e-Methods

Patient evaluation: The basic presurgical evaluation has changed little over the time course of this study. The core evaluation included history and neurological examination, interictal and ictal scalp EEG-video recordings, structural MRI, ^{18}fluro-2-deoxyglucose (FDG) PET, and, when necessary, neuropsychological assessments and intracarotid amobarbital injections (Wada test).[e1] At surgery, intraoperative electrocorticography (ECoG) was performed under standard anesthetic conditions to identify abnormal regions of persistent background slowing, frequent interictal epileptiform discharges, and focal abnormal fast frequencies mapped relative to the zone of cortical abnormality (ZCA) and imaged lesion.[e2] When necessary, sensory mapping with somatosensory evoked potentials (SSEP) and language localization with direct cortical stimulation while awake was performed. The histopathology of the resected cortical specimens was tissue processed and reviewed by essentially the same neuropathology team using standard staining and immunohistochemical protocols.[e3]

Components of the evaluation, surgical procedures, and the clinical approach have evolved from 1986 to 2008. For example, structural MRI, originally at 0.3T, was increased to 1.0T, and then 1.5T in the 1990's. There have also been successive improvements in MRI sequences (FLAIR and DTI), reduced slice thickness (currently 1.8mm), and protocols designed for younger epilepsy patients.[e4] Slice thickness of FDG-PET scans has decreased from 10mm to 3mm, and PET scans have been co-registered with structural MRI since 2004. Magnetic source imaging (MSI) was introduced over the past decade for patients with difficult to localize epilepsy.[e5-e7] In addition, for selected cases fMRI for localization of language areas was utilized since the late 1990's.[e7] Personnel involved with the presurgical evaluation, and operations have changed over the 22 years of the program (see Acknowledgements). Surgically, focal lesions are currently localized in the operating room using 3-D neuro-navigation to delineate their margins relative to ECoG findings more precisely. In addition, surgical techniques, such as hemispherectomy, have evolved to reduce complications and perform complete resections with the initial operation.[e8, e9]

After review of our initial findings from the cohort in 1997, the surgical approach was changed.[e10] Since 1997 we consciously adopted a protocol that emphasizes identifying a possible lesion using multimodality neuroimaging including structural MRI, FDG-PET, MRI/PET co-registration, DTI and MSI. We have also advocated for a complete surgical resection of the lesion with the first operation when possible, and a less aggressive protocol whereby we have taken longer to remove seizure-free patients off of anti-epilepsy drugs (AEDs).

Clinical variables: For resection cases (n=425), clinical variables were abstracted from the medical record. These included age at seizure onset, age at surgery, gender, history of infantile spasms, side of the surgical resection, surgical procedure (defined as hemispherectomy, multilobar, and lobar/focal resections), location of surgery (defined as hemispheric, extratemporal, and temporal), and use of diagnostic intracranial electrodes (Phase II studies). Epilepsy duration was calculated as the interval (in years) from age at seizure onset to surgery. Pre-surgery seizure frequency was dichotomously classified as daily versus less than daily. Based on the MRI and histopathology findings, etiology was ascertained as being cortical dysplasia, hemimegalencephaly, acquired atrophy (e.g. ischemia, stroke, and infections), tumors, hippocampal sclerosis, Rasmussen syndrome, tuberous sclerosis complex (TSC), Sturge-Weber disease, vascular (angiomas), and non-specific gliosis.[e8, e9, e11] Surgical complications, consisting of death (operative and non-operative), serious adverse events, and permanent neurological deficits, were recorded along with reoperations and CSF shunts.

Seizure outcome and number of AEDs were recorded in a standard manner at 0.5, one, two, and five years after surgery.[e10] Seizure outcome was documented as seizure-free or not seizure-free for the three month interval before the recorded time point. A reporting rate per follow up interval was tabulated, consisting of the number of patients with outcome information divided by the eligible patients that should have follow-up data. Outcome information was obtained by direct patient and family contact. The percentage of those not taking AEDs was tabulated at 0.5, one, two, and five years of follow-up. For patients with two and five years of follow-up, they were further classified as always seizure free at all time points measured (Always Sz Free; 0.5 to two or five years after surgery), never seizure free at all time points (Never Sz Free), seizure free at 0.5 and one year after surgery but developing late seizure recurrence at two and five years after surgery (Late Sz Recur.), or becoming seizure free at two and five years after surgery after having postoperative seizures at 0.5 and one year of follow up (Late Sz Free; see Table 3).

e-References

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Hemb et al.