Use of Anterior Temporal Lobectomy for Epilepsy in a Community-Based Population

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Objective: To assess the hypothesis that use of anterior temporal lobectomy (ATL) for temporal epilepsy has diminished over time.


Setting: The Rochester Epidemiology Project based in Olmsted County, Minnesota.

Participants: Residents of Olmsted County.

Main Outcome Measures: Poisson regression was used to evaluate changes in ATL use over time by sex.

Results: Over a 17-year period, from 1993 to 2009, 847 ATLs were performed with the primary indication of epilepsy (average, 50 procedures/y). Of these, 26 occurred among Olmsted County residents. The use rates declined significantly between 1993 and 2000 (8 years) and 2001 and 2009 (9 years) according to Poisson regression analysis, from 1.9 to 0.7 per 100 000 person-years (P = .01). The rate of ATL use among Olmsted County residents was 1.2 (95% CI, 0.9 to 2.4) per 100 000 person-years of follow-up over this 17-year period. The sex-specific rates were 1.6 (95% CI, 0.9 to 2.4) and 0.7 (95% CI, 0.2 to 1.3) per 100 000 person-years for females and males, respectively.

Conclusions: In this community-based cohort, the rate of ATL use was 1.2 per 100 000 person-years of follow-up. Use of this procedure has declined over time; the reasons for this are unknown but do not include referral pattern changes.


Epilepsy affects approximately 3% of individuals at some time in their lives and occurs in more than 50 million people worldwide.1-3 There are approximately 2.5 million Americans with epilepsy currently receiving antiepileptic drug therapy, and of these, approximately 30% continue to have seizures despite treatment.4,5 Much of the cost of epilepsy in the United States is accounted for by these refractory cases.4,5 Focal or localization-related epilepsy is most common and is often responsible for medically intractable epilepsy. Fortunately, focal epilepsy can be surgically remedied.6,7 The most common surgical procedure aimed at cure is anterior temporal lobectomy (ATL) for temporal lobe epilepsy (TLE), the largest subset of focal epilepsy. In a recent multicenter study, 88% of surgical epilepsy cases with craniotomy and resection for therapy had ATL with mesial temporal resection.8

Anterior temporal lobectomy was popularized in the early 1980s for the treatment of TLE and has been found to be an effective therapy, rendering 60% to 90% of patients undergoing the procedure seizure-free.9 Despite an increasing population in the United States and locally (Olmsted County [OC], Minnesota), we have suspected that the number of ATLs performed for epilepsy has declined over the past 2 decades. This trend has been suspected nationally; however, it has yet to be substantiated. Therefore, we assessed whether this trend could be documented. The Rochester Epidemiology Project (REP) offers a unique opportunity to study whether ATL use is in fact declining because it is a well-detailed stable patient population described in more than 2000 articles to date.1,10 Most importantly, it has been documented that the patients in the REP receive all care within the county, ie, at the Mayo Clinic.1,10 Consequently, this population has an advantage both in assessing the temporal trends of this procedure use as well as in eliminating referral bias as a possible cause for trend changes. Therefore, we undertook this study to assess the hypothesis that at our institution, a tertiary referral center for epilepsy, the frequency of ATLs performed has declined over time. Further, using the REP, we investigated the previously unknown use rate of ATL in a population-based manner. Clinically, a reduction in ATL use may indicate a plethora of causes such as a reduction in incident cases

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or more effective medical treatment, representing an opportunity for further investigation.

METHODS

This protocol was approved by the Mayo Clinic Rochester institutional review board. Cases were identified by searching the database of the neurosurgical department at the Mayo Clinic in Rochester, Minnesota, for epilepsy or medically intractable seizures as the primary indication and temporal lobectomy as the primary procedure. To ensure complete case accrual, we also undertook a second search of the Mayo Clinic medical database using all patients with TLE admitted for ATL (International Classification of Diseases, Ninth Revision, Clinical Modification codes 345.41 and 345.51; primary procedure code, 01.53). These records were then reviewed to ensure proper inclusion. All patients undergoing ATL for seizure control of TLE between 1993 and 2010 were included. Temporal lobe epilepsy was confirmed by a neurologist specialized in the treatment of seizures; all patients had appropriate semiology and video electroencephalogram confirmation of this diagnosis.

ROCHESTER EPIDEMIOLOGY PROJECT

Epidemiologic research in OC is possible because of the county’s isolation from other major cities and the comprehensive medical records linkage system of the REP, which includes the records of visits to all providers of medical care to residents of OC.10 All neurosurgical care to local residents is delivered by the Mayo Clinic because there are no facilities where such care is available locally.1,10 According to the US census data, the population of OC was 106,479 in 1990, increased to 124,277 in 2000, and increased further in 2010 to 144,248.10,11 Olmsted County residency was defined as residence within OC for at least 1 year prior to the patient’s ATL.

GENETIC EPIDEMIOLOGY OF SEIZURE DISORDERS IN ROCHESTER STUDY

The Genetic Epidemiology of Seizure Disorders in Rochester Study (GESDR) database, used in this study to assess incidence of both focal epilepsy and febrile seizures in patients with epilepsy, is a population-based investigation of familial risks of epilepsy using REP resources. The GESDR has been previously described.12 Briefly, the GESDR comprised all residents of Rochester born in 1920 or later who had incidence of either epilepsy (2 or more unprovoked seizures) or an isolated unprovoked seizure from 1935 through 1994.13 Information on each patient’s history of febrile seizures was obtained through a comprehensive review of all information in the medical record.

OVID MEDLINE PUBLICATION SEARCH

Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1948 to Present (Ovid Technologies, Inc) were used to search mesh terms epilepsy, temporal lobe with surgery. Then these publications were binned by year from 1980 to 2010 to demonstrate the overall publications related to ATL.

STATISTICAL ANALYSES

We computed use rates for ATL using as the numerator surgeries among OC residents and as the denominator the OC population size as determined by census data with linear interpolation for the intercensal years according to published methods.10,11 Statistical analysis was performed with JMP version 8.0 (SAS Institute Inc) for analysis of variance and Kruskal-Wallis trend tests; further specialty programming with SAS was used to perform Poisson regression analysis. Linear regression of trends was performed in GraphPad Prism (GraphPad Software Inc).

RESULTS

MAYO CLINIC ATL USE

Over a 17-year period, from 1993 to 2009, 847 ATLs were performed with the primary indication of medically intractable epilepsy. Fifty procedures were performed on average per year. Of these, 26 were performed on OC residents. One patient declined research use of his or her medical records and was therefore excluded. Table 1 re-

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Cases</th>
<th>% of Total Cases</th>
<th>95% CI</th>
<th>OC Cases</th>
<th>% of Total Cases</th>
<th>95% CI</th>
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<td>8</td>
<td>2-24</td>
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<tr>
<td>1997</td>
<td>68</td>
<td>8</td>
<td>6-10</td>
<td>3</td>
<td>12</td>
<td>4-29</td>
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<td>3-6</td>
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<td>6</td>
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<tr>
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<td>1-19</td>
</tr>
<tr>
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<td>40</td>
<td>5</td>
<td>3-6</td>
<td>2</td>
<td>8</td>
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</tr>
<tr>
<td>2008</td>
<td>34</td>
<td>4</td>
<td>3-6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2009</td>
<td>28</td>
<td>3</td>
<td>2-5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>847</td>
<td>100</td>
<td>26</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: OC, Olmsted County, Minnesota.
ports the number of cases per year, percentage of total cases per year, and the 95% CIs for both the total cases performed and OC cases. The first 5 years (1993–1997) had significantly more cases than later years (Figure 1). Linear regression analysis demonstrated a negative slope of −0.37 (95% CI, −0.47 to −0.25; \( P < .001 \)). Overall, there is a reduction in cases over the study period.

Population-based analysis

To determine whether this change resulted from changes in referral patterns or a reduction in ATL use over time, we analyzed population-based ATL use. Because of small numbers, we divided the data into 2 periods: 1993 to 2000 (8 years) and 2001 to 2009 (9 years). The use rates declined significantly between these 2 periods according to Poisson regression analysis, from 1.9 to 0.7 per 100 000 person-years (\( P = .01 \)) (Figure 2). The population-based use rate of ATL in OC was 1.2 (95% CI, 0.9 to 2.4) per 100 000 person-years of follow-up over the 17-year period. Use rates were higher in females than males (1.6; 95% CI, 0.9 to 2.4 vs 0.7; 95% CI 0.2 to 1.3 per 100 000 person-years; \( P = .03 \)).

**TLE AND SURGERY PUBLICATIONS**

Publication trends should reflect contemporary practice activity and may give insight into use of a procedure. Certainly publication trends would not increase the incidence of ATL; however, they likely reflect the procedure’s increased use. Our Ovid MEDLINE search revealed 2327 publications pertaining to mesh terms temporal lobe epilepsy and surgery. From 1980 to 2010, 2099 articles were published. Figure 3 demonstrates the trend in publications over this period. There was a significant increase in publications starting after 1988 (\( P < .001 \), linear regression analysis).

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**Figure 1.** Trend in total temporal lobectomies performed at the Mayo Clinic from 1993 to 2009. From 1993 to 2009, 847 anterior temporal lobectomies were performed for medically intractable epilepsy. This figure demonstrates the trend in cases over this period. The y-axis is the percentage of total cases performed in that year; the black box is the estimated percentage of the total for that year with error bars representing the 95% CI. The line demonstrates the linear regression of this trend, which has a slope significantly less than zero (slope = −0.37, 95% CI, −0.47 to −0.25; \( P < .001 \)). Overall, there is a reduction in cases over the study period.

**Figure 2.** Population-based use rates. A, Kaplan-Meier curve representing the total number of cases and loss over time with 95% CI. Note the large reductions in numbers in the first 5 years to 1997, ie, the median time to 50% of cases is in 1996 or 4 years into the 17-year study. B, Population-based use rates for anterior temporal lobectomy with 95% CIs for each year of the study. This difference was significant based on Poisson regression (\( P = .01 \)).
therefore, this study was undertaken to provide evidence have noted a significant reduction in ATL use for TLE, and Rochester residents in the same REP population.12 with incidence of focal epilepsy of unknown cause among of a history of antecedent febrile seizures in individuals of focal epilepsy of unknown cause and the prevalence possibility, we used the GESDR data to assess the incidence of focal epilepsy or a risk factor leading to focal epilepsy, such as febrile seizures. To evaluate this possibility, we used the GESDR data to assess the incidence of focal epilepsy of unknown cause and the prevalence of a history of antecedent febrile seizures in individuals with incidence of focal epilepsy of unknown cause among Rochester residents in the same REP population.12 Figure 4A demonstrates a progressive decrease over time in the cumulative incidence of focal epilepsy of unknown cause among Rochester residents. Further, among individuals with incidence of focal epilepsy of unknown cause, the proportion who had a history of febrile seizures in Rochester was lower in the final decade studied in GESDR (1985-1994) than in the preceding 3 decades. In each of the 3 earlier decades, 10% or more of cases had febrile seizures (15.4% overall, from 1955-1984), whereas in the final decade relative to our data, there was a reduction to 4.9% (P = .08).

FOCAL AND FEBRILE SEIZURES

Patients with focal seizures in which one can identify the seizure-onset zone are potential candidates for surgical therapy for epilepsy. Further, some studies have suggested that occurrence of febrile seizures (either complex or simple) is a risk factor for the development of TLE, although this relationship has not been definitively established.13-16 Therefore, it is possible that a reduction in use of ATL may be caused by a reduction either in the incidence of focal epilepsy or a risk factor leading to focal epilepsy, such as febrile seizures. To evaluate this possibility, we used the GESDR data to assess the incidence of focal epilepsy of unknown cause and the prevalence of a history of antecedent febrile seizures in individuals with incidence of focal epilepsy of unknown cause among Rochester residents in the same REP population.12

Figure 4A demonstrates a progressive decrease over time in the cumulative incidence of focal epilepsy of unknown cause among Rochester residents. Further, among individuals with incidence of focal epilepsy of unknown cause, the proportion who had a history of febrile seizures in Rochester was lower in the final decade studied in GESDR (1985-1994) than in the preceding 3 decades. In each of the 3 earlier decades, 10% or more of cases had febrile seizures (15.4% overall, from 1955-1984), whereas in the final decade relative to our data, there was a reduction to 4.9% (P = .08). for this observation. Several explanations for the decreased use of ATL are possible. First, the referral base for the procedure may be reduced because of more widespread use of the procedure at more centers. Second, it is possible that the source of these surgical cases, ie, focal epilepsy, is reducing or that medical intervention has decreased associated risk factors such as febrile seizures. Third, with improved imaging, perhaps cases previously diagnosed as mesial temporal lobe epilepsy may have been more recently diagnosed as extratemporal epilepsy. Fourth, the higher rate of use in the earlier years of our study may have resulted in part from a lead time bias due to the increased identification of mesial temporal sclerosis (MTS) with the introduction of magnetic resonance imaging in the late 1980s to early 1990s. Finally, the introduction of improved antiepileptic medications may have reduced the need for surgery. Regardless, it is clear from our data that despite the procedure’s popularity and efficacy, the use rate of ATL for TLE has declined and further investigation is warranted as to the cause of this.

Temporal lobectomy as a surgical procedure has been performed throughout the 20th century and is a main-

**COMMENT**

To our knowledge, this is the first study to assess the population-based use rate of ATL for TLE. It is clear that ATL has proliferated over the past 30 years in both procedures performed and publications.17 At our institution, we have noted a significant reduction in ATL use for TLE, and therefore, this study was undertaken to provide evidence
cannot definitively link antecedent febrile seizure and di-
stitution.17 To address this question, we used REP re-
have occurred because of the procedure’s populariza-
plex and simple febrile convulsions.13-15,20,21 Although we
ber of events felt to be the precursor to MTS, such as com-
ervative magnetic resonance imaging. Vaccination programs
mortem but instead has been a common postoperative pa-
ence shows that it usually arises in infancy, often
results, the distribution of the OC cases appears to be pro-
tions do not appear to severely limit this study’s inter-
This may have led to an influx of cases for MTS in the early years of this study disproportionate to the referral rates for the Mayo Clinic in later years. Magnetic resonance imaging led to a similar reported increase in the incidence of acoustic neuromas in the early 1990s that was later revealed to be secondary to increased detection.28,29 Alternatively, proliferation of publications may have popularized this procedure and brought more patients to surgery during this period, as inferred by the number of publications (Figure 3). In either case, a lead time bias related to these possible sources of increased use cannot be ruled out. In conjunction with imaging improvement, it is fur-
possible that patients previously diagnosed with
in use of ATL. Even if these newer drugs did not in-
Escherichia coli)-related meningitides may have produced a re-
duced somewhat because of the small number of OC
nder the Mayo Clinic. Therefore, given this information, we believe that the reduced use rate is highly unlikely to be due to changes in referral patterns, ie, patients seeking care at a facility other than that which is immediately available.
One possible explanation for the reduction in use is a reduction in either the incidence of focal epilepsy or febrile seizures, a potential risk factor for medically intractable TLE. We are unable to confirm with certainty that the incidence of focal epilepsy has declined with time in OC; however, there does appear to be a trend in reduc-
tion of the incidence of focal epilepsy of unknown cause among Rochester residents (ie, a subset of OC). Perhaps this could be due to reduction in an inciting incident such as febrile seizures. Falconer proposed the hypothesis that:
MTS is the most common single lesion to be found post mortem in the brains of chronic epileptics who die a natural death. . . evidence shows that it usually arises in infancy, often as a result of a prolonged febrile convulsion.21(p767)
Fortunately, MTS is currently unlikely to be found post mortem but instead has been a common postoperative path-
ogy of MTS in our surgical cases, preventive care might have an impact on ATL use. As an example, there was a loga-
time. The introduction of these vaccination programs is concordant with our observed decrease in focal epilepsy
and preventive pediatric care may have impacted the num-
stantiated with T2 signal changes were conducted by au-
credibility. Finally, the availability of newer antiepileptic drugs
have a direct influence on ATL use. Table 2 demonstrates the intro-
the number of publications (Figure 3). In either case, a lead time bias related to these possible sources of increased use cannot be ruled out. In conjunction with imaging improvement, it is fur-
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Finally, the availability of newer antiepileptic drugs may have led to better seizure control and a reduction in the use of ATL. Table 2 demonstrates the introduction of multiple medical therapies during the period of this study, which may have contributed to the decline in use of ATL. Even if these newer drugs did not increase the rates of seizure control in individuals with epilepsy, they may have provided more palatable adverse effect profiles and prevented primary surgery.
There are several limitations to this study. Overall, there are low numbers of index cases available to test our primary hypothesis, leading to wide confidence intervals. Although the sample size is small, the unique availability of the REP in our study allows estimation of the population-based use rates of ATL, which were previously unknown. The other limitations in this study are those that have been recognized previously with the REP, namely that the population is predominantly white and has unusually good access to medical care.30,31 Overall, these limitations do not appear to severely limit this study’s internal validity but may affect the generalizability to other settings. Finally, this study does provide compelling evidence to support an overall reduction in the use of ATL; it is not fully equipped to identify the cause of this re-

Table 2. New Anticonvulsant Medications Approved for Use in the United States From 1993 to 2009

<table>
<thead>
<tr>
<th>Antiepileptic Drug</th>
<th>Year of FDA Approval</th>
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<tr>
<td>Vigabatrin</td>
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</tr>
<tr>
<td>Lamotrigine</td>
<td>1990</td>
</tr>
<tr>
<td>Felbamate</td>
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<td>Gabapentin</td>
<td>1993</td>
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<td>1995</td>
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<tr>
<td>Oxcarbazepine</td>
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<tr>
<td>Zonisamide</td>
<td>2000</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>2004</td>
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</table>

Abbreviation: FDA, Food and Drug Administration.

Fosphenytoin sodium is not included because it is not administered orally and it was previously available as phenytoin.
We report a reduction over time in the number of ATLs performed at our institution. Further, population-based use rates of the procedure have declined significantly, from 1.9 to 0.7 per 100,000 person-years. The reasons for this are unknown but may include a rapid use of available local cases, a reduction in the number of surgically treatable cases, or availability of improved antiepileptic drugs. However, referral pattern changes as a cause of reduced use are highly unlikely as shown in this unique population of patients within the REP. Overall, the population-based use rate of ATL in OC is 1.2 (95% CI, 0.9 to 2.4) per 100,000 person-years of follow-up over the 17-year period. Use rates were significantly higher in females than males.

Accepted for Publication: April 6, 2012.
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Conflict of Interest Disclosures: Dr Ottman serves on the scientific advisory board for and holds stock options in TriGeminal Solutions Inc; received funding for travel from the International League Against Epilepsy, the National Institutes of Health, Fallon Medica LLC, EDJ Associates Inc, and Tel Aviv University; has received speaker honoraria for nonindustry-sponsored lectures; serves as a consultant to Ortho-McNeil Jansen Scientific Affairs LLC; received compensation from the Italian Ministry of Health; and received research support from the National Institutes of Health through grants R01 NS043472 (principal investigator), R01 NS036319 (principal investigator), R03 NS065346 (principal investigator), RC2 NS070344 (multiple principal investigators), R01 NS039422 (coinvestigator), R01 NS036630 (coinvestigator), R01 NS039398 (coinvestigator), and P20 HG005535 (coinvestigator). Dr Worrell is on the scientific advisory board for NeuroVista.

Funding/Support: Study data were obtained from the Rochester Epidemiology Project, which is supported by the National Institute on Aging of the National Institutes of Health under award R01AG034676.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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