FULL-LENGTH ORIGINAL RESEARCH

Time to push the age limit: Epilepsy surgery in patients 60 years or older

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SUMMARY

Objective: To summarize the existing literature on resective epilepsy surgery (RES) in older adults (\geq 60 years old) and examine seizure and neuropsychological outcomes in a single-center large cohort of older adults undergoing RES and their comparison to a consecutive, younger (25- to45-year-old) adult population who underwent RES in routine clinical practice.

Methods: First, a comprehensive literature review was performed. Then, we identified older adults who underwent RES at our center (2000-2015). Outcome analysis was performed on patients who had $\geq I$ year of clinical follow-up. A younger cohort of patients who underwent RES during the same period was selected for comparison. The 2 groups were compared with respect to demographic and disease variables as well as key clinical outcomes.

Results: Seizure outcomes on 58 older patients were reported in existing literature; 72% achieved Engel class I outcome \geq I year postoperatively. Sixty-four older adults underwent RES at our center, accounting for 2.8% of all RES during the study period. A total of 51 older adults ($M_{age} = 65$) among them had ≥ 1 -year clinical follow-up; 80% achieved Engel I outcome after a mean follow-up of 3.2 years. This was comparable to the 68% Engel class I outcome among 50 consecutive younger adults, despite later age of onset, longer epilepsy duration, and more comorbidities (all p < 0.001) among older adults. The majority (86%) of older adults were referred to our center after years of suffering from drug-resistant epilepsy. There were no group differences in surgical complications. However, I older adult passed away post-RES. There was no difference in post-RES neuropsychological outcomes compared to younger adults, except significantly higher number of older adults showed a decline in confrontational naming.

Significance: RES in well-selected older adults is a safe and effective therapy, and advanced age should not preclude consideration of surgical therapy in older adults with pharmacoresistant epilepsy.

KEY WORDS: Epilepsy surgery, Older adults, Elderly, Geriatric epilepsy.

Resective epilepsy surgery (RES) remains a significantly underutilized therapeutic modality for patients with drugresistant epilepsy (DRE) despite recommendation for use by the American Academy of Neurology (AAN) and Class I evidence of efficacy in providing freedom from disabling seizures.¹ National data suggest that RES has been offered predominantly to younger adults (average age 31) over the past 2 decades.² However, compared to younger adults, the prevalence of unprovoked seizures almost doubles in patients 60 years or older. There is an almost 5-fold increase in the incidence of epilepsy after age 65.⁴ Despite the high



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KEY POINTS

- We report the largest cohort (more than combined reported literature) of resective epilepsy surgery (RES) in older adults (≥60 years)
- We found seizure outcomes to be similar to that of younger (25- to 45-year-old) adults undergoing RES in routine clinical practice
- Comparable seizure outcomes were achieved in older adults despite significantly longer duration of epilepsy and higher comorbidity burden
- Post-RES neuropsychological outcomes were similar to those in younger adults, except for a more frequent decline in confrontational naming among older adults
- There was no statistically significant difference in RES-related complications; however, 1 post-RES death in older group is a concerning findings

population burden of epilepsy with advanced age, the literature on RES in older adults is sparse, possibly due to concerns of surgical comorbidities^{5,6} and/or inferior surgical⁷ and cognitive⁵ outcomes. The bulk of RES literature in older adults or "elderly" individuals⁵ has included patients 50 years or older, with outcomes reported on approximately 300 cases to date.⁸ However, 2 recent studies focused on patients \geq 60 years old with very encouraging postoperative seizure outcomes.^{9,10}

The elderly population is expected to double over the next 30 years¹¹ and to be healthier, with longer life expectancies than ever before in the developed world.¹² As such, there will be a substantial increase in the number of older adults with DRE who are candidates for RES. In anticipation of these demographic trends, the aims of our study were 2-fold: (1) to perform a comprehensive, systematic literature review on RES seizure outcomes in older adults (\geq 60 years), and (2) to conduct a retrospective, single-center, cohort study comparing RES-related variables and seizure and clinical outcomes between older adults and consecutive, "real-world" young adults who have undergone RES for treatment of DRE.

Methods

Literature review

We performed a systematic literature review on RES in older adults following guidelines set forth by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).¹³ We conducted PubMed, Scopus, and Web of Science database searches with the following search algorithm: ((epilep* AND (surgi* OR surger*) AND (elderly OR older NOT (infant* OR children* OR adolescent* OR young OR pediatric*)) AND (outcome OR prognosis) with filters: 1/1/1990 to 12/31/2016, Humans, English. The search period ended 1/4/2016. All articles reporting seizure outcomes ≥ 1 year following surgery on at least 5 patients aged ≥ 60 years at the time of RES were selected for final analysis.

Cohort study

After institutional review board (IRB) approval, we searched our prospectively maintained epilepsy surgery database to identify patients ≥60 years old who underwent video-electroencephalography (EEG) monitoring at our center followed by RES between 1/1/2000 and 6/30/2015. Patients undergoing tumor-related brain surgery with a prior seizure history were not included. Patients with ≥ 1 year of post-RES clinical follow-up were included in subsequent analyses. For comparison purposes, we selected 50 consecutive younger adults (aged 25-45) who underwent RES at our center in and after 2011 and had ≥ 1 year of clinical follow-up. This time point for cohort selection was chosen specifically, as a majority of the older cohort underwent RES in the last 5 years of the study period. Consecutive patients were selected for comparison to determine the differences in epilepsy and surgical characteristics between older adults and an unbiased sample of young adults routinely undergoing RES in current clinical practice ("realworld"). Patient selection was followed by review of electronic medical records to extract demographic, clinical, and surgical variables relevant to this study. Older and younger adults were compared on demographic and disease variables using chi-square and t-tests.

For the purpose of understanding the reason for delay in undergoing RES among older adults, the duration from initial presentation to RES, along with reason for delay (if \geq 1 years), was analyzed from electronic medical records review.

Seizure outcomes

Seizure outcome was classified into 1 of 2 groups using Engel's criteria¹⁴: Engel class I (free of disabling seizures) versus Engel class II–IV (rare disabling seizures to no worthwhile improvement). Group differences in seizure outcomes were examined using chi-square analysis. Seizure outcome in the older cohort was further characterized as a function of surgical resection type and extraoperative intracranial EEG evaluation.

Cognitive outcomes

Patients were included in these analyses if they had comprehensive neuropsychological evaluations conducted both before and after RES, including measures of intellectual function, attention/working memory, visuomotor processing speed, language, executive function, and memory. Self-report screening measures of mood and anxiety were also completed. A series of *t*-tests and chisquare tests were conducted to examine baseline group differences in demographic, cognitive, mood, and

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surgery variables. Change scores (postoperative score minus preoperative score) were calculated for each cognitive measure and classified as "decline" or "no decline" using established reliable change indices for epilepsy that adjust for test–retest reliability and practice effects.^{15–17} Chi-square analyses with exact tests were then used to examine group differences in cognitive outcome (decline/no decline). Repeated-measure analysis of variance (ANOVA) examined group differences in mood and anxiety symptoms from before to after surgery.

Comorbidities and surgical complications

Because comorbidities in older adults may be a clinical concern in offering RES, Charlson Combined Comorbidity Index (CCI) scores¹⁸ were compared between age groups using a Student *t*-test. In this widely used and validated comorbidity scoring system,¹⁹ each decade of life after 40 adds 1 point along with 1–6 points for 16 different comorbidities (epilepsy not included). We also examined the complications from RES in our cohort, which were considered either transient (no intervention required, and deficit resolved by 6-week clinic follow-up) or permanent, using chi-square analysis.

RESULTS

Literature review

A full text of 44 articles was reviewed after initial identification of 1,662 articles using our search strategy (Fig. S1). Only 6 articles reported seizure outcomes in at least 5 patients who were ≥ 60 years or older and had ≥ 1 -year follow-up.^{5,8–10,20,21} Two articles reported exclusively on this patient population.^{9,10} Forty-two of the 58 patients (72.4%) in these studies achieved an Engel class I outcome ≥ 1 year following RES (Table 1).

Cohort study

Sixty-four older adults underwent RES at our center during the 15-year period under study. This constitutes 2.8% of all RES conducted during that time. Details on this cohort are available in Table 2. Twelve patients were excluded from subsequent outcomes analyses due to insufficient clinical follow-up, and one 67-year-old patient with significant cardiac comorbidities had cardiac arrest 3 days after surgery and died (Fig. S2). Demographic, disease, and outcome variables for the remaining 51 older adults (individual patient data in Table S2) and their 50 younger counterparts are summarized in Table 3.

Not surprisingly, the older adult group had seizure onset later in life [t(74) = 5.6, p < 0.001] and longer duration of epilepsy [t(76) = 3.3, p < 0.001]. In addition, older adults were almost 3 times more likely to have lesional findings on magnetic resonance imaging (MRI) [odds ratio [OR] 2.97 (1.2–7.2), p = 0.02] and significantly less likely to undergo extraoperative intracranial EEG monitoring than the younger cohort [OR 0.41 (0.18–0.92), p = 0.04]. Groups were well matched on other demographic and surgery variables (Table 3).

Delay in RES among the older adults

There was a significantly longer delay of 28 (\pm 22 SD) years in undergoing RES from epilepsy onset among the older adults. Time from initial presentation to our center to RES ranged from <1 month to 135 months. Forty-four patients (86%) were referred to our center for management of DRE, of whom 38 patients underwent RES within 1 year

First author	Publication year	Number of patients	Mean (range) duration of epilepsy	Type of surgery	Follow-up duration	Seizure outcome
Grivas et al. ⁵	2006	11	36 (1–62) years	ATL: I AH: 7 AH + lesionectomy: 3	At least 1 year	Engel class I: 9 Engel II: 1 Engel III/IV: 1
Acosta et al. ^{9,a}	2008	7	34.8 (1–53) years	ATL: 4 Lesionectomy: 2 Frontal resection: 1	I–2 years	Engel I: 4 Engel II: 2 Engel IV: I
Patra et al ²⁰	2014	11	_	_	4.3 (\pm 3.8) years	Engel I: 10 Engel II–IV: I
Bialek et al ⁸	2014	7	_	_	I-2 years	Engel I: 5 Engel II–IV: 2
Dewar et al ^{10,a}	2015	12	26.9 (1–48) years	ATL: 9 Lesionectomy: 2 Frontal resection: 1	3.1 (±2.1) years	Engel I: 9 Engel II: 2 Engel III: 1
Meguins et al ²¹	2015	10	-	ATL: 10	At least 1 year	Engel I: 5 Engel II: 4 Engel IV: I

Table 2. Clinical and surgical data for older patients (≥60) who underwent RES (n = 64)				
Age at RES	65 (±3.8)			
Gender (female)	38 (59%)			
Age of onset, median (range)	45 (0–71) years			
Duration of epilepsy, median (range)	22 (0–64) years			
Lobe of RES (%)				
Temporal	49 (76.6)			
Frontal	8 (12.5)			
Parietal	3 (4.7)			
Multilobar	4 (6.3)			
Pathology (%)				
MTS	21 (31.8)			
FCD	17 (26.6)			
Gliosis/nonspecific	16 (25)			
Tumor	7 (10.9)			
Cavernoma	3 (4.7)			
MTS, mesial temporal sclerosis; FCD, focal co	rtical dysplasia.			

of referral; 3 patients took longer than 1 year to undergo pre-RES testing and 3 were initially reluctant to undergo RES. Of the remainder, 4 patients (8%) had presented after their first seizure and underwent RES within1 year of becoming medically refractory. Two patients were initially reluctant (including the patient with the longest delay, who underwent second RES in his/her 60s) and 1 patient was not considered ideal candidate, but underwent RES 7 years later and achieved Engel class I outcome at the last follow-up.

Seizure outcomes

At last clinical follow-up, a mean of 3.2 (\pm 2.2) years following surgery, 41 of 51 older adult patients (80%) achieved Engel class I surgical outcome and 7 (14%) had Engel class II outcomes. Despite significant differences in age at seizure onset and duration of epilepsy, surgical outcome was similar between the older and younger cohorts [Engel I outcome:

Classical and the second secon	Older adults	Younger adults		- Malu				
	n = 51	n = 50	Odds ratio (95% confidence interval)	p- Value				
Gender (female)	29 (57%)	28 (56%)	1.04 (0.47–2.27)	I.				
Age at surgery (years)	65 ± 4	$35~\pm~5$	N/A	<0.01				
Age at seizure onset (years)	$37~\pm~22$	18 ± 11	N/A	<0.01				
Duration of epilepsy (years)	$\textbf{28} \pm \textbf{22}$	17 ± 11	N/A	<0.01				
Duration of follow-up (years)	$3~\pm~2$	4 ± 1	N/A	0.24				
Side of RES (left)	24 (47%)	31 (62%)	0.54 (0.25–1.2)	0.16				
MRI								
Unilateral	41 (80%)	29 (58%)	2.97 (1.22–7.23)	0.02				
Negative/bilateral	10 (20%)	21 (42%)						
Intracranial EEG evaluation								
Yes	14 (27%)	25 (50%)	0.38 (0.17–0.87)	0.02				
No	37 (73%)	25 (50%)						
Surgical resection								
Temporal	38 (75%)	33 (66%)	1.5 (0.64–3.56)	0.39				
Extratemporal/multilobar	13 (26%)	17 (34%)						
Reoperation								
Yes	4 (8%)	9 (18%)	0.39 (0.11–1.35)	0.14				
No	47 (92%)	41 (82%)						
Pathology								
Mesial temporal sclerosis	18 (35%)	12 (24%)	1.73 (0.73–4.1)	0.50				
FCD	11 (22%)	16 (32%)	0.58 (0.2–1.43)	0.27				
Tumor	7 (14%)	4 (8%)	1.83 (0.5–6.69)	0.52				
Cavernoma	3 (6%)	4 (8%)	0.72 (0.15–3.39)	0.72				
Gliosis/nonspecific	12 (23%)	14 (28%)	0.79 (0.32–1.94)	0.65				
Seizure outcome			· ·					
Engel class I	41 (80%)	34 (68%)	1.92 (0.78–4.8)	0.18				
-	10 (20%)	16 (32%)	• •					
Engel class II–IV								
CCI score ^a (range)	0.92 (0-4)	0.22 (0-2)	N/A	<0.001				
Post-RES morbidity		. ,						
Transient	7 (14%)	4 (8%)	1.83 (0.5–6.69)	0.52				
Permanent	1 (2%)	I (2%)		I				

^aWithout adding scores for age. Time duration presented by means (±standard deviation).

80% vs 68%, respectively, OR 1.92 (0.78–4.8), p = 0.18] (Table 3).

Nine of 13 (69%) older adult patients with extratemporal or multilobar RES achieved Engel class I outcome at the time of last follow-up. Fourteen (27%) older adult patients underwent extraoperative invasive EEG monitoring (Table S2, Fig. S3) and achieved Engel class I surgical outcome. Seven patients (50%) undergoing extraoperative invasive EEG monitoring had extratemporal or multilobar RES. Eight patients were \geq 70 years at the time of RES. One underwent frontal lobe RES with resolution of face, but not hand, epilepsia partialis continua (EPC). The remaining 7 elderly individuals underwent anterior temporal lobe resections with outcomes reported elsewhere.²²

Neuropsychological outcomes

A subset of patients in the older (n = 25) and younger (n = 32) adult cohorts completed neuropsychological evaluations, which was performed prior to and approximately 7 ± 6 months following RES, as part of standard clinical care. There was no clinical concern for dementia in the older cohort patients. The 2 groups were well matched on all baseline variables with the exception of age at time of surgery and age at seizure onset, as expected (Table S1). Decline in confrontation naming on the Boston Naming Test occurred more frequently among the older adults following RES (52%) compared to their younger counterparts [(26%), $\chi^2(1) = 4.05$, p = 0.04]. There was no significant difference in the proportion of patients who declined following surgery on any of the other cognitive measures examined (Fig. 1). Similarly, there was no significant difference between groups in mood or anxiety symptoms across the 2 evaluations.

Comorbidities and surgical complications

The mean CCI score, after accounting for both age and comorbidities, was 3 ± 1.1 in older adults, which translates

to an average 10-year survival likelihood of 75.6%.²³ CCI was significantly higher in older as compared to younger adults [t(73) = 16.23, p < 0.001]. Given that younger adults could not accrue any points due to age, we repeated these analyses without accounting for age and results remained largely unchanged [t(77) = 4.25, p < 0.001] (Table 3).

The proportion of patients who developed RES-related complications did not differ significantly between groups (Table 3). Eight older adults had RES-related morbidity; 4 required subdural hygroma drainage (including 1 who developed pneumonia and required intubation), 1 developed septicemia, 1 had CSF leak and meningitis (treated with antibiotics), and 2 developed possible aseptic meningitis. One of the latter 2 patients developed communicating hydrocephalus that required placement of a ventriculoperitoneal shunt, which was considered a permanent morbidity secondary to RES. Among the young adults, a patient each had transient hand weakness, meningitis, and removal of bone flap due to abscess formation and required 2 units of blood (transfusion). One patient had a basal ganglia infarct leading to right-sided weakness, which was considered a permanent morbidity. Of note, none of the younger adults developed postsurgical subdural hygroma.

DISCUSSION

A comprehensive review of existing literature revealed <60 cases of RES in patients aged 60 or older. With the expected doubling of the elderly population over the next 30 years,¹¹ this will likely compound the existing underutilization of RES for DRE.²⁴ As previously observed, RES is infrequently offered to patients \geq 60 years, even in the most highly specialized epilepsy centers.⁹ At our center, 64 patients aged \geq 60 underwent RES, which accounts for only ~3% of all RES conducted over the 15-year study period



Figure 1.

Cognitive decline following epilepsy surgery as characterized using published Reliable Change Indices for epilepsy. Complete data were not available for all patients in the study. Values in parentheses indicate the number of individuals who completed each measure before and after epilepsy surgery. *Epilepsia Open* © ILAE

and yet is greater than the total number of patients reported in the literature to date. This is comparable to the 3% proportion reported in the 2 other case series limited to patients aged 60 and over.^{9,10} Of interest, this surgery rate is similar to that reported in 1 of the first studies of RES outcomes in "older patients" published in 1991 by Cascino et al,²⁵ who reported on 8 patients undergoing RES at age \geq 50 years. This suggests that the age considered "older" for RES candidates during the last 25 years has shifted upwards by 10 years. Figure S3 demonstrates a steady increase in the number of older adults undergoing RES at our center during the study period.

Around 80% of older adults in our cohort achieved Engel class I outcome, which is comparable to 72% of older patients achieving seizure freedom in our literature review. Seizure outcome in the older group was also comparable to the younger adults in our cohort despite a later onset of epilepsy. However, it is important to note that there may be a potential selection bias stemming from concerns about the likely success of RES in older adults, and hence it may have been offered only to those with a highly favorable risk-benefit ratio. Such bias is suggested by the comparison of RES-related variables among older adults to "real world," consecutive younger adults undergoing RES in routine clinical practice. It showed an almost 3-fold higher likelihood of a unilateral lesion on MRI and one-third likelihood of undergoing intracranial EEG monitoring among older adults compared to their younger counterparts-2 well-known favorable RES prognostic factors.^{26,27} Alternatively, this significant difference in prognostic factors may be interpreted to suggest that young adults undergoing RES in recent times have more complex epilepsy. But the selection bias may not just play a role in the eventual offering of RES to older adults at large epilepsy centers but in referral patterns from the community as well. More than 85% of older adults were referred to our center for evaluation from the community and underwent rapid evaluation and RES. However, the older adult cohort had a mean epilepsy duration of 28 years. This is suggestive of reluctance in referral for RES in the neurological community for older adults. Hakimi et al²⁸ showed that age is an important consideration in at least one-third of community neurologists while referring for RES. A majority of them regarded adults older than 60 years as "inappropriate surgical candidates."28

Epilepsy duration remains a controversial RES prognostic factor.²⁹ Our results show that older adults can achieve good seizure outcomes after RES that are comparable to outcomes in younger adults, despite significantly longer disease duration. Extratemporal RES has often been reported to have inferior outcomes compared to temporal lobe epilepsy.^{30,31} Our analysis of this sub-group found that almost 70% of these patients achieved Engel class I outcome at last follow-up. Notably the number of extratemporal or multilobar RES cases accounted for a one-fourth of all the surgeries in the older adult cohort. This is remarkable compared to only 1 case of extratemporal resection (frontal lobe) among patients ≥ 60 years old in the literature.¹⁰

Another chief concern regarding RES in older adults is the presence of comorbidities. We compared the burden of comorbidities using well-validated and widely accepted CCI,^{18,19,23} which was clearly higher in older adults. However, it also predicted a high likelihood (>75%) of the older adults to survive 10 years.²³ We consider it to be a strong argument for evaluating older adults for RES candidacy and offering it when deemed appropriate, particularly given that, despite more comorbid conditions, there were no differences in RES-related complications or outcomes between our 2 age cohorts. Nonetheless, 1 post-RES death of an older patient with cardiovascular risk factors is a matter of concern. Although the mortality rate of 1.6% in our older cohort is not significantly different from the 0.1-1.4% reported in the literature^{29,32}, our case may serve as a point of caution when considering RES in older patients with significant cardiac history. Of interest, although it did not lead to any longterm morbidity, 4 older adults developed post-RES subdural hygroma requiring evacuation, whereas this was not observed among younger adults. This may be due to ageassociated decreased cerebral volume³³ allowing increased fluid accumulation. Although not statistically different, it is possible that similar complications may lead to different outcomes among older adults compared to their younger counterparts due to advanced age and significantly higher comorbidities and future research may help allay such potential concerns.

Examination of cognitive outcome on a wide range of neuropsychological measures revealed poorer naming outcomes among older adults as compared to their younger counterparts. Specifically, 52% of older adults demonstrated clinically meaningful declines in confrontation naming as compared to 26% decline among younger adults. This could not be explained based on a difference in dominant temporal lobe resection, which was nonsignificant (p = 0.58; Table S1). This finding is consistent with a recent study by Thompson et al.³⁴ that found a higher rate of postoperative naming decline among older adults who underwent temporal lobe RES. This is also consistent with research that has identified older age at time of surgery and later age at seizure onset as risk factors for naming decline following dominant temporal RES.35,36 Combined, these findings suggest a possible interplay of age-related cognitive changes and surgical effect leading to a decline in naming abilities of the older adults. In contrast, there were no significant differences in cognitive outcome as a function of age group on any other cognitive measures. Existing studies report conflicting postoperative cognitive outcomes in older adults (\geq 50 years), ^{5,7,20,34,37} which may be related to a host of factors including study differences in patient characteristics, the measures and methods used to assess cognitive

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outcome, and/or surgical resection side, type, and extent. We attempted to address some of the limitations inherent in prior studies by using reliable change indices to examine cognitive outcome at an individual level while controlling extraneous factors that can affect retest performance (eg, test–retest reliability, practice effects) and ensuring that the 2 age groups under study were well matched on baseline cognitive performance.

Our study suffers from the limitations of a retrospective design. Given that RES in older adults is an uncommon practice currently, we would have liked to understand the motivation of our cohort to pursue surgical therapy. This knowledge can be gained through future prospective studies and used to better identify candidates for RES in this age group. To best serve older adults with DRE, research is required to understand the factors that guide patients and their neurologists to seek or avoid RES evaluation and eventual surgery. In addition,, the impact of RES on the quality of life of older adults, with different socioeconomic demands than their younger counterpart, needs further exploration. Several meta-analysis and systematic reviews have clearly established the benefits and the outcomes to be expected from various RES procedures.^{26,29,30} These results have been arrived at from younger adults or "nonolder adults" population. Therefore, we did not aim to compare outcomes of older adults to a matched cohort of a younger population.

In summary, we report the largest cohort study of RES in individuals aged 60 and older. We found a possible reluctance in referring older adults for RES evaluation in the community. Our data show good surgical outcomes without significant surgical or cognitive morbidity in most individuals. In fact, outcomes among older individuals were comparable to younger adults, despite higher burden of comorbidities, later age at seizure onset, and prolonged duration of epilepsy. However, we would like to emphasize that our results should not be interpreted as an endorsement for RES in all older patients with DRE. The careful assessment of each patient, in light of their individual medical and epilepsy characteristics, remains the cornerstone of good surgical management. This cannot be overemphasized, especially for elderly individuals in whom the balance of risks and benefits associated with RES must be decided in the setting of comorbidities and possibly poor baseline cognitive functioning. Although we have definitely moved away from the days when only individuals between the ages of 12 and 30 were considered "ideal" RES candidates,²⁵ the scarcity of literature on RES among adults 60 or older highlights the fact that age is still a big consideration in offering RES. Our data should help allay some of the primary concerns regarding RES in older adults and hopefully improve their referral for RES evaluation and increase the utilization of this effective treatment strategy in the appropriate candidates, despite their age.

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DISCLOSURE OF CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. PRISMA flow diagram of literature review (*not relevant to search goals).

Figure S2. Flow diagram of older adults included in study.

Figure S3. Number of RES in older adults (≥ 60) at our center over a 15-year time span.

Table S1. Baseline characteristics for study patients who completed pre-/postneuropsychological assessments.

Table S2. Individual data of older adults (n = 51) who had at least 1 year of clinical follow-up after RES.