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Temporal Lobe Surgery in Pediatric Patients: From Temporal Lobe Epilepsy to Temporal Plus Epilepsy

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Purpose: Temporal lobe resection can be categorized as either temporal lobe epilepsy (TLE), which involves cortical resection confined to the temporal lobe, or temporal plus epilepsy (TPE), which entails temporal resection along with involvement of additional extratemporal regions. We compared these forms within a pediatric population.

Methods: We identified 136 patients who underwent temporal resection over a 17-year period and investigated the differences in the clinical profiles and seizure outcomes between TLE and TPE.

Results: Of the total sample, 110 patients (80.9%) presented with TLE and 26 (19.1%) with TPE. Significant differences were observed between the groups in age at seizure onset (TLE: 6.3 years, TPE: 0.9 years; P=0.001), age at epilepsy surgery (TLE: 14.2 years, TPE: 9.2 years; P=0.002), the proportion of patients with a history of infantile epileptic spasm syndrome (IESS) (TLE: 6 [5.5%], TPE: 8 [30.3%]; P<0.001), electroclinical presentation with IESS or Lennox-Gastaut syndrome (LGS) (TLE: 11 [10.0%], TPE: 13 [50.0%]; P<0.001), the presence of focal temporal hypometabolism on positron emission tomography (TLE: 74 [68.5%], TPE: 11 [44.0%], P=0.021), and the use of intracranial electroencephalogram monitoring (TLE: 58 [52.7%], TPE: 21 [80.8%]; P=0.009). Furthermore, multivariate analysis identified the epileptic presentation of IESS or LGS as a significant predictor of TPE (P=0.049). The rates of seizure outcomes of International League Against Epilepsy class 1–3 at 1 year of follow-up were 83.8% for the entire cohort, 89.1% for TLE, and 61.5% for TPE (P=0.002).

Conclusion: TPE appears to represent a substantial subset of pediatric temporal resections. The variation in seizure outcomes between groups underscores the importance of predicting TPE in advance, with implications for effective treatment planning.

Keywords: Epilepsy; Temporal lobe; Pediatrics

Introduction

The term "temporal plus epilepsy (TPE)" was introduced in 2005 to describe a complex epileptogenic network that encompasses the temporal lobe (TL) and adjacent structures, including the orbitofrontal cortex, the insula, the frontal and parietal opercula, and the temporoparietal-occipital junction [1-3].

Studies have reported differences in clinical symptoms and sei-

zure outcomes associated with TPE [2,4]. Several studies have suggested that TPE is a significant factor in the failure of TL resection surgery [4,5], and research has indicated that more extensive resection, tailored with stereoelectroencephalography, may improve surgical outcomes [6]. Pediatric temporal lobe epilepsy (TLE) is characterized by distinct semiology, etiology, and surgical outcomes [7,8]. Reports indicate relatively high rates of dual pathology [9,10] and the presence of extratemporal and multilobar seizure foci in pediatric temporal resection series [11,12]. These clinical features of TPE suggest a relatively complex epileptogenic network and a higher likelihood of TPE in pediatric patients undergoing TL resection. Consequently, distinguishing between children with seizure foci and those with TPE is crucial. To our knowledge, no studies have yet focused on the clinical characteristics and seizure outcomes of TPE in the pediatric population, and only one connectomic analysis using magnetoencephalography has been reported in children [13].

Over the past two decades, we have observed the clinical features and seizure outcomes of pediatric patients who underwent TL resection at our center. In this study, we investigated the differences in clinical profiles and seizure outcomes between TLE and TPE.

Materials and Methods

1. Standard protocol approval

This study was approved by the Institutional Review Board of Yonsei University College of Medicine in Seoul, South Korea (approval number. 4-2023-1139). Written informed consent by the patients was waived due to a retrospective nature of our study.

2. Patients

We identified 136 patients who underwent temporal resection at Severance Children's Hospital in Seoul, Korea between April 2003 and September 2020. Children who underwent cortical resection confined to one TL were classified as having TLE. In contrast, those who underwent additional resections in extratemporal regions, such as the orbitofrontal cortex, the insula, the frontal and parietal opercula, and the temporoparietal-occipital junction, were defined as having TPE.

The exclusion criteria for the study were as follows: (1) the presence of progressive degenerative neurological disorders; (2) a lack of at least 6 months of follow-up data; and (3) a patient age above 18 years.

3. Presurgical evaluation

We categorized the patients into two electroclinical groups based on their clinical presentations and electroencephalogram (EEG) findings. The first group consisted of individuals with focal epilepsy (FE), which is characterized by focal-onset seizures. The second group comprised patients with pediatric-onset epileptic encephalopathy (EE), specifically those with infantile epileptic spasm syndrome (IESS) or Lennox-Gastaut syndrome (LGS) [14]. The presurgical evaluation protocol included video EEG monitoring and magnetic resonance imaging (MRI). For certain cases, additional tests were performed, such as fluorodeoxyglucose-positron emission tomography (PET) and interictal single-photon emission computed tomography.

4. Assessment of seizure outcomes and control patterns

We evaluated seizure outcomes on an annual basis using the International League Against Epilepsy (ILAE) classification system, defined as follows [15]: class 1 represents complete freedom from seizures, without auras; class 2 includes the presence of auras but no seizures; class 3 is characterized by 1 to 3 seizure days per year, with or without auras; class 4 consists of 4 seizure days per year with a 50% reduction from the baseline number of seizure days, with or without auras; class 5 is defined by a less than 50% reduction from the baseline up to a 100% increase in seizure days, with or without auras; and class 6 involves more than a 100% increase in seizure days from the baseline, with or without auras. We considered ILAE classes 1–3 as favorable seizure outcomes (FSOs), whereas ILAE classes 4–6 were categorized as unfavorable seizure outcomes (USOs).

Serial seizure outcomes were evaluated at 1, 1–2, and 2–3 years postoperatively. To monitor the progression of seizures over 3 years, we analyzed the seizure control patterns of 125 patients, classifying them into four categories: pattern A describes patients whose seizure outcome consistently remained an FSO (ILAE class 1–3) following surgery; pattern B refers to patients whose seizure outcome improved by one or more classes, with the final assessment indicating an FSO; pattern C indicates patients whose seizure outcome deteriorated by one or more classes, resulting in a USO (ILAE class 4–6) as the last recorded outcome; and pattern D encompasses those patients whose seizure outcomes were consistently classified as USOs.

5. Statistical analysis

Data analysis was performed using SPSS version 28 (IBM Corp., Armonk, NY, USA). Group comparisons were made using appropriate statistical tests, including the Mann-Whitney test, Pearson chi-square test, Fisher exact test, and linear-by-linear association. Multivariate logistic regression analysis was employed to identify preoperative findings associated with TPE. Odds ratios (ORs)

with 95% confidence intervals (CIs) were calculated to assess differences between groups.

6. Data availability

The deidentified data supporting the present findings can be made available upon reasonable request.

Results

1. Clinical data

The clinical data for the patients are summarized in Table 1. The cohort comprised 136 children and adolescents. The median age at the onset of seizures was 5.8 years, while that at the time of surgery was 12.7 years. Most patients—110 (80.9%)—presented with TLE, while the remaining 26 patients (19.1%) had TPE. Regarding epileptic syndromic classification, 112 patients (82.4%) exhibited FE, while 24 patients (17.6%) were identified as having pediatric-onset EE, including 19 with LGS and five with IESS. Furthermore, 14 patients (10.3%) had a history of IESS during infancy.

2. Etiology

Regarding etiology, the most common cause was malformation of cortical development (MCD), accounting for 33 cases (24.3%). This was followed by hippocampal sclerosis (HS) with 28 cases (20.6%), long-term epilepsy-associated tumors (LEATs) with 27 cases (19.9%), and dual pathology with 21 cases (15.4%). The etiology remained unidentified in 20 patients (14.7%). Brain injuries, such as perinatal asphyxia, infarction, or central nervous system infection, were observed in seven patients (5.1%). Dual pathology was confirmed as follows: HS with a tumor (n=8), with MCD (n=8), with brain injury (n=4), and with vascular malformation (n=1).

HS was identified as the most common etiology in TLE cases, accounting for 25.5%, whereas MCD was responsible for 53.8% of TPE cases. The prevalence of etiologies differed between TLE and TPE. In descending order, TLE was most frequently associated with HS, LEATs, MCD, dual pathology, unidentified causes, and brain injury. In contrast, TPE was predominantly caused by MCD, brain injury, LEATs, unidentified causes, and dual pathology. However, this difference was not statistically significant (linear-by-linear

Table 1. Clinical data

Characteristic	All patients (n=136, 100%)	TLE (n=110, 80.9%)	TPE (n=26, 19.1%)	*P* value[a]
Median range (25th-75th percentile) (yr)				
Age at seizure onset	5.8 (1.0–10.0)	6.3 (1.9–10.9)	0.9 (0.3–6.9)	0.001
Age at surgery	12.7 (7.2–16.9)	14.2 (8.2–17.4)	9.2 (3.6–13.3)	0.002
Epilepsy duration	4.3 (2.3–9.6)	4.4 (2.3–10.7)	3.8 (1.0–7.6)	0.214
History of IESS	14 (10.3)	6 (5.5)	8 (30.8)	<0.001
Epilepsy syndrome				<0.001
Focal epilepsy	112 (82.4)	99 (90.0)	13 (50.0)	
IESS or LGS	24 (17.6)	11 (10.0)	13 (50.0)	
Etiology				0.070
MCD	33 (24.3)	19 (17.3)	14 (53.8)	
Hippocampal sclerosis	28 (20.6)	28 (25.5)	0	
LEATs	27 (19.9)	24 (21.8)	3 (11.5)	
Dual pathology	21 (15.4)	19 (17.3)	2 (7.7)	
Unidentified	20 (14.7)	17 (15.5)	3 (11.5)	
Brain injury	7 (5.1)	3 (2.7)	4 (15.4)	
MRI findings				0.584
Abnormal	110 (80.9)	90 (81.8)	20 (76.9)	
Normal	26 (19.1)	20 (18.2)	6 (23.1)	
PET[b]				0.021
Focal temporal hypometabolism	85 (63.9)	74 (68.5)	11 (44.0)	
Other	48 (36.1)	34 (31.5)	14 (56.0)	
Intracranial EEG recording	79 (58.1)	58 (52.7)	21 (80.8)	0.009

Values are presented as number (%) unless otherwise indicated.
TLE, temporal lobe epilepsy; TPE, temporal plus epilepsy; IESS, infantile epileptic spasm syndrome; LGS, Lennox-Gastaut syndrome; MCD, malformation of cortical dysplasia; LEAT, long-term epilepsy-associated tumor; MRI, magnetic resonance imaging; PET, positron emission tomography; EEG, electroencephalography.
[a]Comparison between patients with TLE and those with TPE using the chi-square, Fisher exact, and Mann-Whitney tests, as appropriate; [b]Excluding three cases that lacked preoperative PET scan results.

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association, *P*=0.070).

The etiologies underlying the 26 cases of normal preoperative MRI findings were diverse: 11 were attributed to mild gliosis, 10 to MCD, three to HS, one to LEATs, and one to dual pathology.

3. Preoperative MRI and PET findings

Abnormal MRI findings were observed in 110 patients (80.9%), while normal findings were noted in 26 patients (19.1%). Of the 110 patients with abnormal MRI findings, 90 were diagnosed with TLE (representing 81.8% of the 110 total patients with TLE), while the remainder had TPE (20/26 total patients with TPE; 76.9%). The remaining 20 patients with TLE (18.2%) and six patients with TPE (23.1%) exhibited normal MRI findings. The *P* value for the comparison was 0.584.

Excluding three cases without preoperative PET scan results, our study identified unilateral focal temporal hypometabolism in 85 patients (63.9%), lateralized hypometabolism in 29 patients (21.8%), diffuse bilateral hypometabolism in 13 patients (9.8%), and no evidence of focal hypometabolism or hypermetabolism in six patients (4.5%). Of these six patients without signs of such metabolic dysfunction, four had TLE and two had TPE (*P*=0.314).

4. Comparative analysis between TLE and TPE

The following factors differed significantly between groups: age at seizure onset (TLE: 6.3 years, TPE: 0.9 years; *P*=0.001), age at surgery (TLE: 14.2 years, TPE: 9.2 years; *P*=0.002), the proportion of patients with a history of IESS (TLE: 6 [5.5%], TPE: 8 [30.3%]; *P*<0.001), the presentation of epilepsy as IESS or LGS (TLE: 11 [10.0%], TPE: 13 [50.0%]; *P*<0.001), focal temporal hypometabolism on PET (TLE: 74 [68.5%], TPE: 11 [44.0%]; *P*=0.021), and the utilization of intracranial EEG monitoring with subdural grids and strips (TLE: 58 [52.7%], TPE: 21 [80.8%]; *P*=0.009).

5. Seizure outcomes and control patterns

At the 1-year mark, 98 patients (72.1%) were categorized as ILAE class 1, two patients (1.5%) as class 2, 14 patients (10.3%) as class 3, seven patients (5.1%) as class 4, 10 patients (7.4%) as class 5, and five patients (3.7%) as class 6. At the last follow-up, ILAE class 1 was observed in 103 patients (75.7%), class 2 in two patients (1.5%), class 3 in 15 patients (11.0%), class 4 in four patients (2.9%), class 5 in eight patients (5.9%), and class 6 in four patients (2.9%).

Serial seizure outcomes were available for 125 patients at Severance Hospital for more than 1 year following surgery. Seizure control pattern A was observed in 105 patients (84.0%), with pattern B in five patients (4.0%), pattern C in three patients (2.4%), and pattern D in 12 patients (9.6%). The distribution of control patterns in the TLE and TPE groups was as follows. In the TLE group, 91 patients exhibited pattern A, four displayed pattern B, one showed pattern C, and seven had pattern D. In the TPE group, 14 patients displayed pattern A, one pattern B, two pattern C, and five pattern D. The proportion of patients exhibiting seizure control pattern A was higher in the TLE group (88.3%) than the TPE group (63.6%); however, this difference was not statistically significant.

Fig. 1 summarizes the postoperative seizure outcomes (Fig. 1A)

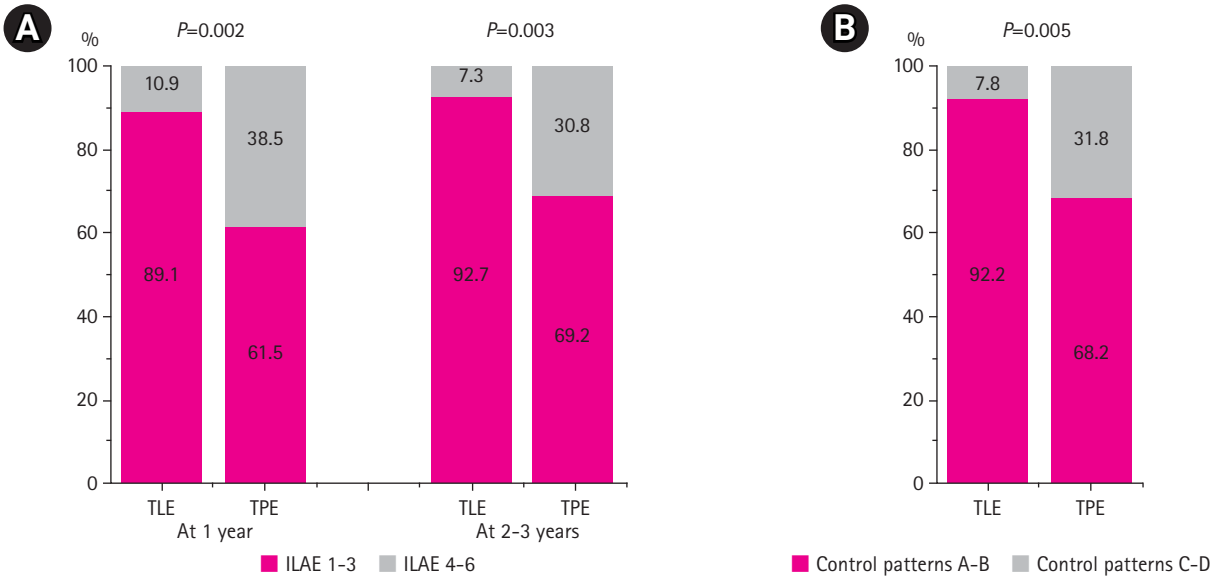

Fig. 1. (A) Seizure outcomes and (B) seizure control patterns of temporal lobe epilepsy (TLE) and temporal plus epilepsy (TPE). ILAE, International League Against Epilepsy.

and seizure control patterns (Fig. 1B) of TLE and TPE. FSOs (ILAE classes 1–3) at 1 year and at the last follow-up, as well as favorable control patterns (A–B), were observed more frequently in TLE than in TPE (P=0.002, P=0.003, and P=0.005, respectively).

6. Preoperative factors associated with TPE

Factors associated with TPE that were significant in the univariate analysis were included in the multivariate model. Logistic regression analysis indicated that the epilepsy syndrome of EE (OR, 3.89; 95% CI, 1.005 to 15.065; P=0.049) was a significant predictor of TPE, as detailed in Table 2. Among the patients with TLE, 12 exhibited seizure outcomes of ILAE 4–6 following their first operation. Upon examining the significant preoperative factors identified in the multivariate analyses, four patients (33.3%) with USO were found to exhibit pediatric-onset EE. However, these findings did not reach statistical significance.

Discussion

This study emphasizes two categories of TL resection in pediatric patients: TLE and TPE. Among the participants, 19.1% presented with TPE, aligning with the previously reported range of 10.7% to 42.9% [2,4,13].

We observed significant differences in several clinical features between the groups. The TPE group exhibited earlier seizure onset, earlier seizure surgery, and more frequent history of IESS, epileptic presentation of IESS or LGS, and intracranial EEG monitoring. Furthermore, the patients with TPE exhibited a lower incidence of focal temporal PET hypometabolism.

Our analysis also revealed that the presence of IESS or LGS as an epileptic presentation was a significant predictor of TPE, exhibiting a high hazard ratio in the multivariate analysis. Thus, such factors may indicate broader abnormalities in brain disorders. For instance, we found that 17.6% of patients who underwent TL resection exhibited electroclinical features consistent with IESS or LGS. Similarly, another study reported that clusters of epileptic spasms occurred in 30% of patients with TLE who experienced onset early in life [16]. This implies that IESS or LGS might represent the electroclinical manifestation of seizures originating in the temporal region in children. This trend is further supported by the high rate of IESS or LGS presentation (32.0%) among patients with focal cortical dysplasia at the same institution [17]. The distinction is important because the interictal findings and semiology of IESS or LGS are different from those of FE and suggest the involvement of a broader and different network in the production of generalized electroclinical abnormalities [18].

When combining the seizure outcomes of TLE and TPE, this study revealed a 72.1% likelihood of achieving an ILAE outcome of 1 at 1 year, which aligns with the 58% to 76% range reported in children after TL resection [7,19,20]. Patients with TLE experienced more favorable outcomes than those with TPE in terms of 1-year and last follow-up results, as well as in patterns of seizure control. Surgical outcomes related to TPE have often been reported as less favorable than those of TLE [4]. In 2005, Ryvlin and Kahane [1] attributed the poorer surgical outcomes for TPE to the onset of extratemporal seizures. Moreover, the risk of surgical failure in TPE is 5.06 times higher when only TL surgery is performed [4]. However, when tailored, multilobar resection is conducted with the aid of stereoelectroencephalography, the surgical outcomes for TPE have demonstrated superior efficacy to those of TLE [6].

In the present study, intracranial EEG monitoring was performed in 58.1% of all TL resections. Notably, a higher rate of utilization (80.8%) was observed in cases of TPE compared to TLE. This study analyzed TL resections starting from 2003, a period when the concept of an "epileptogenic network" and the understanding of TPE were not yet well established. We recognize that TL resection in pediatric patients deviated from the strict definition of TLE, as we sought to improve surgical outcomes by incorporating intracranial monitoring into our surgical strategy.

Regarding seizure recurrence, patients with TLE were confirmed to exhibit significant maintenance of seizure control patterns A and B. In contrast, those with TPE demonstrated less stability in seizure outcomes and control patterns, both in the first year and at the last follow-up. In this study, the clinical factors and surgical outcomes associated with TPE indicate a complex and widespread network disorder, rather than well-circumscribed FE. Thus, clinicians should understand that not all patients with TPE are suitable candidates for surgical intervention. Seizure recurrence is often linked to either incomplete resection or the emergence of new epileptogenic foci [21-23]. To further explore this issue, additional analyses, such as network analyses, are necessary [24].

This study also observed variations in etiology [25]. HS was identified as the second most prevalent cause overall, although its prevalence differed markedly between groups; specifically, HS was the most common cause of TLE, while no instances were reported

Table 2. Results of the multivariate analysis identifying predictors of TPE

Variable	Odds ratio	95% CI	P value
Electroclinical presentation of IESS or LGS	3.89	1.005–15.065	0.049

TPE, temporal plus epilepsy; CI, confidence interval; IESS, infantile epileptic spasm syndrome; LGS, Lennox-Gastaut syndrome.

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among patients with TPE. MCD and dual pathology are significantly more prevalent in pediatric patients, with brain tumors and MCD being identified in up to 40% and 30% of cases, respectively [16]. Although the findings were not statistically significant, MCD accounted for a large proportion of TPE cases in the present study. Furthermore, 14.7% of the pathological results were classified as unidentified, indicating the presence of mild gliosis or mild atrophy in the pathological findings. Cohen-Gadol et al. [26] reported that neuronal gliosis was the predominant etiology in 399 children who underwent definitive TL surgery. Specifically, neuronal gliosis accounted for 59% of the cases, while HS accounted for 28%. Notably, pathological reports of neuronal gliosis do not always indicate complete normality, as histological analyses may not detect changes that could increase susceptibility to seizures or lower the seizure threshold [27,28].

The clinical presentation, etiology, and outcomes of pediatric TL resections are distinct from those performed in adults [8,16,29,30]. This study further establishes that clinical symptoms and surgical outcomes vary between TLE and TPE in children; thus, the known differences between children and adults may be influenced in part by their relative proportions of TPE among TL resections. Variations in brain maturation and epileptogenic neuronal networks may contribute to the different manifestations of TPE, particularly in pediatric patients. The ictal presentation of TLE and the precise localization of ictal and interictal epileptiform discharges pose challenges due to the immature state of the brain and the rapid propagation of seizures [31]. Therefore, identifying presurgical factors associated with TPE could prevent unsuccessful TL surgery and facilitate the development of more effective surgical plans. Our findings emphasize the importance of intracranial recording in patients with suspected TPE, not only to confirm the electroclinical diagnosis but also to precisely define the extent of resection and potentially improve seizure outcomes.

The limitations of this study stem from its retrospective design, small overall sample, and disparity in sample sizes between the TLE and TPE groups.

In conclusion, this study indicates that TPE constitutes a significant subgroup of pediatric temporal resections with distinct clinical features. The variation in seizure outcomes between the groups underscores the importance of predicting TPE in advance, with implications for effective treatment planning.

Conflicts of interest

Heung Dong Kim is an emeritus editor, Hoon-Chul Kang is an associate editor, and Joon Soo Lee is an editorial board member of the journal, but they were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Conceptualization: JCB, HEK, and HDK. Data curation: JCB, HEK, HCK, JSL, and HDK. Formal analysis: JCB and HEK. Funding acquisition: HCK and JSL. Methodology: HCK and HDK. Project administration: JSL. Visualization: JCB and HEK. Writing-original draft: JCB and HEK. Writing-review & editing: JCB, HEK, and HDK.

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