Epilepsy & Behavior 83 (2018) 131–136

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Impact of resective epilepsy surgery on health-related quality of life in children with and without low intellectual ability

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ARTICLE INFO

Article history:
Received 3 March 2018
Revised 28 March 2018
Accepted 28 March 2018
Available online xxxx

Keywords:
Quality of life
Pediatric epilepsy surgery
Developmental disability
Domain-specific

ABSTRACT

Objective: The current study examined pre- and postoperative health-related quality of life (HRQL) across children with and without low intellectual ability. We also aimed to clarify the literature on postsurgical change by assessing domain-specific HRQL pre- and postoperatively in children with drug-resistant epilepsy.
Method: All patients (n = 111) underwent resective epilepsy surgery between 1996 and 2016 at the Hospital for Sick Children in Toronto, comparing baseline and 1-year follow-up HRQL with the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-76). At the group-level, postsurgical change in HRQL was examined through linear mixed-effects modeling. Clinically important change in HRQL at the individual level was quantified using a standard error of measurement (SEM)-based criterion, and estimates were stratified by intellectual ability.
Results: Children with epilepsy and low intellectual ability had lower overall HRQL compared with those with normal intelligence ($b = -10.45$, $SE = 4.89$, $p = .035$). No differences in change in HRQL related to intellectual level were found. In the broader sample, significant postoperative improvements were found for HRQL related to physical activity ($b = 8.28$, $SE = 1.79$, $p < .001$), social activity ($b = 15.81$, $SE = 2.76$, $p < .001$), and behavior ($b = 4.34$, $SE = 1.35$, $p = .001$). Postoperative improvements in physical and social HRQL were associated with better seizure control ($p = .011$). Conversely, cognitive and emotional domains of HRQL did not improve one year postoperatively, even in the presence of improved seizure control.
Significance: Results suggest that children with low intellectual ability can expect to achieve similar improvements in HRQL after epilepsy surgery compared with those with normal intelligence. Further, while overall HRQL is shown to improve in children following epilepsy surgery, domain-specific change is nuanced and has important implications for health practitioners aiming to monitor treatment progress of patients.

1. Introduction

Health-related quality of life (HRQL) is a broad, multidimensional construct that captures the functional impact of an illness and its consequent treatment on a patient, as perceived by the patient, encompassing physical, psychological, and social well-being [1]. Since its recognition as a key measurement for evaluating treatment efficacy by the International League Against Epilepsy (ILAE) Epidemiology Commission [2], HRQL has been increasingly included as an important patient-reported outcome in research examining the impact of epilepsy surgery.

Beyond seizure control and a subset of seizure-related factors, few studies to date have examined the influence of other categories of variables on HRQL outcomes in pediatric epilepsy surgery [3]. More broadly, recent research has highlighted the dominant effects of child and family variables on HRQL outcomes in children with epilepsy, relative to seizure-specific factors [4,5]. However, with the exception of child mood and affective symptoms [3], these variables have yet to be explored in pediatric surgical samples, despite the potential implications for improving prognostication, informing presurgical counseling, and identifying targets for perioperative interventions.

Intellectual disability (ID) is present in 21–40% of children with epilepsy while approximately 30% are found to have mild or subtle cognitive problems [6–9]. Recognizing the harmful effects of early and recurrent seizures on a child's cognitive development [10,11], the potential of early surgical intervention to reduce or prevent further cognitive decline has been explored [12–14]. Findings suggest that, with respect to seizure control, children with low intelligence quotient (IQ) (defined as IQ < 70) obtain similar postoperative surgical outcomes to those with normal intelligence [13,15]. Further, early surgical intervention offers hope to yield improvements in the developmental velocity of cognitive abilities, emphasizing the enhanced potential for functional reorganization and recovery in the developing brain

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https://doi.org/10.1016/j.yebeh.2018.03.036
1525-5050/

[12,16]. Relatedly, studies examining cognitive outcomes from a longer-term perspective (4–11 years [17] and 5–15 years [18] after pediatric epilepsy surgery) suggest that children with lower preoperative IQ are more likely to show a greater increase in IQ relative to those with higher preoperative IQ in long-term follow-up.

While children with epilepsy and ID appear to benefit from early surgical intervention, a related literature suggests that cognitive problems are an important determinant of child HRQL as well as a driving force behind deterioration overtime [19,20]. Independent of seizure frequency and number of antiepileptic drugs (AEDs), parents of children with drug-resistant epilepsy and ID were found to report lower overall and domain-specific child HRQL, compared with the parents of those with normal intelligence [21]. Despite the identification of HRQL as an important outcome measure for assessing treatment efficacy, no studies to date have examined the impact of epilepsy and low IQ on postsurgical change in HRQL. It remains unclear whether children with low IQ will achieve similar gains in HRQL after epilepsy surgery compared with those with normal intelligence.

Few studies to date have compared presurgical and postsurgical data to quantify the impact of pediatric epilepsy surgery on child HRQL [22–27], a necessary condition to determine whether patients improve, decline, or experience no change in HRQL after surgery [3]. Of these studies, three [25–27] utilized an epilepsy-specific measure of HRQL that is well-validated in the literature, the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE). Overall, improved seizure control (both complete seizure control [26] and "worthwhile improvement" in seizure outcome [25]) has been associated with significant improvements in overall HRQL while findings regarding which domains improve after surgery are equivocal. These discrepant results are likely a function of methodological limitations across the limited number of available studies, including variability in duration of follow-up and small sample sizes.

To address these gaps in the literature, the current study examined pre- and postoperative HRQL in children with and without low intellectual ability while accounting for seizure outcome. As a secondary objective, we aimed to clarify the emerging literature on postsurgical change by assessing domain-specific HRQL pre- and postoperatively in the largest sample of children with epilepsy to date.

2. Methods

2.1. Participants

All patients underwent resective epilepsy surgery between 1996 and 2016 at the Hospital for Sick Children in Toronto, Ontario. Prior to undergoing presurgical evaluation, participants had failed to achieve seizure freedom with adequate trials of two or more tolerated and appropriately chosen antiseizure medications, which was confirmed by the child's treating neurologist. Only children who had (1) available HRQL data (as assessed by the QOLCE-76 [28,29]) both prior to surgery and at 1-year follow-up and (2) assessment of preoperative Full Scale Intelligence Quotient (FSIQ) using the age-appropriate Wechsler Intelligence Scale were included in the study. Exclusion criteria included hemispherectomy and corpus callosotomy as those requiring hemispherectomy commonly have significant deficits (e.g., hemiplegia, visual field deficits) even before surgery that could compromise their HRQL independently of seizures and low intellectual ability, and corpus callosotomy is performed for palliative (e.g., to alleviate drop attacks) rather than curative (i.e., to eliminate seizures) purposes.

All patients completed a neuropsychological assessment during evaluation for surgical candidacy (baseline) and were additionally assessed one year following surgery (follow-up) as part of routine care. Data for baseline and follow-up visits were extracted from patients' clinical records. The study received approval from the research ethics board of the Hospital for Sick Children.

Data from approximately 10% of the patients in the current sample have been included in other publications on HRQL in children with drug-resistant epilepsy [5,30,31].

2.2. Measures

Children's HRQL was assessed using the original (Australian) version of the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-76) [28,29]. The QOLCE-76 is a 76-item parent-rated epilepsy specific instrument comprised of five main domains: physical activity (physical restrictions and energy/fatigue), cognition (attention/concentration, memory, language, and other cognition), well-being (depression, anxiety, control/helplessness, and self-esteem), social activity (social interactions, social activities, and stigma), and behavior. The composite HRQL score is the unweighted average of 16 QOLCE-76 subscales (those listed previously and two global items related to general health and quality of life), ranging from 0 to 100. Higher scores indicate better HRQL. The QOLCE-76 has good validity and reliability [28,29].

The FSIQ of all patients was assessed using the age-appropriate version of the Wechsler Intelligence Scale. Intellectual ability was operationalized as a binary variable with levels of normal intelligence (FSIQ ≥ 70) vs low intellectual ability (FSIQ < 70). Further, surgical outcome was quantified using the ILAE classification of seizure outcome following epilepsy surgery [32] and operationalized in two ways: as seizure-free (ILAE I) vs continued seizures (ILAE II–VI) and as improvement (ILAE I–III) vs no improvement (ILAE IV–VI).

2.3. Statistical analyses

All analyses were conducted using R (version 3.1.0 for Windows). Descriptive statistics used to describe the sample included mean and standard deviation for continuous measures and frequency and percentages for categorical variables. Between-group differences across children with and without low intellectual ability were examined using independent samples *t*-tests, Pearson's chi-square, or Fisher's exact test, as appropriate, for all demographic and epilepsy-related variables.

To examine pre- and postoperative HRQL in children with and without low intellectual ability, we conducted a linear mixed-effects model with intellectual ability, surgical outcome (seizure-free vs continued seizures or improvement vs no improvement), and time (baseline vs 1-year follow-up) as fixed effects and time by intellectual ability, time by surgical outcome, and intellectual ability by time by surgical outcome as interaction terms. Backwards selection, such that higher order interactions were sequentially removed from the model if $p > .05$, and an unstructured covariance matrix were used. Significant interactions were followed with simple effects analyses. We further examined clinically important change in HRQL at the individual level utilizing a standard error of measurement (SEM)-based criterion and stratified estimates by intellectual ability status. When employing psychometrically robust measures of HRQL, scores of at least one SEM are considered to represent clinically important intraindividual changes in HRQL [19,33]. Previously published SEM values for the QOLCE-76 composite and domain scores in children with drug-resistant epilepsy were utilized [30]. Change at the individual level was evaluated using χ^2 or Fisher's exact test, as appropriate.

Further, to clarify discrepancies in the literature regarding domain-specific change in HRQL after surgery, linear mixed-effects models using unstructured covariance matrices were fit for the outcomes of physical activity, cognition, well-being, social activity, and behavior. Surgical outcome (seizure-free vs continued seizures or improvement vs no improvement) and time (baseline vs 1-year follow-up) were entered as fixed effects and time by surgical outcome as an interaction term. Sidak corrections [34,35] were used for pairwise comparisons, and significant interactions were followed with simple effects analyses.