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Any Way You Slice It: Corpus Callosotomy in Pediatric Drug-Resistant Epilepsy

A Multi-Center Comparison of Surgical Techniques for Corpus Callosotomy in Pediatric Drug-resistant Epilepsy

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Objectives: Corpus callosotomy (CC) is used to reduce seizures, primarily in patients with generalized drug-resistant epilepsy (DRE). The invasive nature of the procedure contributes to underutilization despite its potential superiority to other palliative procedures. The goal of this study was to use a multi-institutional epilepsy surgery database to characterize the use of CC across participating centers. Methods: Data were acquired from the Pediatric Epilepsy Research Consortium (PERC) Surgery Database, a prospective observational study collecting data on children 0-18 years referred for surgical evaluation of DRE across 22 U.S. pediatric epilepsy centers. Patient, epilepsy, and surgical characteristics were collected across multiple CC modalities. Outcomes and complications were recorded and analyzed statistically. Results: Eighty-three patients undergoing 85 CC procedures at 14 participating epilepsy centers met inclusion criteria. Mean age at seizure onset was 2.3 years (0-9.4); mean age for Phase I evaluation and surgical intervention were 9.45 (.1-20) and 10.46 (.2-20.6) years, respectively. Generalized seizure types were the most common (59%). Complete CC was performed in 88%. The majority of CC procedures (57%) were via open craniotomy, followed by laser interstitial thermal therapy (LiTT) (20%) and mini-craniotomy/endoscopic (mc/e) (22%). Mean operative times were significantly longer for LiTT, whereas mean estimated blood loss was greater in open cases. Complications occurred in 11 cases (13%) and differed significantly between surgical techniques ($p < .001$). There was no statistically significant difference in length of postoperative stay across approaches. Mean follow-up was 12.8 months (range 1-39). Favorable Engel outcomes were experienced by 37 (78.7%) of the patients who underwent craniotomy, 10 (58.8%) with LiTT, and 12 (63.2%) with mc/e; these differences were not statistically significant. Significance: CC is an effective surgical modality for children with DRE. Regardless of surgical modality, complication rates are acceptable and seizure outcomes generally favorable. Newer, less-invasive, surgical approaches may lead to increased adoption of this efficacious therapeutic option for pediatric DRE.

Commentary

It is recognized that prompt referral to a comprehensive epilepsy center for surgical evaluation is strongly recommended for patients with refractory epilepsy who may be deemed surgical candidates.[1] However, delays in referral and prolonged time to an ultimate surgical procedure remains a major issue, during which time injurious seizures occur, quality of life is reduced, and risk of sudden unexpected death in epilepsy remains elevated.[2,3] Multiple factors are associated with delayed referral for surgery, not only in the identification of potential surgical candidates but also on the part of the patient or family, particularly hesitancy to undergo epilepsy surgery. This is abundantly clear when it comes to pediatric epilepsy, where there can be significant resistance regarding discussion about epilepsy surgery.[4]

Corpus callosotomy (CC) is traditionally considered a palliative disconnection procedure targeting injurious, refractory drop seizures. With advances in surgical techniques and increasing adoption of minimally invasive epilepsy surgery, the prospect of less invasive options such as mini-craniotomy/endoscopy (mc/e) approaches and laser interstitial thermal therapy (LiTT) are highly appealing, particularly when it comes to CC, a procedure which has the potential for high

surgical morbidity and typically is reserved for when all else has failed to control a patient's seizures.

Hansen and colleagues[5] performed an observational cohort study of data obtained from the Pediatric Epilepsy Research Consortium surgery database on pediatric patients undergoing epilepsy surgery with CC comparing open callosotomy versus less invasive callosotomy with mc/e and LiTT. The authors looked at operative course including type of procedure, length of surgery, blood loss, postoperative complications, length of hospital stay, readmission rates, and seizure outcomes based on Engel classification to assess if minimally invasive methods are as effective compared to open CC.

Of the 83 patients undergoing CC, most underwent open CC (57%) compared to LiTT (20%) and mc/e (22%). Most children had generalized seizures, although 42% reported a focal semiology. Surprisingly, only 28.9% of the patients in the cohort were experiencing tonic or atonic seizures. Ninety percent of the cohort were reported to have baseline abnormal neurologic examination findings with 86.7% of the cohort having cognitive or developmental delay. There was no information provided on the specific epilepsy syndromes encountered in this series, but one must assume that a number of the patients had Lennox-Gastaut syndrome, however, this is unknown. Operative time was significantly different between the groups, with LiTT CC being a significantly longer procedure. Additionally and not unexpectedly, blood loss was significantly greater in the open CC group compared to the less invasive techniques. Complications were seen in 11 (13%), mainly and statistically significantly in the open CC group, consisting of transient motor weakness, feeding intolerance, respiratory distress, wound infection, meningitis, intracranial abscess, postoperative hydrocephalus, spinal fluid leak, and pneumonia. Disconnection syndrome was not reported as a complication in this series. Five patients in the open group had readmission within 30 days postoperatively for unknown reasons. Favorable seizure outcomes, classified as Engel class I-III were not significantly different between the groups ($P = 0.495$), however, quantitatively were higher in the open CC group (78.7%) versus LiTT (58.8%) and mc/e (63.2%). At last follow-up, 31 children (37.3%) achieved more than 90% seizure reduction (Engel class I and II).

This case series of major U.S. pediatric epilepsy centers shows that less invasive CC techniques are emerging as potential options for pediatric epilepsy surgery. While not significantly different in terms of seizure outcomes, operative morbidity was certainly higher, particularly postoperative complications and the need for hospital readmission, in the open CC group. Interestingly, the length of postoperative hospital stay was not significantly different between the 3 groups perhaps implying that rather than surgical technique determining postoperative recovery, a CC requires similar recovery regardless of how it was performed. As the details regarding postoperative stay were not available, this question remains. These findings are interesting and highlight the need to continue to evaluate the safety and efficacy of CC approaches in the pediatric population.

There are several limitations to this current series. The level of expertise and surgical volumes at a given center should be considered. Two of the hospitals performed over one-third of the procedures in the series, indicating that this series is highly reflective of those centers that contributed the most patients, which may have skewed the results. Based on the range of procedures performed by each center over a 4-year period, at least one center only had one CC during this time, which could be argued is not enough volume to maintain surgical mastery or to develop expertise in newer, less invasive techniques. The lower surgical volumes for pediatric epilepsy surgery did result in this study being underpowered to make meaningful comparisons between the different groups. Additionally, the statistical methods did not account for analysis of multiple comparisons nor were methods such as regression modeling or propensity score analysis utilized for comparative effectiveness assessment of the observational data. Among these 14 major pediatric epilepsy centers, minimally invasive CC was only available at 8 centers. This raises the question of access. We know that delays for referral to epilepsy surgery occur for several reasons, but limited access to care and health care disparities are another major potential cause for underutilization of epilepsy surgery.[6,7] If these less invasive techniques prove to be as effective but with less perioperative morbidity compared to open CC, but are only available at a very limited number of centers, then the goal should be to not only increase adoption of these techniques but also further increase patient access to care. This brings us to the next point, which is earlier referral for CC. If there is more ready access to minimally invasive CC, then certainly families may be more willing to go down this route earlier in the epilepsy course and providers may consider discussing CC earlier than they otherwise would. Additional research may be helpful in determining which patients are the best candidates for minimally invasive CC and who would best be served by open CC.

The seizure outcomes and rates of complications seen in this series were similar to what has previously been reported in the literature.[8,9] This series is a starting point for further studies of the safety and efficacy of less invasive epilepsy surgery in children. Future studies will need to be powered to make meaningful comparisons between surgical techniques and perform comparative effectiveness analyses in order to hopefully demonstrate that pediatric epilepsy surgery should be considered another treatment option rather than a therapy of last resort.

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Declaration of Conflicting Interests

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