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

ANDREW JEA, M.D.,1 SHOBHAN VACHHRAJANI, M.D.,2 KEYNE K. JOHNSON, M.D.,1
AND JAMES T. RUTKA, M.D., PH.D., F.R.C.S.C.2

1Division of Pediatric Neurosurgery, Department of Neurosurgery, Baylor College of Medicine, Houston, Texas; and 2Division of Neurosurgery, Department of Surgery, Hospital for Sick Children, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

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
**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 venography 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.
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).

**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

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**TABLE 2**

Grading system used to evaluate postoperative seizure control after corpus callosotomy

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

Dandy1 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 Herrin29 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. 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.29 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 diminution 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.29 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.13 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.12,24

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 atomic 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). 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 neuro-navigation 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.
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related to surgical manipulation, frontal lobe retraction, and
surgical morbidity, including the disconnection syndromes,
radiosurgery may serve to avoid transient and permanent
the white matter tracts that propagate epileptogenic foci.

Other Surgical Alternatives and Adjuncts

Radiosurgical ablation of mesial temporal structures for
intractable temporal lobe epilepsy was first reported by
Regis et al. in 1995. Leksell designed the Gamma Knife
for functional neurosurgery and realized that a potential tar-
get could be epileptic foci; however, exactly how the irra-
diation 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.

Radiosurgical corpus callosotomy may be a promising
safe and noninvasive alternative to open callosotomy. 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 fol-
low-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 described the use of a rigid endo-
scope 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 dif-
fusion tensor MR imaging coupled with neuronavigation.
Diffusion tensor imaging provides more information about
white matter tracts and may assist in identifying epilepto-
genic pathways. In combination with preoperative neuron-
avigation, the callosotomy could be tailored to section only
the white matter tracts that propagate epileptogenic foci.

This “tailored” corpus callosotomy may help avoid postop-
erative deficits including the disconnection syndromes.

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 encoun-
tered 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 rou-
tinely studied for venous anatomy to effectively plan the
skin incision, bone flap, and dural opening.

Care must be taken when separating the pericallosal ar-
nies. Injury to these vessels or vasospasm from excessive
manipulation can result in lower-extremity weakness sec-
ondary 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 pro-
tected. 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 bia-
choil strips should be placed under the retractor to protect
the brain parenchyma.

Proper corpus callosotomy requires maintaining the mid-
line. An erroneously more lateral corpus callosotomy may
cause fornical injury possibly resulting in memory distur-
bances; or damage to the corona radiata which may lead to
weakness.

Limitations of image-guidance based on archival imag-
ing 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 meningi-
tis/ventriculitis.

Conclusions

Corpus callosotomy is a well-established salvage proce-
dure 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 im-
proved 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.
Acknowledgement

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