Palliative hemispherotomy in children with bilateral seizure onset

Clinical article

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Object. Intractable epilepsy is a significant burden on families and on the cognitive development and quality of life (QOL) of patients. Periinsular hemispherotomy (PIH) for medically intractable epilepsy can benefit patients who qualify for this procedure. The ideal hemispherotomy candidate has ipsilateral ictal and interictal epileptiform activity, unilateral MR imaging abnormalities, contralateral hemiplegia, and a normal contralateral hemisphere. However, certain patients present with a mixed picture of bilateral electroencephalography (EEG) findings and severe intractable epilepsy, prompting consideration of a more aggressive treatment approach. This report introduces the possibility of surgery for patients who normally would not meet criteria for this treatment modality.

Methods. In this retrospective chart review, the authors report on 7 patients with bilateral seizure onset noted on routine or video-EEG monitoring. A QOL phone questionnaire, based on the Quality of Life in Childhood Epilepsy tool, was administered to a parent. The authors reviewed each patient’s chart for surgical complications, changes in examination, QOL, limited neuropsychological outcomes, and seizure outcomes. They also investigated each chart for MR imaging and EEG findings as well as the patient’s epilepsy clinic notes for seizure semiology and frequency.

Results. All patients enjoyed a decrease in seizure frequency and a subjective increase in QOL after PIH. Five patients (71%) achieved Engel Class I or II seizure control. The mean follow-up was 3.64 years (2–5.3 years). One patient is now off all antiseizure medication. No patient had a decrement in Full Scale IQ on postsurgical testing, and 2 (28.5%) of 7 individuals had increased adaptive and social functioning. Postsurgical examination changes included hemiplegia and homonymous hemianopia.

Conclusions. Hemispherotomy in patients with intractable epilepsy is generally reserved for individuals with unilateral epileptiform abnormalities or lesions on MR imaging. Seven patients in this study benefited from surgery despite bilateral seizure onset with improvement in seizure control and overall QOL. Thus, bilateral ictal onset does not necessarily preclude consideration for hemispherotomy in selected patients with severe medically refractory epilepsy.

Key Words • epilepsy • palliative hemispherotomy • surgery • electroencephalography • quality of life

Medically intractable epilepsy is a significant burden on families and patients independent of the etiology of the seizures, and QOL can be greatly improved with a reduction in seizure burden. Despite several newer antiseizure medications developed in the last 2 decades, seizures continue to be medically intractable in 20%–40% of cases. In these cases, surgery can be an important treatment option. Data suggest cognitive and developmental improvement after successful epilepsy surgery.

Ideal candidates for hemispherotomy have traditionally been individuals with unilateral hemispheric lesions and/or unilateral EEG abnormalities. There is an understandable reluctance to offer surgery to patients with bilateral seizure onset or bilateral MR imaging abnormalities. However, recent case series have documented...
patients in whom bilateral lesions were noted on MR imaging or bilateral interictal epileptiform abnormalities were noted on EEG; these patients realized an Engel Class I or II outcome after hemispherotomy. Exceptions to the prescription against the surgical treatment of patients with generalized EEG seizure onset have been identified in the common practice of callosotomy in individuals withatomic seizures as well as in a report of patients with generalized ictal onset who benefited from the resection of unilateral cortical dysplasias. Centers are even more reluctant to offer surgical options to patients with bilateral independent ictal onset. However, Boshuisen et al. described 2 of 4 patients with contralateral ictal EEG onset who became seizure free after hemispherotomy.

Because of the detrimental effects of intractable epilepsy on school work, family life, and the ability to enjoy one’s environment, the risks of surgery in some cases may be outweighed by the benefits, even in nonideal cases.

Quality of life measures have become increasingly important in studying the effects of interventions for epilepsy. The QOLCE tool has been validated as an accurate indicator of QOL in children with epilepsy.

We report the seizure control outcomes, neuropsychological assessments, and QOLCE scores in 7 patients severely affected with confirmed bilateral seizure onset who underwent palliative PIH between 2003 and 2008 at our institution.

Methods

Approval by the Washington University in St. Louis Human Research Protection Office was obtained prior to the initiation of this retrospective study. Patient families gave oral consent prior to participation.

Patient Characteristics

A complete history and neurological examination were obtained in all cases. The charts of patients who underwent hemispherotomy between January 2003 and January 2008 were retrospectively reviewed, including routine and video-EEG reports, neuropsychological assessments, and epilepsy clinic notes. The acquired descriptive data included age at seizure onset, number of antiseizure drugs tried prior to surgery, likely etiology of the epilepsy, frequency of seizures before and after surgery, and examination findings before and after surgery. Magnetic resonance images were acquired on a 1.5- or 3-T scanner prior to surgery in all cases.

All patients had undergone multiple routine and video-EEG studies, which were analyzed using a modified International 10-20 protocol. The presence of seizures with bilateral or generalized onset as well as the number of seizures arising from either hemisphere was noted. A seizure was described as having right, left, or bilateral onset. A seizure was placed into one of the unilateral categories if the primary electrodes involved in the seizure at onset were unilateral; this did not preclude more diffuse involvement later in the seizure. A seizure was described as bilateral if onset was definitively generalized, if symmetric changes were noted in both hemispheres (for example, bifrontally), or if onset was difficult to lateralize.

All EEG studies were read by board-certified pediatric neurologists with epilepsy and neurophysiology training and at least 5 years of experience in interpreting these studies in children.

Seizure semiology, the side and severity of concurrent hemiparesis, ictal EEG data, interictal EEG data, lateralization and severity of MR imaging abnormalities, and severity of seizures were evaluated by the comprehensive pediatric epilepsy center team at St. Louis Children’s Hospital and Washington University prior to surgery. A hemispherotomy, as opposed to focal resection or a staged corpus callosotomy followed by hemispherotomy, was chosen in all cases because of the severity of the lesions ipsilateral to surgery and the predominant electroencephalographic abnormalities noted during routine and video-EEG monitoring. Before surgery, we made all families aware of the possibility of continued seizure occurrence at presurgical frequencies as well as the potential for new neurological deficits.

Both pre- and postsurgical neuropsychological data were obtained when available from neuropsychology charts. Information was obtained about the performance of each patient on age-appropriate versions of the Wechsler Intelligence Scale for Children before and after surgery or, because of age and a lower level of functioning in many patients, on the Bayley Scales of Infant Development or the Mullen Scales of Early Learning. Information about adaptive functioning was available on a few of the patients and consisted of parent-reported scores on the Behavior Assessment System for Children, Second Edition.

Postsurgical records were reviewed for complications. Seizure frequency and pre- and postsurgical examinations were evaluated using clinic notes written by the patient’s epileptologist. Parents were also asked about seizure control as part of the phone questionnaire.

Surgical Technique

The surgical technique used in our group was a variation of the PIH technique based on the description by Shimizu and Maehara. The technique used at our institution was further described by Limbrick et al.

Quality of Life Instrument

Quality of life was evaluated using the cognitive subsection of the QOLCE, which is a nonnormalized parent-rating form. The cognition subscale score of the QOLCE correlates highly (> 0.643, p < 0.0001) with the total QOLCE score, and this subscale has been shown to be most closely related to parental reports of emotional, behavioral, and adaptive functioning. The subscale is made up of 23 questions that assess aspects of cognitive functioning from the parent’s perspective. Two additional questions were added to the phone questionnaire but were not scored as part of the cognition subscale. These questions were “Overall, how much better is your life (parents) after your child’s surgery,” and “Overall, how much better is your child’s life after surgery?” Five answers were possible ranging from “much better” to “much worse.” Current seizure frequency was also questioned at the same time.
Results

Patient Characteristics

We identified 7 patients with bilateral or bilateral independent ictal onset who underwent PIH. Patient age at the time of surgery ranged from 0.4 to 16.4 years (Table 1). Four patients (57%) were male. One patient (14.3%) underwent left-sided hemispherotomy. The mean follow-up was 3.64 years (2–5.3 years). Seizure etiology included trauma (both accidental and nonaccidental) in 3 patients (43%) and Sturge-Weber syndrome, a remote middle cerebral artery infarction, a cortical malformation, and hemimegalencephaly in 1 patient (14.3%) each. Patients had an average of 5.6 years (0.08–15.25) of seizures and had been on an average of 5.9 anticonvulsants (range 4–11 anticonvulsants) prior to surgery.

Seizure Types

Five patients (71.4%) had seizure semiologies that had some localizing features. Three patients (43%) had unilateral tonic, clonic, spasm-like, or tonic-clonic movements at some point in their predominant seizure semiology. Two (28.6%) had head and/or eye deviation at the onset of seizures. Two (28.6%) had generalized spasm-like movements. One patient (14.3%) had multiple seizure types including generalized tonic-clonic seizures, staring episodes, and drop attacks.

Presurgical EEG

Three patients had generalized or nonlocalizing electrographic correlates at the onset of all seizures. These changes included a generalized electrodecrement at seizure onset or diffuse sharp and slow wave discharges. In each case the predominant interictal abnormalities were on the side subjected to hemispherotomy. These abnormalities included both interictal discharges and focal slowing. Three (Cases 2, 4, and 7) of 7 patients had bilateral independent seizures captured on routine or video-EEG (Fig. 1). The most frequent lateralization of seizure onset in all 3 of these cases was on the side subjected to hemispherotomy.

Presurgical MR Imaging

The patient in Case 6 had significant bilateral abnormalities noted on MR imaging after suffering nonaccidental trauma as an infant (Fig. 2). The patient in Case 7, with Sturge-Weber syndrome, had involvement of both hemispheres on MR imaging with predominant involvement of the disconnected side (Fig. 3). All other patients had minimal radiological changes in the hemisphere contralateral to the side of PIH.

Decision Making

All of the aforementioned patient characteristics were taken into account before offering a surgical treatment option (Table 2), and in every case it was believed that the benefits of PIH outweighed the risks. The interdisciplinary comprehensive epilepsy management center at our institution believed that in many cases the side subjected to PIH was so damaged that surgical disconnection would lead to minimal further neurological deficits and that the benefit would be worthwhile.

Postoperative Complications

The patient with Sturge-Weber syndrome demonstrated a postoperative subdural hygroma and a poorly healing scalp incision, which was successfully shunted at the time of local wound revision.

Postoperative Seizure Outcome

Three patients (42.8%) have been seizure free since surgery (Table 3). Two patients have had more than 12 months of seizure freedom, and one of these patients has had only one seizure since surgery. One patient (Case 5) continues to have intractable epilepsy with 2–3 seizure clusters per week; this patient formerly had 40 seizures

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex, Age at Op</th>
<th>Yrs of Szs Before Op</th>
<th>No. of Antiseizure Meds Before Op</th>
<th>Diagnosis/Sz Etiology</th>
<th>Sz Type</th>
<th>No. of Szs Before Op (rt:lt:generalized or bilat)</th>
<th>Szs Ratio Before Op</th>
<th>Hemiplegia</th>
</tr>
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<tr>
<td>1</td>
<td>F, 5</td>
<td>4.6</td>
<td>6</td>
<td>cortical dysplasia</td>
<td>generalized flexor spasms</td>
<td>1/d</td>
<td>10:1:5</td>
<td>mild lt, upper &gt; lower</td>
</tr>
<tr>
<td>2</td>
<td>M, 16</td>
<td>3</td>
<td>6</td>
<td>trauma</td>
<td>lt extremity tonus w/ head &amp; eye deviation</td>
<td>1/wk–3/d</td>
<td>3:1:0</td>
<td>lt</td>
</tr>
<tr>
<td>3</td>
<td>M, 1.9</td>
<td>1.3</td>
<td>4</td>
<td>trauma</td>
<td>rt flexor spasms</td>
<td>5–30/d</td>
<td>0:0:5–30/day</td>
<td>dense rt</td>
</tr>
<tr>
<td>4</td>
<td>F, 5</td>
<td>4.8</td>
<td>5</td>
<td>MCA infarct after aneurysm rupture</td>
<td>lt-sided clonus w/ head &amp; eye deviation</td>
<td>1/wk</td>
<td>8:3:0</td>
<td>lt</td>
</tr>
<tr>
<td>5</td>
<td>M, 0.4</td>
<td>0.08</td>
<td>4</td>
<td>hemimegalencephaly</td>
<td>head drop w/ bilat arm extension</td>
<td>40/d</td>
<td>0:0:50/day</td>
<td>none</td>
</tr>
<tr>
<td>6</td>
<td>F, 10</td>
<td>9.3</td>
<td>11</td>
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<td>generalized tonic-clonic, drop attacks, staring</td>
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<td>lt</td>
</tr>
<tr>
<td>7</td>
<td>M, 16.4</td>
<td>15.25</td>
<td>5</td>
<td>Sturge-Weber syndrome</td>
<td>lt hemiclonic movements</td>
<td>1/d</td>
<td>3:1:0</td>
<td>lt</td>
</tr>
</tbody>
</table>

* MCA = middle cerebral artery; Meds = medications; Sz = seizure.
per day. One patient (Case 7) had an episode of prolonged status epilepticus 4 years after surgery; this was his only seizure event since surgery. The patient in Case 4 has been weaned from all antiseizure medications.

**Preoperative and Postoperative Examination**

Clinic notes from the patient’s board-certified epileptologist were the source of both the pre- and post-surgical examination findings. Before surgery, 6 of 7 patients had contralateral neurological deficits ranging from mildly decreased tone with decreased strength to dense hemiparesis. No patient lost the ability to ambulate after surgery, and the patient in Case 1 is now able to ambulate with support. The patients in Cases 5 and 6 were unable to ambulate prior to surgery, and the patient in Case 1 is now able to ambulate with support. All patients were noted to have a postsurgical homonymous hemianopia. Presurgical testing was difficult to perform in some patients because of their age or mental capacity. The patient in Case 3 had a homonymous hemianopia prior to surgery. After surgery, 1 patient (Case 1) acquired contralateral sensory neglect, and 1 patient (Case 2) acquired significant contralateral hypesthesia. The patient with Sturge-Weber syndrome, whose motor examination was normal prior to surgery, had a dense hemiparesis after surgery (Table 3). The patient with left hemispheric disconnection was nonverbal prior to surgery, and at the last follow-up at the age of 4 years, he was speaking in short phrases and indicating his wants but had significant language delay.
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Quality of Life Questionnaire

Postoperative QOL questionnaires were administered 2–5.5 years after surgery. The average score on the cognition subscale for the entire sample was 30.1 out of 100 (range 10.9–50). Because the cognition subscale may not be accurate in children under 6 years of age, the average score was calculated without 2 patients who were 5 and 3 years of age when the questionnaire was administered. With these patients removed from the analysis, the average score was 32.1 (SD 17.9). All of the parents’ responses to the final 2 questions indicated that the QOL of both their children and themselves was “much better” after surgery.

Postsurgical Neuropsychological Assessment

Three patients (Cases 1, 2, and 4) had full pre- and postsurgical neuropsychological testing. Full Scale IQs for these individuals were unchanged. Verbal IQ increased from 55 to 70 in 1 patient (Case 4). Two patients (Cases 2 and 4) had improvement in social and adaptive functioning. Both of these patients had 10-point increases in their adaptive social functioning after surgery. Both also had more than 10-point increases in their adaptive composite scores after surgery. The patient in Case 1 had no change in these scores after surgery. The lack of formal neuropsychological testing in most of the patients made further analysis impossible.

Discussion

Functional hemispherotomy is generally performed in hemiparetic patients with severe intractable epilepsy arising from one hemisphere and has been shown to be effective in this setting. Recently, data have suggested that patients can become seizure free despite bilateral epileptiform or MR imaging abnormalities identified prior to surgery.

In the present study, we describe 7 patients who underwent hemispherotomy for intractable epilepsy but had bilateral seizure onset confirmed on routine or video-

![Fig. 3](image)

Case 7. The patient in this case had Sturge-Weber syndrome with bilateral abnormalities. A: Gradient echo image demonstrating areas of frontal and occipital calcification (arrows). B: Axial FLAIR image showing abnormally prominent cortical vasculature (arrows). C: Post-Gd T1-weighted image showing abnormally prominent vasculature (arrows).

<table>
<thead>
<tr>
<th>MRI Abnormalities</th>
<th>Rationale for Hemispherotomy*</th>
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<tbody>
<tr>
<td><strong>Case No.</strong></td>
<td><strong>Ipsilat</strong></td>
</tr>
<tr>
<td>1</td>
<td>rt hemispheric polymicrogyria</td>
</tr>
<tr>
<td>2</td>
<td>rt hemispheric encephalomalacia w/ porencephaly</td>
</tr>
<tr>
<td>3</td>
<td>lt hemiatrophy</td>
</tr>
<tr>
<td>4</td>
<td>rt hemispheric atrophy &amp; encephalomalacia</td>
</tr>
<tr>
<td>5</td>
<td>rt hemimegalencephaly</td>
</tr>
<tr>
<td>6</td>
<td>diffuse rt cystic encephalomalacia</td>
</tr>
<tr>
<td>7</td>
<td>diffuse rt hemispheric leptomeningeal angioma</td>
</tr>
</tbody>
</table>

* 1, unilateral MRI abnormalities; 2, predominant MRI abnormalities ipsilateral to side of hemispherotomy; 3, predominant contralateral MRI subcortical abnormalities; 4, low likelihood of new neurological deficits; 5, predominant ictal EEG onset ipsilateral to side of hemispherotomy; 6, predominant interictal EEG abnormalities ipsilateral to side of the hemispherotomy; 7, history of status epilepticus; 8, excessive seizure burden.
Quality of life measures continue to be poor, with an average of 30.1 out of 100 in all patients and 32.1 in patients older than 6 years of age at the time of the questionnaire. These scores are lower than those described by Mikati et al.,22 who reported average QOLCE cognitive subscale scores of 81 ± 14 in a group of postsurgical epilepsy patients. In our cohort, IQs, when measured, were much lower (average 57), which may account for such a dramatic difference between our scores and those of Mikati et al. Despite these low QOL scores, however, all questioned caregivers reported that the lives of both their children and themselves were “much better” than prior to surgery.

A lack of adequate QOL data prior to surgery did not allow us to compare pre- and postsurgical QOL. It is distinctly possible that the subjective feeling of QOL improvement may simply be an outcome bias on the part of the patient’s parents, who in every case were responsible for the decision to proceed with surgery, although it is likely that the seizure freedom achieved in our cohort would improve QOL, as it has in previous studies.1,6,19,21,25 All of the patients in the present study also had a more than 50% decrease in seizure frequency, which is an outcome shown to be associated with a significant increase in QOL.24 Notably, previous research has demonstrated that impaired neuropsychological functioning before and after surgery, which was the case in all of our patients, is associated with lower QOL in and of itself.24

In the future, it will be important to monitor QOL measures in operative patients, and this has been instituted in all pre- and postsurgical neuropsychological assessments at our institution. No objective conclusions can be made in the present study due to a lack of presurgical QOL measures.

All but one patient had a prior abnormal neurological examination finding. No patient acquired unexpected deficits, and all patients now have hemianopia. No changes in ambulation occurred, although one patient who was nonambulatory prior to surgery is now ambulatory. Initial examination of the 5-month-old patient (Case 5) was normal, and at the most recent examination at 6 years of age, a moderate nonspastic hemiparesis was noted. The patient in Case 3, who had disconnection of the left hemisphere, had significant language delay postsurgically but is now able to verbally and nonverbally communicate his wants and desires. The acquired deficits, including homonymous hemianopia, and worsened or acquired hemiparesis are expected complications of this surgery and were discussed with the families before we performed this treatment option.

After careful consideration by a comprehensive epilepsy conference at an institution with significant surgical experience, it was decided that resection was the most likely treatment modality to achieve partial control of the patients’ seizures. In the patient in Case 7, with Sturge-Weber syndrome, some precedent for this surgical treatment has been presented in case reports of hemispherotomy leading to seizure freedom despite bilateral MR imaging abnormalities.1,10

Contralateral abnormalities, such as white matter calcification and atrophy, have been shown to be less likely
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to lead to postsurgical seizure continuation.11 Considering such reports, it was believed that the patients in Cases 7 and 2 would benefit from surgery despite bilateral MR imaging abnormalities, although the families were apprised of the possibility of future seizure recurrence.

In this paper, we presented a series of 7 patients with intractable epilepsy and bilateral seizure onset, including 3 children with bilateral independent seizure onset, identified by routine and/or video-EEG monitoring. All of these patients had a decrease in seizure frequency and a subjective increase in QOL after PIH, with most achieving Engel Class I or II seizure control. According to parental reports, the surgery made the parents’ lives “much better.” The patients had no decrement in Full Scale IQ on postsurgical testing, and some had increased adaptive and social functioning. Because of the small sample size and the retrospective nature of this study, it is necessary for additional patients with bilateral independent and bilateral seizure onset to be studied to identify ideal candidates for resection in these instances. It seems reasonable that, in patients presenting with severe intractable epilepsy, predominant seizure semiology, an MR image with a predominantly unilateral lesion, and/or EEG indicating seizures arising predominantly from the appropriate hemisphere, hemispherotomy can be beneficial as a palliative procedure even if bilateral seizure onset or contralateral seizures are present. This paper introduces the possibility that patients with medically intractable epilepsy who are carefully selected by an experienced pediatric epilepsy center and who do not meet conventional criteria for hemispherotomy could benefit from and should be presented with this treatment option, even those patients with bilateral independent seizure onset.

Conclusions

Hemispherotomy is typically recommended in patients with unilateral epileptiform abnormalities on EEG, seizures that arise from a single hemisphere, and unilateral MR imaging abnormalities that correspond to the side of seizure onset. However, we here describe patients who benefited in terms of both seizure frequency and subjective improvements in QOL from hemispherotomy despite seizures arising from the disconnected hemisphere and the contralateral hemisphere. Palliative hemispherotomy should be considered in patients with a significant seizure burden despite the presence of characteristics that would normally exclude these patients from surgical consideration.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Limbrick, Powers, Smyth. Acquisition of data: Ciliberto, Limbrick, Powers, Munro. Analysis and interpretation of data: Ciliberto, Titus, Smyth. Drafting the article: Ciliberto, Smyth. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ciliberto. Statistical analysis: Smyth. Study supervision: Smyth.

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