Case Report

Single center outcomes of intracranial evaluation and surgical intervention in the elderly population

Hina Dave, Antonio Guerra, Maria Rodriguez, Irina Podkorytova, Bradley Lega

Department of Neurology, University of Texas Southwestern Medical Center, Dallas, TX, United States

Introduction

Elderly with epilepsy

Elderly patients are at a higher risk of developing epilepsy, with the incidence of epilepsy increasing by over four times from the ages of 50 to 70 [1]. Prevalence of epilepsy in the elderly is 1.5 % [2]. Cerebrovascular disease is the most common etiology in the elderly, and seizure etiology is unknown for almost half of all elderly patients [3]. Although 70 % of elderly patients obtain seizure-freedom with anti-seizure medications (ASMs), patients over 60 are at a higher risk of status epilepticus and are less tolerant of ASMs than younger patients [3–6].

Surgical options

Surgical resection is considered a first line treatment for drug-resistant epilepsy patients [7], with some patients requiring intracranial evaluation with stereo-electroencephalography (SEEG) or subdural grid electrodes (SDE) to better understand the seizure focus [8]. SEEG is minimally invasive with a lower risk of complications and the ability to sample deep and superficial regions; SDE usually requires a craniotomy for electrode placement and can provide more extensive mapping [8–11]. Currently, there is sparse literature on the safety and utility of intracranial evaluation in the elderly population [1]. For patients where a well-defined onset is not seen or complete resection is not possible due to eloquent cortex, neuromodulation may be offered including vagus nerve stimulation, deep brain stimulation, or responsive neurostimulation (RNS, manufactured by Neuropace, Mountain View, California, USA) [12].

Complications and outcomes

The literature regarding epilepsy surgical intervention in older patients is predominantly reported in single center studies in patients who underwent resection. Overall, the studies report similar findings with no differences in Engel outcomes between the elderly and younger population, as well as higher complication rates compared to the younger population. To give a few examples, Grivas et al. studied 52 patients > 50 years of age with an overall 7.7 % surgical complication rate, and 71 % Engel class 1 outcome with minimum 12 month follow-up [13], d’Orio et al. evaluated 50 patients > 50 years, who underwent mesial or mesiolateral temporal lobe resections with 3.8 % surgical complication rate.
and 78% Engel class outcome 1 at 2 years [14]. Neuropsychological outcomes varied with Grivas et al., noting a weak baseline performance with a potential for worsening in those 60 years and older (particularly after a temporal lobectomy) contrary to younger patients. d’Orio did not note any statistically significant change in neuropsychological profiles. Overall, it is noted in other literature that elderly patients have a higher reported chance of complications after epilepsy surgery than younger patients [14,15]. Due to the higher risk of complications and pre-existing medical comorbidities, epilepsy surgery is performed less often in the elderly population [6,16]. Nevertheless, the success rate for surgery among elderly patients is shown to remain as high as the success rate among younger patients [14,15,17,18]. In a recent expert consensus from the Surgical Therapies Commission of the International League Against Epilepsy (ILAE), there was no majority consensus regarding the age limit of referral for surgery highlighting differences in expert opinion [19]. Ultimately, the final recommendation was to refer all drug-resistant epilepsy patients up to 70 years of age and those 70 and older if there are no surgical contraindications. Because of the higher rate of medical comorbidities in the elderly and complications during surgery, it is important to consider possible complications and predictors of outcome of any surgical intervention.

There is only one case series evaluating the use of intracranial evaluation for epilepsy surgery in the elderly population. Punia et al. reviewed 21 patients who underwent intracranial evaluation age 60 and older [20]. These patients had a mean age of implantation of 63.8 years. Five patients underwent SDG and 16 underwent SEEG placement. Two complications were seen with one mortality due to intracranial hemorrhage. Of sixteen patients who underwent surgery, eleven achieved Engel class 1 outcome at the last follow-up (mean 2.7 years). The authors felt that intracranial EEG evaluation in this population improved surgical outcomes in the elderly. SEEG mortality in elderly patients can occur, with a high risk of hemorrhage occurring within the first 48 h of SEEG implantation possibly due to vessel wall stiffening due to aging [20,21]. Although there is no literature, underlying cerebral angiopathy may potentially pose a risk as well. There has been a shift towards intracranial evaluation in our center prior to resection or device placement. The purpose of this case series is to examine the feasibility and safety of surgical evaluation and treatment in patients over the age of 55 at a single center.

**Methods**

Institutional IRB exemption was obtained prior to data extraction and analysis. Consent was not required as all data were retrospective. We reviewed the electronic medical charts of adult epilepsy patients from 2016 to 2020 that underwent one or more of the following: intracranial monitoring, resection, or RNS placement. We excluded patients below the age of 55 at presurgical evaluation. Since the aging process is heterogeneous based on lifestyle and genetics, we chose a generous age limit of 55 to encompass as many high-risk individuals as possible. While many studies define elderly as 65 years and above, this cutoff is arbitrary [22]. In addition, multiple studies have shown differences in complication rates between epilepsy populations above and below 50 years of age, so we decided on a lower age-cutoff in order to examine this trend [16,18]. We reported changes in seizure frequency as no change from baseline, still having seizures but at a reduced rate, or seizure free. Seizure outcomes were determined at the most recent clinic visit after the initial intervention. Follow-up periods ranged from two months to four years with an average follow-up period of 23 months (Table 1). Additionally, we looked at morbidity across different groups, examining those with complications during the intracranial evaluation and complications secondary to RNS placement or resection. The number of ASMs a patient was taking pre-intervention and at follow-up was obtained through a chart check. Post-operative neuropsychological testing was not available and therefore neuropsychological profiles were not reported.

**Results**

**Demographics**

We found 17 elderly patients who underwent intracranial evaluation, surgical treatment, or RNS placement at our institution. Three patients were excluded due to one of the following reasons: limited chart data, initial RNS implantation at another institution, and tumor etiology for epilepsy. The mean age at presurgical evaluation was 63.6 ± 4.13 years, with a range of 59 years to 74 years of age. 42.9% (n = 6) of patients were female. The median duration of epilepsy was 15.5 years (IQR = 21.8). The median number of ASMs patients took at presurgical evaluation was 3 with a range of 1–6. 71.4% (n = 10) of patients had a past medical history of neurological disease or symptoms (including cognitive impairment, memory deficit, frequent migraines, traumatic brain injury, and stroke), and 57.1% (n = 8) of patients had a history of cardiac disease. 42.9% (n = 6) of patients had a history of psychiatric disorder.

**Intracranial evaluation**

57.1% (n = 8) of patients underwent intracranial evaluation – six of these patients underwent SEEG evaluation and two underwent SDE evaluation. The year of the intracranial procedure is listed in Table 1. The intracranial evaluation complication rate was 12.5%. None of the patients had complications related to the intracranial implantation. A patient developed respiratory distress requiring high flow oxygen in post-op recovery after SEEG implantation. As this was related to body habitus, it was not attributed to the SEEG implantation itself.

**Surgical intervention**

Ten patients underwent resection, two had resection plus RNS placement, and one had only RNS placement. One patient did not pursue resection after evaluation. The overall surgical complication rate was 14.2%. Post-resection, two patients had major complications related to underlying medical conditions. One patient had 2 systemic complications: uncontrollable hyperglycemia related to her type 2 diabetes and exacerbation of her underlying chronic kidney disease. This was the same patient who experienced respiratory distress during SEEG evaluation. Another patient underwent resection and RNS placement with post-op hypoxic respiratory failure requiring intubation.

**Follow-up**

At the last clinic visit, 58.3% (n = 7/12) of the patients that underwent a resection or resection with RNS placement were seizure-free. The follow-up duration was not standardized, although 11 out of 12 patients that underwent resection had a follow-up period of at least 11 months while the remaining patient had a follow-up period of two months. One patient did not undergo surgical treatment after intracranial evaluation but was also seizure-free at follow-up. This patient was seizure free at the time of pre-surgical evaluation, and as such did not pursue further treatment and remained seizure free at a follow-up period of 45 months. The remaining patients were not seizure free, although some of
| Patient Sex and Age | Epilepsy Duration (years) | # of ASMs (ASMs at Follow-up) | Etiology and past Hx | Semiology | MRI | PET | Autoimmune Epilepsy Testing | Surgical Intervention | Region of Tx | Seizure Freedom | Follow-up Period (months) |
|---------------------|--------------------------|-------------------------------|----------------------|-----------|-----|-----|-----------------------------|----------------------|-------------|----------------|--------------------------|
| F (64)             | 22                       | 3 (3)                         | Neurological, cardiac, psychiatric | FBTC       | SEEG (2019) | Post-surgical changes | R temporal hypometabolism | Negative | Resection | R insula, L hippocampus | No change |
| M (63)             | 57                       | 6 (3)                         | Neurological, psychiatric | Focal      | SDE (2018) | FLAIR L post-central gyrus changes | Negative | Resection | L post-central gyrus | Reduced seizures |
| F (60)             | 57                       | 1 (1)                         | Neurological, psychiatric | Focal      | SEEG (2020) | L mesial temporal sclerosis, R temporal edema | Negative | Resection | L hippocampus | Seizure free |
| F (59)             | 36                       | 3 (2)                         | Neurological | Focal | * | L hippocampal edema | L temporal hypometabolism | | Resection | L temporal lobe | Seizure free |
| M (62)             | 13                       | 5 (2)                         | Neurological, cardiac | Focal | * | L mesial temporal sclerosis, R temporal atrophy, Generalized atrophy | Positive, reflex test negative | RNS | L temporal lobe | Seizure free |
| F (59)             | 21                       | 3 (3)                         | Neurological (stroke), cardiac | FBTC       | SDE (2020 SEEG (2017) | L superior frontal gyrus hyperintensity | | Negative | Resection | L pre-central gyrus | Seizure free |
| M (64)             | 13                       | 3 (3)                         | Neurological, psychiatric | Focal      | SEEG (2017) | L mesial temporal sclerosis, L frontotemporal encephalomalacia | | | Resection | L frontal lobe | Seizure free |
| M (60)             | 15                       | 2 (0)                         | Neurological, cardiac | Focal | * | R temporal edema | R temporal hypometabolism | Negative | Resection | R anterior temporal lobe | Seizure free |
| F (69)             | 16                       | 3 (1)                         | Neurological, psychiatric | Focal | * | R temporal edema | R temporal hypometabolism | Negative | Resection | R anterior temporal lobe | Reduced seizures |
| M (67)             | 10                       | 2 (2)                         | Neurological, cardiac | Focal | * | R temporal edema | R temporal hypometabolism | Negative | Resection | R temporal lobe | Seizure free |
| M (74)             | 3                        | 2 (2)                         | Neurological | Focal | * | R temporal edema | R temporal hypometabolism | | | | No change |
| F (63)             | 63                       | 3 (2)                         | Neurological, cardiac | Focal | * | R mesial temporal sclerosis | R temporal hypometabolism | Negative | Resection | R temporal lobe | No change |
| M (63)             | 8                        | 2 (2)                         | Psychiatric | Focal | * | R mesial temporal sclerosis | R temporal hypometabolism | | | | Seizure reduced |
| M (63)             | 4                        | 2 (2)                         | Cardiac | Focal | SEEG (2016) | Normal | Normal | Negative | | | |

FBTC = Focal Bilateral Tonic Clonic.
* = Not Applicable.
them had reduced seizure burden (Table 1). Of the three patients who had RNS, one patient was seizure-free at 29 months. 66 % (n = 4/6) of our patients who underwent intracranial evaluation obtained seizure-freedom after resection. The median number of ASMs patients took at follow-up was two. 42.9 % (n = 6) of patients saw a reduction in the number of ASMs they were taking, and none of our patients had an increase in ASMs. The presurgical workup and type of surgical procedure performed are outlined in Table 1.

Discussion

Prior literature on elderly epilepsy surgery has focused primarily on resection outcomes. This case series is novel in that it provides insight on the outcomes and complications of a variety of surgical interventions among elderly persons with epilepsy at a single center and more specifically in those who underwent intracranial evaluation. To our knowledge, this is one of two case series to evaluate outcomes of invasive EEG evaluations in the older population. A 2019 study reported a higher surgery success rate among adult SEEG patients over adult SDE patients [23]. While we intended to provide insight into the differences between SEEG and SDE with our study, our small sample size prevents us from directly comparing intracranial evaluation groups. Intracranial evaluation may be an important step to achieving seizure-freedom, but this is often skipped in elderly patients [1]. In comparison to Punia et al., our seizure-freedom rates were comparable in the intracranial population (66 % versus 69 %). Although selection bias for ideal surgical candidates cannot be excluded entirely, the findings suggest that the utility of intracranial evaluation may provide an avenue to not only resection but possibly neuromodulatory devices that will lessen the seizure burden (as well as reducing poorly tolerated ASMs in this population).

Our surgical intervention success rate of 58.3 % is comparable to previous studies with similar patient samples (50–90 %) and supports the notion that epilepsy surgery remains successful even among elderly patients [1,15,16]. Surgical intervention success rates for elderly patients vary across studies likely due to low sample size and the lack of multi-center studies [1]. RNS literature in this population cites a seizure-freedom rate of 27.3 % [24]. Our sample size of three RNS patients was too small to make any substantive conclusions.

The surgical complication rate was slightly higher than other centers however, this can be attributed to the smaller sample size. Ichikawa et al. and Bialek et al. have reported surgery complication rates of 3–11.5 % [15,16]. It is important to note that our complications were secondary to underlying medical conditions. This indicates that medical history and physical health are critical when examining potential options for treatment among elderly patients. Both patients with complications after pre-surgical evaluation were not seizure-free at follow-up. The impact of comorbidities in resective surgery is supported by previous findings in this population, as well as recent recommendations by the ILAE highlighting the importance of assessing older patients before resective surgery [1,19]. Nearly half of all patients saw a reduction in their ASMs, and the remaining patients saw no change (Table 1). Among the patients that were not seizure-free at follow-up, 60 % (n = 3) still saw a reduction in ASMs.

There were limitations to our study. Our retrospective design made it impossible to attribute changes in seizure burden to specific intracranial techniques, comorbidities, or intervention. Additionally, we had no control group and as such could not directly compare our outcomes with those of younger patients. We also had a low sample size that diminishes the generalizability of our study. The age cut-off for “elderly” used in this paper is not standardized and was instead based on prior papers in this population [16,18,22]. We kept our age range broad including patients below 60 years old to encompass the heterogeneity of the aging process as well as addressing the trend of increased risk in epilepsy patients above 50 years of age [13,14]. We had two patients below 60 years of age (both 59), nine patients between the ages of 60 and 65, and two patients above the age of 65. Our mean age of 63.6 was similar to that of prior studies (63.8) [20].

Conclusion

Our study shows that intracranial evaluation and treatment can be an efficacious and a safe tool to use in the aging population in carefully selected patients. Evaluating medical co-morbidities is essential in assessing safety and developing a plan for potential complications after any type of surgical procedure – whether it is an invasive evaluation or surgical treatment. Continued retrospective and prospective research into which factors determine seizure-freedom and surgical complications among elderly epilepsy patients will be valuable to the epilepsy surgery community [1,15,17].

Data Availability

All anonymized data can be obtained upon request by contacting the corresponding author HD.

Ethics Statement

This study obtained IRB exemption as all data were retrospective and collected as a result of standard care. As such, consent was not collected as it was not required. Data were anonymized to protect our subjects’ privacy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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