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Corpus callosotomy in children with intractable epilepsy using frameless stereotactic neuronavigation: 12-year experience at The Hospital for Sick Children in Toronto

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Object. Although corpus callosotomy has been used effectively since the late 1930s to treat severe, medically intractable seizure disorders, particularly atonic or drop-attack seizures, controversy remains as to when, how, and how much surgery should be performed. Intraoperative determination of the extent of callosotomy, the need to stage the procedure, and the side of the interhemispheric approach represent technical issues that remain debatable. The authors report the 12-year experience of the senior author as well as surgical outcomes with corpus callosotomy using a frameless stereotactic neuronavigation system (ISG View Wand and BrainLab).

Methods. Thirteen consecutive children at The Hospital for Sick Children underwent single-stage corpus callosotomy for medically intractable seizures. The mean age was 10.3 years. Five children underwent partial callosotomy, and 8 underwent complete callosotomy. The side of operative approach to avoid large parasagittal bridging veins was determined by preoperative study of 3D MR imaging/MR venography reconstructed by the neuronavigation system. The extent of callosotomy was determined using intraoperative feedback from the neuronavigation system and postoperative MR imaging.

Results. The extent of callosotomy determined by intraoperative neuronavigation and postoperative MR imaging correlated closely in all cases. There were no operative deaths. There was no significant postoperative morbidity related to venous infarction. Four of 5 patients in the partial callosotomy cohort and 7 of 8 patients in the complete callosotomy cohort showed significant improvement in seizure control.

Conclusions. The use of frameless stereotactic neuronavigation is a safe, effective, and important surgical adjunct in the planning and execution of successful corpus callosotomy in children with intractable epilepsy.
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Key Words • **corpus callosotomy** • **neuronavigation** • **pediatric epilepsy**

Children with recurrent and intractable epilepsy frequently suffer from developmental, neurological and cognitive delay, and run the risk of personal injury from falls through sudden loss of consciousness from rapid ictal discharges. The latter is particularly common in children with atonic, or drop-attack seizures. In these children, surgical treatment in the form of corpus callosotomy may be considered despite its associated risks.

Atonic seizures typically arise from multifocal, nonlocalizable, and unresectable epileptic discharges. Callosotomy, although not curative, may reduce the rapid generalization of the ictal onset zone, and prevent harmful drop attacks from occurring.[8,16,18,20,23,25,28] Several reports have attested to the value of corpus callosotomy as a palliative procedure to improve the quality of life of children with intractable, generalized epilepsy where one of the main seizure types is drop attacks. Sectioning of the corpus callosum, in very simple terms, will very nearly disconnect the 2 cerebral hemispheres anatomically. Early approaches to callosotomy consisted solely of sectioning of the entire corpus callosotomy. However, more recently, several intriguing consequences of sectioning the corpus callosum have been reported in the literature, and these have been termed the "disconnection syndromes."[10]

The advent of partial callosotomy was an attempt to obtain the surgical benefits of seizure control without the complication of disconnection syndromes. Since then, there has been controversy as to which procedure is most effective. No randomized studies addressing this matter have been published. The inherent difficulty in intraoperative determination of the extent of partial callosotomy

Abbreviations used in this paper: CSF = cerebrospinal fluid; EEG = electroencephalography.

TABLE 1

Demographics and operative data in 13 patients undergoing corpus callosotomy

Case No.	Age (yrs), Sex	Side of Craniotomy	Extent of Callosotomy	Cause of Seizure	Secondary Seizure Type	FU (mos)	Complications	Seizure Outcome†	
								Primary	Secondary
1	15, F	rt	complete	Lennox–Gastaut Syndrome	myoclonic, tonic, tonic–clonic	69	none	5	3
2	10, F	lt	complete	unknown	generalized tonic–clonic	48	none	4	4
3	8, M	rt	partial	tuberous sclerosis	generalized tonic–clonic	61	infected bone flap, CSF leak	4	3
4	10, F	rt	partial	Lennox–Gastaut Syndrome	tonic	106	none	4	1
5	11, M	rt	complete	cerebral palsy	generalized tonic–clonic, absence	57	none	4	4
6	10, F	lt	complete	Lennox–Gastaut Syndrome	generalized tonic–clonic	81	none	5	1
7	6, M	rt	partial	Lennox–Gastaut Syndrome	generalized tonic–clonic, absence	99	none	3	1
8	8, F	rt	partial	congenital CMV infection	tonic, myoclonic, absence	43	none	4	4
9	11, F	rt	partial	unknown	versive, tonic	11	none	5	1
10	8, M	rt	complete	unknown	none	19	subgaleal collection, noninfected	5	4
11	14, F	lt	complete	Lennox–Gastaut Syndrome	generalized tonic–clonic, absence	2	none	5	4
12	5, F	rt	complete	tuberous sclerosis	absence, tonic–myoclonic	2	none	3	1
13	12, M	lt	complete	hypoxic ischemic encephalopathy	myotonic, clonic	2	none	4	4

* CMV = cytomegalovirus; FU = follow-up.

† See the grading system in Table 2.

using visual inspection and landmarks alone may contribute to the lack of strong evidence. The use of an intraoperative neuronavigation system that can accurately determine the extent of resection may therefore settle the controversy and improve surgical outcomes.

For the past 12 years, the senior author (J.T.R.) has used frameless stereotactic neuronavigation to determine favorability for side of approach based on location of parasagittal bridging veins and extent of callosal sectioning. In the present report, we describe the senior author's surgical results and lessons learned from a series of 13 patients using this technique over a 12-year period.

Clinical Material and Methods

Patient Population

Between 1996 and 2008, 13 consecutive patients (age range 5–15 years [mean 10.3 years]) underwent corpus callosotomy assisted by frameless stereotactic neuronavigation for epilepsy at The Hospital for Sick Children (Table 1). All patients had been examined and treated preoperatively for variable durations by the multidisciplinary epilepsy team. All patients were considered refractory to medical treatment prior to neurosurgical referral and had undergone a complete investigative workup to rule out lateralizable and localizable epilepsy including EEG, MR imaging, and admission to the Epilepsy Monitoring Unit.

The patient population consisted of children with a primary seizure disorder characterized predominantly by drop attacks. The primary seizure disorder for all patients was drop attacks. Secondary seizure types were most commonly generalized tonic-clonic, tonic-myoclonic, and absence seizures. Lennox-Gastaut syndrome was the most common underlying diagnosis, which was seen in 5 patients overall, with tuberous sclerosis seen in 2 patients, and hypoxic-ischemic injury, congenital cytomegalovirus infection, and cerebral palsy deemed the underlying cause in one patient each. Three patients did not have a known diagnosis. Patients with significant functional language underwent anterior two-thirds partial callosotomy, and patients with no functional language underwent complete callosotomy. A Wada test was not routinely performed in this group of patients, of whom a significant number were severely developmentally delayed.

An intraoperative neuronavigation system (ISG View Wand, ISG Technologies; or BrainLab, BrainLab AG) was used. The MR imaging/MR venography studies with Gd were performed within 2-4 weeks of scheduled surgery. Archived images were then reformatted and displayed in axial, coronal, and sagittal planes. The 3D MR imaging/MR veinography was then used to locate large, and presumably important, cortical bridging veins that would limit the size of the interhemispheric operative window, especially in the parasagittal paracentral region of the brain. Based on this information, the more favorable side of midline was chosen for the operative approach.

Operative Technique

A craniotomy and microsurgical interhemispheric approach was performed in the usual manner. Once the corpus callosum was exposed, the extent of corpus callosotomy to be sectioned was determined and marked by frameless stereotaxy. Five patients underwent partial callosotomy, and 8 had complete callosotomy.

Postoperative Follow-Up

The mean follow-up was 46 months. All patients were followed by the same epilepsy team at The Hospital for Sick Children and were assessed with respect to immediate postoperative complications, long-term complications, and seizure control. Neuropsychological testing was not performed in every case. A significant number of patients were severely developmentally delayed that precluded standard neuropsychological testing. Therefore, assessment of postoperative disconnection syndromes was limited in our study.

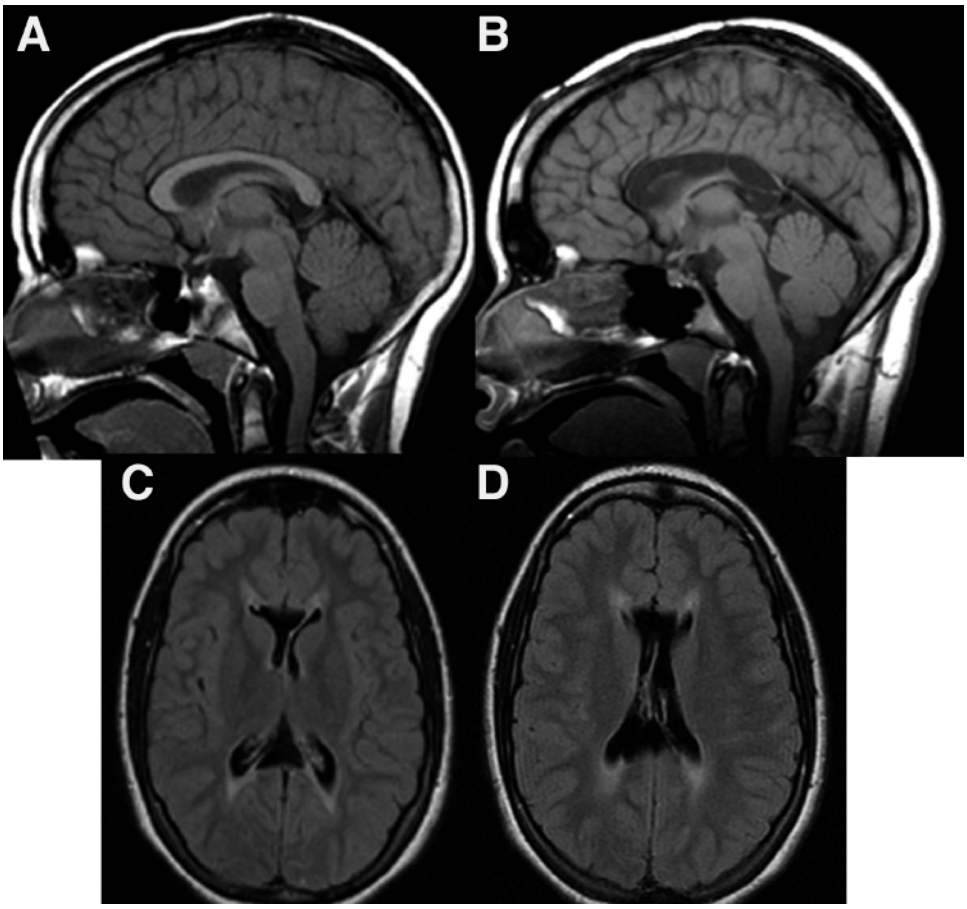

FIG. 1. Magnetic resonance images. a: Sagittal T1-weighted image showing the intact corpus callosum (a). Sagittal T1-weighted (b) and axial FLAIR (c and d) images postcallosotomy demonstrating complete absence of the corpus callosum.

Postoperative MR images were obtained in every case to confirm extent of callosotomy (Fig. 1). Seizure control was assessed using a previously described grading system (Table 2).[9]

Results

Surgical Complications

Only 2 surgical complications were observed in the series. One patient developed a wound infection with an infected bone flap; this patient also developed a CSF leak at the incision site that ceased after lumbar CSF drainage. Another patient developed a large subgaleal collection at the craniotomy site; it was not infected and needle drainage of this was performed without complication. No patient died. The presence of postoperative disconnection syndromes could not be reliably assessed.

Surgical Technique

The majority of cases were approached from the right side due to venous anatomy. Postoperative MR imaging showed excellent concordance with the extent of callosotomy shown by frameless stereotaxy in all cases. There were no unplanned returns to the operating room to complete a callosotomy based on radiographic findings.

Seizure Control

Significant benefit (Grade 4 or 5) was observed with respect to atonic seizures in both the partial and complete callosotomy groups. Four of 5 patients who underwent anterior two-thirds callosotomy achieved good seizure control, and 7 of 8 patients undergoing total callosotomy exhibited these results. Patients in the partial callosotomy

TABLE 2

Grading system used to evaluate postoperative seizure control after corpus callosotomy

Seizure Grade	Postop Status
5	no residual seizures
4	significant improvement in seizures > 75%, consisting of: patient does not require helmet use, improvement in anticonvulsant management, increase in activity of daily living/speech
3	some improvement in seizures but not to the level of grade 4; may involve improvement in seizure severity or mild improvement in frequency
2	no change in seizure pattern, severity, or frequency
1	worsened seizures, or new seizure type

group did not benefit as much when considering secondary seizure control: only 1 such patient achieved good seizure control. By contrast, 5 of the 8 patients who underwent complete callosotomy derived secondary seizure benefit. No patients experienced worsening of their atonic seizures after surgery compared with their preoperative state; however, 5 patients developed worsening frequency or new secondary seizure semiology after corpus callosotomy. One patient underwent completion callosotomy 7 years after initial partial callosotomy; this patient continued to have medically intractable seizures, and vagal nerve stimulator therapy failed.

Discussion

Dandy[3] approached a congenital cyst of a cavum septum pellucidum and cavum vergae in a 4.5-year-old boy in 1931, by sectioning the corpus callosum. In addition to the original aim of the surgery, he unintentionally freed his patient from a seizure disorder and set the stage for a new treatment modality for epilepsy. Van Wagenen and Herrin[29] ushered in the era of commissurotomy for the treatment of clinically refractory epilepsy with the report of their initial series of 10 patients in whom corpus callosotomy was performed between February and May 1939. Over the ensuing decades, several series have reported seizure outcomes which vary widely, but in general do not show enviable seizure control outcomes.[5] The only seizure type for which a demonstrable benefit has been reliably shown following callosotomy is the drop attack.[8,16,18,20,23,25,28]

Extent of Callosal Resection

The extent of callosal resection has long been the subject of debate among epilepsy surgeons. In the past, complete corpus callosotomy also included resection of a fornix, the anterior commissure, and the hippocampal commissure; this degree of resection led to a high rate of morbidity.[28] Various modifications, including partial and staged sectioning of the corpus callosum, evolved to ameliorate the high complication rate.

A partial callosotomy involves sectioning of the anterior two-thirds of the corpus callosum from the border of anterior commissure up to the splenium, preserving this important structure. Partial callosotomies are thought to decrease the incidence of disconnection syndromes by sparing the splenium. Posterior sectioning of the corpus callosum alone is ineffective, even when the EEG abnormalities are posteriorly located.[28] The resection in a complete callosotomy is carried through the splenium to the arachnoid of the quadrigeminal cistern; the vein of Galen may usually be seen through this arachnoid.

Oguni et al.[16] showed that sectioning of the anterior two-thirds of the corpus callosum had a better seizure control outcome, rather than sectioning of only the anterior half. Spencer et al.[27,28] showed 100% seizure control, either cure or marked dimunition with $>$ 80% decrease, after anterior callosotomy for atonic seizures and 83% seizure control for tonic-clonic seizures. However patients with at least 2 seizure types, verbal IQ $<$ 80, and diffuse ictal EEG patterns had poor outcomes with anterior callosotomies alone, suggesting more diffuse cerebral involvement and encompassing both anterior and posterior cortical regions.[28] For example, complete corpus callosotomy is more efficient than partial callosotomy in children after West syndrome and with bihemispheric malformations of cortical development.[12,20]

Spencer et al.[27,28] showed a 68% seizure control rate after complete callosotomy for tonic-clonic seizures and a 57% seizure control rate for tonic seizures. Of the patients in whom anterior callosotomy failed, 60 and 50% had improved seizure outcomes after complete callosotomy for tonic-clonic and tonic seizures, respectively. It has therefore been shown to be efficacious in taking patients back for completion of a partial callosotomy after failure for tonic and tonic-clonic seizures. Rahimi et al.[21] thought that a complete callosotomy is the most effective treatment for secondary generalized seizures. More recent data have suggested starting with anterior callosotomy for atonic and idiopathic epilepsy consisting of nonlesional generalized tonic-clonic, absence, or myoclonic seizures.[11]

Neuropsychological sequelae in the form of disconnection syndromes may be more pronounced if complete corpus callosotomy is performed. These sequelae are attenuated if some of the corpus callosum, particularly the splenium, is preserved, or if the complete callosotomy is performed in 2 stages, allowing for some neurological recovery between stages, especially in older children with normal to moderately impaired intelligence.[12,28]

Total callosotomy may be conducted for prepubescent children and severely delayed older children with little negative clinical sequelae.[16] It has been suggested that interhemispheric communication is not impaired in cases in which the corpus callosum is absent early in life, whether in the setting of callosal agenesis or due to early callosotomy.[12,15,20] Total callosotomy performed before puberty is not followed by permanent deficits of disconnection syndromes; instead, greater cognitive and social gains may be seen in these children.[14,24]

Our results show that patients in both callosotomy groups achieved improved seizure control with 80% of patients in the partial callosotomy group and 87.5% in the complete callosotomy group showing durable long-term atonic seizure control.

Image Guidance

Image-guided frameless stereotactic sectioning of the corpus callosum has been demonstrated to be an important adjunct in the planning and performing of the procedure in this and other series (Fig. 2).[9] The side of the approach and size of the craniotomy may be determined on the basis of favorability of the bridging veins with respect to the extent of the callosotomy. The extent of the callosotomy may be determined by intraoperative feedback from the neuronavigation device. Traditional operative approaches to partial sectioning of the corpus callosum involve guidance through visual inspection of intraoperative landmarks, such as the Monro foramen , the use of surgical patties or titanium clips to measure the length of the callosum prior to or after sectioning, and/or complicated measuring strategies based on preoperative MR imaging. Image-guidance has improved the accuracy of planned partial callosal resections.

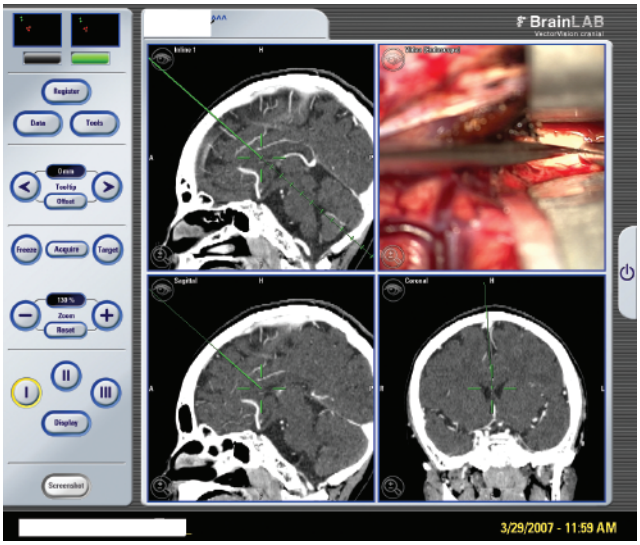

FIG. 2. Screen capture of frameless stereotactic neuronavigation station showing identification of the midline on loaded MR imaging and corresponding intraoperative exposure.

Other Surgical Alternatives and Adjuncts

Radiosurgical ablation of mesial temporal structures for intractable temporal lobe epilepsy was first reported by Regis et al.[22] in 1995. Leksell designed the Gamma Knife for functional neurosurgery and realized that a potential target could be epileptic foci; however, exactly how the irradiation reduces seizure activity is unclear. Since then, the indications for the application of radiosurgery in epilepsy patients have increased with a variable rate of success.[13,17]

Radiosurgical corpus callosotomy may be a promising safe and noninvasive alternative to open callosotomy.[1,4,6,19,26] This modality of treatment can be used in situations where patients have more than 2 seizure types and after a failed partial callosotomy. Small case series and individual case reports have claimed that the noninvasive nature of radiosurgery may serve to avoid transient and permanent surgical morbidity, including the disconnection syndromes, related to surgical manipulation, frontal lobe retraction, and venous injury. These same small reports noted no signs of postradiosurgical side effects in short-and long-term follow-up. However, the true risk of induction of secondary malignancy is unknown. Also, a complete callosotomy cannot be performed in a single radiosurgical procedure due to the large treatment volume so if a total callosotomy is indicated a 2-staged procedure must be planned.

Guerrero and Cohen[7] described the use of a rigid endoscope to enhance microsurgical visualization of the corpus callosum in cadaveric models. Endoscopic dissection was carried out through a narrow corridor without significant brain retraction. The endoscope holds the potential to improve operative exposure in corpus callosotomy.

A new adjunct for presurgical planning may involve diffusion tensor MR imaging coupled with neuronavigation. Diffusion tensor imaging provides more information about white matter tracts and may assist in identifying epileptogenic pathways. In combination with preoperative neuronavigation, the callosotomy could be tailored to section only the white matter tracts that propagate epileptogenic foci. This "tailored" corpus callosotomy may help avoid postoperative deficits including the disconnection syndromes.[2,10,30]

Lessons Learned

Vascular complications may occur when opening the dura toward the sagittal sinus. In addition to sagittal sinus injury and resultant venous congestion, injury to large draining veins and dural venous lakes around the desired interhemispheric corridor can lead to venous infarction. Although our preference is to perform a right-sided approach in all patients who are right-handed, we encountered instances in which a right-sided approach would not have been optimal due to bridging veins that would have limited the interhemispheric corridor or risked venous injury and venous infarction. Therefore, preoperative MR imaging, and even better, image guidance, should be routinely studied for venous anatomy to effectively plan the skin incision, bone flap, and dural opening.

Care must be taken when separating the pericallosal arteries. Injury to these vessels or vasospasm from excessive manipulation can result in lower-extremity weakness secondary to ischemia. As the dissection is continued toward the rostrum and genu of the corpus callosum, the anterior cerebral arteries and perforating arteries must also be protected. Injury to these vessels may cause personality and memory disturbances.

Hemispheric edema has been associated with vigorous and prolonged retraction of the hemisphere. Telfa or biachol strips should be placed under the retractor to protect the brain parenchyma.

Proper corpus callosotomy requires maintaining the midline. An erroneously more lateral corpus callosotomy may cause forniceal injury possibly resulting in memory disturbances; or damage to the corona radiata which may lead to weakness.

Limitations of image-guidance based on archival imaging relate to error caused by brain shift as soon as the bone flap is elevated, the dura is opened, and CSF is lost. We attempt to minimize this error by determining the length of callosotomy as early as possible during the opening before the ventricle was entered and before significant brain shift occurred.

Complications related to violation of the ependyma and entry into the ventricular system may include CSF leak, hydrocephalus requiring a shunt, and chemical meningitis/ventriculitis.

Conclusions

Corpus callosotomy is a well-established salvage procedure for intractable epilepsy. Little has changed regarding its surgical method since its inception in the 1930s. Current surgical adjuncts, such as image guidance, however, have made this procedure safer, more efficacious, and more accurate. Nonetheless it remains to be seen whether improved technical results necessarily translates to improved clinical outcome in terms of seizure control. At present, no randomized studies address this issue. Perhaps, future advances in surgical technique and technology, such as functional tractography with diffusion tensor MR imaging, may help guide the "perfect" extent of corpus callosotomy individualized for each patient.

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