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Case Report

Extra operative intracranial EEG monitoring for epilepsy surgery in elderly patients☆

Vineet Punia [a,*], Juan Bulacio [a], Jorge Gonzalez-Martinez [a,b], Ahmed Abdelkader [a], William Bingaman [a,b], Imad Najm [a], Andrey Stojic [a]

[a] Epilepsy Center, Neurological Institute, Cleveland Clinic, Cleveland, OH 44106, United States of America
[b] Department of Neurosurgery, Neurological Institute, Cleveland Clinic, Cleveland, OH 44106, United States of America

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ABSTRACT

Object: The objective of the study is to investigate and report our experience with extra operative intracranial EEG monitoring for evaluation of epilepsy surgery among elderly (≥60 years) patients.
Methods: After IRB approval, we searched our prospectively maintained epilepsy surgery database to find patients who underwent eiEEG at the age of 60 years or older. Electronic medical records were reviewed to extract clinical and surgery-related information. Patients who underwent resective epilepsy surgery after eiEEG and had at least 1 year of clinical follow-up were assessed for seizure outcome. Categorical and continuous variables were compared using Pearson chi-square and Student's t-test, respectively.
Results: A total of 21 patients, with 13 (62%) women, underwent eiEEG in our center at the age of 60 years or older. The mean age at time of implantation was 63.8 ± 2.7 years. Sub-dural grids (SDG) were implanted in five (24%) patients, whereas sixteen (76%) patients underwent stereo-EEG (SEEG) implantation. Median number of contacts in SDG were 106 (56–136) and depth electrodes in SEEG were 12 (9–14). There were 2 complications, including one mortality due to intracerebral hemorrhage. Sixteen (76%) patients underwent respective epilepsy surgery after eiEEG and eleven (69%) achieved Engel class I outcome on the last follow-up [mean follow-up duration of 2.7 (± 1.8) years].
Conclusion: We noticed an increased utilization of eiEEG in elderly patients after the introduction of SEEG at our center. Overall, we found that eiEEG can help achieve good seizure outcomes in the elderly population. However, the one eiEEG-related mortality serves a word of caution about the potential risks in this population.

1. Introduction

Resective epilepsy surgery (RES) in patients with drug resistant epilepsy can often be planned based on information from noninvasive diagnostic techniques. However, a subgroup of patients may require additional information in the form of extra operative intracranial electroencephalography (eiEEG) monitoring [12]. Recent systematic review and meta-analysis of two most commonly used eiEEG modalities — subdural grids (SDG) and stereo-electroencephalography (SEEG), found them to be generally safe techniques with low surgical complication rates [1,14] They report the mean age of patients undergoing eiEEG ranging from 24 [14] to 37 years [1], which suggests that eiEEG is most frequently used in young adults. However, the incidence of unprovoked seizures and epilepsy starts to rapidly rise after the age of 55 years [10] and may have an almost five-fold increase after the age of 65 years [17].

Today's elderly population is healthier, with a longer life expectancy than ever before [4] and is expected to double over the next 30 years [15] in the developed world. Our recent report on the largest series of 51 elderly patients (≥60 years) undergoing resective epilepsy surgery (RES) showed that 80% of them can achieve Engel I outcome, which was comparable with young adults (25–45 years old) [16]. This evidence of efficacy and safety of RES in elderly [16] in combination with population trends mean that more elderly patients may be candidates for eiEEG. Few case series of SDG [3,19,20] and SEEG [6,13] use suggest that these techniques have been attempted in patients older than 60 years. However, to our knowledge, prior studies have not specifically analyzed the use of eiEEG in this population. Therefore, the aim of our

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* Corresponding author at: Epilepsy Center, Cleveland Clinic, 9500 Euclid Avenue, S-5, Cleveland, OH 44106, United States of America.
E-mail address: puniav@ccf.org (V. Punia).

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study is to report, for the first time in literature, a single center experience with eiEEG in the elderly patients.

2. Methods

After IRB approval, we searched our prospectively maintained epilepsy surgery data base from 01/01/2000 to 12/31/2016 to find patients who underwent eiEEG at the age of 60 years or older. Electronic medical records were reviewed to extract clinical and surgery-related information. The MRI findings were classified into negative (non-lesional), unilateral or bilateral (lesions present in both hemispheres). The indication for undergoing eiEEG was analyzed based on the review of surgical patient management conference note in the clinical chart and was classified as: "Lateralization" — patients with bilateral lesion (e.g. hippocampal sclerosis); "Localization" — for better defining epileptogenic zone and resection strategy; "functional mapping" — for localization of eloquent regions. Patients who underwent RES after eiEEG and had at least 1 year of clinical follow-up were assessed for seizure outcome classified according to Engel's criteria. Categorical variables were described using frequencies and percentages (rounded to nearest integer), while continuous variables were described using mean and standard deviations or medians and quartiles (first and third), as appropriate. Categorical and continuous variables were compared using Pearson chi-square and Student's t-test, respectively.

3. Results

A total of 21 elderly patients, including 13 (62%) women, underwent eiEEG in our center during the study period. The mean age at time of implantation was 63.8 ± 2.7 years with median epilepsy duration of 35 (11–52) years. The first patient to undergo eiEEG had a subdural grid (SDG) implantation in 2008 (Fig. 1).

Five (24%) patients underwent SDG implantation, including 3 with accompanying depth electrodes as well. Sixteen (76%) patients underwent SEEG implantation (Fig. 1; Table 1 — including one with SDG combination approach). Mean number of days of eiEEG monitoring was 8.5 ± 4.2 days (mean SDG duration $= 9 \pm 3$ days; mean SEEG duration $= 8 \pm 4.4$ days; $p = 0.59$). Median number of contacts in SDG were 106 (56–136) and 130 (16–220) in SEEG (including depth electrodes used in combination with SDG). The median number of depth electrodes used in patients undergoing SEEG were 12 (9–14). Maximum number of depth electrodes used were 18 (Table 1 — patient #18), which was a two-staged process where additional 4 depth electrodes were added to the original 14 depth electrodes. Eight patients underwent bilateral depth electrode implantation. All patients received prophylactic antibiotics and perioperative steroids. Details of the study population are provided in Table 1. There were 2 complications — Patient 4 (Table 1) developed transient aphasia and decreased responsiveness requiring emergent explantation of SDG on post-operative day (POD) 4. However, there was no associated long-term morbidity. One patient (Table 1 — Patient #9) passed away 48 h after SEEG implantation.

3.1. eiEEG-related mortality

This patient was a 62-year-old man with no other significant medical history. He suffered from a posttraumatic epilepsy since the age of 10 years. He was taking 3 anti-seizure drugs (lacosamide, zonisamide and phenytoin) along with calcium and multivitamin supplements at time of eiEEG implantation. He underwent bilateral implantation of a total of 14 electrodes using neuro navigation system and a robotic arm. Post operatively, he was noted to be unresponsive with a left dilated unreactive pupil. He received immediate mannitol and a stat CT scan showed large parietal intracranial hemorrhage, with a 17 mm midline shift. Urgent craniotomy and evacuation was performed. Due to the poor neurological status after surgery, the family requested not to pursue aggressive medical treatment, and the patient died after 48 h of eiEEG implantation.

Sixteen (76%) patients underwent RES after eiEEG, of which temporal lobectomy was the most common surgery [44% (7 out of 16) patients] (Table 1). Of the five patients who did not undergo RES, four were not found to be ideal surgical candidates (Table 1 — patients #6, 8, 16, and 21). With an average follow-up duration of 2.7 (±1.8) years, 11 of the 16 (69%) patients had Engel class I outcome on the last follow-up. Since the time of first elderly eiEEG, 53 patients from this age group underwent RES at our center. Of them, 16 (30%) patients required eiEEG to guide RES.

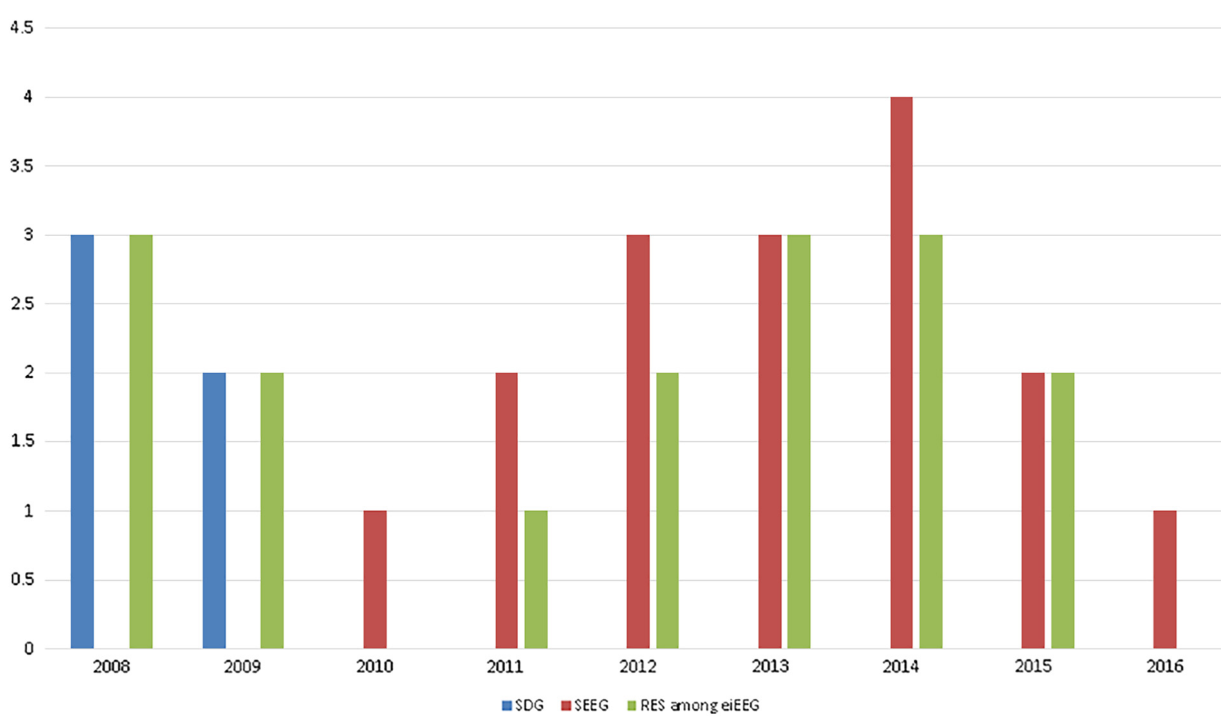

Fig. 1. Number of elderly patients undergoing eiEEG over years at our center.

Table 1
Individual patient data of the study population.

Patient (gender)	Age (years)	Epilepsy duration (years)	MRI findings	Indication for eiEEG	Type of eiEEG	Number of depth contacts (electrodes)	Number of SDG contacts	Duration of eiEEG (days)	Region of RES	Outcome (Engel)
1 (M)	65	3	Bilateral	Lateralization	SDG + Depth	48 (6)	44	9	Right temporal	III
2 (M)	66	59	Unilateral	Localization	SDG	–	141	7	Right frontal	I
3 (F)	68	6	Unilateral	Localization + Functional mapping	SDG	–	90	13	Right parieto-occipital	I
4 (F)	62	22	Unilateral	Localization + Functional mapping	SDG + Depth	16 (2)	160	4	Left frontal	IV
5 (M)	62	58	Bilateral	Localization + Functional mapping	SDG + Depth	42 (5)	122	13	Right temporal	I
6 (F)	66	51	Bilateral	Lateralization	Depth	48 (6)	–	21	N/A	N/A
7 (F)	64	53	Bilateral	Localization	SEEG	158 (15)	–	6	Left parietal	IV
8 (M)	68	3	Bilateral	Localization	SEEG	142 (14)	–	8	N/A	N/A
9 (M)	62	52	Bilateral	Localization	SEEG	144 (14)	–	0	N/A	expired
10 (F)	61	3	Unilateral	Localization + Functional mapping	SEEG + SDG	110 (11)	22	6	Left parietal	I
11 (M)	63	14	Unilateral	Localization	SEEG	130 (13)	–	7	Right frontal	I
12 (M)	64	59	Unilateral	Localization	SEEG	90 (9)	–	7	Left temporal	II
13 (F)	62	48	Bilateral	Localization (deep targets)	SEEG	110 (11)	–	9	Right frontal + Insula	I
14 (F)	60	8	Bilateral	Localization	SEEG	130 (13)	–	15	Left temporal	I
15 (F)	65	49	Unilateral	Localization + Functional mapping	SEEG	114 (9)	–	9	Left temporal	I
16 (M)	60	54	Bilateral	Localization	SEEG	164 (12)	–	5	N/A	
17 (F)	69	55	Bilateral	Localization	SEEG	150 (13)	–	7	Left temporal	I
18 (F)	61	11	Bilateral	Localization	SEEG	220 (18)	–	10	Left temporal	I
19 (F)	65	5	Unilateral	Localization	SEEG	180 (14)	–	8	Right frontal	I
20 (F)	60	25	Unilateral	Localization	SEEG	110 (11)	–	8	Right basal frontal and temporal operculum	II
21 (F)	66	19	Unilateral	Localization (deep targets)	SEEG	150 (15)	–	7	N/A	N/A

N/A = not applicable.

4. Discussion

The first elderly patient to undergo eiEEG in more than 35 years of experience with intracranial EEG implantation at our center [2,9] was in the year 2008. Since then, we have performed 21 such procedures in elderly patients. This temporal trend, which may be not unique to our center, is a likely combination of few converging factors: a) maturing of an epilepsy surgery program after years of performing RES in younger adults; b) a demographical shift towards a healthier, elderly population expected to be the fastest growing population among all age group in the developed world [4,15] and c) changes in eiEEG modality at our center. Therefore, in the face of such changes, our first attempt at analyzing the use of eiEEG in older adults and elderly patients is very timely.

We did not compare our study population to a young adult cohort because all the case series published so far, and the systematic reviews/meta-analysis, are derived from younger patients [1,2,14]. Therefore, they serve as a historical comparison to the elderly patients evaluated in our study. Around 30% of total elderly patients who had RES at our center [16] had undergone a prior eiEEG evaluation which is comparable to the literature [18]. Conversely, 70% of patients who underwent eiEEG subsequently underwent RES, which is again comparable to other larger case series in literature of SDG [3,19] or SEEG [13].

More than two-thirds (69%) of our patients achieved Engel I seizure outcomes, which is comparable or slightly better than the outcomes reported in previous case series of eiEEG [2,19]. The possibility of selection bias — eiEEG being offered to patients with higher pre implantation and/or RES benefit to risk ratio may explain the seizure outcomes. Surgical complications are a significant concern in offering RES and neurosurgical procedures to the elderly patients [7]. Recent meta-analysis have shown a pooled eiEEG-related complication rate of 1.3% [14] to 4% [1] in SEEG and SDG respectively. The first SEEG procedure was performed at our center in March 2009 [5]. As seen in Fig. 1, time period since then coincides with a sharp increase in number of eiEEG performed at our center among elderly — all in the form of SEEG. This may not be a coincidence but rather secondary to the safety and previously reported low morbidity and mortality associated with this procedure [14]. Two of the 6 patients developing complication in a series of 116 SDG and strip implantations were elderly and one of them sustained an intracranial hemorrhage [3]. Hemorrhage is the most common complication due to SEEG [14] and was unfortunately the cause of mortality in one of our patients. This is the only case of SEEG-related mortality at our center [6] and one of the two reported in literature from SEEG-related hemorrhage [14]. Vessel wall stiffening associated with aging [11] may potentially increase the risk of hemorrhage in the older age group. One way to lower such risk could be by limiting the number of implanted electrodes in the elderly as each individual electrode increases the risk of procedure-related morbidity [14]. Another may be the exercise of extra vigilance during implantation in the elderly and to be mindful of slightest resistance to electrode insertion in the OR in this patient population. The initial 48 h is the time period of SEEG-related fatal hemorrhage in the two reported cases in literature [6,8]. Therefore, keeping a low threshold for immediate neuroimaging at times of minor changes in mental status or neurological examination in the elderly may be critical for preventing major complication. Additional factors that may increase the risk of hemorrhage from intracranial electrode implantation in the elderly include their higher likelihood of use of anti platelet agents or possibly having, undiagnosed amyloid angiopathy. Such factors must be considered before eiEEG implantation in this age group. However, of note, our patient who expired post-eiEEG implantation was not on antiplatelet agents and there was no imaging evidence or post mortem pathology report available to suggest amyloid angiopathy.

5. Conclusion

Our study shows that eiEEG can be offered to a well selected elderly patient population. The relatively recent increase in its utilization for presurgical evaluation among the elderly may be secondary to the advent of better tolerated technique of SEEG in North America. Although the experience with eiEEG in elderly is limited the one death in our cohort serves as a word of caution during implantation in this patient population. The outcomes appear similar to that of young adults. Three-quarter of the patients evaluated with intracranial electrodes underwent RES and the majority of them achieved seizure freedom. Therefore, our experience suggests that an elderly patient should not be denied RES due to the need for an eiEEG evaluation. Given the demographical trends of a rapidly aging population, future studies geared towards the identification of elderly patients with the highest benefit to risk ratio for undergoing eiEEG and the subsequent RES is required.

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