Seizure 22 (2013) 752–756

Contents lists available at SciVerse ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Hemispheric surgery for refractory epilepsy in children and adolescents: Outcome regarding seizures, motor skills and adaptive function

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ARTICLE INFO

Article history:
Received 11 February 2013
Received in revised form 31 May 2013
Accepted 3 June 2013

Keywords:
Epilepsy
Children
Hemispheric surgery
Motor function
Outcome
Follow-up
Impairment

ABSTRACT

Purpose: The aim of the study was to report the seizure outcome, motor skills and adaptive motor functions in a series of children and adolescents who underwent hemispheric surgery, analysing the risk-benefits of surgery.
Methods: The clinical course, seizure and motor function outcomes of 15 patients who underwent hemispheric surgery were reviewed.
Results: The mean age at surgery was 9.5, with 1–9 years follow-up. The underlying pathologies were Rasmussen encephalitis, vascular disorders, and hemimegalencephaly. All the patients presented with severe epilepsy and different degrees of hemiparesis, although motor functionality was preserved in 80% of the patients. At last follow-up, 67% were seizure free, and 20% rarely experienced seizures. Antiepileptic drugs were reduced in 60%, and complete withdrawal from such drugs was successful in 20% of the patients. The motor outcome following the surgery varied between the patients.

Despite the motor deficit after surgery, the post-operative motor function showed unchanged for gross motor function in most (60%), while 27% improved. Similar results were obtained for the ability to handle objects in daily life activities. Sixty percent of the children were capable of handling objects, with somewhat reduced coordination and/or motor speed.
Conclusion: Pre-surgical motor function continues to play a role in the pre-surgical evaluation process in order to provide a baseline for outcome. Hemispheric surgery, once regarded as a radical intervention and last treatment resource, may become routinely indicated for refractory hemispheric epilepsy in children and adolescents, with oftentime favourable motor outcomes.

1. Introduction

Hemispheric surgery (HS) is an established treatment for medically refractory epilepsy resulting from diffuse hemispheric disease, and it provides remarkable results in seizure outcome and quality of life.[1–3]

HS can be considered for patients with seizures arising from one hemisphere, with pre-existing structural and functional abnormalities; the other hemisphere is usually normal. This approach is particularly suitable for those with pre-existing hemiplegia and visual field deficit, in whom coexisting cognitive and behavioural impairments are common.[4] HS may be offered to patients without such disabilities, especially in circumstances in which intractable seizures are accompanied by the deterioration of motor and intellectual skills and in cases in which more conservative resections are unsuccessful.[4,5]

The decision making process and consideration of baseline motor function during the presurgical evaluation of patients considered for HS differs among epilepsy surgery centres. Certain centres are more conservative, limiting surgery to patients with preoperative hemiparesis.[2,6] On the other hand, surgery may be indicated in patients with or without minor motor deficits.[1,4,5,7,8]

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http://dx.doi.org/10.1016/j.seizure.2013.06.001

Despite good seizure outcome, the anticipated loss of motor function may prevent a decision to perform the surgery.[9]

The objective of this study is to report the seizure outcome, motor skills and adaptive motor functions in a series of children and adolescents who underwent HS at our centre, analysing the risks (residual motor deficit) and benefits (seizure reduction) of surgery.

2. Methods

We conducted a retrospective review of medical records in 15 children and adolescents (9 males) who underwent HS at Hospital São Paulo, Universidade Federal de São Paulo, between 2003 and 2011. The patients were assessed using a standard presurgical protocol, including clinical, neuroimaging and neurophysiological evaluations. Detailed clinical data were obtained from the patients and their families. All patients were examined by high-resolution magnetic resonance imaging and prolonged video-EEG recording. In the cases in which surgical treatment was indicated, the data were discussed during an interdisciplinary meeting. The records of the motor evaluation of muscle strength and motor function abilities, including the ability to sit, walk, and use both hands were reviewed, and these data were collected. The pre- and post-operative motor functions were assessed for presence and severity of hemiparesis. The muscle strength of the extremities was scored by manual muscle testing, with grades from 0 to 5. The functional level of each patient was evaluated through the Gross Motor Function Classification System (GMFCS) and the Manual Ability Classification System (MACS), which classify patients' movement and manual abilities, respectively. These scores were recorded in the charts or inferred by the available data.[10,11]

The GMFCS determines which of the five levels best corresponds to abilities and limitations in gross motor function, with particular emphasis on sitting (truncal control) and walking: level I denotes patients who walk without limitations, and level V indicates those with severe limitations of head and trunk control who require extensive assisted technology and physical assistance.[10]

The MACS scale is used to assess a patient for coordination in both hands working together; it is not an assessment of each hand taken separately. The five levels are based on a patient's self-initiated ability to handle objects and need for assistance or adaptation to perform manual activities in daily life. The patients classified at level I handle objects easily and successfully, whereas the patients classified at level V do not handle objects, have a severely limited ability to perform simple actions and require complete assistance.[11]

The Fisher exact test was used to compare the results of the pre- and post-operative GMFCS and MAC's scores, grouped according to motor adaptive functions (Group A: satisfactory scores – levels I, II or III; Group B: unsatisfactory scores – levels IV or V).

Seizure outcome was assessed using the Engel scale of seizure outcome after epilepsy surgery.[12]

During the postsurgical appointments, each parent was asked which grade of satisfaction he/she would attribute to the surgical intervention (from zero, minimum satisfaction, to 10, maximum satisfaction) regarding the seizure outcome and cognitive/motor functions in his or her child.

3. Results

3.1. Patients and pre-operative data

The age at seizure onset ranged from 18 days to 7 years (mean 3.1/median 3 years). The age at surgery varied between 1.3 and 16 years (mean 9.5/median 5.8), and the epilepsy duration was 0.2–14 years (mean 5.9/median 2). The post-operative follow-up period ranged from 1 to 9 years (mean 4/median 3) and the follow-up was longer than 2 years in two-thirds of the patients (Table 1).

The underlying pathology was Rasmussen encephalitis in nine patients (60%), vascular disorders in five patients (33%) and hemimegalencephaly in one patient (7%). The left hemisphere was involved in ten cases (67%) (Table 1).

Fifteen patients had daily seizures, and nine had *epilepsia partialis continua*. Fourteen patients were treated with antiepileptic drug (AED) polytherapy, and six had received previous immunomodulatory treatment.

All the patients presented with at least a mild level of hemiparesis, although it was not pronounced in one-half of the patients. Eight patients (53%) had a score of 3 or higher for muscle strength (Table 1). In six patients (40%), fine finger movements were preserved. The GMFCS and MACS scores are shown in Graphics 1 and 2.

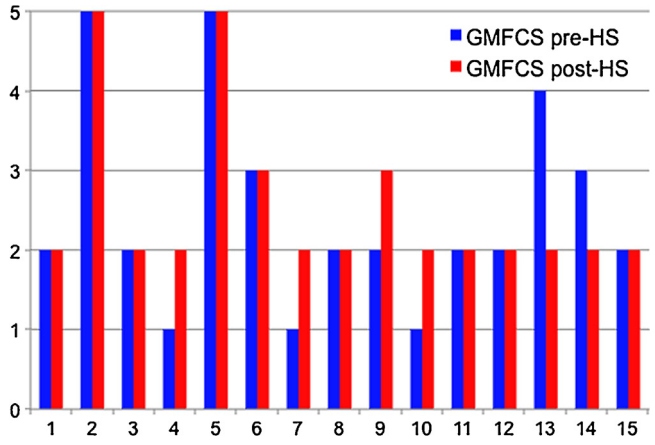
3.2. Operative and complications – potential risks

In 14 patients (93%), a hemispherotomy was performed. One patient had undergone a previous surgery, and hence hemispherectomy was indicated. Mild intra- and/or post-operative complications were reported in all the patients, including minor bleeding and fever. Moderate reversible complications were observed as follows: infections (3 patients), ipsilateral vascular ischaemia (1), diabetes insipidus (1), lung atelectasis (1), and trigeminal neuralgia (1).

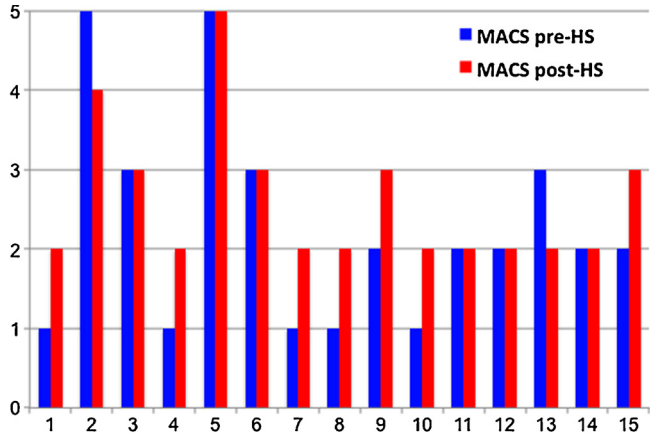
Table 1
Clinical data and pre- and post-operative muscle strength in upper and lower limbs.

	Age at surgery[a]	Pathology	Follow-up[a]	Engel Class	MS-UL Pre-HS	MS-UL Post-HS	MS-LL Pre-HS	MS-LL Post-HS
1	2.3	RE	9	I	4	5	3	4
2	1.3	Vascular	9	I	1	2	2	2
3	5.8	Vascular	9	II	3	4	3	4
4	10.8	RE	4.4	I	4	4	3	4
5	3.3	HME	1	II	2	2	2	3
6	13.6	Vascular	4	III	2	3	2	3
7	9.4	RE	3.6	I	4	4	3	4
8	4.9	RE	3.6	I	4	3	3	4
9	11.3	Vascular	3	III	3	4	3	3
10	6.3	Vascular	3	I	4	4	3	4
11	6.2	RE	2	I	2	3	3	4
12	5.6	RE	2	I	2	3	2	3
13	3.5	RE	2	II	2	2	3	3
14	3	RE	2	I	2	4	3	4
15	16	RE	1	I	4	3	2	4

[a] In years; MS-UL: muscle strength upper limb; MS-LL: muscle strength lower limb; HS: hemispheric surgery; RE: Rasmussen encephalitis; HME: hemimegalencephaly.



Graphic 1. Pre- and post-operative Gross Motor Function Classification System (GMFCS) scores. Level I: Walks without restrictions, limitations in more advanced gross motor skills. Level II: Walks without restrictions, limitations walking outdoors and in the community. Level III: Walks with assistive mobility devices, limitations walking outdoors and in community. Level IV: Self mobility with limitations, children are transported or use power mobility outdoors and in the community. Level V: Self mobility is severely limited, even with use of assistive technology.



Graphic 2. Pre- and post-operative Manual Ability Classification System (MACS) scores. Level I: Handles objects easily and successfully. Level II: Handles most objects but with somewhat reduced quality and/or speed of achievement. Level III: Handles objects with difficulty, needs help to prepare and/or modify activities. Level IV: Handles a limited selection of easily managed objects in adapted situations. Level V: Does not handle objects and has very limited ability to perform even simple actions.

3.3. Seizure outcome – potential benefits

At the last post-operative follow-up appointment (1–9 years of follow-up, mean 4 years), 67% of the patients were seizure free, and 87% were classified as Engel Class I or II. The worst outcome (Engel Class III) was observed in patients 6 (13.6 years at surgery) and 9 (11.3 years). Both of these patients had an underlying vascular lesion as, and their epilepsy duration was 9.6 and 11 years, respectively. Two patients were lost to follow-up. The other patients remained stable with regards to seizure outcome over time, with the exception of patient 3, who went from Engel Class I to II after two years of follow-up.

In the immediate post-operative period, all the patients continued taking the identical AED regimen used before surgery. The AEDs were gradually tapered with safety evaluations concerning seizure relapse. In nine patients, the level of AED therapy was reduced by one-half compared to the pre-operative levels. Complete withdrawal from AED therapy without seizure relapse was successful in three patients.

3.4. Motor function outcome – potential risks

The comparisons between the pre- and post-operative measurements of muscle strength in the upper and lower extremities are shown in Table 1. The scores reflected a post-surgical muscle strength worsening in 40% and improvement in 27% of the patients in the upper extremities. With respect to the lower limbs, in 13% of the patients, the muscle strength decreased; in 33%, it improved; and in 53% it remained unchanged.

Comparisons for the GMFCS and MACS scores are depicted in Graphics 1 and 2. The post-operative motor functional levels decreased in 27% of the patients for gross motor function. Only 27% of the patients had GMFCS scores higher than level III, indicating self-mobility with limitations ($p = 0.029$). Similar findings were seen regarding the ability to handle objects in daily life activities. The two patients who presented post-operative poor scores for the MACS (levels IV or V – ability to handle a limited selection of easily managed objects in adapted situations) had poor pre-surgical MACS scores before the HS ($p = 0.01$).

3.5. Parents' satisfaction with surgery – risks and benefits

All parents reported high levels of satisfaction with the surgical treatment (grades 8–10, mean 9.7)a and 80% attributed grade 10 to the procedure.

4. Discussion

4.1. Seizure outcome – potential benefits

The results show good seizure outcome in our series, with 67% of the patients reaching Engel Class I. This finding is consistent with other series, in which 52–86% of patients became seizure-free after short and long-term follow-up.[1,2,4–8,13–18] Considering that these patients presented with daily seizures or *epilepsia partialis continua* before surgery, Engel Class II, which corresponds to rare disabling seizures,[12] may be considered good seizure outcome. This outcome includes 87% of our series, corresponding to outcomes in the literature with reports of reduction in seizure frequency varying from 58 to 91%.[1,2,4–8,13–18] In this series, the stability of good seizure outcome during the long-term follow-up should be emphasised. The limited number of patients precluded any analysis of the prognostic factors. The worst seizure results were found in two of the three children who were older than 10 at the time of surgery and who had long-term epilepsy. In the majority of the paediatric studies, age at surgery is not considered to be a predictor of seizure outcome.[4,7,16] Kossoff et al. (2003) found that the duration of epilepsy before surgery was shorter in the patients who became seizure free, although this finding did not reach statistical significance. These authors suggest the possibility that delays should be avoided in patients with intractable hemispheric seizures.[8]

In addition to the good seizure outcome, we were able to withdraw or reduce medications in the majority of our patients. Considering that children with epilepsy, especially those with refractory seizures, are at increased risk for cognitive impairment, at least in part due to long-term AED therapy,[19] the possibility of reducing medications can be considered to be a good result. Other authors have previously reported this benefit from HS, with no seizure relapse.[7,8,13,16,20]

4.2. Motor function outcome – potential risks

Regardless of the favourable seizure outcome after HS and considering both the severity of the epilepsies in these patients and the well-known and potentially reversible surgical complications,

the exacerbation or initiation of motor deficits might represent a strong reason to postpone surgery, especially in children without such motor deficits.

4.2.1. Muscle strength

With respect to motor function, at pre-surgical baseline, all of our patients presented with a degree of hemiparesis, which was mild or moderate in half of them. In nine patients (60%), the hemiparesis was disproportionate, more prominent in the upper limbs, and more severe distally, with impairment of fine finger movement. Other authors have observed this disproportionality among the upper and lower limbs in patients evaluated for HS and have noted the difference between proximal and distal impairment, which is more severe in the hands.[8,9,21–23]

The motor function outcome after HS varied between patients and among the upper and lower limbs. The results were worse in the measurements of upper extremity muscle strength, in which the scores reflected a further post-surgical loss of power in 40% of the patients. The scores for the lower limbs remained unchanged in 53% and worsened in 13% of the patients. A degree of muscle strength improvement was observed in 27% (upper limbs) to 33% (lower limbs) of the children. These findings are in accordance with the literature: post-HS motor strength can improve, remain unchanged or worsen, and worsening is observed more frequently in the upper limbs.[2,4–9,14,15,17,21–23] Several features are identified as predictors for improvement or deterioration in motor functioning, including the age at surgery,[16,22] postsurgical seizure remission,[4,7,8] the level of pre-operative cognitive development,[4,16] or previous paresis and/or aetiology.[8,9,22,23] Our sample was too small for statistical analysis aimed at identification of prognostic factors.

4.2.2. Adaptive motor functions

Impairment is defined as a problem in structure leading to significant deviation or loss,[24] reflecting the consequences of a disease at the organ level.[9] Limitations in activities reflect dysfunction in performance and motor activity, and restrictions refer to difficulties encountered in social participation.[9,24]

Hemispheric epilepsy in children represent a functional and/or structural impairment, and seizures can potentially lead to limitations and restrictions. Despite the motor injury that is a consequence of HS, the post-operative motor functional levels showed that the majority of our patients (60%) were unchanged with respect to gross motor function, while 27% improved. The two patients who worsened in post-HS GMFCS had Rasmussen encephalitis. They presented with relatively preserved pre-operative motor strength (level 4), but a higher potential for deterioration caused by the progressive evolution of the disease without surgical treatment.

Equivalent results were obtained for the ability to handle objects in daily life activities. Although more patients showed a decrease in this evaluation, which was expected as a consequence of the HS, 60% of the children were at level II according to the MACS, indicating that they were capable of handling most objects, with somewhat reduced quality and/or speed of achievement.[11] The two children who did not reach satisfactory scores in the MACS did not reach them in the GMFCS either because of severe deficits before surgery.

Our data confirms and expands previous studies. Qualitative functional analysis[2,8,15,17] or the use of international functional motor scales, including the GMFCS[9,16] and the 74 Fugl-Meyer Assessment of Motor Recovery scale,[23] showed similar data. Kossoff et al. (2003) observed that, except for those with major perioperative complications, all the patients (93/105) were walking independently without the use of assist devices, and the majority of these patients had learned to use one hand as a helper. Several have adapted to their disability condition so well that they were able to play the piano, golf, and ping-pong, and were able to dance.[8] The motor impairments, limitations in motor activities and aspects of social participation exist before HS and remain unchanged in the majority of cases, with the pre-operative functionality maintained or improved. These results, including seizure control in particular, indicate overall improvement in epilepsy management.

In the past, the effectiveness of epilepsy surgery was measured predominantly in terms of seizure reduction. In addition to seizure reduction, developmental and cognitive function,[16,20] including motor abilities[8,9,16,23] and language function[20,25] tend to be evaluated with increasing frequency as additional outcome measures, in particular due to their influence on the quality of life. The level of satisfaction of the parents with the surgical procedure supports this hypothesis in our series.

Our data follow the tendency of paediatric epilepsy treatment in general, in which an assessment of daily activities and participation in social life is more comprehensive and more reflective of a patient's needs than an assessment of the impairments themselves.[9,24] According to this concept, the target of HS is an overall good outcome, including seizure frequency, developmental measures and quality of life.

5. Conclusion

The favourable motor functional outcome is relevant because the assessment of pre-surgical motor function continues to play a role in the surgical decision making process. Considering that the seizure outcome is good and that complications are manageable, HS, which was once regarded as a radical intervention and the last treatment resource, may become routinely indicated for refractory lesional hemispheric epilepsy in children and adolescents.

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