Seizure xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Long-term outcomes of surgical treatment for epilepsy in adults with regard to seizures, antiepileptic drug treatment and employment

Kristina Malmgren*, Anna Edelvik

Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University and Department of Neurology, Sahlgrenska University Hospital, Gothenburg, Sweden

ARTICLE INFO

Article history:
Received 1 September 2016
Received in revised form 6 October 2016
Accepted 16 October 2016
Available online xxx

Keywords:
Epilepsy surgery
Long-term outcomes
Seizure outcome
Antiepileptic drugs
Employment outcome
Vocational outcome

ABSTRACT

Purpose: There is Class I evidence for short-term efficacy of epilepsy surgery from two randomized controlled studies of temporal lobe resection. Long-term outcome studies are observational. The aim of this narrative review was to summarise long-term outcomes taking the study methodology into account.
Methods: A PubMed search was conducted identifying articles on long-term outcomes of epilepsy surgery in adults with regard to seizures, antiepileptic drug treatment and employment. Definitions of seizure freedom were examined in order to identify the proportions of patients with sustained seizure freedom. The quality of the long-term studies was assessed.
Results: In a number of high-quality studies 40–50% of patients had been continuously free from seizures with impairment of consciousness 10 years after resective surgery, with a higher proportion seizure-free at each annual follow-up. The proportion of seizure-free adults in whom AEDs have been withdrawn varied widely across studies, from 19–63% after around 5 years of seizure freedom. Few long-term vocational outcome studies were identified and results were inconsistent. Some investigators found no postoperative changes, others found decreased employment for patients with continuing seizures, but no change or increased employment for seizure-free patients. Having employment at baseline and postoperative seizure freedom were the strongest predictors of employment after surgery.
Conclusions: Long-term studies of outcomes after epilepsy surgery are by necessity observational. There is a need for more prospective longitudinal studies of both seizure and non-seizure outcomes, considering individual patient trajectories in order to obtain valid outcome data needed for counselling patients about epilepsy surgery.

1. Introduction

Surgical treatment for epilepsy has long been recognized as a valuable treatment option for carefully selected patients with drug-resistant focal epilepsy. In adults most operations are temporal lobe resections (TLR), and there is Class I evidence for the short-term efficacy (1 and 2 years follow-up respectively) from two randomized controlled studies (RCTs) of TLR [1,2]. Smaller numbers of patients undergo frontal lobe resections (FLR) or other extratemporal resections [3]. Very few adults undergo hemispherectomies [4]. In some patients palliative procedures such as callosotomy or other dissociative procedures may be indicated when resective surgery is not an option [5]. There are no RCTs for any of these surgical treatments.

The neurosurgical advances in epilepsy surgery develop toward minimally invasive techniques, with the ultimate aim to improve or maintain efficacy while reducing adverse effects. These techniques include radiofrequency thermocoagulation, MR-guided focused ultrasound, laser ablation and stereotactic radiosurgery [6]. There are as yet no prospective long-term reports of efficacy and safety for these new epilepsy treatments, the outcomes of which are therefore not addressed in this review. Palliative procedures (e.g., callosotomy) are not considered either due to the scarcity of long-term follow-up studies.

Until recently the knowledge about seizure outcomes after epilepsy surgery procedures was mainly based on short-term follow-ups (1–2 years). Epilepsy surgery candidates, however, are mostly young adults, and as well as information about the short-term chances of seizure control versus risks (complications as well as expected adverse effects), they need detailed advice about likely

* Corresponding author at: Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University and Sahlgrenska University Hospital, Blå Stråket 7, 3rd Floor, SE 413 45 Gothenburg, Sweden.
E-mail address: kristina.malmgren@neuro.gu.se (K. Malmgren).

http://dx.doi.org/10.1016/j.seizure.2016.10.015
1059-1311/

long-term seizure outcome before deciding to undergo brain surgery.

Patients' aims for epilepsy surgery are not limited to seizure relief. To be able to stop antiepileptic drugs (AEDs) and to be employed (or when employed, to be able to work more than preoperatively) are among the most important of these aims [7,8]. Realistic expectations concerning long-term seizure, employment and AED outcomes are therefore part of the information they need to consider.

Long-term outcome studies are by necessity observational since RCTs would be unfeasible as well as unethical. However, observational studies have methodological limitations which are also incorporated in systematic reviews of epilepsy surgery outcomes. In order to compare data from different observational studies, defined quality criteria are needed and a number of requirements for well-conducted studies on the prognosis after epilepsy surgery have been suggested: e.g., prospective study design, representative/population-based study populations, large enough cohorts, well defined inclusion criteria, satisfactory and complete follow-up, longitudinal follow-ups, masked assessment of outcome, clearly defined outcomes, adequate statistical methods and standard definition of prognostic factors [9,10]. When reviewing the literature we have focused on studies which as far as possible fulfill these requirements.

The aim of this review is to focus on outcomes from epilepsy surgery regarding seizures, antiepileptic drug treatment and employment in adults beyond at least a 4-year time period following surgery.

2. Search strategy and selection criteria

For this review we performed a PubMed search without date limits or restriction on type of articles, but with language restrictions to English only.

The following search terms were used in various combinations: "epilepsy surgery" (4153 results) "long-term", outcome*, "antiepileptic drug*", employment, vocational, psychosocial. Titles that clearly indicated e.g., only pediatric populations, non-surgical series, case reports, non-resective procedures and vagus nerve stimulation were not considered further.

For long-term seizure outcomes, the search string "epilepsy surgery" AND "long-term" AND "outcome*" resulted in 348 references, 196 of which were further assessed by reading the abstracts and 95 by screening the full text. For long-term outcomes of AED treatment "epilepsy surgery" AND "antiepileptic drug*" resulted in 200 references, where 31 were assessed by reading the abstracts and 18 in full text. For employment outcomes "epilepsy surgery" AND (employment OR vocational OR psychosocial) yielded 143 titles; 57 were assessed by reading the abstracts and 30 in full text. In addition, reference lists of reviews or meta-analyses were checked for additional articles missed in the electronic search.

3. Reporting of seizure outcomes

When assessing the literature on seizure outcomes after epilepsy surgery it has to be considered that seizure outcome and seizure freedom is not consistently defined. The most commonly used scheme is the Engel classification with one original and one revised version [11,12], another is the International League Against Epilepsy (ILAE) outcome scale [13]. While part of the Engel classification (class I A and I B) takes account of the whole postoperative period, the ILAE classification refers to the seizure outcome the last year of follow-up and the seizure outcome class should be determined for each year at annual intervals after surgery. However, both classifications make it possible to identify patients who have been completely seizure free without auras since the operation (Engel class I A, and ILAE class 1a). In the original Engel classification class I B identifies those patients who have had auras only but no seizures with impairment of consciousness since surgery while the revised version accepts all non-disabling simple partial seizures for a class I B categorization. Both the Engel and the ILAE classifications exclude early postoperative seizures.

Many studies report seizure outcome the last year of follow-up and do not distinguish patients who have been seizure free since surgery, although this is the most important patient group to identify in order to advise surgical candidates about their chances of good outcome. Seizure freedom is most often defined as freedom from seizures with impairment of consciousness, or Engel I (which also includes class I C, i.e., patients who have had some seizures with impairment of consciousness after surgery but then been seizure free at least two years and class I D, i.e., patients who have had secondary generalized convulsive seizures on AED withdrawal). Some studies differentiate into completely seizure-free (Engel I A or ILAE Class 1a) or include patients with auras only in the category of seizure free (Engel I A and B or ILAE Class 1a and 2). Although both scales include a possibility to note worsening of seizure frequency postoperatively, this is seldom reported.

4. Long-term seizure outcomes

During the last decade an increasing number of epilepsy surgery centers have reported long-term outcomes in cohorts of patients following a variety of surgical interventions. The studies which best fulfill at least four of the above-mentioned criteria for well-conducted studies [9,10] have been summarized in Table 1.

Long-term outcome after resective epilepsy surgery is often reported cross-sectionally, which makes it difficult to discern temporal trends. In a meta-analysis from 2005 based on 78 studies, 66% of TLR patients, 46% of patients who had parietal or occipital resections (P/OLR) and 27% of FLR patients were seizure-free at follow-up $\geq$five years post-surgery, but the authors point out that few studies reported sustained seizure freedom from surgery, most report seizure status last year of follow-up and cross-sectionally. Almost all studies described patient cohorts without controls [3].

Several recent studies with prospectively collected long-term data on seizure outcome have provided better information about the chances of sustained seizure freedom. In the largest of these, which is a single-center study of 1160 patients (adults and children) with a cross-sectional follow-up of at least two years (mean follow-up 5.4 years, range 2.0–20.5 years), 50.5% were continuously seizure-free without auras [14]. In another single center longitudinal follow-up of 615 adults, 52% of all patients remained free from seizures with impairment of consciousness from the time of surgery (using an outcome classification which equals Engel I A and B) five years after surgery and 47% at ten years [15]. In a population based national study of 278 patients who had 5 or 10 year follow-up 190 were adults [16]. This study had a control group of 80 adults who had been presurgically evaluated but not had surgery. At long-term 41% of the operated adults had sustained seizure freedom (Engel I A and B [11]) since surgery, compared to none of the controls.

4.1. Long-term seizure outcome after temporal lobe resections

A number of recent longitudinal long-term outcome studies report sustained seizure freedom after TLR. Most are retrospective single center series, only a few are prospective. Sustained seizure freedom is reported as Engel I [17,18], Engel I A [19,20] or Engel I A and B [21] and in a few studies as ILAE class 1 and 2 [15,22]. The proportion of patients with sustained seizure freedom around five

Please cite this article in press as: K. Malmgren, A. Edelvik, Long-term outcomes of surgical treatment for epilepsy in adults with regard to seizures, antiepileptic drug treatment and employment, Seizure: Eur J Epilepsy (2016), http://dx.doi.org/10.1016/j.seizure.2016.10.015