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Successful selection of patients with intractable extratemporal epilepsy using non-invasive investigations

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Purpose: Patients with intractable epilepsy, operated for extratemporal epileptogenic foci, have often been found to have poorer surgical outcome compared with those with temporal lobe foci. The objective of this study is to assess the surgical outcome in patients with extratemporal foci, operated at the All India Institute of Medical Sciences (AIIMS), New Delhi.
Methods: Patients of intractable epilepsy with extratemporal foci on detailed investigation constituted the study group. They were evaluated by the 'Comprehensive Epilepsy Care Team' at the AIIMS with detailed clinical assessment, interictal EEGs, video-EEG studies, magnetic resonance imaging (MRI) with special sequences tailored for evaluation of the temporal lobes and for cortical dysplasias and single photon emission computerised tomography (SPECT) studies. Intraoperative electrocorticography was obtained in some patients. Outcome was assessed on follow-up, and graded according to Modified Engel's Grading System.
Results: Twenty-five patients (18 males, 7 females) with a mean age of 19.7 years (age range 7–45 years) were operated and assessed during the study period, for surgical outcome with a mean follow-up of 16.8 months (range 3 months to 6.5 years). Twenty patients (87%) were found to have a good outcome (Modified Engel's grades I and II), while three had poor outcome, one died and one was lost to follow-up.
Conclusion: We found a good seizure outcome in patients who underwent resection of extratemporal epileptogenic foci, one of the reasons being presence of a lesion in all patients. Careful patient selection even with non-invasive investigations can aid in obtaining a good outcome in this group of patients.

Key words: extratemporal epilepsy; epilepsy surgery; outcome.

INTRODUCTION

Surgery for epilepsy is now an established effective means for treating patients with refractory seizures. Majority of patients operated for intractable epilepsy have temporal lobe epileptogenic foci[1]. However, with several centres now offering this treatment to a large, constantly expanding number of patients, there are a sizeable number of patients with extratemporal foci of seizure onset also. Overall outcome in patients operated for extratemporal foci has been found to be poorer (50–70%)[2–5], compared to seizure freedom in greater than 80% patients with temporal lobe surgery[6]. Most of these patients have cortical dysplasia (~50%) and tumours (37%)[7]. There are also a fair number of patients who, even on sophisticated magnetic resonance imaging (MRI), do not reveal any brain lesion[8]. Poor seizure outcome is possibly due to the more diffuse, ill-localised nature of foci in such patients, the extent of which is not easily demarcated even with the most advanced investigations. Very careful selection of candidates has to be made and surgery should be offered only if there is very good concordance among the various investigations carried out during work-up.

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The objective of this study was to assess the outcome of patients operated for extratemporal seizure foci, as a part of the 'Comprehensive Epilepsy Care Program' at our centre.

MATERIAL AND METHODS

All patients with intractable epilepsy with epileptogenic focus lying outside the temporal lobe, operated for epilepsy surgery at the Neurosciences Center, All India Institute of Medical Sciences (AIIMS), New Delhi, between April 1995 and March 2001, constituted the patient population of this study. The detailed work-up was carried out by a dedicated 'Comprehensive Epilepsy Care Team' comprising of clinical neurologists, clinical neurophysiologists, neurosurgeons, neuroradiologists, nuclear medicine specialist, neuropsychologist and a neuropathologist.

The clinical neurologists defined intractability of seizures when patients had frequent disabling seizures despite a trial of at least two antiepileptic drugs for a sufficient period of time. Clinical evaluation of these patients included details of seizure semiology and type, frequency, duration, response to drugs, family history, social functioning and educational level.

Routine 16-channel interictal EEGs were recorded using the 10–20 International system. For video-EEG, patients were admitted to the Neurology wards and recording was carried out till at least two habitual seizures were recorded. Antiepileptic drug dosages were tapered prior to long-term recording.

MRI using a 1.5 T Siemens Magnetom SP (Erlangen, Germany) or 1.0 T GE (USA) unit, with a special epilepsy protocol, was obtained at least once in all cases. This protocol included T1-weighted inversion recovery sequences, a high contrast T2-weighted pulse sequence like fast spin echo T2-weighted or fast fluid attenuated inversion recovery (FLAIR) sequences.

Interictal single photon emission computerised tomography (SPECT) studies were carried out using Tc HMPAO, comparing radiotracer concentrations in both hemispheres using a dedicated dual head Gamma camera with a fan beam collimator having a 5–6 mm resolution. Hypoperfusion in a particular cortical region was defined as a left to right ratio exceeding 1.10. Ictal SPECT using Tc-ECD was done only in doubtful cases (those with normal MRI or those with discordant interictal SPECT findings).

After completion of the above protocol details of each patient were discussed in monthly meetings of the epilepsy surgery team. Those patients who had well-defined seizure focus based on concordant findings on detailed work-up were cleared for surgery.

Intraoperative electrocorticography (ECoG) (Nihon Kohden Electroencephalograph 2100) was carried out, using subdural Wyler grids (4×4 electrodes), both prior to and following resection in nine patients. The lesion and the surrounding epileptogenic area was excised based on intraoperative ECoG findings. Since this facility was acquired only towards the later part of the study period, it could not be carried out in all patients.

All operative specimens were sent for histopathological, and if required, immunohistochemical examinations.

Postoperatively patients were first monitored in the Intensive Care Unit and usually after 24 hours, in the wards. A note was made about any seizure, new deficits and other complications like infections.

Patients were followed up at 3 months, 6 months and 1 year after discharge. Outcome was assessed using Modified Engel's Outcome Grading System[3] and patients were classified into two broad categories based on surgical outcome:

- *Good outcome*: Modified Engel's grades I and II
- *Poor outcome*: Modified Engel's grades III and IV

All data were collected prospectively and entered on EXCEL spreadsheets. Wherever applicable, descriptive statistics, e.g. mean and standard deviation and percentages were calculated.

RESULTS

Clinical profile

During the study period, 110 patients were operated upon. This included 104 cases operated for focus resection and 6 patients operated for corpus callosotomy. Among these 104 cases, 25 patients (24.03%) underwent surgery for extratemporal foci. The mean age of these patients was 19.7 years (age range 7–45 years). There were 8 patients (32%) below 10 years of age, 11 patients (44%) in the 10–30 year age group and 6 patients (24%) in the 30–50 years age group. Eighteen patients (72%) were males and seven (28%) were females.

The seizure duration ranged between 1 and 18 years with a mean of 3.5 years. Three patients (12%) had seizure duration less than 2 years, 16 (64%) had seizure duration between 2 and 10 years and 6 patients (24%) had duration greater than 10 years. Seizure frequency ranged between 2 and 300 per month with a mean of 65.5 per month.

No patient had a history of perinatal insult or of developmental delay, however, mental retardation was present in three patients. History of significant head trauma was noted in two patients. Only one patient had history of febrile seizures, whereas two patients had positive family history of seizures.

At least one *interictal EEG* was obtained for all patients. EEGs were found normal in four patients (16%). An epileptogenic focus concordant with the lesion on MRI was identified in only 8 patients (32%), while the remaining 13 patients (52%) had either additional foci on the same side as the lesion or contralateral foci on EEG.

Video-EEG was obtained for all except one patient. Findings revealed a focus concordant with the radiological lesion in 16 patients (64%), while in 5 patients (20%), the focus was found to be contralateral or there were more than one foci on the same side. Video-EEG was non-contributory in three patients, with neither any clinical lateralising or localising signs nor any clear focus on simultaneous EEG.

Single unilateral lesions were found in 23 patients (92%), while 2 patients (8%) had bilateral lesions demonstrated on *MRI*.

SPECT revealed an ipsilateral concordant focus in 16 patients (64%). Three patients (12%) showed ipsilateral hypoperfusion on interictal SPECT in another area compared to the radiological lesion. The study was normal in six patients (24%).

Extratemporal resection was the surgical procedure carried out for all the patients. Postsurgery *electrocorticography* could be done in nine cases, out of which six (67%) revealed no spikes, one patient showed occasional spikes and two patients revealed spikes from other areas.

On *histopathological examination*, eight patients were found to have dysembryoplastic neuroepithelial tumours, two had gangliogliomas, four patients had glial tumours and eight patients had gliosis and cystic changes. One patient showed normal findings, one had a hypothalamic hamartoma and one patient had a vascular malformation.

Outcome and course

Seizure outcome

The mean follow-up period for these patients was 16.8 months with a range of 3 months to 6.5 years.

Twenty patients (87%) had a good outcome, while three patients (13%) had a poor outcome. Nine patients had no seizure postoperatively (Modified Engel's grade Ia), while eight others had initial few seizures followed by a running down pattern (grade Ib). One patient had a seizure during intercurrent illness (grade Id). Two patients had worthwhile improvement, with maximum two seizures per year (grade II).

Among the three patients with poor outcome, one had greater than 75% reduction in seizure frequency (grade III) and two patients had no change in frequency (grade IV).

There was one death among these patients. This patient with bilateral frontal gliosis (right more than left) had recurrent focal seizures postoperatively, meningitis, hydrocephalus and brain abscess.

One patient was lost to follow-up; hence seizure outcome could not be determined in this patient.

Postoperative complications

At least one minor complication was seen in 10 patients (a rate of 40%). Hemiparesis, which recovered completely within 5 months to 1 year, was seen in six patients. Two patients developed dysphasia, which also completely improved over a few weeks. Two patients suffered from wound infection and one patient developed meningitis, hydrocephalus and brain abscess and eventually died.

DISCUSSION

This study reveals a good surgical outcome in 87% of intractable epilepsy patients operated for extratemporal focus resection. Patient selection was based on concordant findings on non-invasive investigations.

A favourable outcome has not been found in such a large percentage of patients with extratemporal foci in most previous studies. In a recent study evaluating 126 patients with extratemporal foci, Holmes *et al*.[5] found better outcome in the group with unilateral, unifocal, well-defined discharges (77%), which is also much less as compared to the present study, whereas the overall percentage of patients with good outcome was only 42.9%. In another study in which 60 such children were included, all patients were investigated using CT scanning, MRI and scalp EEG, whereas video-telemetry was used in 40 cases only. Intracranial electrodes were placed in 10 patients, while intraoperative ECoG was used in all patients. Follow-up data were available in 48 patients, out of which 45 (93.7%) were found to have good outcome. There was no standard method of investigation in this study and invasive investigations were used in place of conducting non-invasive tests for all patients. Also, a large number of patients were lost to follow-up (20%), a fact which may reflect that the overall outcome may not have been so good[9]. Zentner *et al*. found a good outcome in 68.3% patients (41/60) operated for intractable extratemporal epilepsy, while a total of 86% patients showed some benefit with surgery. This was despite the fact that invasive subdural grid or strip electrode recording or depth electrode recording was used in all patients in this study[10]. Among 456 patients operated for extratemporal epilepsy (253—frontal and 203—parietal, central or occipital), from 1928 to 1980, a total of 56% patients had seizure freedom or marked

reduction in seizure frequency[11]. Non-availability of sophisticated investigational techniques could be one major factor responsible for poor outcome in a large number of patients. However, seizure freedom was observed in only 28.7% patients and 'marked reduction in seizure frequency' was not clearly defined. However, even later, as observed in the 1991 survey by Engel *et al*., 363 out of 805 patients (45%) with extratemporal resections operated between 1986 and 1990, experienced seizure freedom, while another 35% experienced 'improvement', which is again not clearly defined.

One of the factors predictive of a good prognosis for seizure control among patients with extratemporal epilepsy has been found to be presence of a focal neoplastic lesion. Zentner *et al*. found 80% patients with neoplastic lesions to have a good outcome, compared to only 52% patients with non-neoplastic focal lesions. We had a greater number of patients with neoplastic (56%) than those with non-neoplastic lesions (44%). This could be one of the reasons contributing to favourable outcome. Also, we had no patient with cortical dysplasias in this study, a condition which is more diffuse, with very poorly definable epileptogenic zones.

We observed operative morbidity in many patients, but in most patients, the deficits and complications were short lasting and acceptable since activities of daily living were improved due to good seizure control. This is similar to that observed by other investigators. Postoperative complications and a transient or persistent neurologic deficit was found in 43 out of 100 patients operated for extratemporal epilepsy, reported by Talaraich *et al*.[12]. Among 57 patients operated for extrahippocampal neocortical surgery at the Cleveland Clinic, 88% patients had postoperative complications with 37% patients suffering persistent morbidity with one death[13].

We demonstrate a good seizure outcome in patients operated for intractable extratemporal epilepsy, using a non-invasive investigation protocol and a meticulous preoperative assessment. We, therefore, conclude that careful selection of patients with extratemporal epileptogenic foci, especially those with presence of a lesion, even with non-invasive investigations, can aid in obtaining a significantly favourable seizure outcome without persistent morbidity.

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