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Original Article

Extent of Leptomeningeal Capillary Malformation is Associated With Severity of Epilepsy in Sturge-Weber Syndrome

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ABSTRACT

Background: Individuals with Sturge-Weber syndrome (SWS) often expereince intractable epilepsy and cognitive decline. We hypothesized that the extent of the leptomeningeal capillary malformation (LCM) may correlate with the severity of neurological impairment due to SWS. We tested the hypothesis in a cross-sectional study of seizure severity and electroencephalographic (EEG) findings and a retrospective cohort study for surgical indications related to the extent of the LCM.

Methods: We enrolled 112 patients and classified them according to LCM distribution: (1) bilateral, (2) hemispheric, (3) multilobar, and (4) single lobe. Age at seizure onset, seizure semiology and frequency, and EEG findings were compared. Surgical indications were evaluated for each group by Fisher exact test, and predictors for surgery were evaluated by univariate and multivariate analyses. Therapeutic efficacy was evaluated by the SWS-Neurological Score (SWS-NS).

Results: The bilateral and hemispheric groups had early seizure onset (4.0 months old and 3.0 months old), frequent seizures (88.9% and 80.6% had more than one per month), focal-to-bilateral tonic-clonic seizures (88.9% and 74.2%), and status epilepticus (100% and 87.1%). The groups' EEG findings did not differ substantially. Surgical indications were present in 77.8% of the bilateral, 88.1% of the hemispheric, and 46.8% of the multilobar groups. Seizure more than once per month was a predictor of surgical treatment. Seizure subscore improved postoperatively in the hemispheric and multilobar groups. Even after surgical treatment, the bilateral and hemispheric groups exhibited higher SWS-NSs than members of the other groups.

Conclusion: Our study demonstrated a strong association between extensive LCM and epilepsy severity. Surgical intervention improved seizure outcome in patients with SWS with large LCMs.

Introduction

Seizures affect 75% to 90% of individuals with Sturge-Weber syndrome (SWS), and these patients' seizures are refractory to antiepileptic drugs (AED) almost half of the time.[1,2] Approximately 30% to 60% of patients experience intellectual disability.[3-5] Prevention of cognitive deterioration requires prompt seizure control.[4,6] The therapeutic goal is to maintain or improve mentation and cognition. However, cognitive outcome after treatment is difficult to predict because the seizure severity and the extent of the lesion is not be standardized for comparison between existing

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studies.[3-5] Identification of a somatic mutation in GNAQ[7-9] is responsible for SWS, although the mutation does not predict the severity of the neurological impairment. To optimize the therapeutic management of seizures and cognition in patients with SWS, we analyzed the relationship between the neurological manifestations and the hemangioma extent and its effect on seizure and cognition outcome.

Previous reports on the natural and therapeutic seizure outcomes suggest that seizures starting during the first year of life may gradually stabilize later in infancy.[10,11] However, seizure-free ratios in these series did not reach satisfactory levels.[12] Because the utility of electroencephalography (EEG) for evaluating overall severity is limited,[13] other diagnostic modalities could be required. The contribution of surgery to seizure-free status requires further attention, and only limited indicative data exist on the outcomes of surgical interventions from large series. We describe the therapeutic outcomes following medical and surgical treatment of 112 patients using a single therapeutic protocol.

The extent of leptomeningeal capillary malformation (LCM), the extent of atrophy, and white matter alterations are related to seizure control and psychomotor development in SWS.[14] We hypothesized that patients with extensive distribution of LCM have more severe seizure manifestations, resulting in a poor cognitive outcome. To test our hypothesis, we evaluated seizure severity and EEG findings in a cross-sectional study and surgical indications and outcomes in a retrospective cohort study in patients with SWS according to the extent of the LCM distribution.

Methods

Patients and groups

We enrolled 112 patients (64 male) with SWS who were treated and followed for at least two years at the epilepsy center of Juntendo University Hospital, Tokyo, Japan, from 2006 to 2017. All patients underwent scalp EEG studies using Neurofax (Nihon Kohden, Tokyo, Japan) with the 10-20 international electrode placement system at a sampling rate of 500 Hz. Surgical candidates underwent scalp video-EEG for three days to record their interictal epileptic and seizure discharges and to correlate them with the seizure semiology. All patients underwent a 3.0-T brain magnetic resonance imaging (MRI) with Gd contrast enhancement. The diagnosis of SWS in our cohort was made by the confirmation of LCM on brain MRI together with at least one of the two following findings: facial capillary malformation or elevated intraocular pressure.

LCM distribution was determined using MRI with fluid-attenuated inversion recovery with Gd enhancement (FLAIR-Gd) and susceptibility-weighted imaging (SWI). Two independent reviewers, including a neuroradiologist and a neurosurgeon or pediatric neurologist, determined the affected areas by visual inspection. Patients were classified into the following four groups according to the area affected by LCM: (1) bilateral, (2) hemispheric, (3) multilobar, and (4) single lobe. The definition of the multilobar group included LCMs that involved unilaterally two to three lobes. The incidences of each group were as follows: nine patients (8.0%) in the bilateral, 31 (27.7%) in the hemispheric, 62 (55.4%) in the multilobar, and 10 (8.9%) in the single groups.

Cross-sectional study for the assessment of seizure and EEG severities

Seizure semiology and frequency before antiseizure therapy implementation were obtained from medical records to evaluate seizure severity and age at seizure onset (ASO). Seizure semiology was classified as status epilepticus, focal to bilateral tonic-clonic seizure (FBTCS), focal impaired awareness seizure (FIAS), and focal awareness seizure (FAS). Seizure frequency was classified as "daily" (having at least one seizure a day), "weekly" (having one to six seizures a week), "monthly" (having one to three seizures a month), "yearly" (having one to 11 seizures a year), "rare" (having a seizure less than once a year), or "no history of seizure" (no seizure during clinical history). We compared the ASO and seizure frequency among the four groups, and the incidence of each seizure type in each group.

The EEG records were reviewed and classified using the SWS-EEG score (SWS-EEGS)[13] to assess EEG-based differences among the four groups. The SWS-EEGS ranked the EEG findings as: 0, normal; 1, focal asymmetry (slowing or loss of normal background activity); 2, sporadic with unilateral sharp waves; 3, frequent with occasional semirhythmic unilateral runs of spikes. We conducted an intergroup comparison to determine the ratios of SWS-EEGS.

Retrospective cohort study for therapeutic choice and its outcomes

Our therapeutic strategy was (1) patients were clinically evaluated (neurological condition, seizure characteristics, scalp EEG, MRI, and cognition) every six months, (2) AED treatment began after seizure confirmation, and (3) surgical treatment was indicated when seizures were resistant to AED therapy, progressive cerebral atrophy was observed on MRI sequential imaging, and cognition was deteriorating. The Sturge-Weber syndrome Neurologic Score (SWS-NS) was applied for neurological assessment.[10,15] The SWS-NS included subscores for seizures, hemiparesis, visual deficits, and cognition. Seizure subscores ranged between 0 and 4, with 0 for no seizures ever, 1 for one or more seizures that were currently controlled, 2 for occasional seizures, 3 for monthly seizures, and 4 for seizures at least once a week. Hemiparesis subscores ranged between 0 and 4, with 0 for no weakness, 1 for mild intermittent posturing, 2 for fine motor impairments only, 3 for significant fine and gross motor impairments, and 4 for severe fine and gross motor impairments. Visual field deficit subscores ranged between 0 and 2, with 0 for no field affection, 1 for partial homonymous hemianopsia, and 2 for complete homonymous hemianopsia. Cognitive function subscores ranged between 0 and 5 with 0 for normal, 1 indicating the ability to live independently with some difficulty, 2 indicating the requirement for help, 3 indicating significant difficulties at school and work, 4 for being trainable, and 5 for being under complete care. We continued patients' follow-up every six months after the surgery or for choosing appropriate AEDs. Seizure-free outcome was defined when patients' seizures completely ceased at least for two years after the treatment.

We analyzed the ratio of patients indicated for surgery in each group. The parameters selected for that were as follows: sex, FAS, FIAS, FBTCS, status epilepticus, ASO (earlier than six months or later), seizure frequency (more than a monthly seizure or less), and lesion distribution (more than three lobes or less). We evaluated the significant parameters using univariate analysis of all these categoric variables. Subsequently, multivariate factor analysis was performed using the parameters with statistical significance from the univariate analysis. We summarized AED and aspirin use at the decision point for surgery or after the best medical treatment. Before- and after-treatment seizure subscore of SWS-NS was compared to evaluate the therapeutic outcome in our single therapeutic protocol. Post-treatment SWS-NSs were retrospectively evaluated from the medical records or by telephonic interview. The SWS-NSs after the treatment in each group were compared. The mean follow-up period was 10.2 years and ranged between two and 13 years. The median age at the last evaluation was 15 years and ranged from two to 59 years.

Statistical analysis

SPSS version 26.0 IBM (IBM Japan, Chuo-ku, Tokyo, Japan) was used for data analysis. Evaluation of the sample distribution of the ASO revealed that the data were not distributed normally. Differences in the ASO and seizure frequency among the four groups were evaluated using the Kruskal-Wallis test with the Dunn-Bonferroni posthoc method. The SWS-EEGSs of the four groups were evaluated using the Kruskal-Wallis test. The incidence of seizure type and surgical requirements in each group were compared using Fisher exact test followed by residual analysis. Univariate factor analysis for presence of surgical indications was evaluated using Fisher exact test with binary variables. The binominal logistic regression analysis for surgical requirement was also performed using the significant factors from the univariate analysis. Comparison of SWS-NSs after treatment of the groups with different therapeutic choice was achieved using the Wilcoxon signed-rank test. P values < 0.05 were considered statistically significant.

Institutional review board approval

This study was a retrospective analysis, and data were obtained using the opt-in/opt-out method. Registration and analysis were approved by the ethical committee of Juntendo University (16-163). Parents and patients consented to the collection and storage of their clinical information.

Results

Cross-sectional study for the severity assessment of seizure and EEG changes

The mean age of the 112 patients at seizure onset was 10.3 months. The first seizure occurred within the first year of life in 77.9% of the patients. Medians of ASO were 4.0 months old (MO) in the bilateral, 3.0 MO in the hemispheric, 8.0 MO in the multilobar, and 17.0 MO in the Single groups. ASO was significantly lower both in the bilateral and the hemispheric groups than those in the multilobar and single groups. Both the bilateral and the hemispheric groups showed higher seizure frequency than those of the multilobar and single groups. The incidence of seizures occurring more than once a month in the bilateral and hemispheric groups was 88.9% and 80.6%, respectively (Fig 1).

Seizure semiology and its frequency in each group is shown in Table 1. The incidence of status epilepticus accounted for 54.0% of all patients. Status epilepticus and FBTCS were frequent both in the bilateral and the hemispheric groups. FIAS was the prominent seizure semiology in the hemispheric and multilobar groups.

No significant differences were observed in the SWS-EEGS among the four groups (Table 2). The most frequent EEG pattern was focal asymmetry, corresponding to 1 in the SWS-EEGS. Observations of sporadic unilateral sharp waves and frequent or rhythmic runs of spikes, corresponding to 2 and 3 in the SWS-EEGS, were relatively frequent in the multilobar group.

Retrospective cohort study for therapeutic choice and its outcomes

Medical treatment

Averages and standard deviations of the number of AEDs used initially, at surgery, and at the last visit in our cohort were 1.5 ± 1.1, 1.9 ± 1.1, and 1.2 ± 1.2, respectively (Supplemental Table). The most frequently used AED was carbamazepine at all stages with 48.2%, 68.5%, and 32.1%, respectively. Aspirin use in our cohort at the initial and last follow-up stages was 15.2% and 4.5%.

Surgical indications

Ratios of surgical and medical treatment indications are shown in Fig 2. The hemispheric group was indicated for hemispherotomy

FIGURE 1. Seizure frequency. Seizure ratios of the bilateral and hemispheric groups were significantly higher than those of the multilobar and single groups. Seizure frequency in the multilobar group was higher than that of the single group.

TABLE 1
Incidence of Seizure Type

	Bilateral	Hemispheric	Multilobar	Single	*P* Value
Status epilepticus	100%	87.1%	40.3%	10.0%	<0.001
FBTCS	88.9%	74.2%	50.0%	20.0%	0.003
FIAS	33.3%	71.0%	72.6%	40.0%	0.007
FAS	33.3%	54.8%	38.7%	30.0%	0.592

Abbreviations:
FAS = Focal awareness seizure
FBTSC = Focal to bilateral tonic-clonic seizure
FIAS = Focal impaired awareness seizure
Bilateral and Hemispheric groups had status epilepticus and FBTCS with statistical significance. Hemispheric and multilobar groups presented FIAS.

(HST)[16] in 87.1% of the cases, and that was statistically significant. We had similar findings with statistical significance for the bilateral group regarding application of callosotomy. We performed multilobar disconnection surgery with mainly posterior quadrant disconnection (PQD)[17] for 20 patients and lesionectomy for nine in the multilobar group.

By univariate analysis, FBTCS or status epilepticus in seizure type, early ASO (six months or earlier), frequent seizure (more than a monthly seizure), and wider affected area (three lobes or more) were positive factors for indications to surgery with statistical significance (Table 3). Multivariate analysis using the positive parameters from the univariate analysis showed that frequent seizure (more than a monthly seizure frequency) at the initial stage was a sole predictor to surgery (Table 3).

Therapeutic results

The hemispheric, multilobar, and single groups demonstrated significantly improved seizure subscores on the SWS-NS following therapeutic intervention (Fig 3).

Total callosotomy was indicated in six patients in the bilateral group and had an effect to prevent status epilepticus. The seizure frequency and severity were improved initially but progressed again later in the bilateral group.

The ratio of seizure-free outcomes following HST in the hemispheric group was 85.2%. Second surgery was indicated in four patients to accomplish complete disconnection. A seizure-free ratio of 92.6% was achieved after these procedures. The mean age at HST was 13.8 months (6 to 48 months). Seizure-free ratios comparison between HST carried out before 12 MO and later was 100% and 83.3%, respectively, but the difference was without statistical significance. Cognitive function subscore of SWS-NS between these two groups did not result in significant difference, neither. The drug-free ratio after HST was 70.4%.

Seizure-free outcomes following multilobar disconnection surgery for patients in the multilobar group were obtained in 85.0% after initial surgery. We performed second surgery for two patients, which finally resulted in a seizure-free ratio of 95.0%. The mean age during the disconnection procedures was 39.4 months (7 to 108 months). Seizure and cognitive function subscores of SWS-NS did not show difference between patients who were indicated for disconnection surgery before 24 MO or later. The drug-free ratio after multilobar disconnection surgeries was 55.0%. One patient out of a total of nine (11.1%) in the multilobar group, who was treated with lesionectomy, achieved a seizure-free outcome.

Four patients had indications for vagus nerve stimulation (VNS). A patient who belonged to the bilateral group had VNS after callosotomy. A patient in the hemispheric group had VNS after HST. No effect on seizure severity or cognition was apparent in those patients. Two patients in the multilobar group had indications for VNS after treatment with AEDs. One patient had more than 50% seizure reduction, and the other did not show any effect.

We had no mortality during the perioperative period. A patient in the bilateral group died due to status epilepticus three years after partial callosotomy. We encountered asymptomatic hydrocephalus in 17.2% (5/29), symptomatic hydrocephalus in 6.9% (2/29), and one instance of oculomotor nerve palsy after the HST. One patient had acute encephalopathy one day after the PQD, and another patient was affected by herpes encephalitis six months after PQD in the multilobar group. No sudden unexpected death in epilepsy was recorded during the observation period in all patients including patients on medical treatment.

Comparison of post-therapeutic SWS-NSs among the bilateral with callosotomy, the hemispheric with HST, the multilobar with surgery, the multilobar with medical therapy, and the single groups is shown in Fig 4. We eliminated one patient in the bilateral group and four patients in the hemispheric group with medical treatment from this analysis. The SWS-NS of the bilateral group was worse than those of other groups with statistical significance, especially in seizure and cognitive function subcategories. The SWS-NS of the hemispheric group was also worse than those of other groups except for the bilateral group.

TABLE 2
SWS-EEG Score

Score	Bilateral	Hemispheric	Multilobar	Single
0	22.2%	3.2%	11.3%	30.0%
1	55.6%	87.1%	59.7%	60.0%
2	0%	6.5%	16.1%	10.0%
3	22.2%	3.2%	12.9%	0%

Frequent electroencephalographic pattern was focal asymmetry with slowing or loss of normal background activity regardless the groups.

Discussion

Cross-sectional study for severity assessment of seizures and EEG severity

The average ASO in our series was almost the same as that in the series reported by Kossoff et al.[10] An ASO assessment showed a significantly earlier seizure onset both in the bilateral and the hemispheric groups. The bilateral and the hemispheric groups also showed frequent seizures and a high incidence of status epilepticus and FBTCS (Fig 1). The multilobar groups presented a higher ratio of FIAS. FIAS is a specific seizure semiology in patients with SWS, as we have previously reported.[18,19] Repeated respiratory distress during FIAS may contribute to neurological deterioration. Seizure assessment revealed that a greater extent of LCM was associated with more severe and earlier-onset epilepsy, with frequent and severe seizures.

Our EEG evaluation revealed similar findings to those previously reported,[20,21] and no significant differences among the four groups were observed (Table 2). Kossoff et al. did not observe any clinical correlation between SWS-EEGS and SWS-NS.[13] EEG findings with background abnormalities such as low-voltage slow waves or attenuation of normal background rhythms in affected areas are considered characteristic of SWS. These abnormalities suggest a greater possibility of cortical damage under the LCM. Asymmetry detected by quantitative EEG analysis may be able to detect clinical severity in SWS.[21,22] Iimura et al. reported that electrocorticography using implanted subdural electrodes could reliably detect interictal epileptic and seizure discharges in infants whose scalp EEG did not exhibit spike or sharp waves.[18] Consequently, ordinary scalp EEG analysis has limitations for evaluating clinical severity.

The utility of EEG for early diagnosis and to establish severity is limited; therefore, imaging modalities, such as MRI, play a key role,

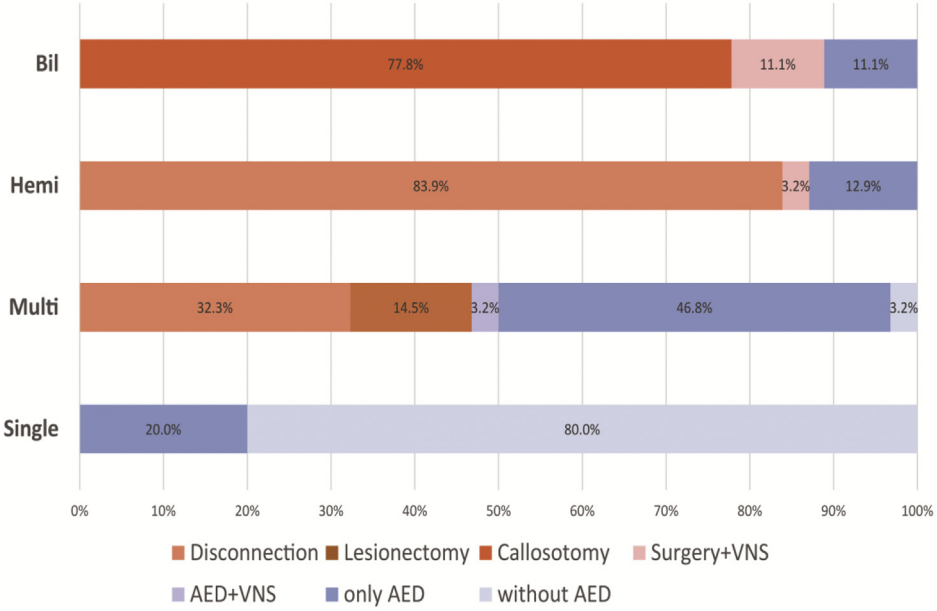

FIGURE 2. Choice of method according to our treatment protocol. Surgery was indicated in 88.9% and 87.1% of patients in the bilateral and hemispheric groups, respectively ($P = 0.04$ in the bilateral, $P < 0.001$ in the hemispheric group). Disconnection surgery was the most frequently indicated curative procedure. All patients in the Single group and 46.8% in the multilobar group did not meet current surgical indications and were treated using AEDs. AEDs could be stopped during follow-up in 3.2% of the multilobar and 80.0% in the Single groups.

with FLAIR-Gd images being the method of choice to visualize leptomeningeal disease[23] but have limitations for establishing SWS diagnosis in certain situations. Adams et al. reported that T1-weighted imaging with Gd and FLAIR-Gd may fail to detect leptomeningeal enhancement until as late as 24 months of age.[24] Transmedullary veins are dilated in brains affected by SWS, and SWI is effective at visualizing these dilated veins.[25] SWI also demonstrates microcalcification in brains with SWS.[26] Therefore, serial MRI studies are required even for patients without enhancement in infancy. Synthetic MRI is an alternative MRI method that can depict prematurely increased white matter myelination in patients with SWS.[27,28] The quantitative apparent diffusion coefficient map can predict a high risk of seizures in SWS.[29] These recent developments in MRI have improved the sensitivity of detecting SWS vascular abnormalities.[29-31] The use of these advanced techniques is recommended for the diagnosis of SWS to facilitate therapeutic management.

TABLE 3
Univariate and Multivariate Analyses Related to Surgical Requirement

	Univariate	Multivariate		
	P Value	*P* Value	Odds Ratio	95% CI
Sex	0.849			
FAS	1.000			
FIAS	0.429			
FBTCS	<0.001	0.347	0.583	0.189-1.794
Status epilepticus	<0.001	0.599	0.709	0.197-2.548
Age at seizure onset (≤6 months)	0.006	0.303	1.677	0.627-4.498
Seizure frequency (≥Monthly)	<0.001	0.014	4.082	1.325-12.458
Lesion distribution (≥3 lobes)	<0.001	0.350	1.724	0.550-5.397

Abbreviations:
FAS = Focal awareness seizure
FBTSC = Focal to bilateral tonic-clonic seizure
FIAS = Focal impaired awareness seizure
Having FBTCS or status epilepticus, age of seizure onset earlier than six months, more than a monthly seizure frequency, and more than three lobes affecting lesion were positive factors from univariate analysis. After logistic regression analysis, only frequent seizures remained a predictor to surgical indications.

Retrospective cohort study for therapeutic choice and its outcomes

Surgical indications in our cohort were based on seizure resistance to optimal AED treatment even after its prompt initiation, progressive atrophy of affected areas, and cognitive deterioration. As we proceeded with early surgical evaluation and management to improve cognitive outcomes in our cohort, interpretation of our data should be carefully considered compared with previous series.[3,11,12,32] Almost 80% of the patients in the bilateral and hemispheric groups met our criteria for surgical treatment. Half of the patients in the multilobar group were also surgically treated (Fig 2). The multivariate analysis results indicated that frequent seizures more than once a month were a sole predictor to the need of surgical requirement. This result came from patients with wider LCM who had frequent seizures (Fig 1), but half of the multilobar group did not have indications for surgery (Fig 2). As a whole, patients with widespread LCMs had greater likelihood of having epilepsy surgery indications after diagnosis. Kossoff et al. reported that more than 70% of patients demonstrated superior outcomes than a breakthrough seizure without surgery, even with clustering seizures before the age one year.[10] In our cohort, indications for surgery were present in 67 of the 112 patients (60.0%), resulting in 92 of 112 patients (82.1%) demonstrating superior outcomes than a breakthrough seizure, including 47 patients (65.2%) being seizure-free. Seizure control using our relatively aggressive therapeutic strategy provided superior outcomes compared with those of a more conservative protocol. HST yielded a high ratio of seizure-free patients (92.6%) in the hemispheric group. Kossoff et al. summarized the surgical outcomes and complications in 32 patients who underwent hemispherectomies,[32] reporting a seizure-free ratio of 81% and complication ratio of 47%. As their data included 16 anatomical hemispherectomies and two hemidecortications, the

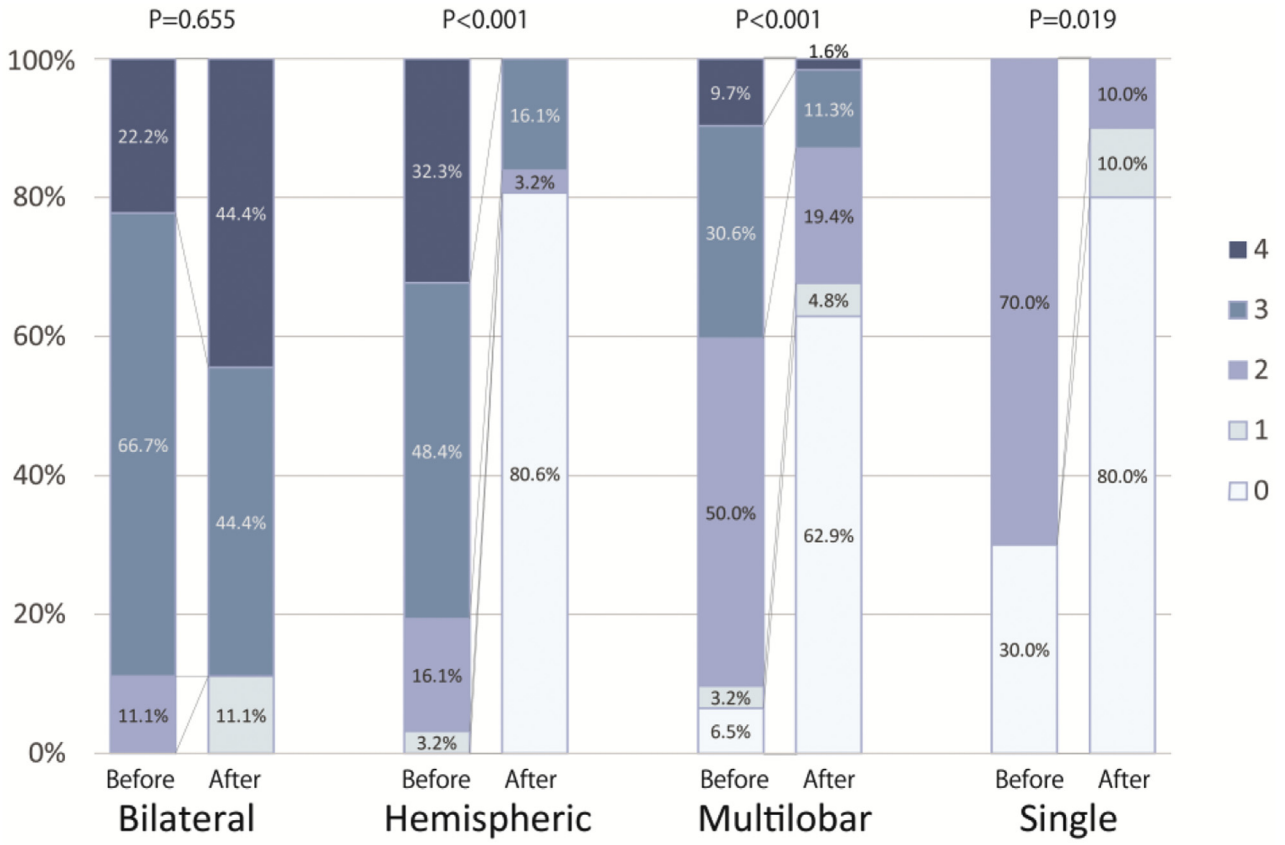

FIGURE 3. Changes in the seizure subscore of the SWS-NS before and after therapeutic intervention. Seizure subscores improved significantly in the hemispheric, multilobar, and single groups. The seizure-free ratios of the hemispheric, multilobar, and single groups were 80.6%, 62.9%, and 80.0%, respectively.

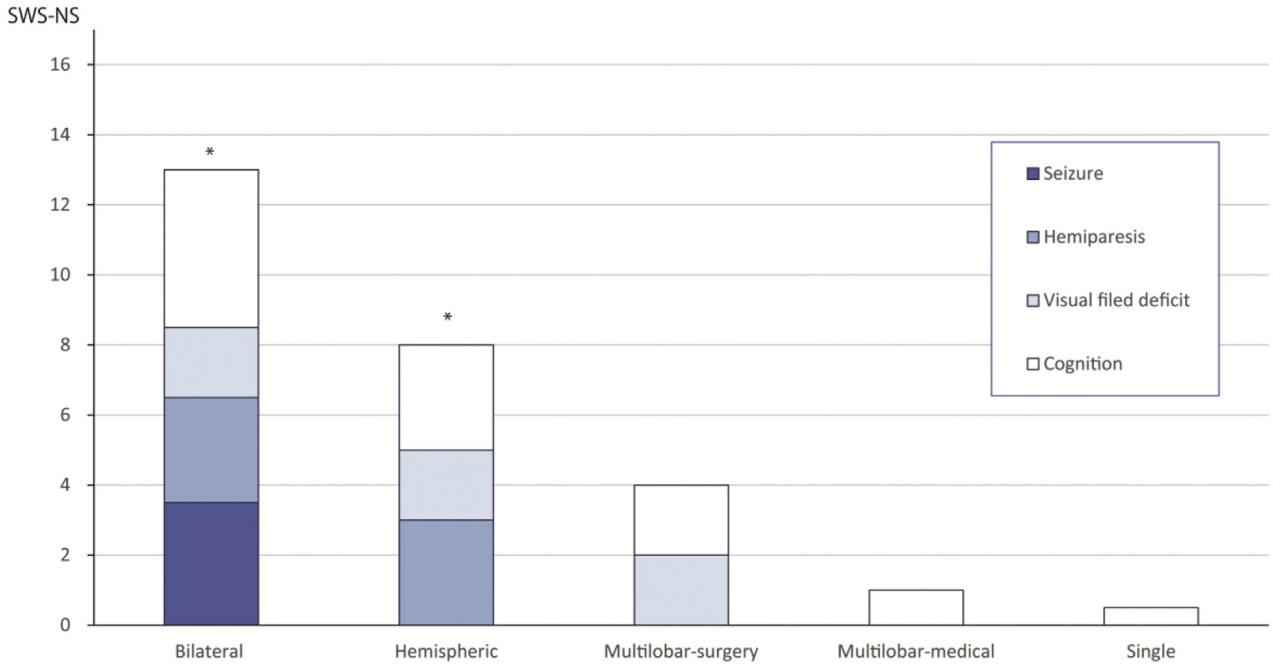

FIGURE 4. Difference of SWS-NS among the groups after treatment. SWS-NSs of the bilateral and hemispheric groups were worse than those of the Multilobar-surgery, the Multilobar-medical, and the Single groups (*$P < 0.001$). SWS-NS between the bilateral and hemispheric groups did not have statistically significant difference. Also, SWS-NSs among the multilobar-surgery, multilobar-medical, and single did not show differences.

complication ratio was higher than that of the currently applied functional hemispherectomy.[16] Disconnection surgery for the multilobar group was indicated in 32.3% of patients with a seizure-free ratio of 95.0% achieved following complete disconnection surgeries. We performed cortical resection in nine patients, and seizure-free outcomes resulted in only 11.1% of patients. Arzimanoglou et al. reported a seizure-free ratio of 53.8% after corticotomy,[33] which is discrepant with our data. Subcortical fiber disconnection may be mandatory to obtain seizure-free outcomes in patients with SWS. Early recognition of seizures and careful management are recommended.[34] Evaluation every six months in our cohort was adequate for optimal surgical timing. We did not find relationships between age at surgery and seizures or cognitive outcome. Delalande et al. reported 10 cases of SWS treated by the same HST procedure as ours[16]; Sugano et al. reported 10 cases of SWS treated by PQD.[17] Their age at surgery was two years and four months and resulted in 80% seizure-free outcome. There were no data for multilobar disconnection surgery in the anterior half of the hemisphere. Therefore, early surgery was not related to seizure outcome in both HTS and PQD for patients with SWS. Serial and meticulous follow-up is important in order to optimize the surgical timing.

Darcy et al. compared intellectual disability among two groups of children with SWS with or without seizures, children with epilepsy alone, and healthy controls. Intelligence in children with SWS with seizures was similar to that of children with epilepsy alone, whereas the intelligence of children with SWS without seizures was similar to that of healthy controls.[35] Bosnyak et al. reported that EEG abnormalities, young age at seizure onset, high seizure frequency, and frontal lobe involvement were predictors of a poorer intelligence quotient.[36] Luat et al. reported that early seizure onset before age one year, high seizure frequency, and long epilepsy duration were predictors of a decline in intelligence quotient.[37] These findings underscore the importance of seizure control at the earliest age possible to maintain cognition. Our data support previous reports that seizure control leads to improvement in cognitive function, especially for surgical cases in the hemispheric and multilobar groups. However, early surgery was not related to cognitive function in our survey. Previous studies have reported that normal mental function was present in only 8% of patients with bilateral involvement.[4] Callosotomy did not improve the seizure subscore in the bilateral group but prevented status epilepticus in 85.7%. Preventing status epilepticus presumably contributed to cognitive improvement in our series. However, patients in the bilateral group did not improve beyond the trainable level, and they required a degree of social support. Patients with widespread LCM are at risk of severe seizures and cognitive decline. Therefore, evaluating the need for surgical intervention at an early stage is necessary to improve cognitive outcomes.

Limitations

Our patients had severe epilepsy compared with those of the previously reported series because primary care physicians introduced their patients to our epilepsy center to be evaluated for possible surgery. Kavanaugh et al. also evaluated cognition using SWS-NS, but their result, especially cognitive function was less severe than in this series.[5] SWS-NS is fundamentally a scale to establish a patient's current status and is not used for serial follow-up or to evaluate therapeutic efficacy. Regarding the multilobar group, we had to analyze separately the anterior and posterior parts of Hemisphere group, but patients with posterior quadrant involvement were the predominant majority with SWS. We merged those two groups into Multilobar for the statistical analysis in this study. Surgical indications were the same throughout this study, but surgical procedures were selected depending on all current patient data at the time of surgery.

Conclusion

Our hypothesis that widespread LCM is associated with more severe seizures and cognitive deterioration was supported by the evaluation of seizures, cognition, and indications for surgery. Patients with wider LCM and frequent seizures (more than once a month despite aggressive medical management) should be considered for surgery. Regular clinical follow-up after initial diagnosis focusing on seizure severity and frequency, progressive cognitive decline, and cortical atrophy is recommended to ensure adequate timing of surgical treatment and to improve cognition.

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The authors have no conflict of interest to declare concerning the materials or methods used in this study or the findings specified in this paper.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pediatrneurol.2020.12.012.

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