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Anterior temporal lobectomy compared with laser thermal hippocampectomy for mesial temporal epilepsy: A threshold analysis study

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ABSTRACT

Purpose: Anterior Temporal Lobectomy (ATL) is the gold standard surgical treatment for refractory temporal lobe epilepsy (TLE), but it carries the risks associated with invasiveness, including cognitive and visual deficits and potential damage to eloquent structures. Laser thermal hippocampectomy (LTH) is a new procedure that offers a less invasive alternative to the standard open approach. In this decision analysis, we determine the seizure freedom rate at which LTH would be equivalent to ATL.
Methods: MEDLINE searches were performed for studies of ATL from 1995 to 2014. Using complication and success rates from the literature, we constructed a decision analysis model for treatment with ATL and LTH. Quality-adjusted life years (QALYs) were derived from examining patient preferences in similar clinical conditions. LTH data were obtained from a preliminary multicenter study report following patients for 6–12 months. A sensitivity analysis in which major parameters were systematically varied within their 95% CIs was used.
Results: 350 studies involving 25,144 cases of ATL were included. Outcomes of LTH were taken from a recently presented multicenter series of 68 cases. Over a 10-year postoperative modeling period, LTH value was 5.9668 QALYs and ATL value was 5.8854. Sensitivity analysis revealed that probabilities of seizure control and late morbidity of LTH are most likely to affect outcomes compared to ATL. We calculated that LTH would need to stop disabling seizures (Engel class I) in at least 43% of cases and have fewer than 40% late mortality/morbidity to result in quality of life at least as good as that after ATL.
Conclusions: This decision analysis based on early follow-up data suggests LTH has similar utility to ATL. These early data support LTH as a potentially comparable less invasive alternative to ATL in refractory TLE. LTH utility may remain comparable to ATL even if long-term seizure control is less than that of ATL. Larger prospective studies with long-term follow up will be needed to validate the true role of LTH in the refractory epilepsy patient population.

Introduction

Mesial temporal lobe epilepsy (mTLE) is the most common indication for epilepsy surgery, accounting for 17–31% of surgical procedures (Pasquier et al., 2002; Piao et al., 2010). Anterior temporal lobectomy (ATL), introduced in 1968 by Falconer and Taylor, is the most common surgical procedure for mTLE (Falconer and Taylor, 1968) and entails removing 4–6 cm of the anterior temporal lobe including the amygdala and hippocampus. Randomized controlled trials (RCT) have demonstrated a significantly greater seizure freedom and improved quality of life (QoL) after surgery compared with medical management alone, with 60–80% of patients achieving effective seizure control (Engel et al., 2012; Wiebe et al., 2001). However, neurocognitive abilities, including verbal memory and naming, are at risk following ATL in the language dominant hemisphere (Sabsevitz et al., 2001; Sherman et al.,

Abbreviations: LTH, laser thermal hippocampectomy.

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2011). As such, there has been a growing interest in more selective procedures to minimize this impairment. Indeed, some studies have indicated that these procedures lead to better neuropsychological outcomes (Clusmann et al., 2004; Helmstaedter et al., 2002).

Stereotactic procedures for minimally invasive treatment of epilepsy offer the ability to ablate seizure foci without damaging surrounding structures. Multiple series have reported that patients undergoing radiofrequency thermal ablation of the amygdala–hippocampus complex achieving 59–77% Engel class I outcome, with good neuropsychological outcomes at 2-year follow-up (Malikova et al., 2013; Quigg et al., 2011; Regis et al., 2004). Recently, the FDA has cleared the first MRI-guided laser interstitial thermal therapy system for use in neurosurgery, which destroys tissue in a focused manner via heat generated by laser light energy absorption. Not only does the stereotactic procedure allow for minimally invasive destruction of the target area, but MRI compatibility also allows precise monitoring of the ablation zone and protection of important surrounding structures (Carpentier et al., 2012; Jethwa et al., 2012). This technology has been recently expanding from treatment of intracranial neoplasms (Leonardi and Lumenta, 2002; Reimer et al., 1998; Schwarzmaier et al., 2006) to ablation of epileptogenic foci. A recent report by Curry et al. (2012) demonstrated that five subjects underwent the procedure without complication and all remained seizure free at up to 13 months postoperatively.

Recently, a consortium of centers reported six-month outcomes following laser thermal hippocampectomy (LTH[1]), which uses laser thermal therapy to selectively ablate an epileptogenic hippocampus (Gross et al., 2013). Given that minimally invasive resections may leave the patient susceptible to seizure recurrence if there is remaining epileptogenic tissue, the risk of undergoing such a procedure would outweigh the benefits if seizures recur. To date, there have been no clinical trials investigating LTH as a minimally invasive alternative to ATL in the treatment of mTLE. To further elucidate the potential risks and benefits of this approach in contrast to ATL, we performed a decision analysis to calculate the seizure freedom rate at which LTH would need to provide QoL improvements equivalent to ATL.

Materials and methods

Outcomes in epilepsy treatment

We take as our base case an adult with medically-refractory temporal lobe epilepsy for several years duration. The possible pathways and outcomes following surgery are illustrated in Fig. 1. The procedure can either be uneventful or be associated with perioperative complications. On follow-up, seizure control can be satisfactory or not. Finally, there may or may not be late onset morbidity. For this analysis, we considered perioperative complications as those related to surgery and occurring within 30 days of operation. These include memory and other cognitive changes associated with surgery, even if not discovered until later than 30 days after surgery. Late onset morbidity, the incidence of which may be influenced by length of follow-up, included severe psychiatric disturbance (depression, psychosis and suicide), sudden unexpected death in epilepsy (SUDEP), and the need for reoperation. Surgical success was defined as Engel Class I (Engel, 1993) or the equivalent *International League Against Epilepsy* (*ILAE*) classes (Wieser et al., 2001). *The process by which we calculated QALYs from outcome parameters is outlined in the Appendix.*

The primary outcome parameter following a given pathway in the model is the QoL, which is expressed in terms of utility, which measures a patient's preference for a given health state and is a quantity between 0 (death) and 1 (perfect health). Multiplying the likelihood of each possible pathway resulting from a treatment by its utility and summing the individual products yields the expected utility of that treatment (Hunink, 2001). To measure the combination of quality and quantity of life, we employ quality-adjusted life years (QALYs) (Pliskin et al., 1980). QALYs are discussed in more detail in the Appendix.

Literature search

We derived data on ATL from a search of Medline, EMBASE and the Cochrane library for articles published since 1995 including the key words "temporal lobectomy" or "hippocampectomy" in the title or text fields. To ensure accurate data transcription, we limited our search to English language publications. We also limited series to those with at least five surgical cases. After excluding abstracts that did not contain original data, we reviewed the remainder and abstracted data of interest, such as perioperative complications, long-term successes and morbidities. All articles and the data abstracted from them were reviewed by at least two authors. Separate searches were performed for QoL associated with each outcome shown in the model (Fig. 1). Although there are no published large clinical study results from LTH, there is one multicenter series with six-to-twelve month data that has been presented recently (Gross et al., 2013). Utility values for the health outcomes used in this study were obtained from the literature.

Data management

Individual complication and morbidity rates were recorded from articles in which they were specifically mentioned. For example, quadrantanopia is common after ATL but not always looked for. Its incidence was calculated only from case series in which it was sought and recorded. In addition, aphasia is expected only after surgeries on the dominant cerebral hemisphere. Accordingly, we recorded aphasia incidence as a proportion of dominant hemisphere procedures. Pooled estimated incidence and success rates were tested to exclude heterogeneity (King et al., 1997) and represent inverse variance-weighted means, using a random-effects, meta-analytic model (Einarson, 1997). Meta-analytic pooling of observational data followed guidelines issued by the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group (Stroup et al., 2000). Outcomes whose incidences were considered likely to change over time (surgical success, late morbidities and mortality) were evaluated using meta-regression (Thompson and Higgins, 2002). Meta-analytic pooling was done using Stata 12 (StataCorp LP, College Station, Texas).

Analysis

Using the decision-analytic model, we calculated the expected QALYs in the ten years following surgery for the two approaches. Our primary analysis involved estimating thresholds of LTH parameters to reach an equivalent outcome to ATL when surgical success was defined as Engel Class I. *Since all our parameters represent point estimates, we employed sensitivity analyses to allow for the uncertainty of our data.* First we varied each parameter in the model for which we had 95% confidence intervals. Then we varied incidences of those parameters for which we had no definitive data (long term results of LTH) between zero and one. Parameters that had the greatest effects on QALYs were then used in two- and three-way sensitivity analyses to test the robustness of our conclusions. Analyses of the model employed TreeAge Pro 2012 (Tree Age Software, Inc., Williamstown, Mass.).