

# The Surgical Effect of Callosotomy in the Treatment of Intractable Seizure

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We evaluated the surgical effects of the callosotomy, particularly with respect to the effect of callosotomy in some seizure types and the extent of surgery. Twenty-one patients with a minimum follow-up of two year were enrolled. The most significant effect of callosotomy was the complete suppression of the generalized seizures associated with drop attack in 12 of 21 patients and seizure reduction of more than 75% in 6 of 21 patients. The surgical effect on the partial seizures was very variable. Transient disconnection syndrome appeared in 4 patients after anterior callosotomy. Total callosotomy by staged operation significantly suppressed generalized seizures associated with drop attack without any disconnection syndrome. Our data show that callosotomy is quite a good approach to the surgical treatment of drop attacks accompanied by disabling generalized seizures.

**Key Words:** Intractable seizure, callosotomy, disconnection syndrome, generalized seizure, drop attack

## INTRODUCTION

In 1940, Van Wagen and Herren reported the control of generalized seizure by dividing the corpus callosum as well as the anterior commissure, massa intermedia, and one fornix.<sup>1</sup> However, they were unable to explain why the procedure controls generalized seizure. Wilson et al. observed that bilateral epileptic discharge became either unilateral or asymmetric after the callosotomy, and suggested that the callosotomy discon-

nect the interhemispheric ictal epileptic discharge along the corpus callosum.<sup>2</sup> It is generally accepted that the surgical indications for callosotomy are seizures that are medically refractory and generalized or partial seizures with a rapid secondary generalized pattern without localized lesion. However, debate has continued on the surgical effect of the callosotomy, particularly with respect to the effect of callosotomy in some seizure types and the extent of surgery. Spencer et al reported that callosotomy was effective in drop attack but less effective in generalized tonic clonic seizure, complex partial seizure and in the absence seizure.<sup>3</sup>

To verify the effect of callosotomy on intractable generalized seizure and other seizure types and to identify possible prognostic factors, we reviewed 21 cases that underwent callosotomy at our institute between 1990 May and 2001 May.

## MATERIALS AND METHODS

### Patient selection

We reviewed the records of 21 patients that underwent callosotomy between 1990 and 2001 and were followed for at least 24 months. Their ages ranged from 7 to 37 years (mean age 19.4 years) and the male to female ratio was 12:9. Mean follow up duration was 57 months (ranging from 32 to 104 months) and the duration of seizure ranged from 2 to 23 years (mean 8 years).

For preoperative work-up, continuous electroencephalogram (EEG) and video monitoring were performed to characterize seizure type in each

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patient. Brain magnetic resonance image (MRI) and EEG were performed pre- and postoperatively. The intraoperative EEG recordings were done in all patients. Nineteen patients underwent neuropsychological test to evaluate their intellectual quotients (IQ) and cognitive deficits preoperatively and 24 months after surgery. Other preoperative evaluations included interictal Single Photon Emission Computed Tomography (SPECT) in 18 patients, ictal SPECT in 10, intracarotid amytal test in 15 and Positron Emission Tomography (PET) study in 7. Subdural electrodes were inserted in 7 patients to identify epileptogenic foci.

Our criteria for surgical candidates were those with medically refractory generalized seizure, or complex partial seizure with no obvious seizure foci, and surgically inaccessible multifocal and wide epileptic discharge.

### Surgical techniques

The length of the callosal section was estimated from genu to splenium on the preoperative sagittal image of the brain MR (Fig. 1). The pre-measured patty string was useful for checking the length of callosal section. After identifying the midline cleft of the corpus callosum just below the bilateral pericallosal arteries, the sectioning of corpus callosum was initiated at the anterior aspect of genu and down to the septum pallidum. The extent of sectioning was 2/3 to 4/5 of the total length of the corpus callosum in first operation. We performed the second operation for the total callosotomy in 4 cases that showed little or no clinical improvement after 6 months postoperative follow up (Fig. 2). For the total callosotomy, the previous craniotomy was reopened

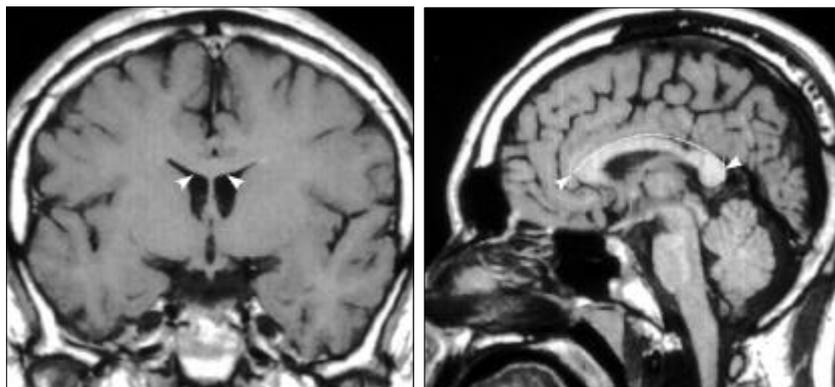


Fig. 1. Measurement of corpus callosum in MRI midsagittal image. The length of the corpus callosum was 59.4 - 81.2 (mean; 65.7) mm.

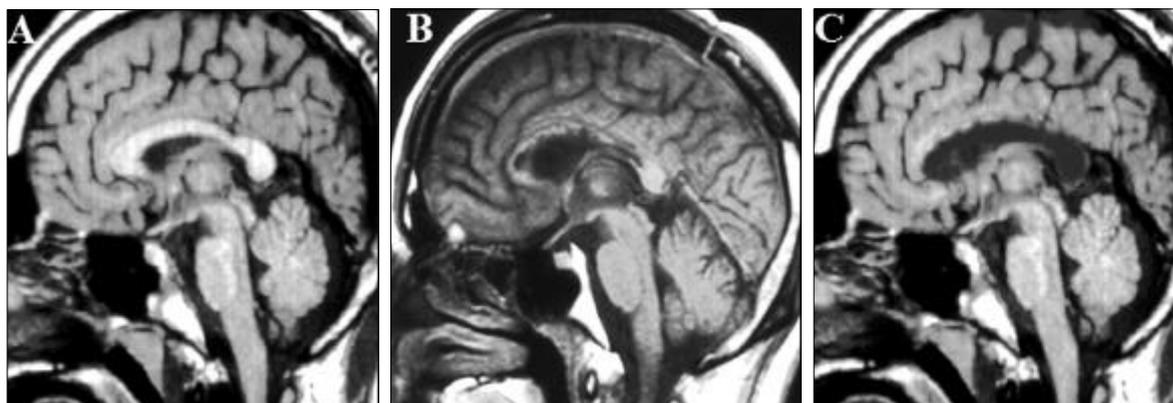


Fig. 2. Pre- and post-operative sagittal images of MR. Preoperative MR images of 21 year-old woman with frequent drop attacks associated with generalized tonic-clonic seizure (A). Follow-up MRI 6 months after anterior callosotomy (B), the frequency of drop attacks had decreased, though they persisted. She underwent total callosotomy. Follow-up MR findings (C) reveal the completion of callosotomy.

and the remainder of the corpus callosum including the splenium was sectioned until the prepineal arachnoids and the vein of Gallen were visible.

**Combined surgery**

Although we could not identify single-isolated focus of seizure activity in any patient on preoperative ictal EEG-video monitoring studies, we suspected 7 patients would have localized epileptic focus and monitored ictal electrocorticogram (ECoG) via the subdural grids. We were able to detect predominant focal epileptic discharge in 5 patients out of them. These focal epileptic discharges were found on parietal lobe in 3 patients, frontal lobe in one, and temporal lobe in one. They received parietal cortisectomy, frontal lobectomy, and temporal lobectomy, respectively. However, multifocal epileptic discharges beyond the resection margin on intraoperative ECoG after lobectomy kept up and additional callosotomy was performed.

**Types of seizure and surgical outcome**

The types of seizure were divided into drop attack, generalized tonic-clonic seizure (GTC), complex partial seizure (CPS) and simple partial seizure (SPS). The drop attacks included atonic, akinetic, tonic and tonic-atonic seizure. Seizure

outcome was evaluated using modified Wyler's classification<sup>4</sup> 12 months after last surgery (Table 1). The favorable outcome was defined as class 1 or class 2.

**RESULTS**

**The types of seizure**

The onset of seizure was variable from birth to 30 years old (mean age: 7 years old) and the mean duration of seizure was 12.5 years (from 3 to 25 years). All patients had more than one type of seizure including generalized seizure. The frequency of seizure was also variable from 1/month to 10/day. In EEG-video monitoring study, the most common type of drop attack was a tonic seizure in EEG-video monitoring. GTC was found in 19 cases, CPS in 17 and SPS in 16.

**Surgical outcomes**

After at least 12 post-operative months, the outcome of callosotomy was evaluated. Favorable outcome was defined as class 1 or 2. Overall outcomes were: 4 cases of class 1, 10 of class 2 and 7 cases of class 3 (Table 2). Favorable outcome was achieved in 14 cases (66.7%). The surgical outcomes were variable according to type of seizure. Drop attack was dramatically improved after

**Table 1.** Classification of Seizure Outcome (Modified Wyler's Classification)

Class	Description
Class 1	Free of seizure; when completely free of motor seizure
Class 2	Significantly improved; decrease in the frequency of the most disabling type of seizures, by at least 75%
Class 3	Unchanged; Little or no change in seizure frequency or postoperative worsening of seizures

**Table 2.** Surgical Outcome of Callosotomy According to the Seizure Types in 21 Patients

Type of seizure	Class 1	Class 2	Class 3
Drop attack	12	6	3
GTC	10	6	3
CPS	3	7	7
SPS	3	7	6
Total (cases)	4	10	7

GTC, Generalized tonic-clonic seizure; CPS, Complex partial seizure; SPS, Simple partial seizure.

callosotomy. Among 21 cases with drop attacks, there were 12 of class 1, 6 of class 2 (favorable outcome 85.7%) and 3 of class 3. Favorable outcomes (class 1 or 2) were 84.2% in GTC. However, favorable outcome in CPS and SPS were much lower than those of drop attack or GTC (Table 2).

Complete callosotomy as a second step was performed in 4 cases: 3 cases with class 3 and 1 case with class 2, who underwent the complete callosotomy by an ardent desire of his parent. After the second operation, 3 cases became class 1 and 1 case class 2.

After the callosotomy, 2 patients developed a new type of seizure with a localized focal spike wave. In one patient, CPS newly developed after the first operation. He underwent frontal lobectomy and then fell into class 2. Another patient, who had multifocal epileptic discharges on the left hemisphere including the motor cortex in preoperative EEG-video monitoring, showed class 3 after the callosotomy. After callosotomy, his seizure focus was well localized on the motor cortex, and then he received MST with little improvement.

Regarding postoperative complications, transient disconnection syndrome developed in 4 cases (19%) after anterior callosotomy. Transient aphasia and hypotonia also developed but those affected fully recovered within 4 weeks. There were no perioperative complications in second operation. One patient developed cranial osteomyelitis after subdural electrode insertion, and another patient suffered from aseptic meningitis after exposure of the lateral ventricle.

### Prognostic factors

We compared the surgical outcomes of 11 pediatric patients (age < 18 years) with those of 10 adults (age ≥ 18). Among 11 children, there were 6 in Class 1, 3 in Class 2, and 2 in Class 3, while among 10 adults; there were 6 in Class 1, 2 in Class 2, and 2 in Class 3. These results indicated the age factors did not influence the surgical outcomes. The duration of seizure didn't have an effect on the surgical outcome.

Preoperative brain MRI showed abnormal findings in 10 cases, which were, diffuse cortical atrophy in 3 cases, mesial temporal sclerosis in 3, focal encephalomalacia in 2, hemiatrophy in 2, and unilateral lissencephaly with multiple angiomas in one, and arachnoid cyst in one. In cases of drop attack ( $p=1.0$ ) and SPS ( $p=1.0$ ), normal or abnormal MRI finding did not influence surgical outcome. No significant difference was found between GTC ( $p=0.58$ ) and CPS ( $p=0.335$ ) but patients with GTC showed a slightly more favorable outcome in the normal MRI findings group and conversely, patients with CPS a slightly better outcome in the abnormal MRI findings group (Table 3).

Neuropsychological evaluation was performed on all patients pre and postoperatively. On preoperative evaluation, IQ was below 60 in 6 cases, between 60 and 90 in 9 cases and above 90 in 6 cases. Three of the 6 retarded patients (IQ<60) were class 3 (50%) and three of the 6 normal patients (90<) class 3 (50%). Our data showed IQ was not involved in the surgical outcome (Table 4). Out of 10 patients showing behavioral abnor-

**Table 3.** Outcome and Extent of Callosotomy According to MR Abnormalities

Type of seizure	MR abnormalities	Class 1	Class 2	Class 3	Total
Drop attack	Yes	6	3	1	10
	No	6	3	2	11
GTC	Yes	4	3	2	9
	No	6	3	1	10
CPS	Yes	3	3	2	8
	No	0	4	5	9
SPS	Yes	1	3	3	7
	No	2	4	3	9

GTC, Generalized tonic-clonic seizure; CPS, Complex partial seizure; SPS, Simple partial seizure.

malities, 8 were improved after callosotomy. One patient presented with schizophrenic symptoms postoperatively.

**EEG findings**

Preoperative EEG findings included diffuse slow spike and wave complex, or polyspike and wave, or bilateral synchronous polyspike and wave. Typically, EEG findings of drop attack due to tonic seizure were a generalized irregular theta/delta burst or diffuse back ground suppression proceeding low amplitude fasting activity with rhythmic activity (4 - 6 Hz).

Postoperative EEG revealed completely abolished bilateral synchronous polyspikes and waves in 2 cases that were classified as class 1, bilateral synchronous polyspikes and waves diminished by more than 3/4 in 16 cases (2 cases in class 1, 9 cases in class 2 and 5 in class 3 (Table 5). Six months after surgery, the complete abolishment of bilateral synchronous polyspikes and waves reappeared in 1 patient. Twelve months after surgery, the bilateral synchronous polyspikes and waves reappeared in 3 of 16 patients in whom the bilateral synchronous polyspikes and waves had diminished by more than three quarters. Nevertheless, clinical features were unchanged.

**Extent of callosotomy**

The length of corpus callosum in the midsagittal plane of the preoperative MRI was measured from

genu to splenium, and found to vary from 59.4 mm to 81.2 mm (mean 65.7 mm). The extent of callosotomy was estimated by MRI 3 months after surgery. Anterior 2/3 callosotomy was performed in 5 patients and in the other cases resection involved more than 2/3 of the corpus callosum. Complete callosotomy was performed as a secondary step in 4 cases. The results of  $2/3 \leq$  anterior callosotomy were as follows: - In 16 drop attack cases, 10 (62.5%) were class 1 and two (12.5%) class 3, and in 5 CPS cases, none was class 1 and 3 (60%) were class 3 (Table 6). After  $< 2/3$  anterior callosotomy, out of 5 drop attack patients two were class 1, two were class 2 and one was class 3 (Table 6). We were not able to find statistically any significant difference in the surgical outcome between  $< 2/3$  and  $2/3 \leq$  anterior callosotomy ( $p=0.422$ ) because of small numbers of cases. However, the rate of favorable outcome in all types of seizures was significantly higher in those patients who underwent  $2/3 \leq$  anterior callosotomy compared to in those of  $< 2/3$  anterior callosotomy (87.5% vs. 80.0% in drop attack, 87.5% vs. 66.7% in GTC, 66.7% vs. 40.0% in CPS, 64.3% vs. 50.0% in drop attack) (Table 6).

**DISCUSSION**

Curtis found that cortical stimulation of one hemisphere evoked potential on the opposite hemisphere.<sup>5</sup> Crowell and Ajmone reported that experimentally induced cortical epileptic activities

**Table 4.** Intelligence Quotient (IQ) and Surgical Outcome in 21 Patients with Callosotomy

IQ	Class 1	Class 2	Class 3	Number of cases
Mental retardation (< 60)	0	3	3	6
Subnormal (60 - 90)	2	6	1	9
Normal (90 <)	2	1	3	6

**Table 5.** Seizure Control and Changes of EEG pattern after Callosotomy in 21 Patients

Changes of synchronous spike wave	Class 1	Class 2	Class 3
Totally abolished	2		
Marked decreased (75% <)	2	9	5
Unchanged		1	2

All patients in our series had preoperatively bilateral synchronous spike wave by scalp EEG and EEG video monitoring.

**Table 6.** Outcome and Extent of Callosotomy According to Seizure Type in 21 Patients

Type of seizure	Extent of callosotomy	Class 1	Class 2	Class 3	Total
Drop attack	<2/3	2	2	1	5
	2/3 ≤	10	4	2	16
	2 <sup>nd</sup> operation	3	1	0	4
GTC	<2/3	0	2	1	3
	2/3 ≤	10	4	2	16
CPS	<2/3	0	2	3	5
	2/3 ≤	3	5	4	12
SPS	<2/3	0	1	1	2
	2/3 ≤	3	6	5	14

GTC, Generalized tonic-clonic seizure; CPS, Complex partial seizure; SPS, Simple partial seizure.

<sup>1</sup>Surgical outcomes after the 2<sup>nd</sup> operation in 4 patients, who showed poor surgical results after the 1<sup>st</sup> callosotomy.

of one hemisphere were also found in the homotopic area of the opposite hemisphere.<sup>6</sup> Therefore, they suggested that a cortical epileptic discharge in one hemisphere is transferred to the other to induce epileptic synchronization. Erickson's experimental report revealed that the corpus callosum was a major pathway for interhemispheric generalization of seizures in monkeys.<sup>7</sup> The corpus callosum may be the major conduit for interhemispheric generalization of seizure in combination with the reticular formation of the mid-brain and the massa intermedia of the thalamus.<sup>8,9</sup> Clinically, many investigators have reported that the synchronization and generalization of seizure may be prevented by callosotomy. Callosotomy may be offered if there is a potential for either functional improvement or an improvement in the quality of life, by reducing the frequency of seizures associated with injury. It is generally accepted that the surgical indications for callosotomy are seizures that are medically refractory and generalized or partial seizures with a rapid secondary generalized pattern without localized lesion. In particular, drop attack including atonic, tonic and tonic-atonic seizures are good indications.<sup>1,3,4</sup> Surgery was also performed to reduce seizure frequency in the case of multiple lesions. The surgical outcomes have reported to be favorable in drop attack (favorable outcomes: 70-90%) but not favorable in SPS or CPS (favorable outcomes: 20-50%).<sup>9-14</sup> Callosotomy outcome in GTC was variable but accepted as relatively good (favorable outcomes: 40-78%).<sup>9,13,15</sup> Our results

were similarly to those of others, i.e., that favorable outcomes were 85.7% in drop attack, 84.2% in GTC, 58.8% in CPS and 62.5% in SPS. The surgical outcomes for CPS and GTC observed were relatively good compared with other reports.<sup>12-14</sup> This may be because callosotomy was performed with lobectomy, MST, and cortisectomy under the guidance of preoperative MRI and pre- and, especially, intraoperative ECoG.

Outcome of 3 cases with primary generalized seizure unrelated to drop attacks revealed 2 in class 1 and 1 in class 2. These results imply that callosotomy is a valid option for reducing the frequency and severity of generalized seizures also in cases with multifocal epileptic foci.

Some authors have reported that patients with low preoperative IQ's are believed to be at greater risk of developing neuropsychological deficits following callosotomy.<sup>16,17</sup> However, our results is strikingly different from reported results and others also maintain that there is no relation between IQ and surgical outcome.<sup>18-20</sup> In terms of the relation between prognosis and age of seizure onset and seizure duration, some have report that seizure onset before 5 years old and of shorter duration are good prognostic factors<sup>4,20</sup> but others disagree.<sup>3</sup> In our series, no relation was apparent between prognosis and age of onset, duration or IQ.

Rossi et al proposed that abnormal findings limited to only one hemisphere is a good prognostic factor.<sup>11</sup> However, this was not found to be true in our study, except for CPS, which

showed no correlation between prognosis and MRI findings in the cases of drop attack and SPS. GTC outcomes in normal MRI were more favorable but without statistical significance. The diminishment of synchrony of the epileptic discharge by postoperative EEG was reported to deserve being treated as a prognostic factor after callosotomy.<sup>21-23</sup> Our results were in agreement, but many of the patients in our series showed a reoccurrence of synchrony with time but without seizure aggravation.<sup>24</sup> This aspect deserves further study.

The greatest variable in callosal surgery is that extent of section. Earlier clinical series often included division of the corpus callosum, the underlying hippocampal commissure, and additional structures, including the anterior commissure and, in some instances, one fornix. Nearly all series today restrict division to the corpus callosum and, in complete callosal section, the hippocampal commissure that is immediately apposed to the ventral aspect of the posterior portion of the callosum. In 1986, Kellachy and Chalupa report that callosal projection was confined to the anterior 2/3 of corpus callosum,<sup>25</sup> which provided a theoretical basis for anterior callosotomy. Manmelak et al supported anterior callosotomy 1/2,<sup>18</sup> as did Sakas et al. 2/3,<sup>13</sup> and Fuiks et al 4/5.<sup>26</sup> There remains variation, however, with regard to which part or how much of the corpus callosum is divided. Spencer et al proposed that the extent of callosotomy should be determined with intraoperative EEG until the bilateral synchrony had diminished.<sup>4</sup> However, Gates reported that there was no correlation between the diminution of bilateral synchrony and surgical outcome,<sup>21,22</sup> and highlighted the fact that it was difficult to distinguish between the surgical and anesthetic effects in intraoperative ECoG. As our results also showed, the larger the surgical extent the better outcome<sup>4,10,11</sup> but the greater the risk of complications.<sup>10,17,19,27,28</sup> Therefore, some investigators staged operation that performed anterior 1/2 section in the first stage and decided second operation during follow up.<sup>3,10</sup> We planned callosotomy on the basis of an anterior 2/3-4/5 section in the first stage and decided upon a second stage operation 6 months after the first in class 3. Posterior section or complete section may disrupt

interhemispheric transfer of visual, tactile, and auditory information and is responsible for the long-term disconnection syndromes associated with this operation. Objects presented solely to the hemisphere that is not dominant for language may not be verbally reported by the patient, but as isolation of such stimuli to one hemisphere usually requires a fairly constrained, laboratory environment, tachistoscopic hemifield visual presentation, it is unusual for this to cause disability. Most patients, as well as many early investigators, have been unaware of the deficit. Although our cases are so tenuous, we did not experience disconnection syndrome in the second stage operation, and were left with the firm impression that the staged operation was both safe and effective.

In conclusion, outcome of callosotomy in drop attack was favorable in 86% of the cases. Callosotomy may be a valid surgical option for patients with medically intractable, multiple epileptic focus, generalized or partial seizures with a rapid secondarily generalized and drop attack. Our data show that the larger the callosal section the better outcome. Staged callosotomy seem to be safe and effective in reducing the frequency and severity of seizure and improved the quality of life with less risk of disconnection syndrome.

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