Surgery for temporal lobe epilepsy in older patients

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Object. The goal of this study was to evaluate the efficacy of surgery for temporal lobe epilepsy (TLE) in older (≥ 50 years of age) patients.

Methods. The authors conducted a review of all patients 50 years of age or older with TLE surgically treated at the Montreal Neurological Institute and Hospital since 1981 by one surgeon (A.O.). Only patients without a mass lesion were included. Outcome parameters were compared with those of younger individuals with TLE, who were stratified by age at operation.

In patients aged 50 years and older, the onset of complex partial seizures occurred 5 to 53 years (mean 35 years) prior to the time of surgery. Postoperatively, over a mean follow-up period of 64 months, 15 patients (83%) obtained a meaningful improvement, becoming either free from seizures or only experiencing a rare seizure. Most surgery outcomes were similar in both older and younger individuals, except for a trend to more freedom from seizures and increased likelihood of returning to work or usual activities in the younger patients. Note that a patient’s long-standing seizure disorder did not negatively affect their ability to achieve freedom from seizures following surgery.

Conclusions. Surgery for TLE appears to be effective for older individuals, comparing favorably with results in younger age groups, and carries a small risk of postoperative complications.

KEY WORDS • temporal lobe epilepsy • epilepsy surgery • seizure surgery • age

Surgery for intractable epilepsy of the temporal lobe is effective in reducing the frequency of seizures in properly selected patients. To date, the preponderance of studies in which epilepsy surgery has been evaluated in adults has included cohorts of patients with average ages in the third or fourth decade of life. The few modern published studies that address epilepsy surgery in older patients contain small numbers of heterogeneous patients and have no analysis of the consequence of seizure duration.

There is always some skepticism about outcomes in older individuals who undergo surgery; they may be in a more frail condition and prone to cardiac, pulmonary, and other complications postoperatively. In addition, epilepsy in older individuals may be more refractory to surgical treatment because it has persisted for a longer duration, with a greater chance for kindling and development of multiple or enlarged epileptogenic zones.

To evaluate the success of epilepsy surgery in the older patient, we retrospectively analyzed patients 50 years of age and older, with no tumor or mass lesion, who had undergone surgery for TLE. If age were an important predictor of surgical impact on seizure frequency or morbidity, one would expect a graded response in analyzing multiple age groups. We, therefore, also investigated younger patients with no mass lesion who had undergone surgery for TLE and stratified them into groups according to their age at the time of surgery. The effect on seizure frequency and surgical morbidity was compared among the groups. Additionally, other pre- and postoperative characteristics that may affect epilepsy or success of surgery were evaluated in each group of patients. The ramifications of seizure duration on the surgical treatment of epilepsy were also investigated by comparing patients grouped by seizure duration irrespective of age.

Clinical Material and Methods

Study inclusion criteria consisted of intractable TLE that was refractory to medical therapy, absence of a tumor or mass lesion on a computerized tomography or magnetic resonance image obtained preoperatively, surgery confined to the temporal lobe, and a postoperative follow-up period lasting 2 years or more. All surgeries were performed by one surgeon (A.O.).

The preoperative evaluation proceeded by following an established protocol that included scalp electroencephalography and neuroimaging to evaluate the temporal lobe and mesial temporal structures. Intracranial recording was performed if there were questions of lateralization or lobar localization. Intracarotid Amytal testing was reserved for cases in which there was uncertain language lateralization or memory reserve. The procedures performed were...
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TABLE 1

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>No. of Patients</th>
<th>Mean Age at Surgery (yrs)</th>
<th>M/F Ratio</th>
<th>Duration of Epilepsy (mean yrs ± SD)</th>
<th>Surgical Technique &amp; No. of Patients</th>
<th>Mean Follow Up (mos)</th>
<th>Temporal Lobe Histopathological Findings</th>
<th>Engel Class of Seizure Reduction</th>
<th>Return to Work or Usual Activities</th>
<th>Anti-convulsant Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–19</td>
<td>16</td>
<td>22:28</td>
<td>10:9</td>
<td>10.9 ± 4</td>
<td>selective AH 11 cortical AH 39</td>
<td>85</td>
<td>abnormal 70 MTS 28 dysplasia 6</td>
<td>II, 46</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>20–29</td>
<td>50</td>
<td>21:29</td>
<td>24:24</td>
<td>15.7 ± 6.7</td>
<td>selective AH 11 cortical AH 39</td>
<td>88</td>
<td>abnormal 80 MTS 42 dysplasia 2</td>
<td>I, 72, 69</td>
<td>6</td>
<td>86</td>
</tr>
<tr>
<td>30–39</td>
<td>50</td>
<td>28:22</td>
<td>34:26</td>
<td>17.6 ± 9.8</td>
<td>selective AH 15 cortical AH 35</td>
<td>79</td>
<td>abnormal 72 MTS 50 dysplasia 4</td>
<td>II &amp; I, 92, 10</td>
<td>4</td>
<td>82</td>
</tr>
<tr>
<td>40–49</td>
<td>50</td>
<td>23:27</td>
<td>44:46</td>
<td>28.8 ± 12.6</td>
<td>selective AH 18 cortical AH 32</td>
<td>51</td>
<td>abnormal 84 MTS 50 dysplasia 2</td>
<td>II &amp; II, 10, 11</td>
<td>10</td>
<td>76</td>
</tr>
<tr>
<td>≥50</td>
<td>18</td>
<td>9:9</td>
<td>54:46</td>
<td>34.9 ± 12.1</td>
<td>selective AH 11 cortical AH 7</td>
<td>64</td>
<td>abnormal 78 MTS 61</td>
<td>I, 61, 22, 4</td>
<td>6</td>
<td>72</td>
</tr>
</tbody>
</table>

* Values in the last five columns represent the percentage of patients. Abbreviation: SD = standard deviation.

either a cortical AH or a selective AH. The decision to perform a selective AH was based primarily on the finding of predominantly mesial temporal spiking on pre-resection electrocorticography or intracranial electroencephalographic telemetry, as well as evidence of MTS on preoperative neuroimaging. The techniques have been described previously.36,38,39

All patients aged 50 years and older who had undergone surgery for TLE at the Montreal Neurological Institute and Hospital and had satisfied the study inclusion requirements were selected from a computer database containing patient information from 1981 to the present. Additional younger patients who met the entry criteria were selected from the database as their names appeared alphabetically until four additional groups stratified by age at surgery contained 50 individuals each: 10 to 19 years of age, 20 to 29 years of age, 30 to 39 years of age, and 40 to 49 years of age (Table 1). The patients may have undergone multiple surgeries, but their age at the last surgery determined inclusion.

Postoperatively, each patient underwent neuropsychological testing. A database of pre- and postoperative characteristics was completed by review of the medical record and/or conversation with the patient by phone or during the office visit (Table 1). The extent of seizure reduction was evaluated by applying an Engel outcome score (Fig. 1).14 Return to work was defined as having held any steady job preoperatively and postoperatively. Return to usual activities signified resumption of preoperative lifestyle and typical activities if the individual was retired or unemployed before surgery.

The consequence of seizure duration was examined by stratifying patients into groups determined by duration of the intractable seizure disorder irrespective of age. All patients were divided into groups of 1 to 10 years, 11 to 20 years, 21 to 30 years, and more than 30 years of chronic intractable epilepsy (Fig. 2). Statistical Analysis

A nonparametric analysis of variance (Kruskal–Wallis test) was used to compare the extent of seizure reduction (Engel class) among the different age groups, followed by nonparametric multiple comparisons among the age groups (Dunn procedure).29,55 To test for a relationship between seizure freedom and patient age at surgery, a 2 × 2 contingency table was constructed to compare Class I results in the 50 years and older patient group compared with all remaining Class I patients. An interrelationship between return to work or usual activities and age at surgery was analyzed using a 2 × 5 contingency table. The same two variables (return to work or usual activities and patient age at surgery) were reanalyzed using a 2 × 2 contingency table combining data from more than one age group, that is, the patients 50 years and older plus those 40 to 49 years of age were compared with those 20 to 29 years of age plus those 10 to 19 years of age. Two-by-two contingency tables were also used to test for differences in other surgery outcome parameters.

Results

Patients Aged 50 Years and Older

Eighteen patients aged 50 years or older had undergone surgery for nontumoral TLE. There were nine women and nine men. Two patients were left handed and 16 were right handed. The patients’ mean age at surgery was 54 years and the oldest patient was 64 years old. The mean age at onset of epilepsy was 18 years and the mean duration of epilepsy was 34.9 years, although there was a range of 48 years. The surgical approach that had been performed was selective AH in 11 patients and cortical AH in seven. Two patients had undergone a repeated operation for additional neocortical or mesial temporal resection. Histopathological examinations of resected specimens had revealed a
striking abnormality in 78% of cases and MTS (gliosis or neuronal loss) in 61%. Follow-up review after surgery had lasted a mean of 64 months.

Seizure outcomes in the group of oldest patients were as follows: Class I in 61%, Class II in 22%, and Class IV in 17% of patients. One patient achieved greater than 50% but less than 90% improvement, and two patients achieved less than 50% improvement in seizure frequency.

Thirteen patients (72%) have been able to reduce or to stop their use of antiepileptic medication since surgery. Of the five individuals who could not lower their dose of anticonvulsant agents, one was unable to reduce the original level of medication and four were switched to different anticonvulsant agents.

A complication resulting from surgery occurred in one patient. This patient experienced a scalp wound infection plus significant upper quadrantanopsia, yielding a complication rate of 6%.

Thirteen individuals (72%) returned to work or to their previously active lifestyle. Four patients (22%) who had been employed before surgery stopped working afterward, and one patient who had been unemployed before surgery did not return to his usual activity level.

**Intergroup Comparison**

Among patients who achieved seizure freedom, individuals 50 years of age or older were at least 11% less likely to have a Class I result in seizure reduction (Table 1). The results of the multiple comparison analysis demonstrated the greatest difference between patients 50 years of age or older and those 30 to 39 years of age, but did not reject the null hypothesis that the groups were similar (p > 0.5). Likewise, a comparison of Engel Class I patients 50 years and older compared with younger Class I patients revealed no significant difference (p = 0.28). Good outcomes of seizure reduction (Classes I and II) were achieved similarly for all age groups, with a trend to better seizure reduction only in the middle age group (p = 0.13; Fig. 3).

The complication rate was comparable among the age groups studied. Complications in the 40- to 49-year-old age group included a cerebrospinal fluid leak, osteomyelitis of the skull, and transient dysphasia. Complications in the 20- to 29-year-old group included aseptic meningitis, otitis, deep venous thrombosis, and corneal abrasion. In the 10- to 19-year-old age group, surgical complications included a mild visual change unrelated to a field defect, a partial visual field defect, and dysphasia. There were no deaths in any groups.

The presence of abnormal histopathological findings in resected specimens was similar between each of the stratified age groups (p > 0.25). Interestingly, MTS occurred less often in the youngest age group (p = 0.01). Dysplasia was not identified in patients in the 50 years and older age group, but was found in 2 to 6% of younger patients.

An intractable seizure disorder was present for a range of 2 to 54 years. A comparison of postoperative seizure reduction in patients stratified by epilepsy duration yielded equivalent successful (Classes I and II) or unsuccessful (Classes III and IV) outcomes (p = 0.11; Fig. 2). The least impact on seizure frequency was recorded in those patients with the shortest epilepsy duration (p = 0.02). An analysis for which the group with the shortest epilepsy duration (1–10 years) was exempt also demonstrated no critical difference among the remaining groups in achieving a successful result (Engel Classes I and II) or seizure freedom (p = 0.73 and p = 0.27, respectively). Likewise, 12% fewer seizure-free outcomes in patients whose epilepsy had lasted longer than 30 years compared with the outcomes in those in the 11 to 20 years duration group demonstrated no meaningful difference (p = 0.11; Fig. 2). Pathological specimens obtained in individuals with the shortest epilepsy duration (1–10 years) displayed MTS in 31% of patients, which was significantly less than the per-

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**Fig. 1.** The Engel postoperative seizure reduction scale.

**Fig. 2.** Bar graph depicting the distribution of postoperative seizure reduction in patients grouped by duration of their chronic intractable epilepsy. n = number of patients.
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There was a trend indicating that patient age at surgery influenced the capacity to return to work or usual activities after surgery (p = 0.27). An analysis in which the two eldest (≥ 50-year-old age group and 40–49-year-old age group) and the two youngest (20–29-year-old age group and 10–19-year-old age group) patient groups were compared revealed a strong tendency for older patients not to return to their preoperative work status or activity level (p = 0.02; Table 1).

Discussion

Authors of recently published series of epilepsy surgery have reported improved results in seizure reduction and lower morbidity rates compared with those of earlier series. Advances in magnetic resonance, single-photon emission computerized tomography, and positron emission tomography imaging techniques have allowed more precise identification of the epileptogenic zone. Additionally, improvements in critical care and anesthesia during the perioperative period have enhanced surgical care in general. Each of these factors benefits surgical patients and increases the likelihood of successfully removing an epileptogenic focus. Despite concerns that older patients with TLE may fare poorly following surgery due to fragile health or longer-standing epilepsy, we found surgery to be effective for all age groups in reducing seizure tendency. Additionally, the complication rate was low in both younger and older patients.

Factors that may influence the effectiveness of surgery include the surgical technique and the cause of the epilepsy. The two different surgical procedures used to treat TLE (cortical AH and selective AH) are expected to be equally effective. A greater number of selective approaches in the older age group may reflect an effort to be more gentle during surgery in older patients by limiting the extent of temporal resection. The presence of a lesion such as a scar or MTS is an important factor in predicting surgical success in patients with TLE. The youngest age group had markedly less MTS identified in resected specimens (p = 0.01), which conceivably is a factor lowering the observed rate of seizure freedom. Additionally, in younger patients more neocortical abnormalities were found during the histopathological examination, possibly reflecting causes of epilepsy different from those in effect in the older individuals. Nevertheless, the lower incidence of pathological changes in the mesial temporal structures is also consistent with a hypothesis of evolving MTS in children who may have the same disease as older persons with TLE, but in whom the stigmata have yet to develop.

Duration of Epilepsy

We found that a very long seizure duration (> 30 years) did not significantly reduce the ability of surgery to produce freedom from seizure (Fig. 2). Bengzon and colleagues came to the same conclusion when they compared patients in whom chronic epilepsy had lasted more or less than 5 years. Kilpatrick, et al., reported no difference in epilepsy duration in eight patients who experienced seizure recurrence after having undergone anterior
Age Effects on Seizure Reduction

There are conflicting reports concerning the impact of epilepsy surgery on seizure frequency in older individuals. Bengzon, et al. reviewed their series of surgically treated patients with TLE and found a striking improvement in seizure reduction in those younger than 30 years of age. Salanova and associates analyzed a larger group including Bengzon and colleagues’ patients who had undergone anterior temporal lobe resection and reported the same finding. They found that patients older than 30 years of age were significantly less likely to achieve freedom from seizure. In the series of temporal lobe resections performed by Falconer and Serafetinides, 20 patients were aged 40 years or older and nine of these became free from seizure or had no more than three seizures per year after surgery. Sperling, et al. found that older patients with TLE were significantly less likely to become seizure free. Cascino and colleagues identified 10 patients 50 to 60 years of age with intractable partial epilepsy who had undergone surgery at the Mayo Clinic. Five had nontumoral TLE and all of these achieved a good outcome (Engel Class I or II). McLachlan and associates reported on 16 patients aged 45 years and older who had undergone temporal resection for epilepsy; these authors identified a trend toward improved seizure control in younger patients. In the current paper we have shown that a large population of patients stratified by age at the time of surgery can realize similarly good outcomes (Classes I and II). The oldest patients (≥ 50 years) were less likely to achieve seizure freedom, amounting to 11% fewer Class I outcomes than patients in the younger group (p = 0.28; Fig. 3). The relationship of this trend to the chronicity of the seizure disorder is not conclusive because patients with long-standing epilepsy were less likely to become seizure free than those with a shorter seizure duration; however, the former fared better than those with the shortest epilepsy history (Fig. 2).

Other Outcome Parameters

We found that return to work or usual activities was influenced remarkably little by the extent of postoperative seizure reduction. Eighteen (49%) of 37 patients in all age groups who did not return to work or their previously active lifestyle were seizure free after surgery. This contrasts with findings of previous studies of TLE, which demonstrate a striking effect of seizure control on the postoperative level of functioning. Enlargement of an epileptic focus has been postulated as a mechanism leading to refractoriness in long-standing epilepsy. The experimental work Morrell has conducted in animals demonstrated a relationship between the chronicity of an epileptic discharge and the development of independent secondary seizure foci. He also found that the likelihood of achieving seizure freedom by excising the primary focus in an animal model was inversely correlated with seizure duration. If enlargement of the seizure focus occurs in long-standing human epilepsy, it seems to have little importance in the surgical control of TLE. This conclusion is supported both by the good results on seizure frequency in patients with epilepsy who had the longest duration of seizures (Fig. 2) and by the fact that the oldest patients underwent the most restrictive resections (Table 1).
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strong relationships among seizure control, improved psychosocial functioning, and quality of life.\textsuperscript{2,28,47} This markedly contrasts with a decline in function identified in patients continuing to have seizures after surgery.\textsuperscript{47} There is a complex relationship between the impact of surgery on the patient’s seizure tendency and psychosocial status, but seizure control remains the most important indicator of improved patient function and satisfaction after surgery. Older patients have a greater tendency for comorbid disease states (such as cardiac or pulmonary dysfunction) that may elevate surgical risks;\textsuperscript{3,11,18,35} however, when properly selected they can realize very low complication rates rivaling those of their younger peers. Despite concern that older individuals may be more prone to complications from surgery, the age group of patients 50 years and older in this series had a low complication rate comparable with that of younger patients.

Conclusions

Older persons with TLE achieve favorable results in seizure reduction after surgery. Although there was a trend toward a lower rate of seizure freedom in the oldest patients, meaningful seizure reduction from surgery (Engel Classes I and II) was comparable among all age groups. A striking age distinction was identified in older individuals who were less likely to return to work or previous activity levels after surgery. Long-standing intractable epilepsy did not prohibit significant seizure reduction as a result of surgery, an outcome similar to that experienced by patients with a shorter history of epilepsy.

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