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Resective focal epilepsy surgery – Has selection of candidates changed? A systematic review

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ABSTRACT

Objective: No standard, widely accepted criteria exist to determine who should be referred for an epilepsy surgical evaluation. As a result, indications for epilepsy surgery evaluation vary significantly between centers. We review the literature to assess what criteria have been used to select patients for resective epilepsy surgery and examine whether these have changed since the publication of the first epilepsy surgery randomized controlled trial in 2001.
Methods: A systematic review was conducted using PubMed and EMBASE, bibliographies of reviews and book chapters identifying focal epilepsy resective series. Abstract, full text review and data abstraction (i.e. indications for surgery) were performed independently by two reviewers. Descriptive historical analysis was done to examine indications over time.
Results: Out of 5061 articles related to epilepsy surgery, 384 articles met all eligibility criteria. Most common criteria for selecting patients for evaluation for resective surgery were: AED resistance ($n = 303$, most commonly >2 AEDs = 46), epilepsy duration ($n = 53$, most commonly >1 year = 42) and seizure frequency (most commonly at least one seizure/month, $n = 29$). Out of the prospective studies the most notable change over time (pre-2000 vs. post-2000) was failure of ≥2 AEDs (8% vs. 43% respectively, $p < 0.001$).
Conclusions: Important variations between studies make it difficult to identify consistent criteria to guide surgical candidacy or changes in indications over time. With increasing evidence that earlier surgery is associated with better outcomes, it is recommended that patients be evaluated as soon as they have failed two AEDs, consistent with the new definition of drug resistant epilepsy. Furthermore, low seizure frequency should not be a barrier to epilepsy surgery. Anyone with drug resistant epilepsy should be promptly evaluated for possible surgery, regardless of seizure frequency.

1. Introduction

No standard, widely accepted criteria exist to determine who should be referred for an epilepsy surgical evaluation. As a result, indications for epilepsy surgery evaluation vary significantly between centers.

In 2003 the International League Against Epilepsy (ILAE) Pediatric Epilepsy Surgery Subcommission proposed that the following individuals be considered possible surgical candidates: (1) those who have failed two appropriate antiepileptic drugs (AEDs); (2) those who are disabled by medication side effects; (3) those with

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seizures that do not fit into a definite electroclinical epilepsy syndrome based on the ILAE classification; and (4) those that have an identified lesion seen on neuroimaging (Cross et al., 2006). In infants and children with frequent seizures, rapid surgical evaluation may be necessary to prevent deleterious effects on brain development (Engel and Shewmon, 1993). In 2009 the American Epilepsy Society consensus conference also underlined the importance of integration of data and care pathways in selecting patients for epilepsy surgery, utilizing a well-functioning multidisciplinary team with a systematic approach to investigations and thus conveying realistic expectations for surgical outcomes to patients and their families (Duncan, 2011). Other recommendations have been published to guide selection of surgical candidates for epilepsy surgery but the recommendations are still very general (Engel et al., 2003; Labiner et al., 2010). Most agree that for a patient to be considered for surgery, the seizures should be disabling; however, this concept is not easily defined. It has been proposed that rather than considering seizure frequency, a physician should consider how significantly the seizures interfere with a patients' quality-of-life (Jones and Andermann, 2000). More recently there is increasing consensus that anyone who meets the new drug resistant epilepsy definition (failed ≥2 AEDs) should be considered for a surgical evaluation (Kwan et al., 2010).

The objectives of this study were to provide estimates of the standard criteria that are used for recruiting patients for epilepsy surgery and to identify sources of heterogeneity between studies. We hypothesized that criteria for selection changed over time and that failure of fewer AED failures would be noted as a criterion in more recent cohorts.

2. Material and methods

2.1. Literature search strategy

A systematic review was conducted as part of a larger project (CASES, the Canadian Appropriateness and necessity Study of Epilepsy Surgery) (www.epilepsycases.com) on the development of an appropriateness and necessity rating tool to identify patients with focal epilepsy who should be referred for an epilepsy surgery evaluation (Jetté et al., 2012). An extensive search using both PubMed and EMBASE databases, bibliographies of reviews, original articles and book chapters were completed to identify English language articles published between January 1965 and June 2008 inclusive (see Appendix A for full search strategy). The aim of the search was to identify all of the focal resective surgical series published since 1965. A separate broader search was also carried out to identify all review articles about epilepsy surgery (including systematic reviews) published for hand searching.

2.2. Study selection

Abstracts were screened independently by two reviewers. Inclusion criteria for the initial search were English language, focal epilepsy or epilepsy with partial seizures (lesionectomy, lobectomy, corticectomy, selective amygdalo-hippocampectomy). Initial exclusion criteria were neonatal studies, non-resective surgery, palliative procedures, stimulation studies and studies with <20 patients. We also required that articles stated clear inclusion or exclusion criteria in the study methods. All abstracts meeting the above eligibility criteria were then reviewed as full text articles again by two independent reviewers, to determine final eligibility for data extraction. Bibliographies of all full text articles meeting final eligibility criteria for data extraction were screened by two reviewers, to make sure no additional studies were missed, as well as bibliographies of book chapters and published reviews about epilepsy surgery.

2.3. Data extraction and analysis

Two authors independently extracted data from the included studies using a standardized form piloted by the authors on an initial sample of articles. Data extracted included the following: year of study, study type, country, sample size, age, and whether the following eligibility criteria (or any additional ones) were used as selection for surgery evaluation, and how they were defined: epilepsy duration, frequency of seizures, disabling seizures, resistance to AEDs, duration of AED failure, number of AEDs failed, intolerable side effects to AED, absence of developmental delay, absence of psychiatric conditions, absence of serious medical conditions, absence of progressive neurological conditions, prior surgery, EEG criteria, neuroimaging criteria.

To further characterize pre-surgical criteria and to examine groupings for these criteria, the studies were divided into prospective (Supplementary Table 1) and retrospective (Supplementary Table 2) series based on when exposure status and outcomes were ascertained. Check marks as seen in Supplementary Tables 1 and 2 indicate the criteria each study used. The aforementioned categories were modified into the following columns: epilepsy duration, seizure frequency, disabling seizures, AED resistance (not further specified), AED trials completed, one AED failed, two or more AEDs failed, duration of AED failure, side effects of medications, EEG, and MRI. If none of these criteria were utilized for the study, the 'other criteria only' column has been marked. If drug resistant epilepsy was documented, the study was placed into the AED resistance (not further specified) column. If AED trials were explicitly mentioned, but the required number of failed drugs not specified, the study was placed in the AED trials completed column. The data were further examined pre- and post-year 2000 within the prospective data to see whether criteria to select patients for surgery evolved over time (Table 1). The year 2000 was selected as it was around the time when results of the first randomized controlled trial of focal resective epilepsy surgery began to be presented at international meetings (Wiebe et al., 2001). The years of data collection were used rather than year of publication.

2.4. Statistical analysis

Descriptive statistics and statistical analysis of proportions were performed. A p-value of less than 0.05 was pre-defined to indicate a statistically significant result. A meta-analysis was not conducted due to heterogeneity between studies.

3. Results

3.1. Literature search

Of the 5061 articles identified from the CASES literature review, 572 articles were either surgical series or review articles on indications or contraindications for surgery evaluation selection. Review articles without original data were excluded, leaving 489 surgical series reviewed in full text and 384 articles meeting all eligibility criteria for data abstraction (Supplementary references) (Fig. 1).

3.2. Study design and population

Study design types were as follows: 73 (19.0%) were prospective, 311 (81.0%) were retrospective and 2 (0.5%) were randomized