



Age is but a number when considering epilepsy surgery in older adults

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ABSTRACT

Background: A quarter of patients with newly diagnosed epilepsy are older, yet they are less likely to be offered resective surgery potentially because of clinical bias that they incur increased surgical risks. There are few peer-reviewed case series that address this cohort and their outcomes.

Objective: In the context of current literature, the objective of this study was to report on all epilepsy surgeries in patients aged 50 years or older from a tertiary care center over 15 years with an average follow-up period of 6 years.

Methods: Patients with epilepsy who underwent surgery between 2001 and 2016 were reviewed retrospectively. Inclusion criteria were age > 50 at surgery, availability of presurgical evaluation data, and minimum one year of follow-up data. We identified 34 patients. Seizure outcome was evaluated using the Engel classification system. **Results:** Thirty-four patients aged 50 years and older out of 276 underwent epilepsy surgery. Average age at time of surgery was 55 years, and average duration of epilepsy was 30 years. Average length of follow-up was 6 years (1–15 years). Twenty-two out of 34 patients (64%) were seizure-free (Engel class I) at their last follow-up visit. Patients with lesional pathology on neuroimaging were more likely to achieve seizure freedom ($p < 0.02$). Parameters associated with poorer outcome included extratemporal epileptogenic focus ($p = 0.07$) and bitemporal interictal epileptiform activity ($p = 0.003$).

Conclusion: Our study cohort is one of the largest and most representative outcome studies of this age group, following the cohort for 6 years. Our findings demonstrated that when considering epilepsy surgery in an older adult, their age should not play a determining role in the decision—a finding that is more common in modern literature.

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1. Introduction

One in four patients with newly diagnosed epilepsy is older [1]. The highest age-related incidence of epilepsy in industrialized countries occurs after 60 years [2]; however, little attention is paid to this particular population with intractable epilepsy [3]. Historically, resective epilepsy surgery has been deemed inappropriate for this age group [4], and this group is thus less likely to be offered surgery. This likely reflects clinical biases that they are at increased surgical risk because of increased comorbidities and that resection might hasten cognitive decline. Studies have shown that longer duration of epilepsy is associated with a poorer seizure outcome [5,6]; thus, this age group is expected to have a reduced chance of favorable surgical outcome. There is a small but growing number of peer-reviewed case series that have described surgical outcomes in patients older than 45 years with mixed outcomes [7–14].

With regard to seizure freedom, most agree that the outcomes reported are good [5,8–12,14] with the majority of patients achieving seizure freedom. These case series are, however, not directly comparable, reporting small numbers with varying age at surgery and varying length of follow-up. It should also be noted that when a comparison is made to a younger cohort, the older cohort has a worse seizure freedom outcome [7,10]. The majority of case series report on temporal lobectomies and exclude other forms of epilepsy [7,10–13]. Other symptomatic epilepsies such as those arising from neoplastic processes are common in this age group [15] and likely account for a higher proportion of resective surgeries when compared with younger age groups. The reported follow-up period also varies; most reports vary from two to four years [10], limiting the long-term predictive value of seizure freedom.

Our study reported on all epilepsy surgeries in patients aged 50 years or older from a tertiary care center over a 15-year period with an average follow-up period of 6 years. The goal was to report on a representative group of this population with follow-up that would allow realistic prognoses to be made.

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2. Methods

The study was approved by the authors' institutional review board (IRB). A retrospective review of a prospectively maintained database of all patients with epilepsy who underwent surgery between 2001 and 2016 was performed. Because of the retrospective nature of the study, the need for patient consent was exempted by the IRB. Inclusion criteria were age > 50 at the time of surgery, availability of presurgical evaluation data (surface or invasive electrophysiological monitoring as well as anatomic and functional imaging studies), and at least one year of follow-up data. This resulted in identification of 33 patients (28 temporal onset seizures and 5 extratemporal).

All pertinent demographic information related to epilepsy outcome was collected. Seizure outcome was evaluated using the Engel classification system. Outcome data were obtained by reviewing clinic visit records and telephone interviews. Information on seizure frequency and antiepileptic drug (AED) usage at the latest follow-up was collected. We further analyzed variables that may correlate with obtaining an Engel class I outcome including age at onset of seizures, total duration of epilepsy, Charlson comorbidity index, preoperative seizure frequency, temporal versus extratemporal seizure location, pathology, and presence of bilateral interictal discharges in temporal lobe cases.

All patients were assessed at a multidisciplinary conference for determination of medically intractable status. All patients underwent continuous video-electroencephalographic (EEG) monitoring (Xltek EEG Systems, Natus Medical Incorporated, Pleasanton, CA, USA) with documented complex partial seizures with secondary generalization. Epilepsy protocol 1.5 or 3 T magnetic resonance imaging (MRI) (Siemens, Munich, Germany) studies were done on all patients. Some patients underwent single-photon emission computed tomography (SPECT) (Siemens, Munich, Germany); magnetoencephalography (Siemens, Munich, Germany); functional MRI (Siemens, Munich, Germany); and subtraction ictal single-photon emission computed tomography coregistered to MRI (SISCOM) using Analyze Software (Mayo Clinic Foundation, Rochester, MN). Preoperative neuropsychological testing was done. Some patients underwent Wada testing. In cases of unclear seizure-focus localization or suspected bilateral onset depth electrodes, subdural or epidural invasive electrodes and grids were placed.

The surgical procedure employed at the authors' center has been previously described [16]. In summary, the procedure consisted of a craniotomy (with general anesthesia unless there was eloquent extratemporal focus in which case the patient was awake) with electrocorticographic monitoring (Xltek EEG Systems, Natus Medical Incorporated, Pleasanton, CA, USA). A tailored approach was used for temporal lobectomies with variable amounts of neocortical resection ranging from 2 to 6 cm of the middle temporal gyrus. Extent of neocortical resection depended on preoperative neuropsychological evaluation, resolution of epileptic discharges after resection of mesial structures, and lack of neocortical involvement on preoperative electrophysiological and functional imaging studies. Resection of the mesial structures included the amygdala to the level of M1 and the endorhinal sulcus. The hippocampal head was removed, and the body was resected to the level of the choroidal point for partial resection or to the level of the collicular plate for a complete resection. Further resection ensued if abnormal spiking was noted on postresection electrocorticography.

Extratemporal resections involved image-guided removal of the lesions along with a 1-cm circumferential margin of gliosis when possible or anatomical resection of previously identified seizure focus based on landmarks and image guidance. Electrocorticographic evaluation of abnormal spiking was also performed to ensure resolution after resection.

All outcome data and variable analysis were evaluated using JMP 12.0 software (SAS software, Cary, NC, USA). The data were summarized initially with descriptive statistics for each variable. Univariate analysis was performed using Wilcoxon rank-sum, chi-square, and Fisher's exact tests to compare patients with seizure-free outcome with patients whose seizures recurred. Statistical significance was set at 5%.

3. Results

3.1. Demographic and clinical parameters

During a 15-year period (2000–2015), 34 patients aged 50 years and older out of 276 underwent epilepsy surgery for intractable epilepsy, representing 12% of this cohort. There were twice as many men ($n=23$) as women ($n=11$) included. The average length of follow-up was 6 years (1–15 years) while the average age at surgery was 55 years (50–69 years). All patients were relatively healthy with an average Charlson comorbidity index of 1.5 (1–4). The average seizure frequency per month was 15 (2–120), which did not affect the outcome of surgery (Table 1). The cohort had a wide range of etiologies for their underlying epilepsy, including hippocampal sclerosis ($n=20$), neoplastic process ($n=5$), vascular malformation ($n=2$), cortical dysplasia ($n=2$), cystic process ($n=1$), tuberous sclerosis ($n=1$), and cryptogenic ($n=3$), none of which affected seizure outcome postoperatively.

3.2. Electroclinical characteristics

The average age at seizure onset was 24 years (2–51 years) with an average duration of epilepsy of 30 years (5–53 years). The average length of follow-up was 6 years (1–15 years). There was no difference in follow-up period between the seizure-free group and those whose seizures recurred. All patients underwent elective inpatient phase 1 (surface) continuous video-EEG monitoring. Interictal epileptiform activity was detected in all while seven patients had bilateral interictal epileptiform activity. Thirty patients had temporal lobe epilepsy, ten from the right and 19 from the left; four had frontal lobe epilepsy, three from the right, one from the left; and one patient had bitemporal epilepsy. Twenty-nine patients had lesions on their MRI. Lesions included hippocampal sclerosis ($n=18$), neoplastic process ($n=5$), cortical dysplasia ($n=2$), vascular malformation ($n=2$), tuberous sclerosis ($n=1$) and cystic process ($n=1$) (Table 2).

3.3. Clinical outcomes

Twenty-two out of 34 patients (64%) were seizure-free (Engel class I) at their last follow-up office visit (mean: 6 years, (Table 3)). Younger age at onset (2–24 years) was associated with the best outcome of Engel class Ia ($p=0.008$) (Table 3). Patients with noted lesional pathology on neuroimaging were more likely to have a good outcome ($p<0.02$) defined as Engel class (Table 2). Parameters associated with poorer outcome (Engel class 3 or higher) were an extratemporal epileptogenic focus ($p=0.07$) and bitemporal interictal epileptiform activity ($p=0.003$) (Table 2). Age at resective surgery had no effect on seizure outcome ($p=0.74$).

3.4. Complications

Ten patients had postoperative complications, seven of which were neurologic in nature. The most common complication was transient aphasia or transient hemiparesis, all of which had resolved upon discharge. Other complications included fever and deep vein thrombosis; however, no patient developed permanent or long-term complications.

4. Discussion

Age should not be a deterrent to performing epilepsy surgery in a patient with intractable epilepsy older than 50 years. Almost two-thirds of our patients had an excellent seizure outcome, a result that is in keeping with other surgical populations both young and old [9,17]. Interestingly, there was no difference in time to surgery after diagnosis with regard to long-term seizure freedom. Similar to younger populations, our patients with bilateral interictal epileptiform discharges, without any lesion on

Table 1
Comparison of demographic and clinical characteristics between seizure-free and not seizure-free groups.

	Overall group (n = 34)	Seizure-free (n = 22)	Recurred (n = 12)	p-Value
Male/female	23/11	17/5	6/6	0.06
Charlson comorbidity index	1.5 (1–4)	1.5 (1–3)	1.4 (1–4)	0.77
Preresection seizure frequency (per month)	15 (2–120)	16 (2–120)	14 (2–60)	0.80
Age at resective surgery (years)	55 (50–69)	54 (50–69)	55 (50–63)	0.75
Age at seizure onset (years)	24 (2–51)	25 (2–51)	24 (2–50)	0.73
Time from diagnosis to surgery	30 (5–53)	29 (19–34)	32 (6–53)	0.64
Follow-up (years)	6 (1–15)	6 (1–15)	7 (2–15)	0.28

MRI or extratemporal epilepsy, were less likely to have a seizure-free outcome.

There is a growing body of case series that suggest advanced age should not be a factor against epilepsy surgery [8,9,11,14]; however, this is not without controversy [6,12,18]. Our findings supported epilepsy surgery in older adults. Larger studies tend to report on slightly younger populations (>45 years) [8,12] while studies reporting on older populations (>60 years) tend to be smaller [9,11]. By including patients 50 years and older, we were able to include a larger number of patients across a wide variety of etiologies and not limit the study to one single underlying pathology or a narrow age group. We did not find an association with advancing age and poorer seizure outcome. At a mean follow-up period of 6 years (range: 1–15 years), we predict a more favorable outcome over a longer time than previously reported [7–12]. Increased risk of surgical complications is both a perceived and reported risk in this population [19]. Our complication rates were low; all were transient and had resolved upon discharge, similar to what is reported in a younger population. It should be noted, however, that all patients who underwent surgery were relatively healthy with a low average Charlson comorbidity index, a bias that is present in the literature reporting on this age group and at the least influences the rate of surgical complications and perhaps seizure outcome.

More homogeneous studies have shown excellent comparable seizure freedom in the setting of resective surgery for mesial temporal sclerosis to younger patients [13]. Other reports on temporal lobectomy have shown less successful outcomes in older patients when compared with younger patients; however, it was felt that this disparity was due to a heterogeneity in etiologies included [7,12]. The majority of our patients had hippocampal sclerosis; however, patients with cortical dysplasia, a neoplastic process, and vascular malformations and one patient with tuberous sclerosis were also included, encompassing a more representative cohort of this older population. No particular underlying pathology was associated with a better or worse outcome. Likewise, neither hemisphere had an effect on seizure outcome despite more left hemispheric surgeries being performed, contrary to previous reports [13].

In most aspects, our patients did not distinguish themselves from younger surgical populations. However, an inherent bias in the choice of patients cannot be excluded; older patients are likely subject to more rigorous screening than their younger counterparts. Those with a visible lesion on MRI that corresponded to an electrographic focus,

as expected [20], had better seizure outcomes ($p < 0.02$). The average seizure frequency per month was 16, and a frequency higher than 20 seizures per month is associated with poorer surgical outcomes [21]; this could account for the favorable seizure freedom rates. Indeed, fewer patients with extratemporal epilepsy were taken for surgery and had little improvement in seizure frequency. This is similar to younger populations where extratemporal surgery is consistently associated with poor seizure outcome [22].

An oft-cited reason to withhold surgery from this age group is the longer duration of disease when compared with younger patients [6,7] because of the proposed effects of secondary epileptogenesis [5,23]. We did not confirm this. Patients with the youngest age at onset of seizures had better outcomes; of those with an Engel class Ia outcome, the oldest age at seizure onset was 24 years (range: 2–24 years, $p = 0.008$). The effects of “age and epilepsy duration” are proposed to affect long-term outcomes at 3–5 years [6]. We could not confirm this as our average follow-up period was 6 years (range: 1–15 years). However, secondary epileptogenesis cannot be ignored. Those with bilateral interictal activity had worse outcomes ($p = 0.003$), again, performing in a similar manner to younger patients [21]. The importance of this finding was that the time to which kindling and secondary epileptogenesis exert an effect may be longer in some patients than others and while it is prudent to perform surgery as soon as necessary, if an older patient with longstanding epilepsy presents with unilateral electrographic disease, they should not be excluded from surgical consideration.

There were limitations to our study. The data were collected retrospectively. Although we report a longer mean follow-up of 6 years, loss to follow-up resulted in shorter recorded follow-up periods, one year being the shortest, limiting the ability of detailed study of long-term seizure freedom postoperatively. Our patient population is heterogeneous and may be seen as a limitation as more homogeneous groups have been reported on previously [13]; however, our group is representative of a population found at a tertiary care center, though, perhaps, not the broader population. Despite an age range spanning almost twenty years, the distribution of age at surgery was skewed to the younger end of the age range prohibiting the cohort to be divided into subgroups and to be analyzed further.

Table 2
Comparison of electrographic and imaging characteristics between the seizure-free and not seizure-free groups.

Electrographic seizure onset	Overall group	Seizure-free	Recurred	p-Value
Right/left temporal	10/19	8/13	2/6	
Right/left frontal	3/1	1/0	2/1	
Bitemporal	1	0	1	
Temporal/extratemporal	30/4	21/1	9/3	0.07
Bilateral interictal epileptiform activity	7	1	6	0.003
Lesional MRI	29	21	8	0.02

Table 3
Detailed seizure outcome with regard to age range at seizure onset using Engel classification.

Engel classification	N	Age at onset (years)
Class I: free of disabling seizures		
A: Completely seizure-free since surgery	11	2–24
B: Nondisabling simple partial seizures only since surgery	4	15–45
C: Some disabling seizures after surgery but free of disabling seizures for at least 2 years	5	20–47
D: Generalized convulsion with AED discontinuation only	2	5–51
Class II: Rare disabling seizures (“almost seizure-free”)		
A: Initially free of disabling seizures but has rare seizures now	4	6–46
B: Rare disabling seizures since surgery	1	2
Class III: Worthwhile improvement	2	5–25
Class IV: No worthwhile improvement	5	7–50

5. Conclusion

We report on the seizure outcomes of all epilepsy surgeries performed on patients aged 50 years and older over a 15-year period. Our study cohort through its inclusivity is one of the largest and most representative outcome studies of the age group, following the cohort for a long period of 6 years on average. More recent series have similar outcomes and should dispel hesitation to perform surgery in this age group. Our findings demonstrated that when considering epilepsy surgery in an older adult, factors known to influence outcomes in younger adults can be used to prognosticate surgical outcomes in a similar fashion in older adults, and their age should not play a determining role in the decision.

Disclosures

There are no funding or financial disclosures to be made.

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