Original article

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Long-term seizure outcome following epilepsy surgery in the parietal lobe: a meta-analysis

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ABSTRACT – *Aim.* Due to a limited number of patients with drug-resistant parietal lobe epilepsy in surgical series, there are insufficient data about long-term seizure outcome following surgery restricted to the parietal lobe. We performed a meta-analysis to asses long-term outcomes in patients with parietal lobe epilepsy who underwent surgery confined to the parietal lobe or resection with major involvement of the parietal cortex.
Methods. An English language literature search for studies on parietal lobe surgery and outcome was conducted using the MEDLINE database, followed by a manual search based on specific criteria. An inverse variance random effect meta-analysis model was used to estimate the pooled proportion of Engel Class I. Meta-regression models were used to examine the association between outcome and potential predictors.
Results. The search yielded seven retrospective studies with a total sample size of 253 patients (mean follow-up: 104.9±74.8 months). Following surgery, Engel Class I surgical outcome was achieved in 62.4% (95% CI: 0.492-0.755). Two independent predictors were identified for positive long-term outcome: interictal EEG localized to the parietal region (p=0.007) and the presence of tumour (p=0.022).
Conclusion. Following surgery confined to the parietal lobe or resection with major involvement of the parietal cortex, the long-term prognosis of patients with parietal lobe epilepsy is favourable.

Key words: parietal lobe epilepsy, surgical outcome, meta-analysis, epileptogenic tumour, interictal EEG

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Although the parietal cortex occupies the second largest cortical surface of the brain (after the frontal lobe) (Tramo *et al*., 1995), parietal lobe epilepsy (PLE) represents only 6% of patients who receive epilepsy surgery in large epilepsy centres (Salanova, 2012). It is hypothesized that PLE prevalence is underestimated in epilepsy surgery centres due to misleading electroclinical presentation attributed to extensive connectivity of the parietal cortex to different and remote brain areas; both interictal and ictal EEG findings are more variable in their anatomical distribution and/or less localizing in PLE patients compared to frontal or temporal lobe epilepsy cases (Ristic *et al*., 2012). Accordingly, these findings underscore the possibility of mislocalization of the epileptic focus to other lobes in patients with PLE, especially in non-lesional cases.

Due to a limited number of patients with PLE in surgical series, there are insufficient data about long-term seizure outcome following surgery restricted to the parietal lobe. It is assumed that surgical management of PLE, substantially aided by high-resolution neuroimaging and invasive neurophysiological evaluation, may provide excellent results (Francione *et al*., 2015). Nevertheless, in early studies (with long-term follow-up lasting from 2 to 50 years), only 20% of patients achieved complete seizure freedom (Engel Class Ia) (Salanova *et al*., 1995a).

The aim of this study was to carry out a meta-analysis to assess long-term outcomes in patients with drug-resistant PLE who underwent surgery confined to the parietal lobe or resection with major involvement of the parietal cortex.

Material and methods

Search strategy

This meta-analysis was conducted in agreement with Preferred Reporting Items of Systematic reviews and meta-analysis guidelines (Liberati *et al*., 2009). The search was based on the MEDLINE database and articles published up to March 31st 2017 were included. The key words used for the search were the following: (surgery OR operative OR outcome OR surgical) AND parietal lobe epilepsy. Articles were then filtered to include only those in English.

Selection criteria

The inclusion criteria were:

– a diagnosis of refractory, intractable, drug-resistant or pharmacoresistant PLE;

– and surgical resection strictly confined to the parietal lobe or mainly involving the parietal cortex. The exclusion criteria were:

– case reports of previously reported surgically treated PLE patients;

– and studies that were not restricted to only PLE patients (*i.e*. posterior cortex epilepsy surgical series and neocortical epilepsy surgical series).

Studies were identified using the search strategy by a single reviewer who also performed data extraction (SPD). When there was uncertainty regarding eligibility and data extraction, a second reviewer was consulted (AJR). The following information was extracted from the studies that met the inclusion/exclusion criteria: name of first author, year of publication, years of patient recruitment, demographic data of the patients, number of analysed patients, age at epilepsy onset, epilepsy duration, age at surgery, mean follow-up period, presence of aura, presence of somatosensory aura, generalized tonic-clonic seizures as part of the clinical presentation, imaging performed or not, positive finding on neuroimaging (brain CT or MRI), localizing interictal EEG, localizing ictal EEG, invasive study performed, presence of tumoural lesion, presence of malformation of cortical development, surgery in the right parietal lobe, and epilepsy surgery outcome (Engel Class I vs. Engel Class II to IV; Engel Class I subdivisions were not available in all studies).

Statistical method

The effect size based on the meta-analysis was the percentage of patients with Engel Class I outcome. An inverse variance random effect meta-analysis model was used to estimate the pooled proportion of Engel Class I patients. Meta-regression models were used to examine association between outcome and potential predictors. Meta-analysis and meta-regression were performed using R software environment for statistical computing (Team, 2014) and R package "metafor" (Viechtbauer, 2014).

Results

Literature research

Initially, we identified 670 studies using the key words. A total of 657 studies were excluded by screening titles and abstracts (including case reports), leaving 13 studies for full-text review. After full-text review, six more studies were excluded:

– one study analysed a surgical cohort of seven patients with predominantly posterior cingulate epilepsy, however, for the purpose of this study,

resection was not considered to involve the parietal lobe (Enatsu *et al*., 2014);
– one study analysed clinical features of 40 PLE patients and surgery was performed in a subset of analysed patients (Kim *et al*., 2004a), however, a similar cohort with complete surgery outcome data from the same centre and the period of recruitment was also published and this was included in the final sample instead;
– three studies analysed surgical outcome data in PLE patients, but surgical outcome was not specified as Engel surgical outcome classification (Williamson *et al*., 1992; Gawel and Marchel, 1998; Kurşun *et al*., 2016);
– and one study analysed surgical outcome in PLE patients, but significant inconsistencies were registered in the presented data (Kasowski *et al*., 2003). Thus, seven studies were included in the analysis (Cascino *et al*., 1993; Salanova *et al*., 1995a, 1995b; Kim *et al*., 2004b; Binder *et al*., 2009; Francione *et al*., 2015; Asadollahi *et al*., 2017).

Study and participant characteristics

All included reports were descriptive studies published in English. All trials were single-centre studies. The basic characteristics of the studies included in the meta-analysis are summarised in *table 1*. A total of 253 patients with refractory PLE were enrolled in seven studies. Mean age at surgery was 27±4.3 years. Somatosensory aura was present in 48% of analysed patients (range: 32%-100%; in one study, data were not available [Binder *et al*., 2009]), secondary generalized tonic-clonic seizures in 49.5% (range: 0-89%), interictal EEG localized to the parietal lobe in 23% (range: 8-40%; in one study, data were not available [Binder *et al*., 2009]), ictal EEG localized to the parietal lobe in 14% (range: 0-21%; in three studies, data were not available [Salanova *et al*., 1995a, 1995b; Binder *et al*., 2009]), and surgery in the right hemisphere in 52.0% (range: 50-55%). The types of surgery in all analysed studies are presented in *table 2*.

Meta-analysis and meta-regression

In all studies, primary outcome was determined as seizure freedom (Engel Class I) after resective surgery. Based on the random-effects model, 62.4% (95% CI: 0.492-0.755) of patients from all studies had Engel Class I outcome (*figure 1*).
The heterogeneity Q test was significant ($p<0.001$; τ^2=0,025 and I^2=80%), therefore, analysis of moderators was performed by meta-regression.
Based on the univariate meta-regression, the following predictors of Engel Class I outcome were identified: interictal EEG localized to the parietal region (p=0.007) and tumour lesion (p=0.022) (*table 3*). Due to the poor ratio of number of analysed studies to potential predictors, multivariate meta-regression was not performed.

Discussion

Meta-analysis of epilepsy outcomes following parietal lobe surgery has not been studied previously. Clearly, the main reason for this is that parietal lobe resections are the least commonly performed resections of the brain and consequently parietal lobe epilepsy surgery has been examined less extensively in the literature with respect to other localization-related epilepsies (Francione *et al*., 2015). Based on a review of studies of epilepsy outcomes following temporal lobe surgery, seizure freedom was reported in 63.2% (95% CI: 60, 66) (Engel *et al*., 2003). Similarly, the median proportion of long-term seizure-free patients following temporal lobe surgery based on a second meta-analysis of 40 studies was reported to be 66% (95% CI: 62, 70) (Tellez-Zenteno *et al*., 2005). In the latter meta-analysis, epilepsy surgery led to a lower seizure-free rate in follow-up studies of patients with surgery in other brain regions (27% with frontal lobe resections [seven studies; 95% CI: 23, 30], 46% with occipital lobe resection [one study; 95% CI: 29, 63], and 46% with parietal lobe resection [one study; 95% CI: 35, 57]). Contrary to previous judgment that success rates are less promising following surgery in the parietal region relative to the temporal lobe (Binder *et al*., 2009), one of our most noticeable findings is that the success rate following surgery confined to the parietal lobe or resections with major involvement of the parietal cortex is equal to that following surgery in the temporal lobe. Although it has been frequently stated that parietal lobe epilepsy poses a challenge for diagnosis, which may affect surgical outcome data (Binder *et al*., 2009; Francione *et al*., 2015; Ristic *et al*., 2012), our analysis shows that many surgical centres over-emphasise selection criteria to justify surgical treatment for parietal lobe epilepsy patients. Our data therefore certainly support the benefit of parietal lobe epilepsy surgery.
Our meta-analysis confirms a previously reported significant correlation between localizing interictal EEG discharges in the parietal lobe and better surgical outcome (Francione *et al*., 2015). Indeed, multiple diffuse EEG patterns or non-localizing scalp EEG findings which characterize parietal lobe epilepsy (Ristic *et al*., 2012) suggest an increased likelihood of misidentification and mislocalization for this localization-related epilepsy. Therefore, presurgical observation of highly diffuse interictal EEG discharge may be perceived as a warning against consideration for surgical treatment which might be related to our finding.

Table 1. Demographic and clinical characteristics and surgical outcome in analysed studies.

First author (year)	Year of recruitment	Pts (*n*)	Mean age at PLE onset (y)	Mean epilepsy duration (y)	Mean follow-up (m)	Pts with aura (*n*)	[a]Pts with positive imaging findings (*n*)	Pts who under-went invasive study (*n*)	Pts with MCD (*n*)	Pts with tumour (n)	Pts with Engel Class I (Ia) outcome (%)
Cascino *et al.* (1993)	1985-1991	10	N/A	8.0	30.4	7 (70%)	10 (100%)	8 (80%)	1 (10%)	5 (50%)	90.0
Salanova *et al.* (1995a)	1929-1988	79	14.5	7.6	245.0	69 (87%)	3 (4%)	59 (75%)	4 (5%)	0 (0%)	45.5 (20.3)
Prior to brain CT/MRI		71	15.6	7.3	261.3	63 (89%)	0 (0%)	54 (76%)	2 (3%)	0 (0%)	43.0 (21.1)
Brain CT/MRI		8	6.1	10.7	84.0	6 (75%)	3 (37%)	5 (62%)	2 (25%)	0 (0%)	25.0 (12.5)
Salanova *et al.* (1995b)	1934-1988	28	28.1	4.4	147.4	23 (82%)	9 (32%)	18 (64%)	0 (0%)	28 (100%)	71.4 (32.1)
Prior to brain CT/MRI		26	27.6	4.5	147.4	21 (81%)	7 (27%)	16 (61%)	0 (0%)	26 (100%)	73.0 (34.6)
Brain CT/MRI		2	37.0	3.0	84.0	2 (100%)	2 (100%)	2 (100%)	0 (0%)	2 (100%)	50.0 (0)
Kim *et al.* (2004a)	1994-2001	38	10.0	N/A	50.7	30 (79%)	26 (68%)	37 (97%)	31 (82%)	3 (8%)	39.5
Binder *et al.* (2009)	1990-2004	40	N/A	13.7	45.0	6 (15%)	38 (95%)	26 (65%)	11 (27%)	16 (40%)	57.5
Francione *et al.* (2015)	1996-2010	40	5.9	15.8	112.8	32 (80%)	36 (90%)	22 (55%)	13 (32%)	19 (47%)	75.0 (57.5)
Asadollahi *et al.* (2017)	1986-2015	18	16.2	13.1	103.2	13 (72%)	14 (78%)	4 (22%)	1 (56%)	5 (28%)	61.1
		Σ=253 $\bar{x}$=36.1±22.1	$\bar{x}$=14.8±8.3	$\bar{x}$=10.4±4.3	$\bar{x}$=104.9± 74.8	$\bar{x}$=69%	$\bar{x}$=67%	$\bar{x}$=65%	$\bar{x}$=24%	$\bar{x}$=39%	

PLE: parietal lobe epilepsy; Pts: patients; MCD: malformations of cortical development; N/A: data not available; [a]angiogram, brain CT, brain MRI (pneumoencephalogram excluded); [b]study involved 82 subjects and follow-up data was available for 79 subjects; [c]study involved 34 subjects and follow-up data was available for 28 subjects.

Table 2. Type of surgery in analysed studies.

First author (year)	Pts (*n*)	Surgery type
Cascino *et al*. (1993)	10	Lesionectomy (10 pts)
Salanova *et al*. (1995a)	79	Lesionectomy (33 pts); Corticectomy (42 pts); Unknown (4 pts)
Salanova *et al*. (1995b)	28	Lesionectomy (28 pts)
Kim *et al*. (2004a)	38	Lesionectomy (34 pts); Lesionectomy+ATL (3 pts); Lesionectomy + callosotomy (1 pt)
Binder *et al*. (2009)	40	Lesionectomy/Corticectomy (29 pts); Lesionectomy/Corticectomy+MST (11 pts)
Francione *et al*. (2015)	40	Lesionectomy/Corticectomy (40 pts)
Asadollahi *et al*. (2017)	18	Lesionectomy/Corticectomy (17 pts); MST (1 pt)

[a]Study involved 82 subjects and follow-up data was available for 79 subjects; [b]study involved 34 subjects and follow-up data was available for 28 subjects; ATL: anterior temporal lobectomy; MST: multiple subpial transections.

The presence of tumour represents another significant predictive element that correlated with favourable surgical outcome in our meta-analysis. A high rate of seizure freedom following surgery for epileptogenic brain tumours is well-documented, with a range of between 71% and 81.7% Engel Class I (Englot *et al*., 2011; Guerrini *et al*., 2013). In two comparable studies from the same centre, better outcome was reported following surgery in patients with tumour pathology (as epileptic aetiology), relative to non-tumour series (Salanova *et al*., 1995a, 1995b). Similarly, in two studies (Francione *et al*., 2015; Cascino *et al*., 1993) with the most favourable rate of surgical outcome analysed in the present meta-analysis, tumour pathology was most prevalent (47% and 50%, respectively). In addition, the tumour group had better outcome following surgery in other series of parietal lobe epilepsy which were excluded from the present analysis (Williamson *et al*., 1992). However, our result should be interpreted with caution since the largest study analysed in the present meta-analysis, that showed poor outcome for parietal lobe epilepsy patients without tumour (Salanova *et al*., 1995a), reflects an era of surgical treatment of epilepsy when imaging was under-developed.

The main limitation of the present meta-analysis is the heterogeneity of the selected trials that was inevitable given the single digit percentage of parietal lobe epilepsy surgery in reported series (Salanova, 2012). As parietal lobe epilepsy surgery is the least commonly performed type of surgery among all focal

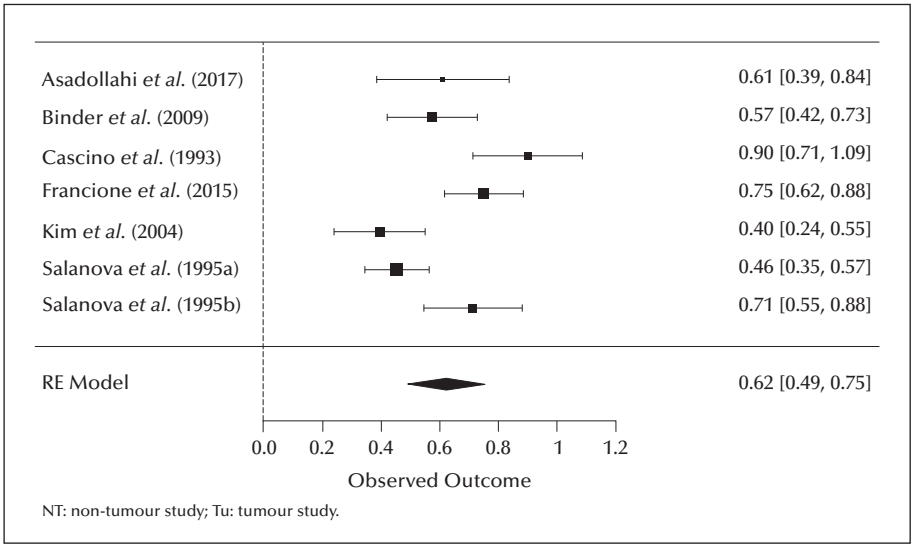

Figure 1. Engel forest plot of the percentage of Engel Class I outcome in analysed studies.

Table 3. Predictors of Engel Class I outcome in analysed studies based on univariate meta-regression.

Independent variable	b	p
Years of patient recruitment	-0,002	0,523
Male patients	-0,002	0,905
Age at onset	0,004	0,726
Epilepsy duration	-0,001	0,956
Age at surgery	0,024	0,120
Mean follow-up (months)	-0,001	0,472
Imaging performed	0,068	0,665
Presence of aura	-0,005	0,989
Somatosensory aura	0,805	0,301
Patients with GTC seizures	-0,147	0,519
Positive finding on imaging	0,229	0,214
Interictal EEG localized to parietal region	1,568	0,007
Ictal EEG localized to parietal region	0,599	0,856
Invasive study performed	-0,218	0,495
Presence of tumour lesion	0,366	0,022
Presence of malformation of cortical development	-0,294	0,263
Surgery on the right side	-0,001	1,000

GTC: generalized tonic-clonic.

pharmacoresistant epilepsy patients, study biases may significantly affect the quality and homogeneity of data. However, the strength of this evaluation lies in the pooling of all available data from studies on parietal lobe epilepsy surgery, which would otherwise not be easy to accomplish even in a multicentre study. □

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.
None of the authors have any conflict of interest to declare.

References

Asadollahi M, Sperling M, Rabiei A, *et al*. Drug-resistant parietal lobe epilepsy: clinical manifestations and surgery outcome. *Epileptic Disord* 2017; 19: 35-9.

Binder D, Podlogar M, Clussman H, *et al*. Surgical treatment of parietal lobe epilepsy. *J Neurosurg* 2009; 110: 1170-8.

Cascino G, Hulihan J, Sharbrough F, *et al*. Parietal lobe lesional epilepsy: electroclinical correlation and operative outcome. *Epilepsia* 1993; 34: 522-7.

Enatsu R, Bulacio J, Nair DR, *et al*. Posterior cingulate epilepsy: clinical and neurophysiological analysis. *J Neurol Neurosurg Psychiatry* 2014; 85: 44-50.

Engel JJ, Wiebe S, French J, *et al*. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* 2003; 60: 538-47.

Englot DJ, Berger MS, Barbaro NM, Chang EF. Predictors of seizure freedom after resection of supratentorial low-grade gliomas. *J Neurosurg* 2011; 115: 240-4.

Francione S, Liava A, Mai R, *et al*. Drug-resistant parietal epilepsy: polymorphic ictal semiology does not preclude good post-surgical outcome. *Epileptic Disord* 2015; 17: 32-46.

Gawel M, Marchel A. Surgical treatment of intractable parietal lobe epilepsy-our own experience. *Neurol Neurochir Pol* 1998; 32: 119-28.

Guerrini R, Rosati A, Giordano F, *et al*. The medical and surgical treatment of tumoral seizures: current and future perspectives. *Epilepsia* 2013; 54: 84-90.

Kasowski H, Stoffman M, Spencer S, *et al*. Surgical management of parietal lobe epilepsy. *Adv Neurol* 2003; 93: 347-56.

Kim C, Chung CK, Lee SK, *et al*. Parietal lobe epilepsy: surgical treatment and outcome. *Stereotact Funct Neurosurg* 2004a; 82: 175-85.

Kim D, Lee SK, Yun CK, *et al*. Parietal lobe epilepsy: the semiology, yield of diagnostic workup, and surgical outcome. *Epilepsia* 2004b; 45: 641-9.

Kurşun O, Karataş H, Dericioğlu H, *et al*. Refractory lesional parietal lobe epilepsy: clinical, electroencephalographic and neurodiagnostic findings. *Noro Psikiyatr Ars* 2016; 53: 213-21.

Liberati A, Altman DG, Tetzlaf J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009; 6: e1000100.

Ristic A, Alexopoulos A, So N, *et al*. Parietal lobe epilepsy: the great imitator among focal epilepsies. *Epileptic Disord* 2012; 14: 22-31.

Salanova V. Parietal lobe epilepsy. *J Clin Neurophysiol* 2012; 29: 392-6.

Salanova V, Andermann F, Rasmussen T, *et al*. Parietal lobe epilepsy: clinical manifestation and outcome in 82 patients treated surgically between 1929 and 1988. *Brain* 1995a; 118: 607-27.

Salanova V, Andermann F, Rasmussen T, Olivier A, Quesney LF. Tumoural parietal lobe epilepsy. Clinical manifestations and outcome in 34 patients treated between 1934 and 1988. *Brain* 1995b; 118: 1289-304.

Team RC. *A Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing, 2014.

Tellez-Zenteno J, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain* 2005; 128: 1188-98.

Tramo M, Loftus WC, Thomas CE, *et al*. Surface area of human cerebral cortex and its gross morphological subdivisions: in vivo measurements in monozygotic twins suggest differential hemisphere effect of genetic factors. *J Cognitive Neurosci* 1995; 7: 292-302.

Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2014; 36: 1-48.

Williamson P, Boon PA, Thadani VM, *et al*. Parietal lobe epilepsy: diagnostic considerations and results of surgery. *Ann Neurol* 1992; 31: 193-201.

TEST YOURSELF

(1) Which localization-related epilepsies are the least common in surgical series?

(2) What is the overall rate of seizure freedom in patients with parietal lobe epilepsy following surgery confined to the parietal lobe?

(3) Which parameters are positive predictors of good surgical outcome in patients with parietal lobe epilepsy?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".