0001
	BP	55.78±21.95†	63.15±25.80‡	85.77±14.06	<0.0001
	SF	56.28±28.87†	65.11±29.49‡	83.55±14.20	<0.0001
	GH	48.52±24.52†	53.13±21.54‡	74.24±13.09	<0.0001
	RE	52.50±42.09†	53.43±43.20‡	90.38±22.63	<0.0001
	VT	42.30±25.37†	48.84±26.36‡	71.07±22.55	<0.0001
	MH	53.92±27.39†	61.64±23.28‡	75.88±12.12	<0.0001
	BDI	23.7±15.3†	18.72±13.23‡	5.08±3.73	<0.0001
	BAI	26.3±17.6†	20.84±16.49‡	6.24±4.94	<0.0001

TLE: Temporal Lobe Epilepsy; ETLE: Extratemporal Lobe Epilepsy; TEMPS-A: Temperament evaluation of Memphis, Pisa, Paris and San Diego Auto-questionnaire; SF-36: Short Form Health Survey; PF: Physical functioning; RP: role limitation due to physical problems; BP: bodily pain; SF: social functioning; GH: general perception of health; RE: role limitation due to emotional problems; VT: vitality; MH: mental health; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory. * p<0.01 for TLE vs. ETLE; †p<0.01 for TLE vs. Controls; ‡ p<0.01 for ETLE vs. Controls.

Table 3. Correlations between SF-36 subscale scores, clinical variables, affective temperaments, BDI and BAI in patients with TLE.

	PF	RP	BP	SF	GH	RE	VT	MH
Seizure frequency/ (past 3 months)	-0.32*	-0.572**	-0.343*	-0.358*	-0.403**	-0.49**	-0.311*	-0.217
Age at disease onset	0.019	0.049	-0.076	-0.018	0.058	-0.031	-0.046	-0.099
Disease duration	-0.248	-0.236	-0.088	-0.233	-0.237	-0.129	-0.201	-0.096
Number of ASMs	-0.149	-0.122	-0.213	-0.22	-0.306*	-0.278	-0.339	-0.194
Depressive	-0.606**	-0.434**	-0.544**	-0.489**	-0.629**	-0.499**	-0.642**	-0.628**
Cyclothymic	-0.341*	-0.42**	-0.488**	-0.464**	-0.466**	-0.446**	-0.541**	-0.393**
Hyperthymic	0.338*	0.17	0.153	0.146	0.326*	0.313*	0.262	0.27
Irritable	-0.174	-0.285*	-0.37**	-0.261	-0.318*	-0.363**	-0.463**	-0.335*
Anxious	-0.499**	-0.451**	-0.53**	-0.435**	-0.638**	-0.531**	-0.712**	-0.607**
BDI	-0.619**	-0.429**	-0.589**	-0.512**	-0.666**	-0.523**	-0.748**	-0.751**
BAI	-0.554**	-0.488**	-0.661**	-0.585**	-0.681**	-0.523**	-0.752**	-0.62**

*p<0.05; **p<0.01; PF: Physical functioning; RP: role limitation due to physical problems; BP: bodily pain; SF: social functioning; GH: general perception of health; RE: role limitation due to emotional problems; VT: vitality; MH: mental health; TEMPS-A: Temperament evaluation of Memphis, Pisa, Paris and San Diego Auto-questionnaire; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; TLE: Temporal Lobe Epilepsy; ASMs: Antiseizure medicines; SF-36: Short Form Health Survey.

Correlation analysis of patients with ETLE

Number of ASMs were negatively correlated with SF-36 subscales except PF and MH. Depressive and anxious temperament and BDI scores were negatively correlated with all SF-36 subscale. Cyclothymic temperament, irritable temperament, and BAI scores, were negatively correlated with all SF-36 subscales, except MH, RE, and VT, respectively. Hyperthymic temperament scores were positively correlated with PF, GH, MH, and VT (Table 4).

Results of multiple linear regression analyses

Patients with TLE

VT (66.8 % of the variance, R=0.830) and GH (54.8 % of the variance, R=0.740) were significantly correlated with BAI and depressive temperament. MH (55.7% of the variance, R=0.752) was negatively correlated with BDI. BP (52.1% of the variance, R=0.735) was significantly correlated with BAI and depressive temperament. PF (45.8% of the variance, R=0.701) was

correlated with depressive temperament, BAI and irritable temperament. RP (44.7% of the variance, R=0.685) was significantly correlated with seizure frequency and BAI. SF (35.1% of the variance, R=0.604) was significantly correlated with BAI. RE (32.5% of the variance, R=0.593) was significantly correlated with anxious temperament and seizure frequency.

These results suggest that TLE patients with higher scores on depressive temperament, irritable temperament, BDI and BAI and increased seizure frequency had a poorer QOL.

Patients with ETLE

The MH subscale of the SF-36 was strongly correlated with BDI, hyperthymic and irritable temperaments with 52.9% of the variance explained (R=0.747). The SF subscale of the SF-36 test (45.5% of the variance, R=0.682) was significantly

correlated with anxious temperament. In addition, PF (37.8% of the variance, R=0.416) was significantly correlated with BDI and anxious and hyperthymic temperaments. In addition, the BP subscale (34.3% of the variance, R=0.586) was significantly correlated with depressive temperament. The RP subscale was significantly correlated with anxious temperament and number of ASMs, with 34% of the variance explained (R=0.583). VT (31.8% of the variance, R=0.588) was significantly correlated with anxious and hyperthymic temperaments. RE was significantly correlated with anxious temperament (29.8% of the variance, R=0.558). GH (24.2% of the variance, R=0.522) was negatively correlated with depressive and hyperthymic temperaments. These results indicated that receiving polytherapy, temperamental disturbances and comorbid depressive symptoms predict QOL in patients with ETLE. Table 5 outlines the statistically significant results.

Table 4. Correlations between SF-36 subscale scores, clinical variables, affective temperaments, BDI and BAI in patients with ETLE.

	PF	RP	BP	SF	GH	RE	VT	MH
Seizure frequency/ (past 3 months)	0.009	-0.077	-0.157	-0.156	-0.119	0.019	-0.004	-0.117
Age at disease onset	-0.141	-0.165	-0.195	0.052	-0.245	-0.182	-0.103	0.262
Disease duration	-0.175	-0.176	-0.104	-0.202	0.003	-0.056	-0.035	-0.114
Number of ASMs	-0.177	-0.375**	-0.304*	-0.345*	-0.284*	-0.309*	-0.347*	-0.276
Depressive	-0.493**	-0.433**	-0.579**	-0.503**	-0.481**	-0.333*	-0.351*	-0.380**
Cyclothymic	-0.47**	-0.473**	-0.406**	-0.472**	-0.349*	-0.406**	-0.332*	-0.236
Hyperthymic	0.316*	0.108	0.196	0.144	0.375**	0.035	0.314*	0.456**
Irritable	-0.307*	-0.310*	-0.317*	-0.405**	-0.319*	-0.178	-0.358**	-0.429**
Anxious	-0.422**	-0.555**	-0.553**	-0.626**	-0.384**	-0.643**	-0.472**	-0.400**
BDI	-0.552**	-0.521**	-0.516**	-0.458**	-0.464**	-0.509**	-0.398**	-0.481**
BAI	-0.423**	-0.559**	-0.511**	-0.441**	-0.343*	-0.470**	-0.418	-0.294*

*p<0.05; **p<0.01; PF: Physical functioning; RP: role limitation due to physical problems; BP: bodily pain; SF: social functioning; GH: general perception of health; RE: role limitation due to emotional problems; VT: vitality; MH: mental health; TEMPS-A: Temperament evaluation of Memphis, Pisa, Paris and San Diego Auto-questionnaire; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; ETLE: Extratemporal Lobe Epilepsy; ASMs: Antiseizure medicines; SF-36: Short Form Health Survey.

Table 5. Multiple linear regression analysis for SF-36 subscale scores in patients with TLE and ETLE.

	R	Adj R2		β	St coeff. β	p
Patients with TLE						
PF	0.701	0.458	Depressive	-3.230	-0.553	0.000
			BAI	-0.716	-0.401	0.003
			Irritable	2.622	0.349	0.009
RP	0.685	0.447	Seizure frequency	-6.115	-0.464	0.000
			BAI	-0.928	-0.396	0.001
BP	0.735	0.521	BAI	-0.655	-0.525	0.000
			Depressive	-1.252	-0.306	0.012
SF	0.604	0.351	BAI	-0.992	-0.604	0.000
GH	0.740	0.548	BAI	-0.591	-0.482	0.000
			Depressive	-1.446	-0.361	0.003
RE	0.593	0.325	Anxious	-3.053	-0.429	0.001
			Seizure frequency	-4.050	-0.301	0.018

Table 5. Cont.

	R	Adj R2		β	St coeff. β	p
VT	0.830	0.668	BAI	-0.539	-0.173	0.002
			Depressive	-1.481	0.559	0.011
MH	0.752	0.557	BDI	-1.344	-0.752	0.000
Patients with ETLE						
PF	0.416	0.378	BDI	-0.735	-0.356	0.011
			Anxious	-1.259	-0.294	0.033
			Hyperthymic	1.544	0.245	0.035
RP	0.583	0.340	Anxious	-3.207	-0.481	0.000
			Number of ASMs	-14.902	-0.246	0.045
BP	0.586	0.343	Depressive	-3.656	-0.586	0.000
SF	0.682	0.455	Anxious	-3.150	-0.682	0.000
GH	0.522	0.242	Depressive	-1.966	-0.377	0.005
			Hyperthymic	1.379	0.278	0.034
RE	0.558	0.298	Anxious	-3.777	-0.558	0.000
VT	0.588	0.318	Anxious	-2.029	-0.492	0.000
			Hyperthymic	1.847	-0.304	0.012
MH	0.747	0.529	BDI	-0.516	-0.293	0.014
			Hyperthymic	2.560	0.477	0.000
			Irritable	-2.452	-0.345	0.004

TLE: Temporal Lobe Epilepsy; SF-36: Short Form Health Survey; PF: Physical functioning; RP: role limitation due to physical problems; BP: bodily pain; SF: social functioning; GH: general perception of health; RE: role limitation due to emotional problems; VT: vitality; MH: mental health; ETLE: Extratemporal Lobe Epilepsy; ASMs: Antiseizure medicines; Adj. R²: adjusted R square; Std. coeff β : standardized beta regression coefficients.

DISCUSSION

This study explored the predictors of QOL and examined the relationship among QOL, affective temperaments, depression, anxiety, and clinical characteristics in patients with TLE and ETLE. Previous reports have demonstrated the crucial role of affective temperaments in the prodromal phases and MDS^{9,10}. Higher scores on depressive, cyclothymic, and anxious temperaments were associated with a diagnosis of major depressive disorder¹⁰. Additionally, individuals with irritable, cyclothymic, and hyperthymic temperaments have a tendency to develop bipolar disease^{9,17}. In our study, TLE and ETLE groups had significantly higher scores on the depressive, cyclothymic, irritable, and anxious subscales of TEMPS-A than healthy controls. Similar to our results, Yazıcı et al. have shown that all temperament scores were significantly increased, except the hyperthymic temperaments, in PWE¹¹. In addition, Taycan et al. found that PWE had higher scores on all TEMPS-A subscales¹². These reports claimed that PWE present temperamental disturbances that can be a potential precursor for the development of MDs. However, no significant differences in TEMPS-A, depression, and anxiety scores were found between the TLE and ETLE groups. Consistent with our results, Sanchez-Gistau et al. compared the prevalence of interictal psychiatric disorders with SCID-I in patients with refractory TLE and ETLE. In that study, the hypothesis that patients with TLE have more psychiatric comorbidities than ETLE was not accepted¹⁸.

In our study, affective temperaments, except hyperthymic, were negatively correlated with almost all SF-36 subscales. Interestingly, we detected a positive correlation with hyperthymic temperament and some SF-36 subscales in both patient groups. This situation may explain why excessively confident, grandiose, energetic, and expansive patterns of people with hyperthymic temperament have a paradoxical tendency to mark optimistic choices of the SF-36 questionnaire. More importantly, in our regression analysis, depressive, anxious and irritable temperaments showed a predictive role for low QOL of patients with TLE. In addition, in our regression model, predictors of low QOL in patients with ETLE were depressive, anxious, irritable, and hyperthymic temperaments. These results indicate the determinative role of subclinical MDs on QOL.

To our knowledge, no published study has compared QOL and affective temperament profiles among patients with focal epilepsy. Our findings showed that patients with TLE and ETLE had higher scores on the depression and anxiety questionnaire than the healthy group. Similarly, recent epidemiological studies have identified a higher prevalence of psychiatric disorders in PWE than in the general population^{2,19}. Approximately, one-third of PWE experience depression or anxiety in their lifetime²⁰. PWE have fear of having seizures and difficulties in participating in social groups and feel alone and rejected, which lead to an increase in psychiatric comorbidities. However, our data does not support the prevalent thought about the superiority of TLE on impaired depression and anxiety scales.

Swinkels et al. emphasized that lateralization and localization do not determine the risk of depression, anxiety, and personality in patients with TLE and ETLE, which is consistent with our results⁸. In a prospective multicenter epilepsy surgery study, Devinsky et al. did not find a relationship between depression and anxiety levels and the side or lobe of the seizure focus prior to surgery²¹. In addition, Sanchez-Gistau et al. studied interictal psychiatric disorders in patients with refractory TLE and ETLE and did not support the hypothesis of temporal lobe's priority in psychiatric disorders¹⁸. In contrast, previous studies have claimed that patients with TLE are more susceptible to affective disorders than those with ETLE or generalized epilepsy^{6,22}. Nevertheless, the effect of temporolimbic hyperconnection in TLE on the development of MDs has been controversial among studies, due to the probable effect of the heterogeneity of seizure classification and methodological approaches.

In our sample, SF-36 subscale scores were lower in patients than in controls, without statistical differences between the TLE and ETLE groups. More importantly, in the linear regression analysis, patients with TLE who had comorbid anxiety, increased seizure frequency, depressive temperament, and depressive symptoms had poorer QOL. Additionally, in patients with ETLE, affective temperamental disturbances, depressive symptoms, and polytherapy were predictive factors of lower QOL. Our results confirmed the important role of psychiatric status, frequent seizures, and ASMs in QOL. In patients with TLE, all SF-36 subscale scores were significantly correlated with depression and anxiety scores. All subscales, except MH, were negatively correlated with seizure frequency. In our study, depressive symptoms and comorbid anxiety were the strongest predictors of QOL in the TLE group. Kutlu et al. compared the SF-36 scores of 60 PWE and 33 healthy people and found a correlation between vitality and increased seizure frequency and variables such as educational status, age at seizure onset, disease duration, ASMs, and types of seizures²³. Similar to this study, Mutluay et al. revealed that PWE with good treatment response had significantly better scores on the SF-36²⁴. A hospital-based study conducted in the Czech Republic confirmed that seizure frequency, employability, and psychiatric comorbidities are strong predictors of QOL in PWE²⁵. A systematic review from the UK summarized 93 QOL studies found in Medline, Embase, and Cochrane Library databases that were published before July 2010. This review pointed out the associations among seizure frequency, seizure severity, and levels of depression and anxiety with reduced QOL in PWE²⁶. Similar to our report, many studies have shown that comorbid depression and anxiety have stronger effects than demographic and disease-related factors^{27,28}. On the contrary, some studies have demonstrated the superiority of clinical factors on QOL.

A hospital-based Chinese study claimed that adverse effects of ASMs had a stronger influence than number of ASMs, depression, and anxiety on poorer QOL²⁹. A hospital-based study from Russia reported that increased seizure frequency was the strongest predictor of QOL³⁰. In the MEPSY study, QOL was assessed

using the Quality of Life in Epilepsy Inventory (QOLIE)-10 in 702 people with epilepsy from Korea, and the strongest predictor was adverse effects of ASMs, followed by depression, seizure control, anxiety, and household income³¹. However, these studies have compared the determinants of QOL in mixed groups of PWE. Previous reports support our findings that psychiatric status has a stronger effect than disease-related variables on determining QOL^{32,33}. In addition, a number of studies have examined the QOL of patients with refractory TLE and documented a significant association between frequent seizures on poorer QOL^{34,35}. Our results agreed with those of previous studies where frequent seizures predicted poorer QOL in TLE. Dourado et al. used the QOLIE-31 to assess the correlation between seizure-related variables and QOL in patients with TLE, ETLE, and idiopathic generalized epilepsy³⁶. They found similar scores among patient groups, and increased seizure frequency was a predictor for worse QOL. Consistent with these results, we found no significant differences in SF-36 scores between patient groups. However, in our regression model, seizure frequency was not a predictive factor of poorer QOL in ETLE. Ertem et al. assessed the effects of psychiatric comorbidity, demographic factors, and clinical features on QOL in patients with mesial temporal lobe epilepsy, juvenile myoclonic epilepsy, and healthy controls using the QOLIE-89. In their report, only psychiatric comorbidity in PWE affected QOL regardless of seizure syndrome³⁷. Similar to our study, Chen et al. explored the predictive factors of QOL in patients with TLE using the QOLIE-31 inventory³⁸. In their study, depression, anxiety, long epilepsy duration, and adverse effects of ASMs were significant predictors for lower QOL. Previous studies that investigated QOL in TLE have controversial results. This difference may be related to the variability in sample size, psychiatric evaluation, methodological process, and heterogeneity of QOL tests.

In psychiatric practice, ASMs have mood-stabilizer and anxiolytic potentials in addition to their antiseizure effect. The beneficial effect of ASMs on QOL and MDs has been well established in PWE³⁹. Nevertheless, many studies have reported that polytherapy and side effects of ASMs can lead to impaired QOL^{29,38}. In our sample, the number of ASMs was correlated with worse general health in patients with TLE, whereas a significant correlation was detected in all SF-36 subscales, except physical functioning in ETLE. In the linear regression analysis, the number of ASMs in the ETLE group had a negative predictive role on the physical subscale of SF-36. Further studies are needed to elucidate the effect of ASMs on QOL in patients with focal epilepsy.

This study had several limitations. First, our study was carried out in a single center with a relatively small sample from a tertiary care hospital. Second, we classified seizures based on the International League Against Epilepsy 1989 criteria, which is a noninvasive tool for the localization and lateralization of epilepsy¹³. Third, we did not consider the type of ASMs and time interval between seizures, which might interfere with behavioral and cognitive changes. Fourth, participants were not

assessed using the SCID⁴⁰. Finally, our study included nonrandomized patients, which might have biased the results due to the selection of individuals who possibly have better cognition and QOL. Thus, further studies with larger groups are needed to assess predictive factors of QOL in different epilepsy types.

Our study has several strengths. To our knowledge, this is the first study that investigated affective temperaments, disease characteristics, and psychiatric status as possible predictors of QOL in patients with TLE and ETLE. Previous studies have assessed affective temperaments only in patients with mixed types of epilepsy. Second, our study provides a new insight into

subclinical manifestations of MDs in focal epilepsy. Third, all questionnaires were validated and applied by an experienced psychiatrist.

In conclusion, affective temperamental disturbances, comorbid psychiatric disorders, and disease-related variables can affect the QOL of patients with TLE and ETLE. An important but overlooked topic is the negative effect of affective temperaments. From a clinical perspective, our findings suggest that evaluating factors that may impair QOL in patients with different epilepsy types can improve treatment strategies for subclinical MDs and comorbid psychiatric disorders.

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