Title: Epilepsy and adverse quality of life in surgically resected meningioma

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# Running title:

Epilepsy and adverse QoL in meningioma

# Introduction

Meningiomas are central nervous system neoplasms that originate from the cap cells of arachnoidal granulations and are usually attached to the inner dural layer of the cranial meninges1. They account for 20% of intracranial tumors with an approximate annual incidence of 6 cases per 100,000 people2,3. Prognosis in benign meningioma is good with a 10 year survival rate of 80%4. Quality of life (QoL) is therefore important to patients with meningioma and their clinicians. Seizures are common occurring pre and post-operatively despite pharmacological therapy5. Anti-epileptic drugs (AEDs) and increased seizure frequency are known to reduce QoL in non-tumor epilepsy patients, but whether this is true in meningioma is uncertain6-11. Our aim was to investigate the impact of epilepsy and its treatment on quality of life in patients with surgically treated meningioma.

# Material and methods

A cross-sectional postal questionnaire study was conducted at the Walton Centre NHS Foundation trust between November 2012 and August 2013 with full ethical approval (NRES: 12/NW/0747). Patients were recruited into three groups: meningioma without epilepsy, meningioma with epilepsy, and a matched epilepsy without meningioma group. Meningioma patients were identified from the local histology database and epilepsy patients were identified using clinical coding. Eligible patients were invited to participate by post. We adopted a self-selection sampling technique and non-responders were contacted by telephone to maximize sample size. The primary outcome was comparing QoL between meningioma patients with and without epilepsy, and between epilepsy patients with and without meningioma. The term QoL is used to encompass health related quality of life and functional status. QoL, current employment status, seizure frequency and AED use was determined by postal survey and all other data by case note review. Independent variables were compared between each group and used in regression analyses to identify significant determinants of QoL as secondary outcomes.

## Participants

### Meningioma

Patients who had undergone surgical resection of a supratentorial World Health Organization (WHO) grade 1 meningioma were considered for inclusion. They were excluded if they had: (i) infratentorial meningioma; (ii) WHO grade 2 (atypical) or 3 (malignant) meningioma; (iii) surgical excision or radiotherapy within 6 months of study participation; (v) neurofibromatosis type 2; (vi) dementia or learning difficulties; (vii) other intracranial tumors. Meningioma patients were considered to have epilepsy if they experienced at least two seizure episodes, or one seizure episode for which AED therapy was commenced. One seizure episode was defined as the occurrence of any number of seizures within a 24 hour period.

### Epilepsy patients without meningioma

Patients with focal seizures of symptomatic or cryptogenic etiology were included if they experienced at least two seizure episodes, or one seizure episode for which AED therapy was commenced. Patients were excluded if they had: (i) primary generalized seizures; (ii) idiopathic generalized epilepsy; (iii) intracranial surgery within 6 months of study participation; (iv) dementia or learning difficulties; (v) a non-benign intracranial lesion. Participants in the epilepsy without meningioma group were matched to patients in the meningioma groups by sex, age (±5 years) and duration of disease (±3 years).

## Outcome Measures

Three QoL questionnaires were used: a generic measure of functional health and wellbeing; the Short Form 36 version 2 (SF-36), a brain cancer specific measure; the Functional Assessment of Cancer Therapy with Brain Subscale (FACT-BR), and an AED adverse effects measure; the Liverpool Adverse Events Profile (LAEP). All are reliable, widely used and validated9,12-17. FACT-BR combines FACT-G, a generic questionnaire, with questions pertinent to patients with brain tumors (BRCS). FACT-BR compared QoL in meningioma patients with and without epilepsy. The BRCS subscale did not compare QoL in epilepsy patients with and without meningioma. Clinically meaningful differences in QoL score were defined on the basis of validation studies18. In SF-36, this was defined as 3.0 points in physical component score (PCS) and 4.6 points in mental component score (MCS)19. A meaningful difference in FACT-BR total was 9.0, 6.0 for BRCS and 2.0 for all other subscales20,21. For LAEP a difference of 11 points was clinically meaningful22.

## Data Analysis

Independent variables (Tables 1 and 2) were compared between patient groups to identify confounding factors. Significance was ascertained with Fisher’s exact t-tests, student’s t-tests and chi squared analyses. QoL data was treated as continuous data; which is robust in our sample size23. Normality testing of QoL data, and thus suitability for parametric testing, was performed with q-q plots, histograms, Kolmogorov-Smirnov tests, and Shapiro-Wilk tests24. All subscale and summary scores had a Crohnbachs alpha coefficient >0.70. Two tailed student t –tests compared QoL between groups. IBM SPSS v.20 was used for all analyses and significance was set at the *p* = 0.05 level. Missing data was handled differently for each questionnaire. The FACT-BR utilized a prorated subscale scoring method with a 50% missing data threshold per subscale. The SF-36 package includes missing data software that utilizes simple mean imputation, item response theory modelling and regression analysis. For the LAEP, simple mean imputation was used to estimate summary scores with a threshold of 3 missing questions per patient. There were 81 cases (35%) with missing items in a questionnaire and only 14 questionnaires (2%) had to be excluded from the QoL analysis. Between groups, there was no proportional difference in missing data. For the regression analysis, data was pooled into two new groups; a meningioma regression group, which consisted of data from the meningioma groups with and without epilepsy, and an epilepsy regression group, which consisted of data from the meningioma with epilepsy and epilepsy without meningioma group. Multiple regression analyses were performed with a selection of independent variables chosen on account of findings from univariate analyses and Pearson correlation tables. Some variables were re-coded to simplify the regression (Table 4). The selected variables were organized into four blocks and each block was sequentially inserted into a hierarchical stepwise multiple regression analysis by block in the order: demographics, comorbidities, meningioma variables and epilepsy variables.

# Results

Of the 697 patients that were invited 229 (33%) took part. Patients with meningioma and epilepsy were less likely to participate than meningioma patients without epilepsy (*X*2 (1, *n* = 350) = 3.90, *p* = 0.048), and patients with meningioma and epilepsy were more likely to participate than patients with epilepsy and no meningioma (*X*2 (1, *n* = 486) = 24.31, *p* < 0.001).

The mean age of all participants was 59.9 years and the majority were female (81%). The majority of participants (43%) classed themselves as retired, while 32% were employed and 16% unemployed. Demographics were comparable between each group. There was a mean of 2 (SD = 2) comorbidities per person. The characteristics of our meningioma cohorts were comparable (Table 1) except for an increased proportion of patients with tentorial meningiomas (*X*2 (1, *n* = 165) = 3.98, *p* = 0.046) and visual complications (*X*2 (1, *n* = 165) = 6.03, *p* = 0.014) in the meningioma patients without epilepsy group. Median time since surgery was 3.9 years with a range of 0.8 to 11.5 years. Thirteen participants (8%) had recurrence from previous meningioma resection and 18 (11%) received radiotherapy.

Epilepsy patients without meningioma were more likely to experience seizures (*X*2 (1, *n* = 120) = 9.46, *p* = 0.02), take AEDs (*X*2(1, *n* = 120) = 438.20, *p* < 0.001), and were more likely to be currently prescribed Levetiracetam (*X*2(1, n = 120) = 10.43, p = 0.001) (Table 2). Epilepsy patients without meningioma were also more likely to experience dyscognitive seizures (*X*2 (1, *n* = 120) = 6.51, *p* = 0.011) (not tabulated) and commence AED treatment with lamotrigine (*X*2(1, *n* = 120) = 14.70, *p* < 0.001). Patients with meningioma were more likely to commence AED treatment with phenytoin (*X*2 (1, *n* = 120) = 20.21, *p* < 0.001). There was no significant difference in disease duration, or years spent on AEDs. The etiology of epilepsy in the epilepsy without meningioma group was unknown in the majority of cases (64%); stroke was the most common identified etiology (20%). Stroke was more prevalent in epilepsy patients without meningioma compared to meningioma patients with epilepsy (*X*2 (1, *n* = 120) = 5.29, *p* = 0.022) but the distribution of all other comorbidities was comparable.

### Quality of life Scores

Compared to meningioma patients without epilepsy, all QoL scores were impaired in meningioma patients with epilepsy, with exception to bodily pain (BP) in SF-36 (Table 3). Differences in FACT-BR summary score (*t* (92.9) = -2.55, *p* = 0.012) and the BRCS subscale score (*t* (161) = -3.14, *p* = 0.002) were significant. Participants in the meningioma with epilepsy group were significantly more likely to report the presence of shaky hands on the LAEP (*t* (76.5) = -3.57, *p* < 0.001). Individual items from the LAEP are not tabulated. Meningioma patients with epilepsy had impaired PCS and MCS scores compared to age adjusted United States (US) population norms25. Meningioma patients without epilepsy had impaired MCS but not PCS summary scores. Overall, epilepsy patients without meningioma had impaired QoL scores compared to patients with meningioma and epilepsy but none of these differences were statistically significant (Table 3). The mean SF-36 summary scores for both epilepsy groups were impaired compared to age adjusted US population norms. The Bonferroni method was applied post-hoc to reduce the impact of type one error. Subscale and summary scores were considered separately, as were group comparisons, changing alpha to 0.003 in subscale and 0.0125 in summary score. This did not alter the outcome of significance testing.

## Regression Analysis

### Hierarchical Regression Models

In a stepwise hierarchical regression model of our meningioma participants the demographics variable block accounted for a significant amount of variance in all questionnaires. The comorbidities block was significant in all questionnaires except LAEP, the meningioma block was significant in all measures except SF-36 MCS, and the epilepsy block was significant in FACT-BR and LAEP. When looking at individual factors, unemployment, diabetes, depression, number of meningioma symptoms and current AED treatment were consistent and significant predictors of impaired QoL (Table 4). In the stepwise hierarchical regression model of our epilepsy patients, demographics, co-morbidities and epilepsy variables accounted for significantly increased variance all questionnaires. The meningioma block was significant in SF-36 MCS and PCS. When looking at individual factors, unemployment, the number of comorbidities, stroke, cognitive/emotional effects of meningioma, and current Levetiracetam treatment were consistent and significant predictors of impaired QoL (Table 4).

### Post-Hoc Analysis

In the meningioma regression analysis AEDs consistently predicted impaired QoL. A post-hoc analysis was performed comparing QoL in meningioma patients by AED use. All measures, except for SF-36 PCS, suggested that QoL was significantly impaired in an AED treated population (Table 5). The differences in SF-36 MCS and FACT-BR were clinically meaningful.

# Discussion

Our cohort of 165 meningioma patients was typical of a post-resection meningioma population4. Of these 56 patients (34%) fulfilled the meningioma with epilepsy criteria which is similar to approximations of seizure frequency in the literature5. Meningioma patients with and without epilepsy had comparable demographics, comorbidities and meningioma profile except for tumor location. The proportion of tentorial tumors was higher in patients without epilepsy. Similar findings have been reported previously5.

We included a matched epilepsy group without meningioma. These patients had a different epilepsy profile. Patients without meningioma experienced more seizures and dyscognitive seizures, were more likely to be prescribed an AED, and were more likely to be prescribed Levetiracetam, which is prescribed in drug resistant focal epilepsy27*.*

QoL was measured with the SF-36 version 2, FACT-BR/FACT G and LAEP. None were considered to be a sole primary outcome variable due to a paucity of data on this subject. Patients with meningioma and epilepsy had consistently impaired QoL scores when compared to patients with meningioma.

Differences in QoL score were statistically and clinically significant in the BRCS subscale score, the FACT-BR summary score and one individual item in the LAEP: “shaky hands”. The differences in QoL appeared small and this could be due to a number of factors. Poor correlation in SF-36 scores to epilepsy factors was demonstrated in our regression analyses. Previous research has demonstrated that the SF-36 is unable to detect QoL differences between milder severities of epilepsy28. There was a relatively low epilepsy burden in our meningioma and epilepsy group; only 12% of patients experienced a seizure in the preceding 6 months and only 57% were currently taking AEDs; a result of our inclusive epilepsy definition. A non-significant difference in LAEP score could be due to the low epilepsy burden and a low incidence of AED toxicity in our meningioma with epilepsy group22. Scores above 45 in LAEP have previously been associated with AED toxicity, and the average score in the meningioma with epilepsy group was below this29.

When comparing QoL in the epilepsy groups, scores were consistently more impaired in patients without meningioma; but none of these differences were large or significant. The increased severity of epilepsy in patients without meningioma was expected to result in significantly impaired QoL scores. As this was not the case, this could be due to the insensitivity of the SF-36 to epilepsy and LAEP in the absence of toxicity. For FACT-G, non-significance could be explained by the omission of the brain tumor subscale (BRCS). This subscale was omitted because of the potential bias towards patients with meningioma but the BRCS subscale was sensitive to epilepsy in the meningioma analysis and may be useful in future studies.

In the multiple regression analyses demographics and comorbidities were consistently associated with impaired QoL. This was mainly due to unemployment, depression, diabetes and stroke. All are known to influence QoL30-32. In the meningioma multiple regression analyses, the number of meningioma symptoms, as opposed to any individual meningioma symptom, was consistent in predicting impaired QoL scores. The addition of the epilepsy variables block to the multiple regression analysis accounted for an increased amount of variance in FACT-BR and LAEP, but not SF-36. When looking at individual variables, AEDs, not seizure frequency, predicted impaired QoL scores. In light of this, we performed an unplanned post-hoc analysis in our meningioma patients, comparing the mean QoL scores of meningioma patients with and without AEDs. Patients in receipt of AEDs demonstrated significantly impaired SF-36 MCS, FACT-BR and LAEP scores. These differences were clinically significant in SF-36 MCS and FACT-BR. The concept that AEDs reduce QoL is not novel. Baker et al reported that in an epilepsy population, 88% of patients receiving AEDs describe adverse effects33. Furthermore, it has been demonstrated that patients in seizure remission and in receipt of AED monotherapy still have impaired QoL 34. In our study population, this concept is reinforced by impaired scores in the LAEP; a questionnaire designed to identify adverse effects of AEDs17.

In the epilepsy regression, meningioma related factors were largely non-significant. The epilepsy block of variables accounted for significantly increased variability in FACT-G and LAEP score. When looking at individual variables, Levetiracetam was particularly significant. Seizures however were not.

The current literature base for meningioma, epilepsy and QoL is small and heterogeneous, but does suggest that epilepsy impacts QoL in meningioma patients11. Two studies report an association between seizures and impaired Karnofsky performance scale (KPS) in meningioma patients, but do not comment on AED use7,10. The KPS is limited as it does not represent global QoL26. Another study states that AEDs impairs activities of daily living, but provides no data to support this8. Waagemans et al stratified meningioma patients by AED use, and compared SF-36 scores in each subgroup. Patients with AEDs had greater impairments in QoL than patients without AEDs when both were compared to a healthy cohort9. However, QoL was not directly compared between patients with and without AEDs or by any other epilepsy variable. They performed a multiple regression analysis and demonstrated that AED use, not seizures, accounted for variance in QoL, which is in keeping with our study.

Our study is limited by a reliance on case notes to collect co-morbidity, epilepsy and meningioma data. Recent seizure status and AED use was ascertained with patient completed questionnaires which were subject to recall bias. Our inclusive definition of epilepsy meant that many patients in the meningioma with epilepsy group were in seizure remission. A larger sample size would have obtained more patients with seizures allowing an effective evaluation of seizure recency, seizure frequency and seizure severity. The poor response rate, particularly in our meningioma with epilepsy group, compounds this issue and may have produced a healthy responder bias. In addition, the LAEP may not have been an effective epilepsy specific measure for this study as it focuses on AEDs and adverse effects. The SF-36 was not pertinent to patients with epilepsy. The measure of QoL at one point in time is another limitation. Multiple hypothesis testing increased the risk of type 1 error. Bonferroni correction was used for QoL comparisons but not demographic comparisons or regression analyses as they were secondary outcomes.

In conclusion this study demonstrates that epilepsy impairs QoL in patients who have undergone surgical resection of a benign intracranial meningioma. Patients who take AEDs represent a subgroup with particularly impaired QoL and AEDs seem to have a greater impact on QoL than seizures. A causal relationship between AED use and impaired QoL could not be determined in our study, since AEDs are used only by patients with meningioma and epilepsy. Nevertheless, the epilepsy in meningioma patients appears to be mild. Patients should be fully counselled about AEDs, which our study suggests impairs QoL, and unnecessary AED treatment should be avoided.

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# Conflicts of interest

We certify that there are no actual or potential conflicts of interest in relation to this article for all authors

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**Table1: Meningioma characteristics and significance testing of group differences between the meningioma without epilepsy and meningioma with epilepsy groups**

|  |  |  |  |
| --- | --- | --- | --- |
| Meningioma Characteristics | Meningioma without epilepsy(n=109) | Meningioma with Epilepsy(n=56) | Total(n=165) |
|  |  | **n** | **(%)** | **n** | **(%)** | **n** | **(%)** |
| Simpsons Grade | 1 | 29 | (26.9%) | 24 | (43.6%) | 53 | (32.5%) |
| 2 | 47 | (43.5%) | 17 | (30.9%) | 64 | (39.3%) |
| 3 | 6 | (5.6%) | 5 | (9.1%) | 11 | (6.7%) |
| 4 | 26 | (24.1%) | 9 | (16.4%) | 35 | (21.5%) |
| Meningioma location | Convexity | 24 | (22.0%) | 16 | (28.6%) | 40 | (24.2%) |
| Intraventricular | 1 | (0.9%) | 0 | (0.0%) | 1 | (0.6%) |
| Parafalcine | 27 | (24.8%) | 17 | (30.4%) | 44 | (26.7%) |
| Skull base | 28 | (25.7%) | 11 | (19.6%) | 39 | (23.6%) |
| Sphenoid Wing | 19 | (17.4%) | 12 | (21.4%) | 31 | (18.8%) |
| **Tentoriala** | **10** | **(9.2%)** | **0** | **(0.0%)** | 10 | (6.1%) |
| Number of Symptoms | 0 | 49 | (45.0%) | 24 | (42.9%) | 73 | (44.2%) |
| 1 | 37 | (33.9%) | 26 | (46.4%) | 63 | (38.2%) |
| 2 | 15 | (13.8%) | 4 | (7.1%) | 19 | (11.5%) |
| 3 | 7 | (6.4%) | 1 | (1.8%) | 8 | (4.8%) |
| 4 | 1 | (0.9%) | 1 | (1.8%) | 2 | (1.2%) |
| Symptoms | **Visuala** | **29** | **(26.6%)** | **5** | **(8.9%)** | 34 | (20.6%) |
| Cognitive/Emotional | 10 | (9.2%) | 8 | (14.3%) | 18 | (10.9%) |
| Headache | 12 | (11.0%) | 3 | 5.4%) | 15 | (9.1%) |
| Motor/Sensory | 7 | (6.4%) | 8 | (14.3%) | 15 | (9.1%) |
| Infection | 6 | (5.5%) | 5 | (8.9%) | 11 | (6.7%) |
| Cranial Nerve | 9 | (8.3%) | 1 | (1.8%) | 10 | (6.1%) |
| CSF problems | 5 | (4.6%) | 4 | (7.1%) | 9 | (5.5%) |
| Balance/Co-ordination | 5 | (4.6%) | 1 | (1.8%) | 6 | (3.6%) |
| Cosmetic | 3 | (2.8%) | 2 | (3.6%) | 5 | (3.0%) |
| *a = p* < 0.05 (*X2)* (Significant results also underlined and in bold) |

**Table 2: Epilepsy characteristics and significance testing of group differences between the meningioma with epilepsy and epilepsy without meningioma groups**

|  |  |  |  |
| --- | --- | --- | --- |
| Epilepsy Characteristic | Meningioma with Epilepsy(n=56) | Epilepsy without Meningioma(n=64) | Total(n=120) |
| **n** | **(%)** | **n** | **(%)** | **n** | **(%)** |
| Number of Seizures in 6 Months | **0a** | **49** | **(87.5%)** | **39** | **(60.9%)** | 88 | (73.3%) |
| 1 | 2 | (3.6%) | 6 | (9.4%) | 8 | (6.7%) |
| 2 - 3 | 4 | (7.1%) | 6 | (9.4%) | 10 | (8.3%) |
| 4 - 5 | 1 | (1.8%) | 6 | (9.4%) | 7 | (5.8%) |
| 6 - 9 | 0 | (0.0%) | 2 | (3.1%) | 2 | (1.7%) |
| 10+ | 0 | (0.0%) | 5 | (7.8%) | 5 | (4.2%) |
| Number of AEDs | **0a** | **24** | **(42.9%)** | **5** | **(7.8%)** | 29 | (29.3%) |
| **1a** | **27** | **(48.2%)** | **42** | **(65.6%)** | 69 | (89.7%) |
| 2 | 4 | (7.1%) | 16 | (25.0%) | 20 | (28.6%) |
| 3 | 1 | (1.8%) | 1 | (1.6%) | 2 | (2.5%) |
| Current AED | Lamotrigine | 8 | (12.7%) | 21 | (25.6%) | 29 | (20.0%) |
| **Levetiracetama** | **4** | **(6.3%)** | **21** | **(25.6%)** | 25 | (17.2%) |
| Sodium Valproate | 10 | (15.9%) | 9 | (11.0%) | 19 | (13.1%) |
| Carbamazepine | 5 | (7.9%) | 12 | (14.6%) | 17 | (11.7% |
| Phenytoin | 10 | (15.9%) | 5 | (6.1%) | 15 | (10.3%) |
| Gabapentin | 1 | (1.6%) | 2 | (2.4%) | 3 | (2.1%) |
| Other | 2 | (3.2%) | 7 | (8.4%) | 9 | (6.3%) |
| *a* = *p* <0.05 (*X*2) (Significant results also underlined and in bold) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Questionnaire Subscale and Summary Score | Meningioma without Epilepsy(n=109) | Meningioma with Epilepsy(n=56) | Epilepsy without Meningioma(n=64) | Difference in QoL mean: |
| **Meningioma without epilepsy and meningioma with epilepsy** | **Meningioma with epilepsy and epilepsy without meningioma** |
| **Mean** | **(SD)** | **Mean** | **(SD)** | **Mean** | **(SD)** | **Mean** | **Mean** |
| SF-36 | **Subscale** | Physical Function | 46.8 | (11.6) | 44.5 | (13.0) | 44.8 | (13.3) | -2.3 | +0.3 |
| Role Physical  | 46.2 | (11.5) | 44.0 | (12.0) | 42.7 | (12.3) | -2.2 | -1.3 |
| Bodily Pain | 48.6 | (11.2) | 48.8 | (10.7) | 47.6 | (11.8) | +0.2 | -1.2 |
| General Health | 49.5 | (11.3) | 46.3 | (12.4) | 44.1 | (13.9) | -3.2 | -2.2 |
| Vitality  | 49.0 | (11.3) | 47.6 | (10.6) | 43.7 | (12.3) | -1.4 | -3.9 |
| Social Functioning | 47.9 | (11.0) | 44.1 | (13.7) | 42.7 | (13.0) | -3.8 | -1.4 |
| Role Emotional | 46.9 | (11.8) | 44.0 | (12.2) | 41.7 | (14.3) | -2.9 | -2.3 |
| Mental Health | 49.0 | (11.2) | 48.2 | (11.3) | 43.9 | (12.0) | -0.8 | -4.3 |
| **Summary** | **Physical Component PCS (47.4)c** | **47.5** | **(11.2)** | **45.8** | **(11.2)** | **45.6** | **(11.9)** | **-1.7** | **-0.2** |
| **Mental Component Score MCS (51.7)c** | **48.9** | **(11.4)** | **46.8** | **(11.7)** | **42.8** | **(12.8)** | **-2.1** | **-4.0** |
| FACT | **Subscale** | Physical Wellbeing  | 22.9 | (5.5) | 21.2 | (6.2) | 20.4 | (6.9) | -1.7 | -0.8 |
| Social Wellbeing  | 22.4 | (5.7) | 20.3 | (7.0) | 20.6 | (6.0) | -2.1 | +0.3 |
| Emotional Wellbeing  | 19.5 | (4.5) | 18.6 | (5.2) | 16.7 | (5.7) | -0.9 | -1.9 |
| Functional Wellbeing  | 20.5 | (6.7) | 19.1 | (7.7) | 18.1 | (7.7) | -1.4 | -1.0 |
| **Brain Cancer Subscale*b*** | **60.1** | **(14.1)** | **52.6** | **(14.8)** | **-** | **-** | **-7.5*b*** | **-** |
| **Summary** | **FACT-BRa** | **146.1** | **(29.6)** | **131.7** | **(35.9)** | **-** | **-** | **-14.4a** | **-** |
|  | **FACT-G** | **-** | **-** | **79.1** | **(22.9)** | **75.8** | **(23.2)** | **-** | **-3.3** |
| LAEP | **Summary** | **LAEP** | **36.1** | **(10.4)** | **39.4** | **(13.7)** | **40.8** | **(11.3)** | **+3.3** | **+1.4** |
| a = *p* = *< 0.05 b = p* = <0.01 (students t-test) (Significant results underlined, in bold and significant despite Bonferroni correction) *c = Age adjusted SF-36 summary score for normal US population* |

**Table 3: Quality of life scores of meningioma without epilepsy, meningioma with epilepsy and epilepsy without meningioma groups**

**Table 4: Hierarchical stepwise multiple regression analyses; selected dependent variables versus all QoL measures for meningioma regression and epilepsy regression**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Regression Cohort** | **Variable Blocks** | **Variables** | **PCS** | **MC*S*** | **FACT** | **LAEP** |
| **Beta** | ***p*** | **Beta** | ***p*** | **Beta** | ***p*** | **Beta** | ***p*** |
| **Meningioma Regression****n = 165** | **Demographics****Variable Block** | **Age** | **-0.202** | **0.005** | **0.185** | **0.011** | 0.035 | 0.596 | -0.060 | 0.394 |
| Female | -0.071 | 0.294 | 0.050 | 0.467 | 0.058 | 0.354 | 0.020 | 0.764 |
| **Unemployed** | **-0.286** | **< 0.001** | **-0.286** | **< 0.001** | **-0.312** | **< 0.001** | **0.246** | **0.001** |
| **Comorbidities****Variable Block** | Number of Comorbidities | -0.089 | 0.203 | -0.068 | 0.342 | -0.093 | 0.153 | -0.016 | 0.823 |
| **Arthritis** | **-0.141** | **0.039** | 0.045 | 0.517 | -0.009 | 0.883 | -0.079 | 0.245 |
| **Depression** | -0.061 | 0.382 | **-0.172** | **0.017** | **-0.152** | **0.019** | 0.092 | 0.181 |
| **Diabetes** | **-0.137** | **0.049** | **-0.149** | **0.036** | **-0.147** | **0.024** | **0.147** | **0.034** |
| **Neoplasm** | **-0.171** | **0.012** | 0.032 | 0.637 | -0.062 | 0.327 | 0.019 | 0.775 |
| **Meningioma****Variable Block** | **Meningioma Complications** | **-0.236** | **0.003** | **-0.166** | **0.040** | **-0.234** | **0.001** | 0.139 | 0.077 |
| **Motor/Sensory** | -0.100 | 0.172 | -0.026 | 0.724 | **-0.139** | **0.043** | 0.120 | 0.100 |
| Cranial Nerve | -0.041 | 0.582 | -0.084 | 0.276 | -0.083 | 0.223 | 0.120 | 0.110 |
| **Recurrence** | -0.136 | 0.054 | 0.003 | 0.965 | -0.076 | 0.254 | **0.160** | **0.023** |
| **Epilepsy****Variable Block** | Meningioma with Epilepsy  | -0.080 | 0.402 | 0.068 | 0.485 | 0.025 | 0.782 | -0.104 | 0.276 |
| **Seizure in Past 6 Months** | -0.008 | 0.914 | 0.035 | 0.652 | -0.105 | 0.145 | **0.187** | **0.014** |
| **Current AED** | 0.052 | 0.604 | **-0.202** | **0.048** | **-0.218** | **0.020** | **0.220** | **0.027** |
| **Epilepsy Regression** **n = 120** | **Demographics****Variable Block** | **Age** | -0.136 | 0.175 | **0.234** | **0.025** | 0.097 | 0.332 | -0.148 | 0.159 |
| Female | 0.032 | 0.703 | 0.047 | 0.642 | 0.037 | 0.667 | -0.020 | 0.737 |
| **Unemployed** | **-0.386** | **< 0.001** | **-0.237** | **0.027** | **-0.293** | **0.001** | **-0.181** | **0.032** |
| **Comorbidities****Variable Block** | **Number of Comorbidities** | **-0.332** | **0.001** | -0.128 | 0.211 | -0.164 | 0.079 | **0.290** | **0.009** |
| **Depression** | -0.045 | 0.595 | **-0.200** | **0.017** | -0.105 | 0.153 | 0.130 | 0.109 |
| Diabetes | -0.048 | 0.674 | -0.131 | 0.109 | -0.062 | 0.305 | 0.052 | 0.454 |
| Neoplasm | 0.047 | 0.592 | -0.084 | 0.352 | -0.008 | 0.830 | -0.018 | 0.923 |
| **Stroke** | -0.021 | 0.766 | **-0.203** | **0.036** | **-0.234** | **0.009** | 0.063 | 0.502 |
| **Meningioma****Variable Block** | Cranial Nerve | -0.106 | 0.191 | -0.082 | 0.522 | -0.133 | 0.190 | 0.147 | 0.116 |
| **Cognitive/Emotional** | **-0.172** | **0.041** | 0.024 | 0.843 | **-0.161** | **0.039** | 0.132 | 0.127 |
| **Epilepsy****Variable Block** | Epilepsy without Meningioma | -0.024 | 0.730 | 0.011 | 0.607 | 0.104 | 0.113 | -0.111 | 0.194 |
| **Levetiracetam** | -0.138 | 0.224 | -0.120 | 0.191 | **-0.230** | **0.013** | **0.207** | **0.011** |
| 1 to 3 Seizures in 6 Months | -0.061 | 0.571 | 0.043 | 0.526 | -0.177 | 0.080 | 0.161 | 0.059 |
| > 4 seizures in 6 months | -0.097 | 0.470 | -0.006 | 0.674 | -0.075 | 0.263 | 0.069 | 0.212 |
| **Current AED**  | 0.121 | 0.301 | **-0.168** | **0.014** | -0.124 | 0.110 | 0.195 | 0.090 |
| Significant results are underlined and in bold |

**Table 5: Post hoc analysis; Quality of life of meningioma patients with and without anti-epileptic drugs**

|  |  |  |  |
| --- | --- | --- | --- |
| Questionnaire Summary Score | Meningioma without AED(n=133) | Meningioma with AED(n=32) | Difference In Mean |
| **Mean** | **(SD)** | **Mean** | **(SD)** | **Mean** |
| PCS | 46.9 | (11.2) | 46.9 | (11.5) | 0.0 |
| MCS | **49.1** | **(11.0)** | **44.2** | **(13.0)** | **-4.9a** |
| FACT-BR | **145.5** | **(29.2)** | **123.7** | **(39.4)** | **-21.8c** |
| LAEP | **36.0** | **(10.6)** | **42.1** | **(14.7)** | **+6.1b** |
| *a = p < 0.05* *b = p < 0.01**c = p < 0.001* *(Significant results also underlined and in bold)* |  |