Postoperative Quality of Life Outcome and Employment in Patients Undergoing Resection of Epileptogenic Lesions Detected by Magnetic Resonance Imaging

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Abstract
The long-term postoperative improvement of quality of life (QOL) and employment were investigated in patients undergoing resection of epileptogenic lesions detected by magnetic resonance (MR) imaging to identify the associated preoperative factors. Thirty of 47 patients who underwent lesionectomy between 1987–2001 replied to questionnaires. Patients with extratemporal resection outnumbered those with temporal lobe resection. The mean follow-up period was 12.4 ± 3.7 years. An arbitrary score for quantitatively assessing QOL was assigned. The mean increases in QOL score points were significantly higher in the late childhood onset group than those in the early childhood onset group, and were also significantly higher in the temporal resection group and extratemporal resection of non-dysplastic cortical pathology group than in the extratemporal resection of dysplastic cortical pathology group. Postoperative QOL improvement and occupational status of patients depended on the completeness of seizure control. Resection of lesions detected by MR imaging in patients with intractable epilepsy resulted in effective long-term QOL improvement and postoperative occupational status. Favorable outcome was related mainly to the pathology of the epileptogenic lesions, whether the lesion site was temporal or extratemporal, and the completeness of seizure control.

Key words: epilepsy surgery, long-term outcome, quality of life, employment, magnetic resonance imaging

Introduction
Epilepsy surgery has seen a dramatic resurgence of interest in the past two decades, associated with remarkable advances in magnetic resonance (MR) imaging techniques for identifying epileptogenic lesions of the brain in patients with refractory epilepsy.2,21) Studies of long-term outcome have found mounting evidence of late seizure recurrence in the last few years,19) but almost all of these studies have been limited to temporal lobe resections,20,23) with few long-term follow-up studies of the outcomes of epilepsy surgery involving extratemporal resection.22)

We previously developed a protocol that introduced MR imaging as an essential tool for the diagnosis of epileptogenic lesions amenable to surgical treatment, which was applied to epilepsy surgery in both children and adults.10) Our previous study of postoperative long-term seizure outcome, 5 years or more after epilepsy surgery, in patients undergoing lesionectomy under this protocol found that the outcome was related mainly to the pathology of epileptogenic lesions and whether the lesion site was temporal or extratemporal.17)

The present study evaluated the long-term efficacy of lesionectomy on improvement of quality of life (QOL) in the same series, which includes more extratemporal than temporal lobe resections, and also investigated the preoperative factors associated with long-term QOL improvement.

Materials and Methods
The protocol for the diagnosis of epileptogenic le-
sions amenable to surgical treatment was as follows: MR imaging was performed on patients with intractable epilepsy to identify the epileptogenic lesions. The epileptogenicity of any identified lesion can be determined by non-invasive methods, including ictal electroencephalography (EEG) analysis using ambulatory and/or video-EEG recordings, and regional cerebral blood flow measurements by single photon emission computed tomography. Any confirmed epileptogenic focus was then surgically treated.

Craniotomy was performed under general anesthesia with tracheal intubation, induced by intravenous administration of thiopental sodium and maintained by inhalation of halothane or sevoflurane with nitrous oxide (N₂O). The lesion and the eloquent area were localized in the brain intraoperatively by referring to the findings of preoperative MR imaging, inspection, palpation, laser Doppler flowmetry, B-mode ultrasonography, and EEG studies. The location and limits of the epileptogenic zone were identified, extent of resection decided, and completeness assessed by intraoperative cortical EEG and/or depth EEG. Somatosensory and/or motor evoked potential monitoring was performed to localize primary afferent and/or efferent areas.

Patients included in this clinical analysis of long-term outcome of epilepsy surgery had a lesion on MR imaging but no mass effect and/or contrast enhancement; had undergone resective surgery in accordance with our protocol, by a single neurosurgeon (K.M.); and had been followed up for at least 5 years postoperatively. A total of 47 patients were selected from among those who underwent surgery between December 1987 and April 2001 at two hospitals, Kyoto University Graduate School of Medicine and Shimane University School of Medicine. These patients received questionnaire surveys by post or telephone regarding postoperative seizure control. Thirty patients replied to the questionnaire (reply rate 64%) and became the subjects. The mean follow-up period was 12.4 ± 3.7 years.

The 30 patients (19 males and 11 females) were divided into two groups according to the resection site of the brain: 11 (5 males, 6 females) who had undergone temporal resection, i.e., resection in the temporal lobe (T group); and 19 (14 males, 5 females) who had undergone extratemporal resection, i.e., resection in the cerebrum other than in the temporal lobe (ExT group). The predominant side of lesionectomy was the right in the T group (right 7, left 4) and the left in the ExT group (right 8, left 10, bilateral 1). The patients were also divided into three clinicopathological categories: Temporal resection (T group), extratemporal resection of non-dysplastic cortical pathology (Non-CD exT group), and extratemporal resection of dysplastic cortical pathology (CD exT group).

The patients were divided into three groups according to age at seizure onset: 10 patients with early childhood (less than 3 years of age) onset, 14 with late childhood (3 to 15 years) onset, and 6 with adult (more than 15 years) onset. Patients in the T group were almost evenly distributed over the three seizure onset groups, but less than 20% of patients in the ExT group belonged to the adult onset group. The patients were divided into three groups according to the preoperative duration of epilepsy: 7 patients with short (less than 6 years), 9 with medium (6 to 10 years), and 14 with long (11 years or more) duration.

Seizure outcome was coded into 4 classes according to the degree of seizure reduction at the longest follow up, using Engel’s criteria as follows: Class I (free of disabling seizures), Class II (rare disabling seizures, almost seizure-free), Class III (worthwhile improvement), and Class IV (no worthwhile improvement). To assess the surgical results quantitatively with regard to postoperative reduction in seizure frequency, a score for Engel's grades was assigned as follows: Class I, 5 points; Class II, 3 points; Class III, 1 point; and Class IV, 0 points.

Postoperative QOL in terms of disability in daily living at the longest follow up was divided into four grades as follows: normal range (work or study possible), slightly disturbed (independent daily living possible), moderately disturbed (partial care required in daily living), and severely disturbed (care required for all activities of daily living). An arbitrary point system was assigned as follows: normal range, 5 points; slightly disturbed, 4 points; moderately disturbed, 3 points; and severely disturbed, 1 point. The grading gap of 2 points was left between moderately disturbed and severely disturbed from the practical viewpoint of QOL. The degree of improvement in QOL was evaluated by the postoperative increase or decrease in QOL points.

The items in the questionnaire were compared with age at seizure onset, duration of epilepsy (period between seizure onset and surgery), and clinicopathological features to investigate the factors affecting long-term QOL outcomes. All personal data items were subject to privacy protection.

All values are expressed as means ± standard deviation. Statistical analysis used the chi-squared ($\chi^2$) test, Kruskal-Wallis H test, Spearman’s test, and Scheffe’s method, and were conducted with Excel 2004 (version 11.2.3; Microsoft, Redmond, Wash., U.S.A.) and SPSS (version 8.0 for Windows; SPSS, Chicago, Ill., U.S.A.) with significance accepted at the 5% level.

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Table 1 Distribution of postoperative quality of life (QOL) grading in patient groups classified according to clinicopathological category

<table>
<thead>
<tr>
<th>Clinicopathological category</th>
<th>n</th>
<th>Nor (5)</th>
<th>Sl (4)</th>
<th>Mod (3)</th>
<th>Sev (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T group</td>
<td>11</td>
<td>8</td>
<td>2</td>
<td>1</td>
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<tr>
<td>ExT group</td>
<td>19</td>
<td>7</td>
<td>7</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Non-CD exT group</td>
<td>15</td>
<td>7</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CD exT group</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>15</td>
<td>9</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>


Table 2 Distribution of postoperative increase and mean value of quality of life (QOL) point score in patient groups classified according to clinicopathological category

<table>
<thead>
<tr>
<th>Clinicopathological category</th>
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<th>2</th>
<th>1</th>
<th>0</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>T group</td>
<td>11</td>
<td>1</td>
<td>9</td>
<td>1</td>
<td>1.00 ± 0.45*</td>
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<tr>
<td>ExT group</td>
<td>19</td>
<td>1</td>
<td>12</td>
<td>6</td>
<td>0.74 ± 0.56</td>
</tr>
<tr>
<td>Non-CD exT group</td>
<td>15</td>
<td>1</td>
<td>12</td>
<td>2</td>
<td>0.93 ± 0.46*</td>
</tr>
<tr>
<td>CD exT group</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0.83 ± 0.52</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>2</td>
<td>21</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significantly different from CD exT group (p < 0.005). CD: with cortical dysplastic pathology, ExT: extratemporal resection, Non-CD: without cortical dysplastic pathology, T: temporal resection.

Results

Mean overall postoperative increase in QOL point score was 0.83 ± 0.53. Mean postoperative increase in QOL score was 0.70 ± 0.67 in the early childhood onset group, 0.93 ± 0.47 in the late childhood onset group, and 0.83 ± 0.41 in the adult onset group. Mean postoperative increase in QOL point score was 0.71 ± 0.49 in the short duration group, 0.89 ± 0.60 in the medium duration group, and 0.86 ± 0.53 in the long duration group. No significant differences were found in QOL point score between any of these groups.

The histological diagnoses of the epileptogenic lesions were shown previously. The most prominent findings were neuronal loss and gliosis, which was associated with cerebral scarring or porencephaly after head injury, infection, or vascular malformation, or was of unknown origin. Mesial temporal sclerosis was found in 6 patients, and cortical dysplasia and cryptic angioma in 3 patients each.

Table 1 compares the distribution of patients in terms of postoperative QOL grading according to the site of lesionectomy and the three clinicopathological categories. Ten of the 11 patients in the T group and 14 of the 19 in the ExT group belonged to the higher two grades of postoperative QOL.

Table 2 compares the distribution of patients in terms of postoperative increase and mean QOL point score according to the site of lesionectomy and the three clinicopathological categories. Postoperative increase in QOL point score was higher in patients in the T group than in those in the ExT group, though not significantly. However, 10 of the 11 patients in the T group and 13 of the 15 in the Non-CD exT group achieved 1- or 2-point increases in postoperative QOL, whereas none of the patients in the CD exT group achieved any point increase. The mean postoperative increases in QOL point score in the T and the Non-CD exT groups were significantly higher than that in the CD exT group (p < 0.005).

Examination of the relationship between postoperative seizure outcome and postoperative employment status in the 28 patients who replied found that 11 of the 14 patients in Engel Class I worked full time, 2 worked part time, and 1 did not work at all; 2 of the 9 patients in Engel Class II worked full time and 7 worked part time; and none of the 5 patients in Engel Class III or IV worked full time, 2 worked part time, and 3 did not work at all. Almost all patients in Class I or II worked full time or part time. One of our patients, who had become free from seizures after temporal lobectomy, could not work, mainly because of moderate mental retardation and psychosis she had suffered since before the surgery. There was significant correlation between the score for Engel’s grade of seizure control and employment status (p < 0.005, Spearman’s test). Two patients who worked full time in spite of residual seizures (Class II) were supported by good understanding of their seizures and cooperation from partners at home and/or colleagues in the workplace.

Discussion

The QOL of patients improves after surgery. Postoperative QOL is clearly related to seizure outcome. Health-related quality of life (HRQOL) im-

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provement occurs primarily among patients who have achieved complete freedom from seizure,\(^5\) which may be necessary to improve the HRQOL for epilepsy surgery patients.\(^4,13\) Deterioration in QOL occurs with less than 90% seizure reduction.\(^15\) On the other hand, improvement in HRQOL may not be evident until the 2nd postoperative year,\(^15\) and is significantly greater at the 2-year follow up than at the 1-year follow up.\(^13\) Patients free of seizures and those with at least 90% reduction in seizure frequency reported significant improvements in HRQOL at 24 months.\(^15\)

Our previous study\(^17\) on the long-term seizure outcome in the same subjects indicated that lesionectomy based on MR imaging in patients of intractable epilepsy was effective for long-term seizure control and the postoperative seizure outcome was related mainly to the pathology of the epileptogenic lesions, with excellent seizure outcome in patients in the Non-CD exT group and poor in those in the CD exT group. The present study of long-term QOL outcome showed compatible findings.

Focal cortical dysplasia forms a distinct subgroup of malformations of cortical development with favorable outcome after resection, but the epileptogenic zone often extends beyond the abnormalities found on neuroimaging.\(^7\) The type of pathology negatively influences the prognosis. Symptomatic seizures associated with cortical dysplasia or tuberous sclerosis in the youngest patients are among the most intractable.\(^18\) Children with acquired epileptogenesis, such as posttraumatic focal gliosis, appear to have a better outcome than those with dysplastic pathologies, such as cortical dysplasia or tuberous sclerosis.\(^14\)

Seizure-free patients are clearly employable after successful surgery, but few studies of QOL have assessed occupational achievement and income acquisition after epilepsy surgery. The occupational status of subjects has been shown to improve significantly after surgery from unemployed to higher categories of professional achievement.\(^11,12\) Adult patients who are seizure-free 2 years after resective epilepsy surgery were most likely to still be seizure-free 10 years later, and most were working.\(^1\) Employment rates were significantly different between groups categorized according to the seizure outcome: 80% of seizure-free patients and 53% of patients with no more than 10 seizures a year were in gainful employment postoperatively, compared with 28% and 27% of patients with 10 or more seizures a year or those who were unsuitable for surgery.\(^10\) One of our patients, who had become free from seizures after temporal lobectomy, could not work, mainly because of moderate mental retardation and psychosis she had suffered since before the surgery. Psychosocial long-term outcomes do not change dramatically with time and do not depend on seizure freedom.\(^8\) Social phobia is frequently seen before anterior temporal lobectomy, and the postoperative period in these patients may involve major depressive disorder.\(^9\)

Our study found a significant correlation between the degree of seizure control and employment status. Surgical treatment of intractable epilepsy under our protocol was effective to improve long-term QOL and postoperative occupational status of the patients. These outcomes were related mainly to the pathology of the epileptogenic lesions and depended on the completeness of seizure control. QOL improvement and postoperative occupational status of patients also depended on the completeness of seizure control. Despite the marked limitations of this retrospective study, the results of our survey are expected to serve as a guide for selecting patients suitable for surgical treatment for intractable epilepsy and for predicting postoperative QOL outcome.

References

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We read with interest the study on postoperative quality of life (QOL) and employment in patients undergoing resection of epileptogenic lesions detected by MRI. There are several aspects of the study to be commented. The fact that all four of the patients with extra-temporal lobe lesions and cortical dysplasia do not improve, and show severe disability post-operatively, adds more evidence that malformations of cortical development likely portend a worse prognosis than other etiologies — not only in terms of seizure freedom (as the authors showed in their previous study), but also in the patients’ postoperative QOL (as shown in this study). This goes against other studies, of course, so the debate continues. Also, it is interesting to see that Engel’s criteria significantly correlate with employment status — as the authors have shown. Employment status is not commonly analyzed, so this is a nice contribution to the literature. With most studies following patients for a mean of 5 years for long-term outcomes, this study provides a relatively excellent follow-up period (a mean of 12.4 years). Another useful aspect of this study is that while most outcome studies do not look at extratemporal lobe epilepsy (32% of studies), a majority of the cases in this study are extratemporal.

We do suggest, of course, a few areas where the study might have been more robust. Although a valiant effort, it is surprising that no significant differences are found in QOL scores in either “duration-of-epilepsy” or “age-of-onset” groups. Perhaps a higher powered study than the thirty responders could achieve a statistical significance to shed light on these important questions in the future. While the study finds that QOL is related to anatomical and pathological characteristics, and that seizure outcome correlates with employment status (for which the authors wisely and correctly used Spearman’s test to find statistical significance), it would have been interesting to see how these variables are related to one another. For example, a future analysis might examine whether QOL and employment are related, or whether — in the more heated question in the epilepsy

Commentary


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community — seizure-outcome and QOL are related. Future questionnaires to answer such questions might also use a more standardized QOL measure, such as the QOLIE-31, etc., for increased reliability, rather than the authors’ chosen ranking of QOL based on disability.

Overall, we are thankful for the addition of this QOL and employment data into the literature. We hope, like the authors, that such studies help us to continue to improve our patient selections and our ability to give informed prognostic information to patients and their families.

References


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This is an important contribution of a very well documented study of patients operated on for temporal epilepsy (11 cases), extratemporal non-dysplastic (15 cases) and dysplastic cortical pathology (4 cases). After a study of their 30 cases — out of 47 operated on — in spite of the fact that this represents a small sample of patients if compared to the larger series in the medical literature, the authors deserve great credit thanks to the very careful analysis they made of this series, in which they found practically all of the neurological and psychiatric manifestations of intractable and refractory epilepsies, thus establishing definite guidelines for selecting patients suitable for neurosurgical treatment of their incapacitating epilepsy problems, and also in predicting their health related quality of life improvement and outcome.

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This study confirms previous studies’ findings of a correlation between seizure outcome and quality of life (QOL) outcome measures in a retrospective analysis of 30 patients with at least five-year follow-up. It is difficult to determine from the analysis if the pathological substrate (cortical dysplasia versus other) was a predictor of QOL improvement independent of seizure outcome. As a potentially preoperative parameter, however, such imaging diagnostic capability assumes even greater importance.

Quality of life in this assessment may be measuring different things in the different subgroups of this analysis. For the majority of patients it appears to be largely a marker of employment status; for the extratemporal cortical dysplasia group (of which, it should be noted, there are only four patients), all are in the most severely disabled group (“care required for all activities of daily living”), presumably secondary to major disability across cognitive and physical domains, improvement out of which may be exceedingly difficult with or without seizures.

Despite the limitations of such a retrospective study, including selection bias, response bias, and reliability of 5-year recall, this report reminds us of the ultimate importance of long-term QOL outcomes.

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