RACE 611: Clinical Epidemiology and Evidence-based Medicine

Assignment VII: CAT presentation

CAT FOR PROGNOSIS

"Temporal plus epilepsy is a major determinant of temporal lobe surgery failures"

Clinical Question: Does temporal plus epilepsy (TPE) account for temporal lobe epilepsy (TLE) surgery failure?

Patients: patients with temporal lobe epilepsy

Intervention or Exposure: temporal plus epilepsy (TPE)

Comparison: temporal lobe epilepsy (TLE)

Outcome: seizure relapse rate

Citation: Barba C, Rheims S, Minotti L, Guenot M, Hoffmann D, Chabardes S, et al. Temporal plus epilepsy is a major determinant of temporal lobe surgery failures. Brain: a journal of neurology. 2016;139(Pt 2):444-51. doi: 10.1093/brain/awv372. Epub 2015 Dec 22. (5-year impact factor 10.545)

A. **Study Characteristics**: This is a retrospective cohort study.

1. **Patients included** –Patients included in this study were selected from the epilepsy surgery cohorts launched in Grenoble and Lyon in 1990.

Inclusion criteria were:

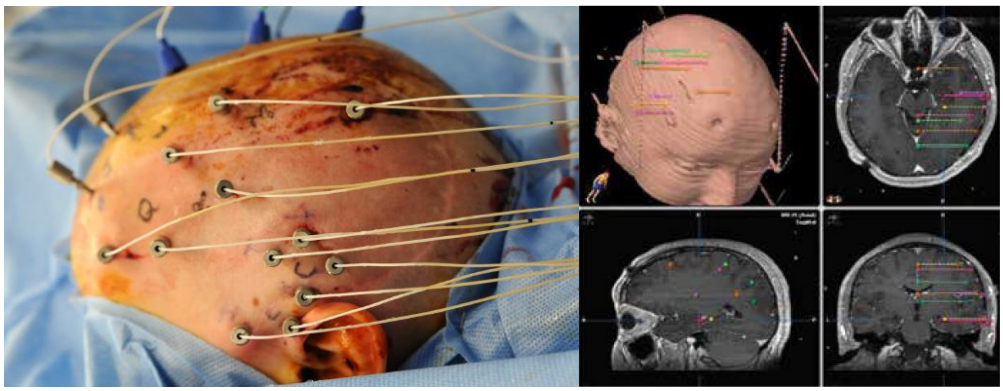
1) epilepsy surgery performed between January 1990 and December 2001
2) TLE surgery encompassing the anatomical boundaries of a standard anterior temporal lobectomy (ATL) as defined by Spencer et al. (1984): resection of the anterolateral 4.5 cm of

the temporal lobe and of the medial temporal structures from the amygdala to the lateral ventricular atrium

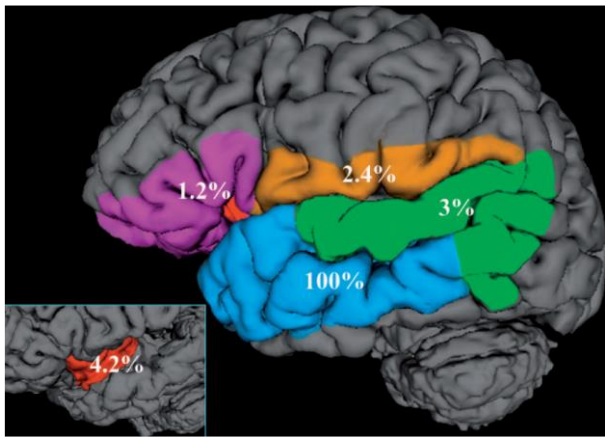
3) MRI either normal or showing signs of hippocampal sclerosis

4) postoperative follow-up □ 24 months for all patients classified as Engel outcome class I (Engel, 1993).

2. **Exposure** – Temporal plus epilepsy (TPE) proved by SEEG findings. TPE was defined as an epileptogenic zone including part of the temporal lobe and extending to neighboring regions, such as the insula, the suprasylvian operculum, the orbito-frontal cortex and the temporo-parieto-occipital junction (Ryvlin and Kahane, 2005; Barba et al., 2007).



SEEG technique



Blue = temporal lobe

Neighboring regions are orbito-frontal cortex (violet), suprasylvian operculum (brown), insular (red), and temporo-parieto-occipital junction lobe (green

3. **Outcome** – Postoperative seizure outcome was assessed using the Engel postoperative outcome scale (Engel, 1993).

B. **Validity Criteria**:

1. **Sample of patients, representative?**

- Since this study was performed in two referral epilepsy centers, this can lead to a referral bias.

- In this study the patients who did not undergo SEEG were all considered to be suffering from TLE. In addition, there was some limitations in spatial sampling and qualitative interpretation of the SEEG. This can lead to erroneous conclusions or overestimation of the seizure onset zone. Both conditions may lead to misclassification bias.

2. **Patients sufficiently homogenous with respect to prognostic risk?**

- Between TLE and TPE groups, statistically significant different characteristics were history of febrile seizures in childhood ($p = 0.012$), presence of hippocampal sclerosis on MRI ($p = 0.005$), and the number of cases needed to perform SEEG recordings ($p < 0.001$). Clinically but not statistically significant different characteristics were history of traumatic or infectious brain insult ($p = 0.058$), presence of secondarily generalized seizures ($p = 0.068$) and presence of postoperative hippocampal remnant. These differences result in “susceptibility bias” as groups being compared are not equally susceptible to the outcome of interest.

3. **Was follow-up sufficiently complete?**

- Yes. Surgical outcome was assessed at last follow-up. Time since the surgery until the assessment may be different in each patient, but postoperative follow-up had to be □ 24 months for all patients classified as Engel outcome class I. Mean follow-up periods of both TLE and TPE

groups were slightly different (85.4 ± 36.1 versus 90.3 ± 39.2 months), but did not reach statistical significance. It is therefore that outcome of all patients in both TLE and TPE groups were used for analysis.

4. **Were objective and unbiased outcome criteria used?**

Yes. In both TLE and TPE groups, widely-used surgical outcome assessment criteria so-called "Engel's classification" was employed.

C. **Results** [Risk factors of seizure recurrence (Engel class II-IV) with multivariate analysis]:

Outcome	Point Estimate (adjusted HR)	95% Confidence Interval	P value
1. History of traumatic or infectious brain insult	2.15	1.12 – 4.15	0.022
2. Secondarily GTCs	2.16	1.11 – 4.18	0.023
3. Temporal plus epilepsy (TPE)	5.06	2.36 – 10.82	< 0.001
4. Postoperative hippocampal remnant	4.62	1.88 – 11.30	0.001
5. MRI signs of hippocampal sclerosis	0.94	0.47 – 1.87	0.863
6. SEEG recording	1.46	0.69 – 3.08	0.320

One of the major biases that could affect the main findings of this study is susceptibility bias. Even though independent predictors for seizure relapse were identified after multivariate analysis, a valid association between TPE and seizure relapse is still in doubt since some factors that could be confounding factors are related to the surgical outcome—history of traumatic or infectious brain insult and secondary generalized seizures, are more prevalent in TPE patients.

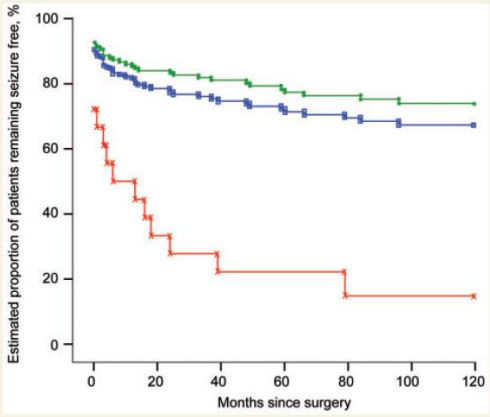


Figure 2 Long-term risk of seizure relapse following temporal lobe surgery. Kaplan-Meier analysis of time to seizure recurrence for all patients (blue/rectangles curve), patients with temporal lobe epilepsy (green/circles curve) and patients with TPE (red/cross symbols curve).

D. **Applicability**:

1. **Were the study patients and their management similar those patient in my practice?**

Yes. The study patients were similar to the patients in my practice since the King Chulalongkorn Memorial Hospital (KCMH) is also a referral epilepsy center. However, the SEEG has not yet been available at KCMH. At the KCMH, we have another method which is also considered to be a gold standard used to assess the area of seizure onset zone.

2. **Was follow-up sufficiently long?**

Yes. In most previous studies, long-term surgical outcome was assessed at more than 5 years after the surgery.

3. **Can I use the results in the management of patients in my practice?**

Yes. As also mentioned in the discussion part of this article, my initial interpretation of this kind of patients compatible with the TPE as described in this study was thought to be representing the patients with TLE but with very fast propagation to other neighboring areas -- resection of the very initial seizure onset zone in the temporal area would not necessarily affect postoperative outcome.

The results from this study showed that in TPE patients, resection in the extent of standard anterior temporal lobectomy (ATL) would give only 16.7% of the patients to be seizure-free (Engel class I). This is probably due to the fact that other neighboring areas which are not included in the area of standard ATL are left unresected. We should not therefore offer standard ATL to TPE patients.

Author's Conclusion:

Temporal plus epilepsy represents a hitherto unrecognized prominent cause of temporal lobe surgery failures. In patients with temporal plus epilepsy, anterior temporal lobectomy appears very unlikely to control seizures and should not be advised. Whether larger resection of temporal plus epileptogenic zones offers greater chance of seizure freedom remains to be investigated.

Reviewer's Conclusion:

This study was carried under difficulty in defining the TPE since it needs an invasive, costly, and highly specialized technique (SEEG) to confirm. This could result in a small number and limited variability of the patients included.

The researchers showed the important findings which can be used for the patients in a referral setting. They provide the first ever the surgical outcome of the TPE patients and suggest not to offer the surgical option in these patients. This has a large impact on decision of treatment, particularly for epileptologists who have to deal with complicated epilepsy cases. However, as mentioned earlier, some potential biases including a referral, misclassification, and susceptibility bias are found in this study. These biases inevitably compromise the study validity. Further studies with more study patients in different epilepsy centers are required to prove this association.

Reviewer: Chusak Limotai **Date**: 28 November 2016