Seizure outcome from anterior and complete corpus callosotomy

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Eighty patients underwent anterior corpus callosotomy for treatment of generalized seizures. The patients' mean age was 18.3 years (range 4 to 53 years); the mean age at seizure onset was 5.27 years (range 0.1 to 27 years). The mean intelligence quotient (IQ) of 41 testable patients was 71.12 (range < 30 to 114). The seizure outcome was as follows: 13% were seizure-free, 65% were significantly improved, and 22% were unchanged. Ten patients subsequently underwent a second operation to complete the callosal sectioning which resulted in additional seizure improvement in only five of them. Five complications resulted from 90 operations: two epidural hematomas, one delayed subdural hematoma, one bone flap infection, and one postcallosotomy disconnection syndrome; two patients died. A younger age at onset of seizures, a higher IQ, and generalized tonic-clonic, atonic, complex-partial, and mixed seizure types were associated with improved seizure outcome.

KEY WORDS - corpus callosotomy - seizure - epilepsy surgery - outcome

Corpus callosotomy is a surgical option for patients with medically uncontrolled seizures who do not have a unilateral, restricted epileptogenic focus. Callosotomy was first introduced in 1940 by Van Wagenen and Herren. Since then, numerous refinements in operative technique have reduced the morbidity and mortality associated with the procedure, but several issues remain controversial. First, what extent of callosotomy is sufficient for acceptable seizure outcome? Second, if complete callosotomy is elected, should it be performed in one or two stages? Third, does a certain type of seizure respond best to callosotomy? We report a series of 80 patients who underwent anterior corpus callosotomy and use data derived from this group to address some of these issues.

Clinical Material and Methods

Inclusion Criteria

Patients who had failed treatment with Dilantin (phenytoin), Tegretol (carbamazepine), phenobarbital or Mysoline (primidone), and Depakene (valproic acid), in mono- or combination therapy, were referred for surgical evaluation. Most patients also had evidence of seizure-related bodily injury.

Preoperative Evaluation

Surgical evaluation was carried out using a sequential protocol. Patients were initially evaluated with magnetic resonance (MR) imaging to identify a possible causative lesion. They were then admitted for long-term electroencephalographic (EEG)/video seizure monitoring; a complete neuropsychological test battery was administered if possible. Patients with no causative lesion and who were found to have a typical primary generalized seizure type (tonic, atonic, or myoclonic), were considered for corpus callosotomy. However, patients who had either complex partial seizures or seizures that were not easily classified were considered for invasive long-term seizure monitoring.

At our center invasive monitoring is performed by implantation of subdural strip electrodes. Unless there are compelling reasons for an alternative montage, we use a bifrontal and bitemporal array of electrodes similar to those reported previously. A minimum of three typical seizures were clearly recorded before monitoring was discontinued.

Patients were given the option of corpus callosotomy if a clear unilateral focus could not be demonstrated during strip-electrode monitoring. Put another way, patients who were not candidates for focal resection or
hemispherectomy and who were known not to have a neurodegenerative disorder (progressive juvenile myoclonic epilepsy, for example) were considered for corpus callosotomy.

Surgical Procedure

All operations were carried out under general anesthesia. Surgery was performed with the patient in the supine position in 41 cases (from August 2, 1985, until July 14, 1988) and with the patient in the lateral decubitus position in 39 cases (from July 14, 1988, until February 1, 1990). We have favored the lateral decubitus position (Fig. 1) because it provides gravity retraction to the dependent hemisphere and eliminates manual retraction.

Following anesthesia induction, the patient is placed in the lateral decubitus position, and a lumbar cerebrospinal fluid catheter is inserted at the L4–5 interspace and allowed to drain until the majority of the callosum has been sectioned. The neck is kept in a neutral position to minimize venous pressure, and the operating table is tilted with the patient approximately 30° head-up. Hyperventilation maintains the pCO₂ at 25 torr. Diuretics are seldom needed. A rectangular craniotomy is centered over the intersection of the sagittal and coronal sutures. The dura over the dependent hemisphere is opened and dissection is carried down to the corpus callosum. The corpus callosum is divided into the septum pellucidum without entering the ventricular system. The genu and rostrum are sectioned and the body of the corpus callosum is dissected to the level of the trigone of the ventricle.

In 10 patients, completion of the callosotomy was performed in an attempt to improve seizure outcome; these operations were carried out with six patients in the supine position and four in the lateral decubitus position.

Outcome Measurement

Seizure outcome was classified as seizure-free, significantly improved, or unchanged. Because acute postoperative seizures may occur for various reasons, seizures in the first few postoperative days were not considered when judging outcome. The seizure-free category includes patients who have been completely seizure-free; patients who experience auras are not considered seizure-free. Patients in the significantly improved group had a total decrease of all seizures of at least 50%. In patients having more than one type of seizure preoperatively, the seizure frequency took into account the sum of all seizures. This criterion was maintained postoperatively. Thus, patients with a decrease in atonic seizures but an increase in tonic seizures may have shown no significant change if the two changes were equal. The unchanged group represents any result that is neither seizure-free nor significantly improved. A patient might be considered a failure if there was no change in seizure frequency within the first 3 months after surgery. But a patient was not considered seizure-free unless followed for a period of at least 9 months. Any patient who did not have a satisfactory seizure outcome was re-evaluated with MR imaging to show the extent of callosal section. Fifteen patients also underwent repeat long-term EEG/video monitoring.

Statistical Methods

To determine which, if any, of the potential demographic variables (such as age at onset, age at surgery, duration of seizures, gender, seizure type, and intelligence quotient [IQ]), were associated with seizure outcome, we used the chi-square test for the categorical variables (such as seizure type or gender) and analysis of variance for the continuous variables (such as age at surgery or IQ).

Results

Demographic Data

Eighty patients who underwent 90 operations from August 2, 1985, to February 1, 1990, are presented. Although the follow-up period was short, no patient was considered seizure-free unless at least 9 months of follow-up data had been amassed. No patient was followed for less than 6 months. The average follow-up period was 25 months with a range of 6 to 59 months. The mean age at seizure onset was 5.27 years with a range of 1 month to 27 years. The mean age at the time of anterior callosotomy was 18.3 years with a range of 4 to 53 years. Forty-four patients were male and 36 were female. Seventy-one patients were right-handed, eight were left-handed, and one was ambidextrous. Forty-one patients underwent neuropsychological testing prior to surgery, including either the Wechsler Adult Intelligence Scale, Revised (28 patients) or the Wechsler Intelligence Scale for Children, Revised (13 patients). The mean full-scale IQ for the entire group was 71.12, ranging from less than 30 to 114. Thirty-nine patients were not tested either because of severe mental retardation or problems in scheduling assessments.

Ictal Onset

In 41 patients who underwent invasive monitoring, the electrocorticographic ictal onsets were classified as:
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<tr>
<th>Type of Seizure</th>
<th>Seizure Outcome</th>
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<tr>
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<td>No Change</td>
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<tr>
<td>atomic</td>
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<tr>
<td>generalized</td>
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<td>tonic-clonic</td>
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<td>4</td>
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* Two of the 80 original patients died.

1) bilateral mixed frequency polyspike and spike-wave discharge in eight patients; 2) generalized spike-wave discharges in eight; 3) bilateral decremental response in six; 4) bilateral onset of low-voltage rhythmic fast discharges in four; 5) generalized spike- and slow-wave discharges in three; 6) generalized slow-wave discharge in two; 7) bilateral polyspike discharges in two; 8) bifrontal and bitemporal slow-wave discharge in one; 9) intermixed spike- or slow-wave discharge for either right or left frontal regions in one; 10) bilateral frontal-polar sharp- and slow-wave discharges in one; 11) bilateral diffuse polyspike and slow-wave discharge in one; 12) focal temporal decremental event with rapid (<5-second) spread to the contralateral temporal lobe in one; 13) rhythmic fast activity alternating between the right and left temporal lobes in one; 14) bilateral polyspike and spike-wave discharge in one; and 15) spike-wave discharge initially involving the right temporal strips, subsequently involving the right frontal, then left frontal and temporal strips in one patient.

Seizure Types

During long-term EEG/video monitoring, 55 patients (69%) demonstrated either generalized tonic-clonic or mixed seizures. Of 26 patients with mixed seizures, seven had four or more seizure types, six had three seizure types, and 13 patients had two seizure types. The seizure types represented in the mixed group included: generalized tonic-clonic in 19 cases; myoclonic in 12; tonic in 12; atonic in 11; complex partial in 11; atypical absence in five; absence in three; and clonic in one.

Seizure Outcome

Table 1 presents postoperative seizure outcome as a function of seizure type. Ten (12.8%) of the 78 surviving patients are seizure-free; of these, four had generalized tonic-clonic, four had mixed, one had atonic, and one had complex partial seizures. Fifty-one (65.4%) of 78 patients are significantly improved. Improvement was seen in 86% of the patients with generalized tonic-clonic seizures, 88% of those with complex partial seizures, 83% of those with atonic seizures, 73% of those with mixed seizures, but only 50% of those with tonic seizures. Seventeen of 78 patients did not improve following anterior callosal sectioning: four had generalized tonic-clonic seizures, seven had mixed seizures, one had atonic seizures, one had complex partial seizures, and four had tonic seizures.

The age at onset of epilepsy, age at surgery, duration of seizures, and IQ were correlated with outcome. Although none of these variables was significantly associated with improved outcome, there was a highly suggestive trend that a younger age at onset and a higher IQ were related to improved outcome. As a group, those patients with IQ's greater than 70 had somewhat better seizure outcomes than those with IQ's less than 70.

Completion of Callosotomy

Ten patients subsequently underwent completion of the corpus callosotomy. The seizure diagnoses in this group included: atonic seizures in five patients; mixed seizures in three; and generalized tonic-clonic seizures in two. Of the 10 patients, two achieved considerable but not significant improvement, three had modest improvement (<50% reduction in all of their seizure types), and five experienced no improvement from the surgery. In no case did completion of the callosotomy move the patient from one outcome category into another. For example, it did not make a significantly improved patient seizure-free nor did it move a person who was initially in the no-change group to the significantly improved category.

Complications

There were five postoperative complications and two deaths in this series. The complications included one subdural hematoma, one deep wound infection, one protracted disconnection syndrome, and two cases of epidural hematoma. Two of the patients who developed postoperative hematoma were receiving Depakote perioperatively, and that drug is known to be associated with blood clotting problems. All five patients recovered from their complications without long-term sequelae.

Of the two deaths in the series, one was due to an air embolism during a second craniotomy for completion of callosotomy and the other was caused by unexplained respiratory arrest during the first postoperative night.

Discussion

Histological Perspective

Van Wagenen and Herren\(^5\) reported an initial series of 10 callosotomy patients in 1940. They sectioned the body and the genu of the corpus callosum in eight patients. Because seizures continued in three of these, a second operation was performed to complete the callosal sectioning. Two other patients received a total callosotomy and division of the left fornix. Their results were variable and the follow-up period was brief. There
were no further publications on this surgical procedure until the early 1960's when Bogen and Vogel reported their series of commissurotomy. Harbaugh, et al., described two operations, one being a complete cerebral commissurotomy in which they divided the corpus callosum, hippocampal commissure, massa intermedia, and the anterior commissure. The other operation was a frontal commissurotomy in which only the rostrum, genu, anterior body of the corpus callosum, one fornix, and anterior commissure were sectioned. The complete commissurotomy led to an acute disconnection syndrome consisting of unilateral tactile anomia, left hemialexia, mutism, and unilateral apraxia. Skepticism about the utility of complete cerebral commissurotomy emerged in 1975 when Wilson, et al., reported a 37% morbidity rate primarily from aseptic meningitis and hydrocephalus. Changes in surgical technique, including microsurgical instrumentation, have decreased operative morbidity. In 1982, Wilson, et al., demonstrated that callosal sectioning alone was as effective in treating generalized and mixed seizures as was cerebral commissurotomy. Eighty-four percent of their patient sample achieved substantial seizure reduction. Since Wilson's encouraging report, others have described successful results from callosotomy. Overall, 62% to 100% of patients have attained substantial seizure reduction from callosal sectioning.

**Indications for Callosotomy**

In the 1970's, the common indication for corpus callosotomy was the occurrence of generalized epilepsies, particularly generalized tonic-clonic, myoclonic, and akinetic seizures. Patients with unilateral brain damage (for example, infantile hemiplegia) or unilateral hemispheric lesions were also felt to be good surgical candidates. In the 1980's, the indications for callosotomy expanded to include individuals with mixed seizures, tonic/atactic seizures with rapid secondary generalization, and complex partial seizures of multifocal origin. A comparison of seizure outcomes cannot be made between reported series because of the difference of inclusion criteria for callosotomy within various surgical centers. Nonetheless, most reports claim that partial or complete callosotomy is helpful for patients with atonic/tonic seizures characterized by falls and tonic-clonic seizures. Geoffroy, et al., noted the eradication of atonic seizures in two of three children by this means. Rayport, et al., observed the elimination of drop attacks in two patients after corpus callosum section and Gates, et al., documented resolution of atonic seizures in eight and a substantial reduction of atonic seizures in the remaining 16 of 24 patients so treated. Other reports have documented that callosotomy benefits patients with generalized tonic-clonic seizures.

While callosotomy for complex partial seizures is controversial, anterior callosotomy may be indicated in specific situations. At our center, patients who have complex partial seizures but demonstrate either bilateral ictal onset (during invasive recordings) or an interhemispheric propagation time between the temporal lobes of less than 5 seconds are considered candidates for anterior corpus callosotomy. In the present series, nine patients had complex partial seizures, of whom seven achieved a good and one an excellent seizure outcome. Ictal monitoring established bitemporal seizure foci in seven patients and bilateral extratemporal foci in two. Other investigators have found successful outcomes in patients with complex partial seizures.

**Analysis of Current Results**

In our series of 80 patients, 70 underwent anterior corpus callosotomy and 10 complete callosotomy. Two patients died, yielding 78 patients for follow-up analysis. The seizure outcomes were as follows: 10 (12.8%) seizure-free patients; 51 (65.4%) significantly improved; and 17 (21.8%) unchanged. Anterior callosotomy resulted in substantial seizure reduction in 78% of our patients. Many of these patients underwent postoperative MR imaging to assess the degree of callosotomy, and those who have done well had approximately 80% of the anterior callosum sectioned (this implies all of the genu and the anterior portion of the body for a total of 80% of the entire callosus). Completing the callosal sectioning, on the other hand, resulted in additional seizure reduction in just five of 10 patients. Only two of these had substantial seizure reduction to warrant classification in the significantly improved group and none achieved seizure-free status. Moreover, in no patient was seizure outcome upgraded from unchanged to significantly improved as a result of posterior callosotomy.

**Anterior vs. Complete Callosotomy**

While our series supports anterior (80%) callosotomy for the treatment of generalized epilepsy, controversy exists between the need for anterior or complete callosotomy for optimal seizure outcome. The Yale group advocates complete callosal sectioning in those who fail to improve substantially following anterior callosal sectioning. In their hands, 77% benefited after total sectioning whereas only 33% improved after partial sectioning. Their procedure is staged to minimize the acute disconnection syndrome. This syndrome may be permanent following complete corpus callosotomy and occurs in those who do not have mixed cerebral dominance.

Purves, et al., supported the contention that anterior callosotomy may be sufficient for many patients, reporting that this procedure resulted in improvement in 75% of their series. Seven of 24 patients developed a truncated disconnection syndrome marked by mutism and left hemiataxia, but these disturbances cleared over a few days. Murro, et al., reported that 17 (68%) of 25 patients experienced significant reduction of gen-
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geralized tonic-clonic seizures following anterior corpus callosotomy. One problem in comparing patient series is not knowing how much is resected during an "anterior" callosotomy.

Complications

Temporary left hemiparesis can follow partial or complete corpus callosotomy and usually disappears over a matter of days or weeks. Its cause is attributed either to retraction of the medial hemisphere or to damage to the venous drainage of this region. In our experience the acute disconnection syndrome or left hemiparesis did not occur frequently. Postoperative transient mutism occurred frequently but lasted only 1 to 4 days. The low incidence of long-lasting disconnection syndrome can be attributed to performing an anterior callosotomy only (80%) rather than a complete sectioning. However, we found that the incidence and severity of this complication has diminished greatly since we abandoned the supine operative position for the lateral decubitus position (the latter position eliminates the need for retraction of medial frontal cortex).

Our series contained no patients with crossed cerebral dominance: that is, individuals who have cerebral dominance on the same side as preferred handedness. In such patients postoperative communication deficits may occur following total or partial callosotomy.

Correlates of Outcome

An improved clinical seizure outcome has been correlated with higher IQ and younger age at seizure onset. Wilson, et al., Blume, and Spencer, et al., have noted a relationship between retardation and poor seizure relief following callosal section. Why mental retardation is associated with a less favorable seizure prognosis is not completely understood. It has been suggested that in many cases mental retardation reflects more generalized damage to the central nervous system. Thus, the seizure syndrome may be more refractory to any form of treatment, medical or surgical. Although this trend was also seen in our series, it is not absolute because one of our longest-followed seizure-free patients is also mentally retarded.

The trend between younger age at seizure onset and a favorable seizure outcome has been noted in previous reports. Wilson, et al., on the other hand, observed that age at seizure onset had no relation to seizure outcome. We have also found a suggestive trend between older age at seizure onset and poorer outcome from callosal sectioning. Primary generalized epilepsy occurs in younger patients, and it may be that individuals with this type of seizure do better following callosotomy than those who have other types of epilepsy (secondarily generalized or multifocal). Because individuals who are older at seizure onset are less likely to have primary generalized epilepsy, they may not fare as well following corpus callosotomy.

Conclusions

We have reported our experience with 80 patients treated with anterior corpus callosotomy. Ten of these patients subsequently had the remainder of the callosum sectioned. Anterior section alone was effective in helping 61 (78%) of 78 patients, but only a small percentage (12%) of patients were completely seizure-free. Although completion of callosotomy helped an additional five of 10 patients, the actual gains in seizure reduction were rather modest. The majority of postoperative complications occurred in the group who underwent completion of callosotomy. We have found that an initial sectioning of 80% of the callosotomy provides an optimal outcome for the majority of patients who are likely to benefit from callosotomy, and we no longer routinely consider completion ofcallosal section. A younger age at seizure onset and a higher IQ were associated with better outcome, although neither factor achieved statistical significance (p < 0.05).

References

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