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Epilepsy surgery in children: Trends and challenges

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Summmary

Investigators from the Pediatric Epilepsy Research Consortium (PERC), a collaboration of 21 US pediatric epilepsy centres, reports patient characteristics, evaluation strategies and postoperative outcomes in children with drug resistant epilepsy, who undergo evaluation for epilepsy surgery [1]. The cohort included 437 children, of whom 71 children were younger than 3 years at the time of referral for surgery. The baseline patient demographics and epilepsy characteristics were compared between children who were referred at a younger age ($\leq$3 years) and those referred after 3 years age. Pre-surgical evaluation strategies, including MRI findings and ancillary testing used if any, were reported and compared between these two groups. The type of surgery, intent of procedure (definitive or palliative), need for invasive monitoring and surgical outcomes were recorded for those who underwent surgery. The investigators identified abnormal neurological examinations (p=0.002) and imaging findings (p=0.042), frequency of seizures (p=0.01) and proximity to referral centres (p=0.05) as factors which contributed to early referral in the younger age group. 85% of the children who were evaluated for surgery had focal onset seizures, with 71% having abnormal MRI. The most commonly identified etiology was structural (multilobar and hemispheric malformations (55%) and unilobar abnormalities (45%)). In the younger age group, use of ancillary testing was less frequent compared to older children, with 48% of the group having only MRI/EEG testing. The utility of tests such as positron emission tomography, among others, was noted to be higher for children with normal MRI or those without circumscribed malformations. It was noted that there was no difference in the rates of surgery between the two groups; but the younger age group more often underwent larger procedures such as hemisperectomy. Among those referred for surgery at $\leq$3 years, 11 children had normal MRI of whom only 1 was offered surgery. Among the children who had onset of seizures at <3 years (n=202), 176 (87%) had drug resistant epilepsy (DRE) at the time of referral. The investigators sought to compare the characteristics of those with early DRE diagnosis (<3 years) to those with later DRE diagnosis among children with early epilepsy onset and found no significant differences. Factors that contributed to delay in surgical referral (defined as > 1 year after DRE diagnosis) among those with early onset DRE (n=79) were found to be abnormal neurological examinations and generalized or focal aware seizure types and the intent of referral was mostly for palliative procedures. Thirty four patients <3 years old underwent surgery. The type of surgery offered was more often focal resection and the mean follow-up post-surgery was 23 months (4-40 months). Favourable outcomes were identified in a significant proportion of the cohort, with Engel class I outcomes in 59% and class II in 18%. Surgical complications or developmental outcome following surgery were not analysed in the study.

The investigators concluded that surgery is effective but may be disproportionately offered to children with severe presentations, as those with normal MRI and better neurological status had lower rates of referral for surgery. They attribute this to lower utilization of ancillary testing and recommend further studies into the prevalence of nonlesional DRE.

Commentary

Drug resistant epilepsy occurs in 35-65% of children with epilepsy <3 years old and contributes to significant morbidity and health care burden. Epilepsy surgery can result in seizure freedom in appropriately chosen candidates and can improve developmental outcomes. Previous retrospective studies have shown that seizure-free survival can be attained in 50-80% children who undergo resective surgeries for DRE, with positive or static effects on cognitive outcomes [2, 3]. A single centre randomized control trial performed at a tertiary care institute in India compared seizure freedom and quality of life in children under 18 years with DRE [4]. It was found that 77% in the surgery group attained seizure freedom at 12 months versus 7% in the medically treated group. A retrospective study from Japan that reported the surgical and developmental outcome in children under 3 years who underwent epilepsy surgery over a period of 13 years, concluded that seizure freedom was attained in 82%

of children, with nearly 30% of them completely stopping anti-seizure medications by their last follow up [5]. Another retrospective study on the developmental outcome after epilepsy surgery in infancy reported that patients who were operated on at younger age and with epileptic spasms showed the largest increase in developmental quotient after surgery [6]. Few prospective studies exist that evaluate patient characteristics and surgical techniques in children <3 years. The present study, with a prospective design and large study population, captures the pre-surgical evaluation in this younger cohort comprehensively. Barriers to early referral include seizure types such as focal aware and generalized seizures and abnormal neurological status at baseline. The routine and ancillary testing used for evaluation, types of surgery performed, and invasive monitoring used during surgery were described in detail. Those children with DRE, normal MRIs and less severe seizures were under-represented in the cohort. Significant heterogeneity is likely between centres regarding factors that determine time delay, time points of intervention and decision making with regard to ancillary tests. The effect of completeness of resection or disconnection as evident from MRI, utility of intra-operative electrocorticography and the value of post-operative EEG as predictors of seizure free outcome cannot be gauged from the current study. Given the multicentre design of the study, longitudinal epilepsy, cognitive and quality-of-life outcomes up to the period of transition into adulthood are potential data that can be anticipated from this study group. Post-surgical assessment of developmental outcome as well as data on surgical complications would have added to the understanding of efficacy and safety of epilepsy surgery in the younger age group under 3 years. Further studies are required to evaluate the effect of surgery in non-lesional DRE. The study highlights the necessity for prompt referral of young children with DRE for comprehensive evaluation and potentially remediable epilepsy surgery given the debilitating seizures that often present in this group with consequences on neurological, particularly long-term development outcomes. Its utility in children with ostensibly 'non-debilitating' seizure subtypes with respect to anti-seizure medication reduction or cessation, cognition and quality of life needs to be prospectively understood. This will help prevent 'referral hesitancy' among pediatricians and neurologists as well as help to reduce the treatment gap among infants and toddlers with surgically remediable syndromes.

Competing interests

The authors have declared that no competing interests exist.

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