RESEARCH PAPER

Surgery in patients with childhood-onset epilepsy: analysis of complications and predictive risk factors for a severely complicated course

Piergiorgio d'Orio,[1] Michele Rizzi,[1,2] Valeria Mariani,[1] Veronica Pelliccia,[1] Giorgio Lo Russo,[1] Francesco Cardinale,[1] Michele Nichelatti,[3] Lino Nobili,[1,4] Massimo Cossu[1]

[1]"Claudio Munari" Epilepsy Surgery Centre, Azienda Socio Sanitaria Territoriale Grande Ospedale Metropolitano Niguarda, Milano, Italy
[2]Department of Neuroscience, University of Parma, Parma, Italy
[3]Service of Biostatistics, Azienda Socio Sanitaria Territoriale Grande Ospedale Metropolitano Niguarda, Milano, Italy
[4]Child Neuropsychiatry Unit, DINOGMI, University of Genoa, Genoa, Italy, Istituto Giannina Gaslini, Genova, Italy
Child Neuropsychiatry Unit, Istituto Giannina Gaslini, DINOGMI, University of Genoa, Genoa, Italy

Correspondence to
Dr Massimo Cossu, "Claudio Munari" Center for Epilepsy Surgery, Azienda Socio Sanitaria Territoriale Grande Ospedale Metropolitano Niguarda, Milan 20162, Italy; massimo.cossu@ospedaleniguarda.it

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ABSTRACT

Object To compare the occurrence of surgery-related complications in patients with childhood-onset focal epilepsy operated on in the paediatric or in the adult age. To investigate risk factors for surgery-related complications in the whole cohort, with special attention to age at surgery and severe morbidity.

Methods A cohort of 1282 patients operated on for childhood-onset focal epilepsy was retrospectively analysed. Occurrence of surgery-related complications, including a severely complicated course (SCC: surgical complication requiring reoperation and/or permanent neurological deficit and/or death), was compared between patients operated on in the paediatric age (<16 year-old; 452 cases) and, respectively, in adulthood (≥16 year-old; 830 cases). The whole cohort of patients was also evaluated for risk factors for a SCC.

Results At last contact (median follow-up 98 months), 74.5% of patients were in Engel's class I (78.0% of children and 73.0% of adults). One hundred patients (7.8%) presented a SCC (6.4% for children and 8.6% for adult patients). Postoperative intracranial haemorrhages occurred more frequently in adult cases. At multivariate analysis, increasing age at operation, multilobar surgery, resections in the rolandic/perirolandic and in insulo-opercular regions were independent risk factors for a SCC.

Conclusions Surgery for childhood-onset focal epilepsy provides excellent results on seizures and an acceptable safety profile at any age. Nevertheless, our results suggest that increasing age at surgery is associated with an increase in odds of developing severe surgery-related complications. These findings support the recommendation that children with drug-resistant, symptomatic (or presumed symptomatic) focal epilepsy should be referred for a surgical evaluation as early as possible after seizure onset.

INTRODUCTION

Surgery is recognised as a useful and effective treatment option for drug-resistant focal epilepsy. Its effectiveness and safety have been demonstrated for both adults[1 2] and children.[3] Excellent results on seizures have been reported also in more heterogeneous series for every age range.[4–6]

Childhood-onset epilepsy is often refractory to drug treatment, and the detrimental effects of ongoing seizures, abnormal electrical activity and antiepileptic drugs on brain development, cognitive functions and psychosocial outcome have been widely reported.[7] Furthermore, childhood-onset drug-resistant epilepsy has been recognised as a significant risk factor for epilepsy-related mortality.[8] For these reasons, early surgical treatment of children with symptomatic focal epilepsy has been advocated, in order to contrast the harmful impact of epilepsy on health-related quality of life in the paediatric age.[9]

Nevertheless, despite a general increase in volume of surgeries in children, including complex and severe cases,[10] this treatment option appears to be still largely underused.[11] As a consequence, many ideal candidates for paediatric surgery are operated on during adulthood after several years of disease duration.

Potential morbidity associated with epilepsy surgery has been claimed as one possible cause of reluctance to refer for surgery of youngest patients with intractable epilepsy.[12] Although data concerning factors associated with a complicated postoperative course, including age, are not univocal, several recent studies reported a low rate (5.5%–12%) of complications in the paediatric age.[13–16]

In this retrospective single-centre study, we have addressed the issue of risk factors for surgery-related complications in a large series of patients with childhood-onset epilepsy. Our main hypothesis was that surgery performed during the paediatric age is burdened by a lower surgical risk.

METHODS

Patients

We searched our institutional database and clinical charts for patients with childhood-onset (<16 years) focal epilepsy treated surgically from 1996 to 2016.

All eligible patients were included in the present cohort. Presurgical investigations and surgery were performed only after the patients or their tutors had given their informed consent. The local Ethical Committee approved the present study.

Presurgical evaluation

A comprehensive presurgical workup included: clinical history, neurological examination, interictal

scalp encephalography (EEG) and, when needed, intensive video-EEG monitoring with at least one ictal recording. All patients were imaged by high-resolution brain MRI (1.5 T magnet Philips ACS-NT & Achieva) using appropriate sequences. In selected cases, fluorine-18 fluorodeoxyglucose positron emission tomography/CT scan was obtained. When non-invasive evaluation failed to appropriately localise the epileptogenic zone (EZ), invasive monitoring with stereotactically implanted multilead intracerebral electrodes (stereo-electro-encephalography, SEEG) was performed. In no case subdural electrodes were employed.

Surgery

Once patient's anatomo-electro-clinical data were reviewed, a tailored, navigation-assisted microsurgical resection (and/or disconnection) was performed, with the aim to remove the EZ and to preserve neurological functions. Lobar/multilobar disconnective techniques were adopted since June 2002. For presurgical anatomical and functional planning, we constantly updated the workflow of neuroimage postprocessing to the standards available at time of operation. Intraoperative neurophysiological monitoring was employed whenever required with the patients under general anaesthesia. No patient of the present cohort underwent awake surgery.

Surgery-related complications

By searching our institutional database, in which patients' clinical information were prospectively collected, and by reviewing patients' clinical charts, we categorised three types of surgery-related complications: medical, neurological and surgical complications.

Medical complications included any internal-medicine disorder occurring during the postoperative period (eg, deep vein thrombosis, airway problems, electrolyte imbalance and urinary tract infections).

Neurological complications were defined as new, unwanted, unexpected neurological deficits developed after a diagnostic or therapeutic procedure. They were defined as transient (cleared within 6 months postoperatively) and permanent (still present 6 months postoperatively). Hence, expected permanent neurological sequelae (for instance: haemianopia after an occipital lobe resection, quadrantanopia after temporal lobectomy, haemiparesis after hemispheric surgery) were not considered as complications. Indeed, our assumption was that expected neurological consequences of surgery may be regarded to as side effects, which are fully discussed with and unequivocally accepted by the patient or patient's family in the preoperative counselling.

Surgical complications were categorised as minor (for which a surgical correction was not necessary) and major (those requiring return to the operating room for reoperation).

The postprocedural course of a patient presenting a major surgical complication, a new unexpected permanent neurological deficit or decease (or a combination of them) was defined as a severely complicated course (SCC).

Histology

Surgical specimens were routinely processed for histological and immunohistochemical investigations.

Histological findings were grouped as follows: malformations of cortical development; hippocampal sclerosis (HS); low-grade epilepsy-associated tumours (LEAT); dual pathology; vascular disorders (ischaemic or malformative); unremarkable findings. Focal cortical dysplasias (FCD) type III were assigned to the group of the principal diagnosis associated to the FCD. In fact, there is evidence that both electroclinical phenotype and surgical results of patients with FCD type III and those of cases with the corresponding solitary principal diagnosis are similar.[17]

Postoperative follow-up

The first two postoperative visits were scheduled 6 months and 1 year after surgery. Subsequently, follow-up controls were performed with yearly frequency. A control MRI study was performed at the first follow-up visit for all patients.

Postoperative seizure outcome according to the Engel's classification[18] was assessed at each follow-up visit. Seizure outcome at the final assessment (last available data from outpatient visit or direct telephone contact) was classified as favourable (free from disabling seizures, corresponding to Engel's class I) and unfavourable (corresponding to Engel's classes II–IV).

Data analysis

Several presurgical, surgical and postsurgical variables were compared between patients operated on in the paediatric age (<16 years) and, respectively, in adulthood (≥16 years). The same two groups were also analysed to compare the occurrence of neurological complications, surgical complications, medical complications and SCC. In this phase, the two-tailed Fisher's exact test was used to analyse categorical variables and the Kruskal-Wallis rank sum test was used for numerical variables.

The whole cohort of patients was then analysed to investigate which variables were associated with an increasing odds to develop a SCC. The following variables were analysed using a univariate logistic regression with the Wald's test: age at surgery (as a continuous variable), duration of epilepsy (as a continuous variable), sex, single/multiple procedures, extent of surgery (unilobar/multilobar/hemispheric), temporal lobe resection, rolandic/perirolandic resection, operculo-insular resection, type of surgery (resection/disconnection/resection plus disconnection) and histological diagnosis.

A multivariate logistic regression model was then built in order to identify variables independently associated to the odds of SCC, after exclusion of reciprocally correlated variables. The variables maintained in the multivariate regression were chosen as follows. First, a draft multivariable model was set including all the variables showing a $p<0.25$. Second, a deep analysis searching for possible correlations between independent variables was carried out; in case of association, we maintained in the model only the clinically more relevant variable. Then, a backward stepwise selection was performed to include in the model only significant variables.

Statistical significance was assumed at $p<0.05$. Statistical analysis was performed using the statistical software STATA (V.15.1, Stata, College Station, Texas, USA).

RESULTS

Patients

One thousand two hundred and eighty-two patients were included in this study. They represent 77.6% of 1652 patients who underwent surgical treatment for drug-resistant epilepsy in our Centre during the examined period. According to the adopted selection criteria, this cohort includes all the paediatric patients and all adults with childhood-onset epilepsy operated on in our Centre. Patients with adult-onset epilepsy have been excluded. Table 1 details the main presurgical, surgical and postsurgical data of the entire population and of the paediatric and adult groups.

Table 1 Main presurgical, surgical and postsurgical data in the whole cohort and in patients operated on in the paediatric age and in adulthood

	Total cohort	Paediatric (%)	Adult (%)	P values*
Number of patients	1282	452	830	
Sex				NS
Males	692	251 (56)	441 (53)	
Females	590	201 (44)	389 (47)	
Age at seizure onset (years)				<0.0005
Median (range)	5 (0–15)	2 (0–14)	6 (0–15)	
Duration of epilepsy (years)				<0.0005
Median (range)	15 (0–59)	5 (0–15)	22 (1–59)	
Frequency of seizures†				<0.0005
Daily	517	256 (57)	261 (31)	
Weekly	532	99 (22)	433 (52)	
Monthly	136	34 (7)	102 (12)	
Sporadic	97	63 (14)	34 (4)	
MRI				<0.0005
Positive	1154	435 (96)	719 (87)	
Negative	128	17 (4)	111 (13)	
SEEG				<0.0005
Yes	386	95 (21)	291 (35)	
No	896	357 (79)	539 (65)	
Repeated SEEG				NS
Yes	21	7 (2)	14 (2)	
No	1261	445 (98)	816 (98)	
Surgical procedure				<0.0005
Resection	1167	382 (85)	785 (95)	
Disconnection	75	48 (10)	27 (3)	
Resection + disconnection	40	22 (5)	18 (2)	
Repeated surgery				0.0079
Yes	70	35 (8)	35 (4)	
No	1212	417 (92)	795 (96)	
Extent of surgery				<0.0005
Unilobar	891	268 (59)	623 (75)	
Multilobar	339	143 (32)	196 (24)	
Hemispheric	52	41 (9)	11 (1)	
Site of surgery				<0.0005
Temporal	555	128 (28)	427 (51)	
Extratemporal	727	324 (72)	403 (49)	
Histology				<0.0005
MCD	456	208 (46)	248 (30)	
Hippocampal sclerosis	249	36 (8)	213 (26)	
LEAT	254	107 (24)	147 (18)	
Dual pathology	50	13 (3)	37 (4)	
Vascular	102	40 (9)	62 (7)	
Unremarkable	171	48 (10)	123 (15)	
Seizure Outcome				NS
Engel's class I‡	954	351 (78)	603 (73)	
Engel's classes II-IV	328	101 (22)	227 (27)	

*Comparison between patients operated on in the paediatric and adult age. Two-tailed Fisher's exact test was used for categorical variables and Kruskal-Wallis rank sum test for numerical variables.
†Including also auras and focal seizures without impairment of awareness.
‡Engel's class I includes classes Ia, Ib, Ic and Id.
LEAT, low-grade epilepsy associated tumour; MCD, malformations of cortical development; NS, not significant; SEEG, stereo-electro-encephalography.

Surgical procedures and seizure outcome

Three hundred and eighty-six patients (30%) required a SEEG evaluation; a repeat SEEG exploration was performed in 21 cases and therefore the total number of implantations was 407 (range 0–2 per patient).

A total of 1356 therapeutic surgical procedures were performed in the 1282 patients. Seventy patients (5.5%) received more than one operation: 67 were operated on twice, 2 patients received three resective procedures and 1 was operated on four times.

Age at seizure onset and duration of epilepsy were significantly higher in adult patients, while seizure frequency was significantly higher in children. Adult patients had more frequently an uninformative MRI and were more likely to require an SEEG exploration. Microsurgical disconnections and reoperations were more often performed in children. Multilobar and hemispheric surgeries were more frequent in children, who were less likely to receive temporal lobe resections compared with adults. Significant differences were also observed as to histology of resected specimens, with cortical malformations and LEATs prevailing in children and HS in adults. The median postoperative follow-up of the whole population was 98 months (range 12–246): at last contact, 954 patients (74.5%) were in class I, 112 patients (8.7%) in class II, 106 patients (8.3%) in class III and 109 patients (8.5%) in class IV. Among patients in class I, 735 (57.4%) were in class Ia, 68 (5.3%) were in class Ib, 93 (7.3%) were in class Ic and 58 (4.5%) were in class Id. Seizure outcome was somewhat more favourable in children, but this difference did not reach statistical significance (p=0.0522, table 1).

Surgery-related complications: age-group analysis

Seventeen out of 386 patients (4.4%) experienced surgery-related complications after SEEG implantations: 4 patients (1%) presented a medical complication, 10 patients (2.6%) had a surgical complication (one of them developed a permanent motor deficit—0.2%) and 3 patients (0.7%) had a transient neurological deficit. No statistically significant differences were found comparing the paediatric with the adult group.

After microsurgical procedures, medical complications occurred in 31 (6.9%) children and in 64 (7.7%) adults (p=0.5777). One patient, operated on at the age of 19 years, deceased for meningitis followed by Waterhouse-Friderichsen syndrome (overall mortality rate 0.0008%).

Details on neurological and surgical complications related to microsurgical procedures in the two groups of patients are provided in tables 2–4. Among neurological complications, the rates of transient speech impairment and transient cranial nerve

Table 2 Neurological complications associated to microsurgical procedures in patients operated on in the two age groups

	Transient			Permanent		
Neurological complications	Paediatric n (%)	Adult n (%)	P values*	Paediatric n (%)	Adult n (%)	P values*
Motor deficit	34 (7.5)	39 (4.7)	0.0433	13 (2.9)	18 (2.2)	NS
Cranial nerve deficit	3 (0.6)	20 (2.4)	0.0265	2 (0.4)	2 (0.2)	NS
Speech disturbance	6 (1.3)	39 (4.7)	0.0013	3 (0.7)	13 (1.6)	NS
Sensitive deficits	0	4 (0.5)	NS	0	4 (0.5)	NS
Total	*43* (9.5)	*102* (12.3)	*NS*	*18 (4)*	*37 (4.5)*	*NS*

*Comparison between paediatric and adult groups by two-tailed Fisher's exact test.
NS, not significant.

Table 3 Type and severity of permanent postoperative neurological deficits occurring in the paediatric and adult groups of patients

	Paediatric	Adult
Permanent neurological deficit	**n**	**n**
Haemiparesis	13	18
Mild	2	5
Severe	11	13
Cranial nerve palsy	2	2
Mild	1	2
Severe	1	0
Speech impairment	3	13
Mild	3	13
Severe	0	0
Sensitive impairment	0	4
Mild	0	4
Severe	0	0
Total	*18*	*37*

palsy were significantly higher in adult patients, whereas children presented more frequently a transient motor deficit. No significant difference was found as to the occurrence of permanent neurological deficits between the two groups of patients. Major surgical complications, in particular intracranial haemorrhages requiring surgical evacuation, were significantly more frequent in adult patients, who presented also a significantly higher rate of minor intracranial haemorrhage not requiring reoperation.

Overall, a SCC occurred in 100 patients (7.8%; eight patients presented a permanent neurological deficit secondary to a surgical complication requiring reoperation). The rate of SCC was higher in the group of adult patients (71 cases, 8.6%) if compared with the paediatric group (29 cases, 6.4%), but this difference was statistically not significant (p=0.1915).

Risk factors for SCC

Evaluation of risk factors for the development of SCC in the whole cohort of patients is detailed in table 5. A significant association was found between SCC and: multiple procedures, extent of surgery, site of surgery, type of surgery, histology.

Table 4 Surgical complications associated to microsurgical procedures in patients operated on in the two age groups

	Minor			Major		
Surgical complications	**Paediatric n (%)**	**Adult n (%)**	**P values***	**Paediatric n (%)**	**Adult n (%)**	**P values***
Intracranial haemorrhage	4 (0.9)	37 (4.5)	<0.0005	1 (0.2)	19 (2.3)	0.0034
CT hypodensity	3 (0.6)	4 (0.5)	NS	0	0	
Wound infection	0	1 (0.1)	NS	2 (0.4)	9 (1.1)	NS
Hydrocephalus	0	0		3 (0.7)	5 (0.6)	NS
CSF leak	0	0		1 (0.2)	3 (0.4)	NS
Other	3† (0.6)	2‡ (0.2)	NS	6§ (1.3)	3¶ (0.4)	NS
Total	*10 (2.2)*	*44 (5.3)*	*0.0084*	*13 (2.9)*	*39 (4.7)*	*NS*

*Comparison between paediatric and adult groups by two-tailed Fisher's exact test.
†Ischaemic optic neuropathy (two cases), brain oedema (one case).
‡Ischaemic optic neuropathy (one case), subdural hygroma (one case).
§Subdural hygroma (three cases), instability of the cranial flap (three cases).
¶Brain oedema (one case), instability of the cranial flap (one case), abscess at the site of a skull-clamp pin (one case).
CSF, cerebrospinal fluid; NS, not significant.

Table 5 Risk factors for a SCC: results of univariate statistical analysis.

Variable	OR	95% CI		P values*
Age at surgery (years)	1.0147	0.9993	1.0303	0.062
Duration of epilepsy (years)	1.0162	1.0000	1.0326	0.050
Sex (male vs female)	1.0457	0.6938	1.5760	0.831
Multiple procedures	2.0258	1.3429	3.0559	0.001
Extent of surgery†				
Multilobar	3.5205	1.6251	7.6264	0.001
Hemipheric	2.3142	1.5000	3.5702	<0.0005
Temporal lobe Surgery	0.4581	0.2903	0.7229	0.001
Rolandic/perirolandic resection	3.0333	1.7764	5.1796	<0.0005
Operculoinsular resection	4.9402	2.3099	10.5655	<0.0005
Type of surgery‡				
Disconnection	1.9835	0.9832	4.0015	0.056
Res+Dis	2.2752	0.9289	5.5728	0.072
MCD	1.6039	1.0633	2.4195	0.024
Hippocampal sclerosis	0.4384	0.2247	0.8555	0.016
LEAT	0.6389	0.3569	1.1439	0.132
Dual pathology	1.3298	0.5157	3.4294	0.555
Vascular	1.4818	0.7644	2.8724	0.244
Unremarkable histology	1.0628	0.5896	1.9159	0.839

*Univariate logistic regression by Wald's test.
†Reference category: unilobar.
‡Reference category: resection.
LEAT, low-grade epilepsy associated tumour; MCD, malformation of cortical development; SCC, severely complicated course.

The fitted multivariate logistic regression model indicated increasing age at surgery, multilobar surgeries, rolandic/perirolandic and operculo-insular resections as independent risk factors for the development of SCC (table 6).

DISCUSSION

Our study indicates that surgery for childhood-onset epilepsy may allow excellent results on seizures with an acceptable risk profile at any age. Nevertheless, patients operated on in the paediatric age are more likely to present with a lower rate of severe complications, as compared with patients operated on in adulthood. We identified increasing age at surgery, along with extended resections and surgery in highly eloquent areas, as an independent risk factor for a severely complicated postoperative course.

There is a great variability in the presentation and interpretation of available data in the literature on complications of epilepsy surgery. For instance, the distinction between complications and

Table 6 Output of the fitted multivariate logistic regression model of risk factors for a SCC

Variables	OR	95% CI		P values†
Age at surgery (years)	1.0257	1.0093	1.0424	0.002
Extent of surgery*				
Multilobar	5.2520	2.3271	11.8535	<0.0005
Hemispheric	1.3663	0.7840	2.3812	NS
Rolandic/perirolandic resections	3.5890	1.8763	6.8652	<0.0005
Operculoinsular resections	5.3322	2.1870	13.0004	<0.0005

*Reference category: unilobar.
†Multivariate logistic regression.
NS, not significant; SCC, severely complicated course.

expected postoperative deficits (ie, side effects) is disregarded in some studies. Also, neurological deficits resulting from surgical complications are frequently reported separately, leading to an overestimation of the rate of adverse events. In order to simplify the analysis of our data, we identified patients with a SCC, thus including in a single variable the occurrence of one or more major surgery-related complications (death, return to the operating room for a surgical complication, permanent neurological deficit), which allows assigning to a specific patient's postoperative course a distinct profile of severity.

Age groups

The comparison between the two age groups indicated that, despite no significant difference was observed in the occurrence of a SCC between the two groups, a subset of surgery-related complications, including postoperative intracranial haemorrhages requiring return to the operating room, was significantly higher in the adult group. Higher frequency of postoperative intracranial haemorrhage in the adult group is not easy to explain; indeed, the results of studies on the effects of age on intracranial postoperative bleeding are not conclusive.[19] We can hypothesise a role of the prophylactic use of low-molecular-weight heparin in the postoperative period in adult patients as well as of the presence of occult hypertensive disease in the same group.

Our two age-groups differ significantly for several factors, suggesting that delay of surgery may be due to a number of reasons. For instance, patients operated on in adulthood probably experience a less disabling impact with their seizures, as suggested by the significant difference of seizure frequency between the two age groups. Furthermore, patients without a discrete lesion at MRI, who prevail in the adult group, are frequently referred with reluctance for surgery.[20] Also, we cannot exclude that the possible presence of longer periods of responsiveness to antiepileptic drugs during childhood in adult group patients might have led their neurologists to search for an effective drug regimen rather than for a surgical solution.

Risk factors for SCC

The multivariate analysis in the whole group of patients indicated multilobar resection, surgery in the rolandic/perirolandic and insulo-opercular regions and increasing age at surgery as independent risk factors for a SCC.

Multilobar resections have been previously recognised as procedures at significant risk of developing complications,[21 22] with a rate of new postoperative motor deficits ranging up to 11%.[23] An increased risk of major neurological complications has been described after surgery within or around eloquent areas.[22] A recent series described 18 out of 66 patients (34%) who developed a new sensorimotor deficit after surgery for seizures arising from the rolandic/perirolandic region,[24] with similar or even worst results having been reported by previous studies.[25–28] In our patients operated on in or around the rolandic region, a SCC was detected in 18.2% of cases, a proportion that compares favourably with previous reports. Insulo-opercular resections are burdened by the risk of injury to both dominant perisylvian cortex and to subcortical bundles, including arcuate, corticospinal and thalamocortical fascicles. Nevertheless, recent studies on surgery for epilepsy arising from this region report an acceptable rate of morbidity, which ranges from less than 10% of permanent deficits[29] to exclusively transient neurological impairments.[30] Procedures in the operculo-insular area resulted in 27.8% of patients with a SCC in our series, a considerably worse morbidity profile compared with recent reports. It is noteworthy that many of our patients, according to the epileptological indications, required resections of both insular and opercular cortex. As already underlined by others, additional morbidity may be expected when an insulectomy is extended to the overlying opercula,[31] owing to either direct injury to functional cortex or to perforating vessels supplying subcortical pathways.[32 33]

Surgery in the rolandic/perirolandic and insulo-opercular areas is still a challenging task and it should preferably be performed in high-volume epilepsy surgery centres with appropriate facilities and expertise in order to counteract the risks of disabling complications. An essential role in achieving better functional results is played by advanced presurgical anatomofunctional planning[34] combined with neuronavigation and intraoperative neurophysiological monitoring.

The relationships between age at surgery and risk of surgery-related unexpected complications are still unclear. Several studies have reported higher rates of complications in older patients.[35–37] Conversely, other recent studies failed to reveal significant associations between age at surgery and occurrence of postoperative adverse events.[6 22 38–41] Even, Hader *et al* reported that children were more exposed to postoperative complications compared with older patients.[12] In our study, the OR for age at surgery indicates that each 1 year increase in age determines a+2.57% increase in odds of developing a SCC. Although this odds increase is apparently small, since it is measured on a single-year difference, the relevant clinical impact of the relationship between age at surgery and SCC is clearly shown by the strong significance of their association (p=0.002).

Our findings show that patients operated on as adults are exposed to a significantly higher risk to develop severe postoperative complications. The design of this study, which includes only patients with childhood-onset epilepsy, does not allow disentangling the respective roles of age at surgery and illness duration as risk factors for surgery-related complications. Indeed, these two variables were highly correlated, as found during multivariate model building. Further studies, including patients unselected for age at seizure onset, are warranted to address this issue.

Limitations and strength

The more obvious limitation of our study is its retrospective and single-centre nature, which limits the general relevance of the presented results. A multicentric study with possibly prospectively collected data is needed to reliably assess the risk factors of complications after epilepsy surgery, with specific attention to age at operation. Furthermore, the group analysis might be biased by the different representation of some variables between the two groups of patients, as discussed above. On the other hand, the selection of a large sample of patients with childhood-onset epilepsy operated on at different ages allowed investigating the impact of age at surgery on complications in a subset of patients who could have been selected for surgery in the same age range.

CONCLUSION

The excellent results on seizures and the more favourable safety profile of surgery conducted in the paediatric age support the recommendation that children with drug-resistant, symptomatic (or presumed symptomatic) focal epilepsy should be referred for a surgical evaluation as early as possible after seizure onset, especially when an aetiology with a recognised high risk to induce drug-resistance has been diagnosed.

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MN. Drafting the article: PdO, MC. Critical revision of the article: GLR, LN, MC. Final approval of the version to be published: all the authors.

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