



Surgical outcomes in two different age groups with Focal Cortical Dysplasia type II: Any real difference?



Jorge Luis Ramírez-Molina^a, Roberta Di Giacomo^b, Valeria Mariani^{c,d}, Francesco Deleo^{e,f}, Francesco Cardinale^d, Angélica María Uscátegui-Daccarett^g, Pablo Lorenzana^a, Laura Tassi^{d,*}

^a Neurology Unit, Department of Internal Medicine, Universidad Nacional de Colombia, Carrera 30 No. 45-03, Bogotá, Colombia

^b Department of Neuroscience, Imaging and Clinical Sciences, University "G. D'Annunzio", Neurological Clinic "SS. Annunziata" via dei Vestini, 66100 Chieti, Italy

^c "C. Mondino" National Neurological Institute, Pavia, Italy

^d "Claudio Munari" Epilepsy Surgery Centre, Niguarda Hospital, Piazza Ospedale Maggiore 3, 20162 Milan, Italy

^e Clinical and Experimental Epileptology Unit, Istituto Neurologico "Carlo Besta", Via G. Celoria, 11, 20133 Milano, Italy

^f Department of Neurology, Montreal Neurological Institute and Hospital, McGill University, Montreal, Quebec, Canada

^g Neuropediatrics Unit, Department of Pediatrics, Universidad Nacional de Colombia, Carrera 30 No. 45-03, Bogotá, Colombia

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ABSTRACT

Objective: Focal Cortical Dysplasias (FCDs) represent a common architectural cortical disorder underlying drug-resistant focal epilepsy. So far, studies aimed at evaluating whether age at surgery is a factor influencing surgical outcome are lacking, so that data on the comparison between patients harboring Type II FCD operated at younger age and those operated at adult age are still scarce. We compared presurgical clinical features and surgical outcomes of patients with histopathologically diagnosed Type II FCD undergoing surgery at an earlier age with those operated after 20 years of age.

Methods: We retrospectively analyzed 1660 consecutive patients operated at the "Claudio Munari" Epilepsy Surgery Centre. There were 289 patients (17.4%) with a neuropathological diagnosis of Type II FCD. We included two different groups of patients, the first one including patients operated on at less than 6 years, the second sharing the same seizure onset age but with delayed surgery, carried out after the age of 20. Seizure characteristics and, neuropsychological and postoperative seizure outcomes were evaluated by study group.

Results: Forty patients underwent surgery before the age of 6 and 66 patients after the age of 20. Surgical outcome was favorable in the whole population (72.6% were classified in Engel's Class Ia + Ic), independently from age at surgery. In the children group, 32 patients were classified in Class I, including 30 (75%) children in classes Ia and Ic. In the adult group, 53 belonged to Class I of whom 47 (71%) were in classes Ia and Ic.

The percentage of permanent complications, the surgical outcomes, and AED withdrawal did not significantly differ by study group.

Conclusion: Our results indicate that there is no difference between the groups, suggesting that outcome depends mainly on the histological findings and not on timing of surgery.

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1. Introduction

Focal Cortical Dysplasias (FCDs) are a subset of malformation of cortical development characterized by disorder of cortical lamination,

maturation, and neuronal differentiation frequently found in patients suffering from drug-resistant focal epilepsies [1]. Focal cortical dysplasias include a wide range of white and gray matter abnormalities from a mild cortical disruption and dyslamination, without cytological alterations, to complete disarrangement of the neocortical lamination associated with dysmorphic giant neurons accompanied or not by balloon-shaped cells (BCs) [1,2].

Despite the discovery of supplementary neuropathological features and the advent of classifications based also on electro-clinical and neuroimaging features [2–6], the original subdivision of Type IIa (without) and IIb (with BCs) has remained fixed.

Type II FCD has a high epileptogenic potential and is often associated with early-onset drug-resistant focal epilepsy, constituting an important cause for admission to epilepsy surgery programs [6,7]. This entity

Abbreviations: FCDs, Focal Cortical Dysplasias; BCs, balloon cells; EZ, epileptogenic zone; AEDs, antiepileptic drugs; MRI, Magnetic Resonance Imaging; IQR, Interquartile Ratio; SD, Standard Deviation.

* Corresponding author.

E-mail addresses: joramirezmo@unal.edu.co (J.L. Ramírez-Molina), roberta.digiacomob4@gmail.com (R. Di Giacomo), valeriamariani85@gmail.com (V. Mariani), francesco.deleo@istituto-besta.it (F. Deleo), francesco.cardinale@ospedaleniguarda.it (F. Cardinale), amuscateguid@unal.edu.co (A.M. Uscátegui-Daccarett), plorenzanap@unal.edu.co (P. Lorenzana), laura.tassi@ospedaleniguarda.it (L. Tassi).

is encountered in approximately 30–40% of children with epilepsy and can manifest with neurological, cognitive, and psychosocial alterations [8–10].

Previous studies reported 50–85% of patients with FCDs become seizure-free after surgery. The best predictor of a good seizure outcome is the complete removal of the epileptogenic zone (EZ), which often coincides with the culprit lesion [6,11–14].

In the pediatric population, the detrimental effect of frequent seizures at an early age on cognitive potential and neuronal plasticity is well known, and it seems to be independent from the epileptogenic pathology. Moreover, infants with longer duration and earlier onset of epilepsy performed worse on developmental testing [8,9,15,16].

Cognitive, social, and developmental outcomes are better the earlier surgery is performed [8,15,17–19]. However, these data have been extrapolated from various groups, with different epilepsy syndromes and diverse ages from infancy to late adolescence [9,20–22].

Data are still scarce concerning the comparison between patients harboring Type II FCD operated at young and/or adult age, investigating whether age at surgery is an important factor influencing surgical outcome. Some evidence exhibits no significant difference in the surgical outcome between children and adults, regardless of the onset age [8,23,24], even in a selected FCD Type II population [18].

The aim of our study was to compare presurgical clinical features and surgical outcomes of patients with histopathologically identified FCD II, the first group operated on at less than 6 years, the second sharing the same seizure onset age but with a delayed surgery, carried out after the age of 20 years.

2. Material and methods

Among 1660 consecutive patients operated on at the “Claudio Munari” Epilepsy Surgery Centre from June 1996 to June 2016, 289 patients with a histologically proven diagnosis of FCD Type II were selected. Only patients suffering from this cortical malformation and sharing an epilepsy onset before 6 years and with a minimum of 12 months of follow-up after surgery were enrolled.

A first group of children (40 patients) with early seizure onset and surgery performed before the age of 6 years was selected. In the comparison group (66 patients), epilepsy similarly arose before the age of 6, but surgery, for various reasons, was carried out after the age of 20. Globally, 106 patients were included in the analysis.

Surgery was performed for strictly therapeutic reasons, after obtaining informed consent from the patients and/or their caregivers, and after a comprehensive presurgical evaluation. Clinical and demographic data were analyzed. The pre-surgical work-up was compared, as well the pharmacological history and the histopathological results. The outcomes were compared by periodical monitoring (i.e. at 6, 12, 24, 36, and 60 months from surgery) using Engel's classification [25], and for monitoring surgery complications, antiepileptic drugs (AEDs) therapy management, and the neuropsychological outcomes.

2.1. Magnetic resonance imaging

Magnetic resonance imaging (MRI) protocols were assessed according to Colombo et al. [26,27], including transverse double-echo spin-echo (SE) sequences of the entire brain during the early period of the study, later replaced by T2-weighted transverse and coronal turbo spin-echo (TSE) and T2-weighted transverse coronal and sagittal TSE fluid-attenuated inversion-recovery (FLAIR) sequences, and T1-weighted coronal inversion recovery (IR) sequences. Intravenous contrast was injected only in the rare cases of an uncertain diagnosis.

2.2. Stereo-EEG procedure

Stereo-EEG recordings were considered mandatory in patients for whom data on ictal events obtained by Video-EEG, along with MRI data

and clinical aspects of the seizures, were considered insufficiently reliable to identify the epileptogenic zone (EZ). Stereo-EEG was tailored to the patients' individual anatomical and electro-clinical characteristics [28].

2.3. Surgery

The final surgical resection was performed in order to remove the cortical areas involved in seizure generation, that is the EZ. In each case, the extent of resection was carefully planned taking account of the severity of the epilepsy and other neurological symptoms, as well as the risk of postsurgical neurological deficits.

2.4. Histopathology and classification

The surgical specimens were fixed (10% neutral buffered formalin) and paraffin-embedded sections (4–10 m) were stained using hematoxylin and eosin, thionin, Klüver-Barrera, and Bielschowsky techniques.

Routine immunocytochemical investigations were also performed using anti-glial fibrillary acid protein (GFAP, Roche Diagnostics, Mannheim, Germany) and anti-neurofilament (2F11 monoclonal, DAKO, Denmark). The diagnosis of FCD types Ia and Ib was performed according to the classification criteria by Blümcke et al. [3].

2.5. Neuropsychological outcomes

We reviewed data concerning the neuropsychological assessment before surgery and at different time points after surgery (i.e. at 12, 24, 36, 48, and 60 months).

In children, the neuropsychological test battery was tailored to the age of patients. Parents underwent Vineland Adaptive Behavioral Scale (VABS). The Preschool Neuropsychological Test was assessed as well [29]. We also used the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-3), the revised Griffiths Mental Development Scales that was made for children between 2 and 8 years, and the Beck Depression Inventory.

Adult patients included in the comparison group underwent a standard neuropsychological test battery assessing language, reading skills, verbal memory, visuospatial memory, visual constructive functions, visual explorations, attention and executive functions, visual perception, abstract reasoning, and depressive symptoms. Building on an overall index score, we classified the neuropsychological outcomes after surgery as improvement, unchanged or worsened state, compared with the presurgical state.

2.6. Statistical analysis

Age at epilepsy onset, the duration of epilepsy, age at surgery, seizure frequency, and follow-up duration in the two age groups were expressed as median and interquartile range (IQR) and compared using a Mann Whitney U test. The number of tried AEDs before surgery was expressed as media \pm SD and compared using a Mann Whitney U test. The associations between the presence of complications and presence of permanent complications, surgical outcome (Engel's Classification Class Ia + Ic), and AED withdrawal for both age groups were evaluated using a contingency table analysis. Independence of rows and columns were evaluated using a Fisher's exact test. A p value of 0.05 was considered significant. All statistical analyses were made using SPSS software, v. 22.

3. Results

3.1. General characteristics

The children group included 40 patients (29 males and 11 females), the adult group comprised 66 patients (36 males and 30 females).

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