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Hemispheric surgery for severe epilepsy in early childhood: a case series

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ABSTRACT

Objective. Hemispheric surgery is an effective and cost-effective option for hemispheric epilepsy. Data specifically focusing on very early infancy are scant. In our study, we report the results of hemispheric surgery in children under three years of age, along with clinical, neuroradiological and EEG features, from two Italian epilepsy surgery centres.

Methods. After reviewing our epilepsy surgery databases (2008-2018), we identified 14 patients (seven males) submitted to hemispheric surgery, under three years (range: 2-29 months), with a follow-up of at least 12 months.

Results. No deaths occurred, and surgical complications were observed in 3/17 procedures. At final follow-up visit (mean: 30.8 months; range: 12-90), 10/14 patients (71.4%) achieved Engel Class I (eight Class 1A, one Class 1B, and one Class 1C). Antiepileptic drugs were completely discontinued in three and reduced in eight, thus a significant decrease in drug regimen after surgery was achieved in 11/14 patients (78.6%). Before surgery, severe developmental delay was present in 10 patients, moderate in two and mild in two. At the last follow-up visit, the degree of developmental delay changed from severe to moderate in five patients, remained unchanged in six cases (four severe and two moderate), and changed from mild to moderate in two following surgery.

Significance. In many cases, hemispheric surgery in children under three years is effective in achieving seizure freedom or reducing seizure frequency, with the possibility of simplifying complex drug regimens. Moreover, it appears to be a safe and well tolerated procedure, leading to improvement in cognition and posture.

Key words: diffuse hemispheric epilepsy; hemispherotomy; hemispherectomy; early childhood; seizure outcome

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Catastrophic, diffuse hemispheric epilepsy (DHE) may occur in infancy and early childhood as a consequence of different congenital (hemispheric cortical dysplasia, hemimegalencephaly, polymicrogyria), acquired (encephalomalacia from remote aetiologies) and progressive (Rasmussen encephalitis, Sturge-Weber syndrome) pathologies. Typically, affected children develop drug-resistant seizures and an epileptic encephalopathy with progressive developmental delay (DD). In these cases, hemispheric surgery (either resective or disconnective) has proved effective in both controlling seizures and improving the patients' cognitive development [1-4]. Indeed, recent series of

hemispheric surgery in children with DHE showed that seizure freedom may be achieved in a high proportion of cases, including those operated on in early infancy [3, 5-8]. In addition, patients who underwent surgery at younger ages showed larger increases in developmental quotient (DQ) after surgery [3, 8-14]. Thus, early surgery has been recommended to prevent the negative effects of high-frequency intractable seizures on the developing brain [15].

Nevertheless, in the past, hemispheric resections (or "anatomic hemispherectomy") were offered with reluctance to very young children, owing to the high rate of intraoperative complications and mortality, as a consequence of the large volume of brain tissue that has to be removed and massive intraoperative blood losses in patients with a low body weight [16, 17]. Moreover, anatomical hemispherectomy is burdened by a significant rate of postoperative complications, including superficial hemosiderosis and hydrocephalus [18-20].

In order to significantly reduce the number of complications associated with hemispheric surgery, there has been a progressive shift from anatomical hemispherectomy to disconnective surgical procedures, which have provided functional results comparable to those of anatomical hemispherectomy with a lower complication burden [18, 21]. The aim of these techniques is to remove small amounts of tissue while disconnecting the residual hemisphere. In 1983, Rasmussen described a disconnective technique, which was named "functional hemispherectomy" [22]. This consisted of removal of the temporal lobe and of a considerable amount of the suprasylvian region, with disconnection of the frontal and parieto-occipital remainders of the hemisphere through an intraventricular commissurotomy. In subsequent years, different procedures of hemispheric deafferentation ("hemispherotomy") were introduced, in which resection was limited and more brain was disconnected [23-27]. These techniques, with slight or major modifications, are currently the procedures of choice in most epilepsy surgery centres, with excellent surgical, epileptological and functional results. Furthermore, they have significantly decreased the risks and complications associated with hemispheric surgery, and are therefore recognized as the most appropriate strategy in very young children [28].

Nowadays, there is a considerable body of evidence on the outcome of hemispheric surgery in children. However, although some surgical series of children under three years of age have been reported, recent data specifically on hemispheric surgery in this specific age group are scant [3, 16, 29-33].

In our study, we report the results of hemispheric surgical procedures in children under three years of age, along with their clinical features, from two Italian epilepsy surgery centres.

Materials and methods

By retrospectively reviewing the clinical records and the prospectively maintained databases of patients who received surgery for refractory epilepsy during the period 2008-2018 at two epilepsy surgery centres in Italy (IRCCS Istituto Giannina Gaslini, Genoa, Italy and Niguarda Hospital, Milan, Italy), we selected patients meeting the following criteria: hemispheric surgery (either resective or disconnective) for DHE, under three years of age at the time of surgery, and postoperative follow-up of at least 12 months.

Presurgical evaluation

Collected data included complete personal and medical history, family history of epilepsy, age at seizure onset, type of seizures, epilepsy duration, comorbidities, estimated seizure frequency, and evaluation of psychomotor development considering physiological milestones and neurological examination [34]. Given the retrospective nature of the study and the non-homogeneous developmental tests performed before surgery, we considered DD as a delay in two or more developmental areas, identified based on clinical and neurological evaluation (gross motor, fine motor, cognition, speech/language, personal/social, or activities of daily living). Mild DD was defined as a functional age of 66% of chronological age, moderate DD as a functional age of 34% to 66% of chronological age, and severe DD as a functional age below 33% of chronological age [35, 36].

Current and previously administered antiepileptic drugs were noted. Routine interictal electroencephalogram (EEG) and ictal video-EEG recording were acquired. In all patients, brain magnetic resonance imaging (MRI) was performed under deep sedation using an Achieva 1,5T or 3T magnet (Philips Healthcare; Best, The Netherlands). MRI phase-contrast angiographic sequences, as well as X-ray digital subtractive angiography, were also acquired to image vascular brain anatomy.

The indication for surgery was discussed in a multidisciplinary consensus conference and based on the presence of unilateral brain abnormalities as visualized on MRI and lateralization of interictal and ictal EEG abnormalities to one affected hemisphere, consistent with clinical semiology and MRI findings. Nevertheless, the propagation of interictal and/or ictal EEG abnormalities to the contralateral hemisphere was not a reason to exclude surgery [37].

Surgery

Selection of the appropriate surgical technique was made according to aetiology and on the basis of anatomical, EEG and clinical findings. Anatomical hemispherectomy (removal of the entire affected hemisphere) [38] and functional hemispherectomy (temporal lobectomy, resection of the rolandic-perirolandic region, disconnection of the residual frontal and posterior residual tissue, according to Rasmussen [22]) were mainly reserved for cases with hemimegalencephaly and hemispheric cortical dysplasia, while we opted for a lateral (or peri-insular) hemispherotomy (hemispheric disconnection through a peri-insular approach, following resection of infra- and supra-sylvian opercula, as described by Villemure and Mascott [23]) in cases with an atrophic hemisphere. Microsurgical procedures were performed using neuronavigation (StealthStation® S7® System, Medtronic, Minneapolis, Minnesota, USA).
Intraoperative blood loss was calculated using Moore's formula for estimating total blood volume and Gross' method for estimating blood loss [39].
All patients underwent brain computerized tomography immediately after surgery to rule out perioperative complications, and were monitored for 12 to 24 hours in the intensive care unit, until extubation and recovery of normal hemodynamic parameters.
Histopathological analysis of surgical specimens was performed for all patients, according to previously released recommendations [40].
The study was approved by the local ethical committees, and patients' parents or tutors gave their informed consent for the diagnostic and therapeutic procedures.

Postoperative evaluation

In the case of more than one surgery, we considered the last surgery as the index procedure, but the first surgical approach was reported as well. Both surgical complications and the occurrence of acute post-operative seizures were recorded. Seizure outcomes were classified according to Engel's outcome classification at the last available follow-up visit [41]. Patients were re-evaluated by routine EEG, brain MRI and neurological examination six months after surgery and then yearly with clinical examination and routine EEG. Data on evaluation of psychomotor development, considering physiological milestones and neurological examination, were collected at the last available follow-up visit. In families who accepted to complete a developmental questionnaire, the Vineland Adaptive Behaviour Scales were administered.

Results

Fourteen patients (seven males and seven females) who met the inclusion criteria were identified, representing 1.1% (14/1240) and 29.8% (14/47) of all patients and patients under three years of age, respectively, who received resective epilepsy surgery during the study period (2008-2018) at the two participating institutions.

Presurgical evaluation

Clinical, EEG and neuroradiological findings are summarized in *table 1*. Mean age at seizure onset was 1.3 months (range: 0-7 months). Ten patients had seizures within three days after birth. Mean age at surgery was 14.5 months (range: 2-29); 12 patients underwent surgery ≤18 months and five before 12 months. Mean time from epilepsy onset to surgery was 13.2 months (range: 2-29). At the time of surgery, seizures occurred daily in 11 cases, weekly in two and monthly in one. Six patients experienced status epilepticus before surgery (three of them underwent surgery during the status; Patients 3, 6 and 7).
The preoperative neurological evaluation revealed contralateral hemiparesis in 11 cases, asymmetric quadriparesis in one (Patient 7) and hypotonia in eight. Severe DD was present in 10 patients, moderate in two cases and mild in two (*table 1*). None of the patients could walk autonomously or with help and only four could sit autonomously.
MRI findings were suggestive of large unilateral hemispheric malformations of cortical development in nine cases (hemimegaloencephaly in six cases), post-haemorrhagic poroencephalic cysts in two, perinatal ischemic lesions in two and hemispheric atrophy in one. Seven patients showed atrophy of the cerebral peduncle ipsilateral to the affected hemisphere (including all those with perinatal damage or hemispheric atrophy). Interictal EEG abnormalities were confined to the affected hemisphere in 11 cases, while involvement of the contralateral hemisphere was shown in three cases. The ictal video-EEG showed a discharge originating on the affected hemisphere in all cases, with contralateral diffusion recorded in seven subjects.

Surgery and postoperative course

Details on surgical procedures and postoperative findings are reported in *table 2*. We performed nine lateral peri-insular hemispherotomies, three functional hemispherectomies and two anatomical hemispherectomies.

▼ **Table 1.** Preoperative clinical, EEG and MRI findings.

Pt	Sex/age at seizure onset/age at surgery* (months)	Type of seizures	Seizure frequency	Neurological examination	Developmental delay	Status epilepticus	Number of AEDs pre-surgery	Interictal EEG	Ictal video-EEG	MRI findings	Unilateral atrophy of cerebral pedicle
1	M/0/14	Lt tonic-clonic and secondary generalized	Daily	Lt hemiparesis	Severe	No	7	Rt subcontinuous epileptic discharges with BS, rare contralateral diffusion	Rt discharges with contralateral diffusion	Rt hemispheric FCD	No
2	F/0/16	Rt myoclonic and clonic, rare secondary generalized	Daily	Global hypotonia, Rt hemiparesis	Severe	Yes	2	Lt subcontinuous epileptic discharges	Lt subcontinuous epileptic discharges	Lt HME	No
3	F/0/2	Lt tonic-clonic and secondary generalized	Daily	Global hypotonia	Severe	Yes (surgery during SE)	2	Rt subcontinuous, multifocal epileptic discharges with BS	Rt discharges with contralateral diffusion	Rt HME	No
4	M/2/26	Lt tonic, spasms	Monthly	Lt hemiparesis, global hypotonia	Severe	No	6	Rt central and posterior epileptiform abnormalities with diffusion to vertex	Asymmetric spasms, right focal discharges	Polylobar Rt HME	No
5	F/0/17	Rt tonic-clonic, blinking, horizontal nystagmus	Daily	Rt hemiparesis	Severe	Yes	6 + steroids	Lt subcontinuous, pseudoperiodic epileptic discharges with contralateral diffusion	Lt discharges with contralateral diffusion	Lt hemispheric FCD	No

▼ **Table 1.** Preoperative clinical, EEG and MRI findings (*continued*).

Pt	Sex/age at seizure onset/age at surgery* (months)	Type of seizures	Seizure frequency	Neurological examination	Developmental delay	Status epilepticus	Number of AEDs pre-surgery	Interictal EEG	Ictal video-EEG	MRI findings	Unilateral atrophy of cerebral pedicle
6	M/0/14	Rt clonic and tonic	Daily	Global hypotonia, Rt hemiparesis	Severe	Yes (surgery during SE)	4	Lt, subcontinuous epileptic discharges	Lt discharges with contralateral diffusion	Lt HME	No
7	M/3/16	Ocular version with nystagmus	Daily	Global hypotonia, asymmetric quadriparesis with Rt predominance	Severe	Yes (surgery during SE)	2	Lt posterior subcontinuous epileptiform discharges with BS	Posterior left discharges	Lt post-haemorrhagic poroencephalic cyst in GM/IVH	Yes
8	M/0/29	Lt focal motor with automatism and secondary generalization	Daily	Lt hemiparesis	Severe	No	11 + steroids	Rt fronto-central epileptic discharges	Rt discharge with contralateral diffusion	Rt diffuse FCD	Yes
9	M/0/10	Rt focal clonic	Daily	Global hypotonia, Rt hemiparesis	Severe	Yes	6	Lt continuous epileptic discharges	Lt discharge	Lt HME with prosencephaly	Yes
10	M/5/15	Lt focal motor	Daily	Lt hemiparesis	Moderate	No	Steroids	Rt hypsarrhythmia	Rt discharges with contralateral diffusion	Rt perinatal ischemic lesions	Yes
11	F/1/6	Ocular deviation followed by generalized tonic-clonic events and spasms	Weekly	Global hypotonia	Mild	No	3	Lt epileptiform abnormalities	Lt discharge	Lt HME	No

▼ **Table 1.** Preoperative clinical, EEG and MRI findings (*continued*).

Pt	Sex/age at seizure onset/age at surgery* (months)	Type of seizures	Seizure frequency	Neurological examination	Developmental delay	Status epilepticus	Number of AEDs pre-surgery	Interictal EEG	Ictal video-EEG	MRI findings	Unilateral atrophy of cerebral pedicle
12	F/7/11	Rt focal tonic with secondary generalization; nystagmus	Weekly	Rt hemiparesis	Mild	No	1	Lt continuous spike-waves with contralateral diffusion	Lt discharge	Lt post-haemorrhagic poroencephalic cyst	Yes
13	F/0/9	Focal with motor automatisms	Daily	Hypotonia, Lt hemiparesis	Severe	No	5 + steroids	Rt slow and epileptiform abnormalities	Rt discharges with contralateral diffusion	Rt hemispheric atrophy	Yes
14	F/0/18	Focal with motor automatisms	Daily	Lt hemiparesis	Moderate	No	4	Rt temporo-occipital epileptic discharges	Rt discharge	Rt perinatal ischemic lesions	Yes

*Age at last surgery for patients who received more than one surgery.
Pt: patient; AEDs: anti-epileptic drugs; Lt: left; Rt: right; DD: developmental delay; SE: status epilepticus; BS: burst suppression; FCD: focal cortical dysplasia; HME: hemimegalencephaly; GM/IVH: germinal matrix/intraventricular haemorrhage; NA: not acquired.

▼ **Table 2.** Surgical and postoperative data.

Pt	Sex/age at seizure onset/ age at surgery * (months)	Type of surgery	Surgical complications	APOS	Histology	Engel scale	AEDs changes after surgery	Neurological examination	Developmental delay VABS	Follow-up (months)
1	M/0/14	Rt LH	Yes, hydrocephalus (external CSF shunt)	No	FCD IIa	IA	Withdrawal of AEDs	Autonomous gait with Lt hemiparesis	Moderate; C:71,DL:73, S:72, MS:64, Total score 67	34
2	F/0/16	Lt FH	No	No	HME	III	Reduction of number of AEDs (currently on monotherapy)	Rt hemiparesis, gait with support	Severe; C:59, DL:54, S: 59, MS:49, Total Score 58	54
3	F/0/2	Rt LH	No	No	HME	IB	Reduction of number of AEDs (currently on monotherapy)	Lt hemiparesis, gait with support	Moderate; C:69, DL:59, S:64, MS:49, Total Score 64	90
4	M/2/26	Rt FH (after previous TPO disconnection)	No	No	FCD Ia	IA	Reduction of dosages of AEDs (currently on 3 AEDs)	Lt hemiparesis, autonomous gait	Moderate NA	14
5	F/0/17	Lt LH (after previous TPO disconnection)	No	No	FCD IIb	IA	Withdrawal of AEDs	Rt hemiparesis, autonomous gait	Moderate; C:100, DL:93, S:92, MS:70; Total Score: 86	13
6	M/0/14	Lt AH (after previous left LH)	No (IDC and infection after first surgery with VPS)	No	HME	IA	Reduction of number and dosage of AEDs (currently on 2 AEDs)	Rt hemiparesis, autonomous sitting	Severe; C:66, DL:69, S:56, MS:62; Total Score: 61	12
7	M/3/16	Lt LH	Yes, hydrocephalus with VPS	Yes	Gliosis	III	Increase in dosage and number of AEDs	Symmetric quadriparesis, no posture acquired	Severe; C:42, DL:46, S:55, MS:37, Total Score: 43	48
8	M/0/29	Rt FH	No	No	FCD IIb	IV	Unchanged	NA	NA/NA	24
9	M/0/10	Lt AH	Yes, DI, transient SE	Yes	FCD IIb	IID	Reduction in number and dosage of AEDs	Severe DD, Rt hemiparesis, no posture acquired	Severe NA	24
10	M/5/15	Rt LH	No	No	FCD IIId	IA	Withdrawal	Moderate DD, Rt hemiparesis, autonomous sitting	Moderate NA	12

▼ **Table 2.** Surgical and postoperative data (*continued*).

Pt	Sex/age at seizure onset/ age at surgery * (months)	Type of surgery	Surgical complications	APOS	Histology	Engel scale	AEDs changes after surgery	Neurological examination	Developmental delay VABS	Follow-up (months)
11	F/1/6	Lt LH	No	No	HME	IA	Reduction in number of AEDs (currently on monotherapy)	Moderate DD, Rt hemiparesis, autonomous gait	Moderate; C:91, DL:89, S:84, MS:82, Total Score 84	33
12	F/7/11	Lt LH	No	No	FCD IIId	IA	Unchanged	Moderate DD, Rt hemiparesis, gait with support	Moderate; C:91, DL:83, S:95, MS:57, Total Score 78	28
13	F/0/9	Rt LH	No	No	FCD IIa	IC	Reduction in number of AEDs	Moderate DD, Lt hemiparesis, no posture acquired	Moderate NA	34
14	F/0/18	Rt LH	No	No	Gliosis	IA	Reduction in number of AEDs	Moderate DD, Lt hemiparesis, autonomous gait	Moderate; C:66, DL:71, S:68, MS:74, Total Score 66	12

*Age at last surgery for patients who received more than one surgery.
APOS: acute post-operative seizures; AEDs: antiepileptic drugs; CSF: cerebrospinal fluid; Rt: right; Lt: left; LH: lateral hemispherotomy; AH: anatomical hemispherectomy; FH: functional hemispherectomy; TPO: temporo-parieto-occipital disconnection; IDC: intravascular disseminated coagulation; VPS: ventriculo-peritoneal shunt; DI: diabetes insipidus; SE: status epilepticus; FCD: focal cortical dysplasia; HME: hemimegalencephaly; TS: tuberous sclerosis; NA: not available; VABS: Vineland Adaptive Behaviour Scales; C: communication; DL: daily living; S: socialization; MS: motor skills.

Three patients were operated on twice. Two did not benefit from a previous posterior quadrant disconnection and received a functional hemispherectomy (Patient 4) and a lateral peri-insular hemispherotomy (Patient 5), respectively. In the remaining patient, an anatomical hemispherectomy was carried out after that a lateral peri-insular hemispherotomy failed to control seizures (Patient 6).

Mean estimated blood loss volume (EBLV) was 234.9 mL (range: 98-472.9 mL), representing a mean 29.9% of estimated total blood volume (ETBV) (range: 7-72%).

Regarding surgical complications, two patients presented with acute hydrocephalus, which cleared after placement of a temporary external CSF (cerebrospinal fluid) shunt in one and ventriculo-peritoneal shunt in the other. One child (Patient 6) had a haemorrhagic complication followed by infection after a first surgical approach with lateral peri-insular hemispherotomy; after ventriculo-peritoneal shunting for secondary ventricle dilatation, a second approach with anatomical hemispherectomy was performed without complications.

Two patients suffered with acute post-operative seizures (Patients 7 and 9), in one case associated with diabetes insipidus which regressed after appropriate medical treatment.

Histology disclosed type II FCD in five cases (type IIb in three and IIa in two), type Ia FCD in one, type IIId in two, and gliosis in two. In four subjects, findings were compatible with hemimegalencephaly.

Mean post-operative follow-up was 30.8 months (range: 12-90). At the final available assessment, 10 patients (71.4%) were classified as Engel Class I (eight Class IA, one Class 1B, and one Class 1C). One patient was classified as Engel Class IID, two as Class III, and one as Class IV. Both patients who experienced acute postoperative seizures had unsatisfactory seizure control at the last follow-up visit (Engel Class III and IID, respectively). Postoperatively, 11/14(78.9%) patients benefited from discontinuation (three cases) or reduction (eight cases) of antiepileptic drugs.

For one patient (Patient 8), we had no available data concerning psychomotor development at follow-up.

At the last available psychomotor and neurological evaluation, 13 patients presented with motor deficits (hemiparesis in 12 and asymmetric quadriparesis in one) on neurological examination. Eight of 10 patients, who were able to sit autonomously, could walk (autonomously in five cases and with assistance in three). In one patient (Patient 8), neurological and psychomotor evaluation was not possible as the patient lived abroad, and only data on seizure outcome was available. DD was present in all cases (severe in four cases and moderate in nine cases). In five patients, the degree of DD changed from severe to moderate after surgery, in six cases it remained unchanged (four severe and two moderate), and in two changed from mild to moderate following surgery.

The Vineland Adaptive Behaviour scale was administered at the last follow-up visit in 9/13 patients. Total IQ (intellectual quotient) scores resulted from low to moderately low (range: 43-86). The lowest scores were recorded on the motor skills subscale (range: 37-82) and the highest scores on socialization and communication skills subscales (*table 2*).

Discussion

Our series confirms that hemispheric surgery offers a significant opportunity to achieve seizure control and improve psychomotor developmental outcome in infants younger than three years, affected by severe/catastrophic DHE [3, 16, 17, 29-33, 42]. Moreover, our results confirm that this type of surgery, if performed in paediatric epilepsy surgery centres with a solid expertise in hemispheric procedures, can be carried out with an excellent safety profile.

In this case series, the choice of surgical techniques depended mainly on aetiology. Anatomical and functional hemispherectomy were preferred in cases with hemispheric dysplasia or hemimegalencephaly, as tissue exuberance and anatomical abnormalities may obscure landmarks that are essential to complete an effective disconnection. Anatomical hemispherectomy may be the ideal option after failure of disconnective techniques. A typical case is represented by Patient 6, who presented with DHE, symptomatic of left hemimegalencephaly, and was rendered seizure-free by anatomical hemispherectomy after a failed lateral peri-insular hemispherotomy. A lateral peri-insular approach was always chosen in cases with an atrophic hemisphere, which allows easier access to the ventricular cavities.

Vertical parasagittal hemispherotomy (VPH) [27] was not performed in any of our patients. It has been reported that the disconnection length is shorter and blood loss is lower with VPH compared to lateral approaches, and that this might represent an advantage in very young infants with low total blood volume. Nevertheless, all three neurosurgeons (MC, GLR, AC) who performed the surgical procedures in our case series were trained in lateral approaches, and we believe that one of the factors that impacts surgical safety and effectiveness is the choice of technique based on that best mastered by the surgeon.

The vast majority of our patients presented with highly frequent seizures (daily occurrence) and three of them underwent surgery during status epilepticus.

In all subjects, video-EEG recording documented seizures originating from the anatomically abnormal hemisphere with contralateral diffusion in half of them, confirming that this latter aspect does not represent an exclusion criterion for surgery [37].
The predominant presurgical MRI findings were hemimegalencephaly (six patients) and sequelae of ischemic or haemorrhagic events (four patients). Seven patients showed evident atrophy of the cerebral peduncle ipsilateral to the affected hemisphere; this data was observed in all patients with perinatal damage or hemispheric atrophy (five patients). The type of hemispheric surgery was tailored to the individual case, on the basis of the anatomical-electro-clinical features and the type and degree of alteration of the hemispheric anatomy, reserving the most aggressive approaches (anatomical and functional hemispherectomy) for those cases in which the surgical anatomy was more subverted (as in some hemispheric cortical malformations) and where, consequently, it would have been more difficult to recognize the anatomical landmarks to perform disconnective approaches. We performed an anatomical hemispherectomy in two cases (in one following a previous lateral peri-insular hemispherotomy), a functional hemispherectomy in three patients (in one following previous temporo-parieto-occipital disconnection), and a lateral peri-insular hemispherotomy in the remaining patients (in one following previous temporo-parieto-occipital disconnection). The reason for a second surgical approach was, in all three re-operated cases, the persistence of severe drug-resistant seizures.
No deaths occurred in our sample. Surgical complications were reported in three patients (21.4%), with necessity of permanent ventriculo-peritoneal shunt in two of them. This rate of complications is comparable to what has been reported in other recent similar surgical series [3, 7].
The most common aetiologies in our patients were malformations of cortical development, in line with previous studies on the same age group [3, 16, 29-33, 43].
After a mean post-operative follow-up of 30.8 months (range: 12-90), we observed a total of 10/14 (71.4%) patients in Engel Class I, with eight of these in Class Ia. Moreover, a withdraw or reduction of the antiepileptic regimen was obtained in 78.6% of our patients. These positive results are in line with those reported by studies conducted on similar populations showing percentages of seizure-free subjects (Engel Class I) ranging from 60% to 80% [3, 7, 16, 31, 44]. None of the two patients with acute post-operative seizures (Patient 7 and 9; one in the context of diabetes insipidus), resulted seizure-free at the end of follow-up, confirming that post-operative seizures appear to be a negative prognostic indicator for the success of this kind of surgery [45, 46].
Previous studies have reported significant worse outcome in patients with a developmental pathology with respect to those with an acquired pathology [27, 47, 48]. However, other studies did not reveal any correlation between seizure outcome and etiology [49]. The relative small size of our series does not allow for a definitive evaluation of this aspect, however, our data do not suggest different outcomes related to aetiology.
Catastrophic and drug-resistant epilepsy can manifest from very early infancy, often leading to a life-threatening condition with dramatic effects on cognitive and behavioural development [50]. In DHE, the severity of motor and cognitive impairment can be the consequence of both structural brain alteration and epileptic activity itself. All of our patients showed DD before surgery that was severe in 10, moderate in two and mild in two patients. At the last follow-up visit, an amelioration from severe to moderate DD was observed in 5/13 (38.5%) patients; no information was available concerning psychomotor development in one patient during follow-up. Before surgery, 11 patients had clear hemiparesis and one presented with asymmetric quadriparesis; only four were able to sit independently and none were able to walk, even when helped. During follow-up, all the evaluated patients had motor deficits disclosed by neurological examination, including the two cases with no previous hemiparesis. However, we observed a progressive improvement in motor deficit over months. Indeed, eight patients could walk (autonomously in five cases and with assistance in three). On the other hand, it is important to point out that these patients still had an intellectual deficit based on post-operative evaluation, with a total IQ score from low to moderately low and higher scores in socialization and communication skills subscales with respect to motor skill subscales.
In conclusion, our results confirm that early hemispheric surgical procedures in children younger than three years, affected by severe/catastrophic epilepsy related to DHE, are sufficiently safe, with positive effects not only on seizures but also on developmental outcome and motor autonomy, highlighting specific features of brain plasticity in infants. ■

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

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

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TEST YOURSELF

(1) When is hemispheric surgery considered an option for the treatment of epilepsy during early childhood?

(2) Which surgical techniques are recommended for hemispheric surgery during early childhood?

(3) Is surgery effective for diffuse hemispheric epilepsy when performed during early childhood?

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