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Diffuse low grade glioma after the 2016 WHO update, seizure characteristics, imaging correlates and outcomes

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ABSTRACT

Objective

The majority of patients with supratentorial diffuse grade II glioma present with seizures, which adversely affect quality of life. The exact mechanism of epileptogenesis is unknown and the influence of tumour characteristics, radiological and histological, are not well studied, particularly following the introduction of molecular genetics in the 2016 WHO reclassification of gliomas. We sought to define predictors of seizure development and outcome in low grade glioma.

Patients and Methods

A retrospective review of patients who underwent resection of a supratentorial grade II glioma in a single institution. All patients underwent surgery at initial presentation with the aim of maximal safe resection. Presenting symptoms and radiological variables were recorded, including eloquent location, cortical involvement, tumour margins and tumour volume. Extent of resection (EOR), surgery type (awake vs asleep) and seizure outcome were analysed. Using molecular genetics data the original histology was reclassified according to the 2016 WHO update.

Results

63 patients were included, 45 (71%) presented with seizures. 36 (57%) had oligodendroglioma and 27 astrocytoma. IDH-1 mutation was present in 53 (84%). 18 (29%) had tumour in an eloquent location. 33 (73%) were Engel class I following surgery at median follow up of 43 months. 6 patients were Engel II, 6 class III. Complete and near total resection were associated with improved Engel class compared to subtotal resection. No factors such as age, tumour location, tumour margins or tumour molecular genetics (including IDH-1 mutation) predicted better seizure outcome. Updated histological subtype did not predict the presence of seizures at initial diagnosis, only tumour heterogeneousity on initial MRI (p=0.043). More patients who underwent awake craniotomy with intraoperative mapping were Engel class 1 post-operatively than those operated under general anaesthetic (84% vs 65%). Tumour volume at presentation did not correlate with seizure outcome but impacts on the EOR.

Conclusion

Seizure outcome is directly related to EOR in low grade glioma, which can be predicted by the initial tumour volume. Tumour histological subtype, including updated molecular genetic classification did not predict seizure development or outcome in this series. The use of awake craniotomy results in greater EOR and improved Engel Class following surgery.

Key words

Low-grade glioma; seizure outcome; extent of resection; updated molecular genetics; risk factors

1. Objective

World Health Organisation (WHO) grade II gliomas (low-grade gliomas; LGGs) are a heterogeneous group of primary central nervous system (CNS) tumours arising from glial cells (1). LGGs are shown to exhibit an average growth rate of around 4mm/year and will eventually undergo malignant transformation (2,3). The recent WHO classification system of LGGs classifies them as either astrocytoma or oligodendroglioma, emphasising the use of molecular genetics to distinguish tumour type. Previously, an additional classification of oligoastrocytoma existed, however, this has been removed in the recent updated classification system (4).

Most patients with LGGs present within the third or fourth decades of life with an overall incidence of 0.63-1.8/100,000 adults per year (5,6). They are highly epileptogenic tumours with 60-88% of patients presenting with seizure activity (7–10). The exact mechanisms of tumour epileptogenesis are not fully understood but multiple factors appear to play roles. Potential factors predominantly involve peritumoural changes in metabolism, perfusion, electrolytes and enzyme activity. (11). For example, *IDH* mutations occur in up to 80% of LGGs and are believed to contribute to epileptogenesis by causing production of a structurally similar compound to glutamate and thus activating NMDA receptors (11).

Previously, management of LGGs involved a 'watch-and-wait' approach. However, there has been a recent shift towards earlier and more aggressive management due to the inevitable malignant transformation (2,12). A range of studies have shown more favourable outcomes with early surgical resection, particularly with a greater extent of resection (EOR) (13,14). In terms of seizure outcome, studies have shown seizure freedom in up to 65-81% of patients post-resection, but the exact prognostic factors that influence seizure outcome are not yet fully understood (6,8,9,15).

This study aimed to assess seizure outcome in a series of operated LGG patients and identify any pre- or post-operative predictors which may influence eventual seizure outcome, including tumour type based on the up-to-date molecular genetic analysis of the 2016 WHO classification update.

2. Patients and Methods

2.1 Patient Population

A total of 63 patients with operated supratentorial grade II gliomas were included in this study, consisting of 36 oligodendrogliomas and 27 astrocytomas (according to WHO 2016 classification). All patients underwent surgical resection of their tumour at initial presentation, between May 2011 to December 2016 in a single institution. Those patients that only underwent biopsy were excluded from the study. Additionally, all cases with tumours classified grade II/III were excluded.

Clinical records were retrospectively analysed for symptoms at presentation, seizure type, type of resection (awake vs asleep), adjuvant treatments, seizure outcome (Engel class; table 1) and the presence and grade of tumour recurrence. Seizure outcome was assessed at 3, 6 and 12 months post-operatively and at most recent clinic follow up (median follow up time of 40 months). Tissue samples were analysed for all but 2 patients in terms of their immunohistochemistry (IHC) and molecular genetics and tumours were reclassified according to the 2016 system retrospectively. Reclassification was performed on the basis that a tumour with an IDH mutation plus 1p19q mutation is an oligodendroglioma and an IDH mutation plus ATRX mutation is an astrocytoma. All tissue samples in our institution have had IDH1 mutation IHC and molecular genetics performed since 2011 enabling retrospective reclassification in the majority of cases.

Table 1 – Overview of Engel classification system; from Tanriverdi *et al.* [16].	
Engel class	
I	Seizure free without aura; seizures only on withdrawal of anti-epileptic drug (AED)
II	Rare disabling seizures
III	Worthwhile improvement
IV	No worthwhile improvement/worsening seizures

2.2 MRI Analysis

The recorded MRI information included laterality (left or right hemisphere), location (frontal, temporal, parietal, insular or a combination), presence of cortical involvement, mass effect and location in an eloquent region. Tumours were also described with relation to their borders (distinct vs indistinct) and tumour signal on MRI (homogenous vs heterogenous). Tumour size was analysed using the widest diameter in three directions and tumour volume calculated (ellipsoid method volume=D1xD2xD3/2). EOR was described as complete, near-total (>90%) and subtotal (<90%), based on immediate post-
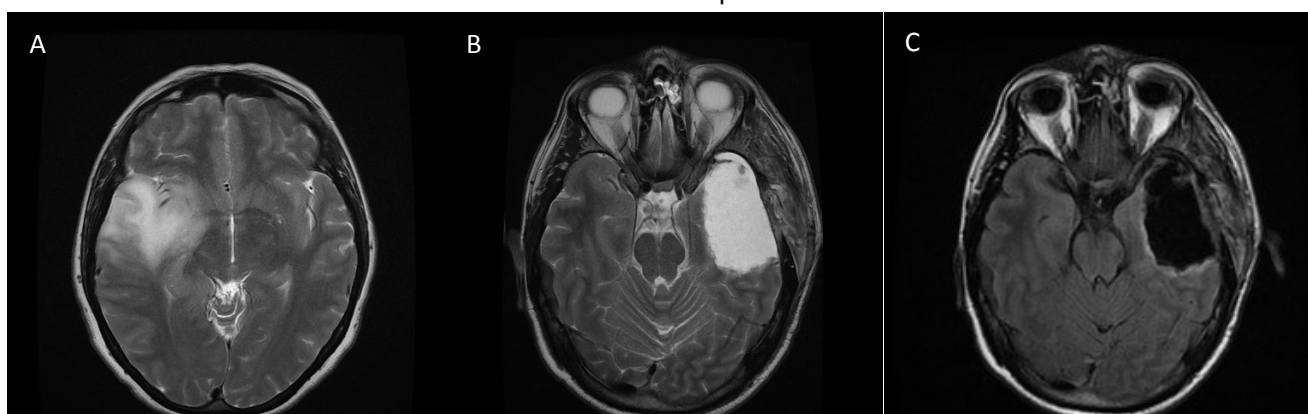
Figure 1 – Axial MRI images from two patients. A) Shows an example of a heterogenous glioma with indistinct borders on T2. B) shows an example of a homogenous LGG with distinct borders. C) Post-operative surgical cavity on FLAIR after resection of tumour B.

operative MRI.

Statistical analysis was performed using SPSS, Version 24 IBM Corp, Armonk NY. Univariate analysis was performed using $\chi2$ and Fishers exact test where appropriate and paired t tests for continuous variables. A P value of <0.05 was considered significant.

3. Results

Our cohort included a total of 63 patients, 43 male and 20 female, with a median age of 34 years. 36 patients had oligodendogliomas and 27 had astrocytomas with 30 being located in the right hemisphere and 33 in the left hemisphere. The key clinical and demographic characteristics are

> **Table 2** – Summary of overall patient parameters. Tumours situated within the supplementary motor area (SMA) have been included in the eloquent group.

displayed in table 2.

Parameter	Total number of cases
Total patients	63
Males	43 (68%)
Females	20 (32%)
Median age	34
Median follow up time	40 months
Deceased patients	4
Median time to death	29 months (range 11-44)
Tumour	
Oligodendroglioma	36 (57%)
Astrocytoma	27 (43%)
IDH-1 mutation	53 (84%)
Right hemisphere	30 (48%)
Left hemisphere	33 (52%)
Eloquent region (+ SMA)	18 (29%)
Non-eloquent	45 (71%)
Seizures	
Total seizures	45 (71%)
GTC	17 (38%)
Partial	15 (33%)
Combined GTC and partial	13 (29%)
Surgery	
Awake	25
General anaesthetic (GA)	38

The main presenting complaint was seizure in 45 (71%) patients, of which 17 (38%) were generalised tonic-clonic seizures (GTC), 15 (33%) were focal seizures and 13 (29%) had a combination of focal and generalised. Other presenting symptoms included headache (3%), focal neurological deficit (5%), a combination of the two (11%) or were incidental findings (5%). There were 53 patients with IDH-1 mutations present (84%) of which 41 presented with seizures (77%). Four oligodendrogliomas and four astrocytomas did not have IDH-1 mutations present and thus classify as

oligodendroglioma, NOS, and astrocytoma, NOS, respectively. Two patients with morphological astrocytomas did not have molecular genetics available.

3.1 Patients Presenting with Seizures

Seizure outcome was assessed using the Engel classification system (table 1). 33 out of 45 patients (73%) presenting with seizures were Engel class I post-operatively at a median follow up of 43 months. All remaining patients gained some benefit from resection (6 patients were Engel class II, 6 were class III). Seizure outcome was assessed at 3, 6 and 12 months post-operatively as well as up to most recent status. 41 patients were Engel class I at 3 months (91%), 39 at 6 months (87%) and 36 at 12 months (80%). No patients were Engel class IV. Median and mean times to seizure recurrence were 10.5 months and 17.8 months respectively (range 3-48 months). Of the 12 patients with seizure recurrence, 6 (50%) had evidence of tumour recurrence at the time. Seizure recurrence was not significantly associated with tumour recurrence or progression, with seizure recurrence or new seizures occurring in only 8 out of the 25 patients (32%) with tumour recurrence in the series.

We analysed data for other variables that might predict eventual Engel class after surgery. Greater EOR tended to give better seizure outcome, with complete and near-total resection resulting in Engel class I in 76% and 87.5% respectively compared to 62.5% of subtotal resections. Complete resection is the strongest predictor of seizure freedom compared to either near or subtotal resection (p=0.066). Demographics including patient age, IDH status and type of surgery did not significantly predict seizure outcome, but this may be related to the small sample size within subgroups. Tumour type did not significantly predict seizure outcome, whether using the 2016 WHO classification system or the previous system. Based on the 2016 classification system, patients with oligodendrogliomas had a slightly greater seizure freedom rate than those with astrocytomas, but this is not significant (79% vs 67%; p=0.299). This is similar to results based on the previous classification system, where 88% of oligodendrogliomas, 61% of astrocytomas and 60% of oligoastrocytomas were seizure free. More patients who underwent an awake craniotomy with intra-operative functional mapping were Engel class I post-operatively compared to those under GA but this was non-significant (84% vs 65%; p=0.80). There were no radiological variables that significantly predicted seizure outcome, including eloquent location, cortical involvement, border distinction, mass effect or tumour signal.

Figure 2 – Seizure outcomes using Engel classification system based on pre-operative factors (tumour type, seizure type and tumour location as either eloquent (including SMA) or non-eloquent. Blue bars indicate Engel class I, orange bars indicate Engel class II or above. Data only used from patients presenting with seizures (n=45). Individual bar totals are the total number of patients presenting with seizures within each category.
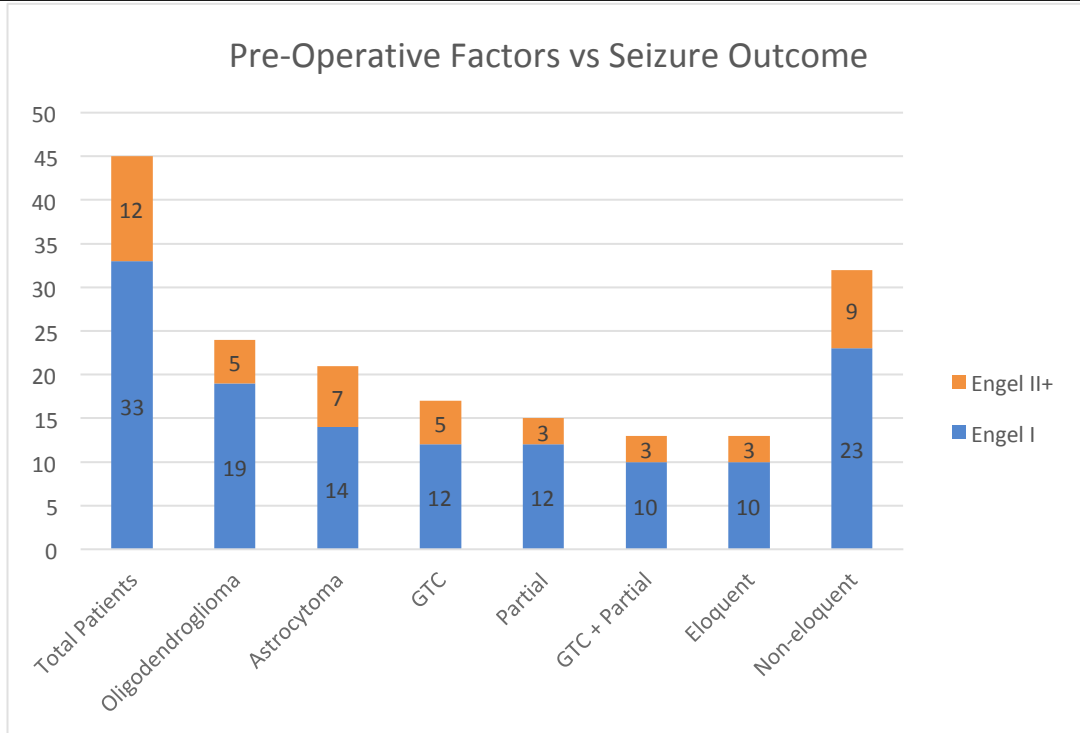
Figure 3 - Seizure outcomes using Engel classification system based on operative factors - EOR (complete, near-total or sub-total) and type of surgery (awake vs GA). Blue bars indicate Engel class I, orange bars indicate Engel class II or above. Data only used from patients presenting with seizures (total n=45). Individual bar totals are the total number of patients presenting with seizures within each category.
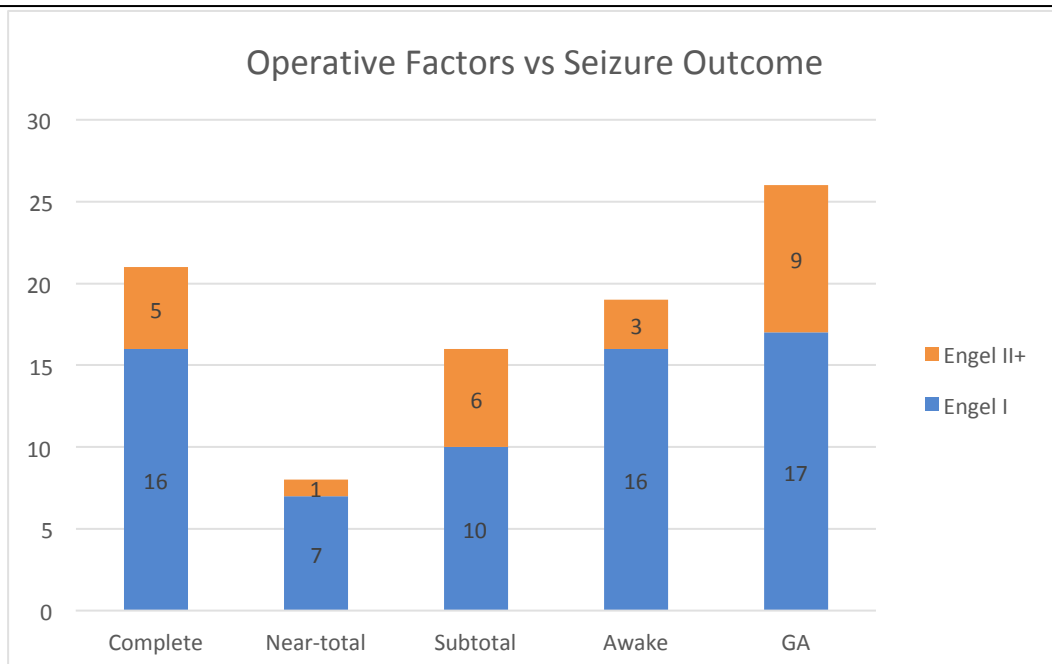
We also analysed data to identify if any factors predicted whether seizures were the presenting symptom. The only variable to significantly predict seizures as a presenting symptom was tumour signal on MRI, where 81% of tumours with a heterogeneous appearance produced seizures compared to 58% of homogenous tumours (p=0.043). Other demographics including age, IDH status and tumour volume and radiological variables of eloquent location, cortical involvement, mass effect and border distinction did not significantly predict whether seizures were the presenting symptom.

We tried to identify whether any variables correlated with tumour type based on the 2016 WHO classification system. More oligodendrogliomas had indistinct borders (59%) compared to astrocytomas (35%), p=0.05. No other factors, including seizures as a presenting symptoms, IDH status, tumour recurrence and tumour signal on MRI, significantly correlated with reclassified tumour type.

Tumour volume at presentation did not correlate with eventual seizure outcome (p=0.70). However, EOR was significantly greater in tumours with smaller volumes. The mean tumour volume in patients who underwent complete or near-total resection was 23.8 cm^3 compared to 54.9 cm^3 in those who underwent subtotal resection (p=<0.01). Tumours in eloquent locations had significantly smaller volumes than those in non-eloquent locations, with mean volumes of 22.0 cm^3 and 37.7 cm^3

Parameter	Number of cases

respectively (p=0.035).

3.2 Patients with no seizures at presentation

Total patients	18
Tumour type	
Oligodendroglioma	12 (67%)
Astrocytoma	6 (33%)
IDH mutation	
Present	16 (89%)
Absent	2 (11%)

Table 3 – Parameters for patients whom did not presenting with seizures. * indicates percentage of seizure cases	

Complete	9 (50%)
Near-total	6 (33%)
Sub-total	3 (17%)
Eloquent	5 (28%)
Non-eloquent	13 (72%)
Cortical involvement	7 (39%)
Mass Effect	6 (33%)
Distinct borders	10 (56%)
Homogenous appearance	11 (61%)

18 patients did not present with seizures and their key parameters are outlined in table 3. As previously stated, the only variable that significantly predicted seizures as a presenting symptom was heterogeneous MRI appearance, with those with heterogenous tumour signal being more likely to present with seizures, although this did not correlate with a specific tumour type. Median tumour size in patients who did not present with seizures was 14.55cm^3 compared to 36.85cm^3 in those who did.

7 patients did eventually develop seizures (6 GTC; 1 partial) at a median time of 29 months. Of these new cases of seizures, 6 were oligodendrogliomas and 1 was astrocytoma. Only one new seizure case was associated with radiological tumour progression recurrence of an oligodendroglioma which

Grade at Recurrence	Complete resection	Near-total resection	Subtotal resection

had undergone subtotal resection. There were no factors that predict which patients would go on to develop seizures. EOR was complete or near total in 5 patients with new seizures (71%) compared to 10 out of 11 patients who never had seizures (91%).

3.3 Tumour Outcome

Tumour recurrence or progression occurred in 25 (40%) patients in the series, with median time to recurrence of 22 months. Of these, fourteen recurred as grade II, eight as grade III and three as grade IV.

In patients presenting with seizures (n=20) the median time to recurrence was 22.5 months vs 21 months in those who did not present with seizures (n=5) Figure 1. Table 4 shows the EOR and tumour grade at recurrence for the 25 patients who progressed. In this cohort, patients who underwent subtotal resection were more likely to have progression than those with complete or near-total resection, with progression occurring in 52% of subtotal resections and 27% of complete/near-total resections (p=0.044). Importantly, of tumours recurring as grade III or IV, only one out of nine patients had undergone complete resection (11%).

Table 4 – comparison of EOR rates in different grades of tumour recurrence	

II	6	3	5
II/III	2		
III	1	1	4
III/IV			1
IV		1	1

Larger tumours were also more likely to recur. The mean tumour volume in patients who had recurrence was 44.2 cm^3 compared to 26.0 cm^3 in patients with no recurrence (p=0.008). Mass effect was also predictive of tumour recurrence, where recurrence occurred in 67% of patients with evidence of mass effect on pre-operative MRI, compared to 19% of those with no mass effect evident (p=<0.01). IDH status, type of surgery and radiological variables of border distinction, cortical involvement and tumour signal did not significantly predict recurrence.

Overall, greater EOR was generally achieved with awake craniotomy with 13 undergoing complete resection (52%), 7 near-total (28%) and only 5 sub-total (20%). In comparison, in the general anaesthesia (GA) group a complete resection was achieved in 17 patients (45%), near-total in 7 patients (18%) and sub-total in 14 patients (37%). However, this did not statistically predict seizure freedom (p=0.80).

Most patients were treated before the publication of the RTOG 9802 study, therefore the use of adjuvant treatment was mixed. 17 patients received adjuvant therapy after initial tumour resection due to significant residual disease. 8 received radiotherapy alone, 2 received chemotherapy alone and 7 received combined chemo-radiotherapy. 11 (65%) had oligodendrogliomas, the remainder had astrocytomas. Of the patients who initially presented with seizures (n=45), 9 received adjuvant therapy, compared to 8 patients out of those who did not present with seizures (n=18). 11 patients who had adjuvant treatment were Engel class I (65%). Our data did not show a statistically significant improvement in seizure outcome after adjuvant therapy compared to no adjuvant therapy (p=0.33).

3.4 Outcomes Before and After the 2016 WHO Update

After reclassification there were 36 patients with oligodendroglioma and 27 with astrocytoma. Based on the original histological classification before the 2016 update there were 28 with oligodendroglioma, 24 with astrocytoma, 11 with oligoastrocytoma. Of the oligoastrocytomas, 7 were reclassified to oligodendroglioma and 4 to astrocytoma.

Table 5 – Comparison of cases before and after reclassification using 2016 WHO update

	Total cases	Seizures	Engel I	Engel II+
Before Update				
Oligodendroglioma	28	18	16 (89%)	2 (11%)
Astrocytoma	24	17	11 (63%)	6 (37%)
Oligoastrocytoma	11	10	6 (60%)	4 (40%)
After Update				
Oligodendroglioma	36	24	19 (79%)	5 (21%)
Astrocytoma	27	21	14 (67%)	7 (33%)

As shown in table 5, tumours previously classified as oligoastrocytoma were most likely to present with seizures. Oligodendrogliomas were also more likely to be Engel class I post-operatively, whereas oligoastrocytomas were least likely. More oligoastrocytomas were reclassified as oligodendroglioma than astrocytoma, which may have affected Engel class outcomes post-update as there were 10% fewer oligodendroglioma patients Engel class I after reclassification. However, seizure outcome was virtually unchanged in astrocytomas before and after the update.

In new cases of seizures, there was no change between pre- and post-updated classification, with 6 cases of new seizures in patients with oligodendrogliomas and 1 with astrocytoma.

Tumour recurrence was not significantly impacted after the updated classification. 25 patients had tumour recurrence, 12 of which were oligodendroglioma and 13 astrocytoma. Before reclassification, these 25 patients were made up of 9 oligodendrogliomas, 11 astrocytomas and 5 oligoastrocytomas.

4. Discussion

The main outcome of this study was to assess seizure outcome in patients with LGGs and identify any imaging, molecular or operative predictors of seizure development and seizure freedom based on the 2016 WHO classification system (4).

Our result of 73% patients being Engel class I post-operatively is in keeping with other data, with a range of 67-81% reported (6,8,15,16). The proportion of our patients being Engel class I decreases with time post-operatively, as shown by the seizure freedom rates at 3, 6 and 12 months post-operatively (91%, 87% and 80% respectively).

EOR appears to be a strong predictor of seizure freedom (Engel class I) after resection (8,15,17). Our results of Engel class I for complete (76%), near-total (87.5%) and subtotal resection (62.5%) show preferable seizure outcome with greater EOR. This is in keeping with other literature, for example Xu *et al.* (15) found an EOR >80% gave better seizure outcome (Engel class I) and a meta-analysis showed 80% seizure freedom from gross-total resection compared to 53% of subtotal resections (17), again similar to our data. Seizure freedom in 62.5% of subtotal resections still shows the surgical benefit to seizure outcome even when a lower EOR is achieved. The widespread push towards maximal early resection appears to provide improved seizure outcomes. In fact, "supratotal" resection, whereby the tumour is removed along with a margin visible on FLAIR-weighted MRI, has been shown to produce favourable seizure outcomes as well as a significant reduction in the risk of malignant transformation (14). This is reflected in the fact that in this study EOR was also a significant predictor of tumour recurrence as tumours were significantly more likely to recur with an incomplete EOR compared to near-total or complete, despite adjuvant therapy. Adjuvant therapy did not appear to give favourable seizure outcomes in this cohort (p=0.33) which may be due to the fact that adjuvant therapy tended to be used in those with significant residual disease (incomplete EOR) which is a negative prognostic factor in itself.

Our data also show that seizure outcome is improved when resection is performed as awake craniotomy with intra-operative functional mapping compared to under GA (84% Engel class I vs

65%). This may be due to an overall greater EOR in those operated awake compared to those operated under GA. Of the 19 patients who underwent awake craniotomy and resection, 74% had complete or near-total resection compared to 58% of those operated under GA. The increased number of subtotal resections in the GA group may contribute to the reduced rate of seizure freedom.

When comparing seizure outcome in patients with oligodendrogliomas to astrocytomas based on the 2016 WHO update, slightly more patients with oligodendrogliomas were Engel class I (79% and 67% respectively), however this is not statistically significant. In contrast, Chang *et al.* (8) report that patients with oligodendrogliomas are more prone to seizures due to a tendency to be located cortically. It was generally thought that more cortically located tumours are more prone to developing seizures, which included the no longer used classification of oligoastrocytoma. Where astrocytomas were thought to be mainly found in white matter tracts they were thought to have less seizures apart from protoplasmic astrocytomas which were linked to chronic epilepsy. After reclassification, tumour type did not have an impact on seizure outcome in our cohort. There is somewhat mixed data assessing outcomes based on tumour type. Previous studies have shown both improved outcome with certain tumour type (oligodendroglioma; (18) or no difference in outcome (19). Furthermore, there is conflicted evidence that oligodendrogliomas are more likely to have seizures as a presenting symptom (9,20) but in our cohort tumour type did not predict which patients would present with seizures initially, with no significant difference between oligodendrogliomas and astrocytomas in terms of seizures as a presenting symptom. Additionally, although oligodendrogliomas had more indistinct borders than astrocytomas based on the 2016 classification (59% vs 35%), there was no difference in EOR or seizure outcome in this series , which may reflect the small numbers in each subgroup and requires further study.

The 2016 WHO update has not shown significant changes in prognosis in our series. The greatest difference was in seizure freedom rates of oligodendrogliomas, where 89% were Engel class I post-operatively based on the old classification system compared to 79% after reclassification. This may be due to fact that the majority of oligoastrocytomas, which had the highest proportions of patients presenting with seizures (89%) and lowest proportion Engel class I post-operatively (40%), were reclassified as oligodendrogliomas and thus reduced the rate of seizure freedom. Aside from this, there was very little impact on rates of tumour recurrence between tumour types and no change between rates of new seizures. Larger long term case series will be required to demonstrate differences in clinical features and outcome after the 2016 update.

Delfanti et al. aimed to correlate imaging characteristics with tumour classification based on the 2016 update in a retrospective study of 40 patients (21). They identified that tumour classification had an impact on tumour location, appearance of borders on MRI and progression free survival (PFS), where patients with no IDH mutation had significantly shorter PFS (24). It may be that tumour histology under the new classification has less importance to seizure outcome compared to the old system but has a greater impact in relation to patient demographics, imaging characteristics and prognosis. In our study, pre-operative radiological variables including cortical involvement, mass effect, eloquent location, border distinction and tumour signal did not significantly impact on seizure development, outcome or the ability to achieve maximal EOR. Interestingly, tumour signal (homogenous vs heterogenous) on MRI was significantly related to whether seizures were the presenting symptom, which may reflect as yet unknown molecular differences within tumours.

IDH mutation status has previously been shown to be associated with seizures as a presenting symptom and increased risk of future malignant transformation (5,13,25–27). However, our data showed no significant correlation between *IDH* mutations and seizures as a presenting symptom, seizure outcome, tumour type or recurrence. Therefore the use of *IDH* mutation status alone as a prognostic marker was limited in our cohort.

Tumour volume did not influence seizure outcome, with similar mean tumour volumes in patients who were Engel class I compared to class II or above post-operatively (33.8 cm^3 vs 30.3 cm^3 respectively). However, tumour volume did influence tumour outcome, as cases where progression occurred had significantly larger initial tumour volumes compared to those which did not (p=0.008; mean volumes 44.2 cm^3 vs 26.0 cm^3 respectively). This is likely linked to the potential EOR achievable with larger tumours, as mean tumour volume was significantly greater in patients who underwent subtotal resection compared to those who had near-total or complete resection (54.9 cm^3 vs 23.8 cm^3; p=<0.01). Thus, larger initial tumour volumes appear to reduce the possible EOR, which has also been shown elsewhere (1). We did not identify a link between tumour volume and seizures as a presenting symptom whereas others have shown that larger tumours tended to present with seizures (28).

For patients that did not present with seizures, it is not obvious as to what specific factors predict the absence of seizures or what led to development of seizures in 7 of the 18 (39%) as our data show no statistically significant predictors. The majority of patients who went on to develop seizures had oligodendrogliomas (86%) which correlates with some that oligodendrogliomas tend to be more cortical and are more prone to seizure activity, but this result was not significant and there is mixed evidence in the literature (8,9,20). Previous studies have suggested that larger tumours are indicative of a longer period of silent growth, with more time for seizures to develop (28). It is possible that more patients would have gone on to develop seizures had they not presented with other symptoms or as an incidental finding. Leading on from this, our finding that tumour volume was significantly smaller in tumours located in eloquent regions compared to non-eloquent regions (22.0 cm^3 vs 37.7 cm^3) is most likely due to eloquently located tumours producing symptoms at an earlier stage in their growth.

We identified several key factors that predict tumour recurrence, in line with recent studies (1,26). Evidence of mass effect on pre-operative MRI, larger tumour volumes and reduced EOR all statistically correlated with an increased likelihood of recurrence. Mass effect may play a role by affecting resection, whereby compression of nearby structures limits the achievable EOR. Tumour volume and EOR appear to interlink in their effect on tumour recurrence, whereby larger tumour volumes correlate directly with tumour recurrence and also reduced EOR, which indirectly correlates with survival as reduced EOR is associated with tumour recurrence. Similar data has been shown in other studies in that EOR is reduced in larger tumours as well as tumour volume being an independent prognostic factor for tumour recurrence (1,29).

Overall, pre-operative radiological variables did not predict seizure outcome in our cohort, with tumour volume the only variable that influences EOR and hence seizure outcome. Even tumour location in an eloquent region does not influence EOR so it seems that with judicious use of awake craniotomy it is possible to achieve significant resection and lead to a favourable outcome. Tumour volume appears to be an important variable relating to factors such as EOR and tumour recurrence

but does not affect seizure outcome. In this study, the majority of patients achieved seizure freedom and thus were able to return to driving, which is a considerable benefit to quality of life, particularly due to the young age and previous good health of the majority of LGG patients.

This study has several limitations including the retrospective analysis of a single institution series. With multiple variables it is possible that the lack of statistical significance is related to small sample size. However, our findings regarding EOR and outcome are in line with the current LGG literature and further larger multicentre studies of radiological and molecular genetic variables are required.

5. Conclusion

Our data are consistent with similar studies when assessing seizure outcome after resection of LGG, in that a greater EOR gives improved seizure freedom. Even when EOR was subtotal, most patients were still Engel class I, indicating that the newer strategy of earlier and more aggressive resection may result in a better overall prognosis for patients with LGGs and improve quality of life with regards to seizure freedom. Radiological variables did not impact seizure outcome, indicating that cautious resection, particularly with the use of intra-operative functional mapping, is still possible in the majority of tumours even when eloquently located. Regardless of pre-operative variables, it appears the most important predictor of seizure outcome is maximal safe resection, regardless of tumour type.

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Conflicts of interest

None declared.

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