Callosotomía: técnicas, resultados y complicaciones. Revisión de la literatura

Callosotomy: techniques, results and complications - Literature Review

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Abstract

Background: Patients with intractable seizures who are not candidates for focal resective surgery are indicated for a palliative surgical procedure, the callosotomy. This procedure is based on the hypothesis that the corpus callosum is an important pathway for interhemispheric spread of epileptic activity and, for drug resistant epilepsy. It presents relatively low permanent morbidity and an efficacy in the control of seizures. Based on literature, the corpus callosotomy improves the quality of life of patients that has the indication to perform this procedure because it allows reducing the frequency of seizures, whether tonic or atonic, tonic-clonic, absence or frontal lobe complex partial seizures. **Aim:** The aim of this literature review is discuss the technical details, modalities, risks, complications, results as well de prognosis of callosotomy based on critical literature review and the authors experience. **Casuistry and Methods:** It was performed bibliographical consultation, using the databases MEDLINE, LILACS, SciELO, utilizing language as selection criteria, choosing preferably recent articles in Portuguese, Spanish or English, with publication year higher than 2000. **Conclusion:** According to author's experience and references, callosotomy is a safe procedure when indicated to selected cases and the success rate is proportional to the extent of callosal resection. A greater resection can reduce the seizure frequency, however the morbidity may also be larger. There is no important study comparing VNS *versus* Callosotomy *versus* VNS plus callososotomy, what would be for future necessary for an important source of data about this topic.

Key words: Drug Resistant Epilepsy, Drug Refractory Epilepsy, Corpus Callosum.

Resumen

Introducción: Los pacientes con convulsiones intratables que no son candidatos para la cirugía de resección focal están indicados para un procedimiento quirúrgico paliativo, la callosotomía. Este procedimiento se basa en la hipótesis de que el cuerpo calloso es una importante vía para la propagación interhemisférica de la actividad epiléptica y, para la epilepsia resistente a fármacos. Presenta relativamente baja morbilidad permanente y una eficacia en el control de las convulsiones. Sobre la base de la literatura, la callostomía mejora la calidad de vida de los pacientes que tiene la indicación para realizar este procedimiento, ya que permite reducir la frecuencia de las crisis, ya sean tónica o átona, tónico-clónicas, ausencia o lóbulo frontal crisis parciales complejas. **Objetivo:** El objetivo de esta revisión de la literatura es discutir los detalles técnicos, modali-

dades, riesgos, complicaciones, resultados y de pronóstico de callosotomía basado en la revisión crítica de la literatura y la experiencia de los autores. **Casuística y Métodos:** Se realizó la consulta bibliográfica, utilizando la base de datos MEDLINE, LILACS, SciELO, que utiliza el lenguaje como criterios de selección, la elección de los artículos recientes preferiblemente en portugués, español o Inglés, con el año de publicación superior a 2000. **Conclusión:** De acuerdo con la experiencia y las referencias del autor, callosotomía es un procedimiento seguro cuando indicado para casos seleccionados y la tasa de éxito es proporcional a la extensión de la resección del cuerpo calloso. A mayor resección puede reducir la frecuencia de las crisis, sin embargo, la morbilidad puede ser también mayor. No hay ningún estudio que compara la estimulación del nervio vago frente a frente callosotomía VNS más callososotomy, lo que sería la futura necesaria para una importante fuente de datos sobre este tema.

Palabras clave: Epilepsia refractaria, epilepsia resistente a fármacos, Cuerpo calloso.

Introduction

Corpus callosotomy is a palliative surgical approach that aims to control potentially harmful seizures, for instance, atonic or drop seizures, preventing the spread of epileptic electrical activity[4].
This technique was described by Van Wagnen and Dandy[16,56] and was highlighted as a surgical method after 60s. In the following decades, Bogen reintroduced the callosotomy[6] and later was reduced indication due to the use of vagal nerve stimulation (VNS).
The disconnective syndrome, the consequence of the section of the corpus callosum fibers, it was proven by experimental callosotomy in monkeys[28,29]. Although VNS results have shown minor complications, some patients continue to have atonic seizures, tonic and clonic seizures, even after treatment. In these cases, it would be indicated the additional callosotomy. In Lennox Gastaut Syndrome, both kinds of surgery has been used, however few authors have used for disconnection of partial lateral syndromes secondarily generalized. If we consider only the refractory atonic seizures, there is no superiority between these surgical methods, even VNS presenting minor complications[4,17].
The most important complications of corpus callosum transection are mutism, the disconnection syndrome and hemiparesis[35].
This article aims to clarify technical details about callosotomy, allowing avoid damaging to important neural structures as fornix, ventricle wall, arteries, thalamic connections, forceps minor and major. A serious complication and cause of postoperative death is injury to vessels close to the corpus callosum, as the veins and pericallosal and calloso marginal arteries.
In over 60% of cases, callosotomy shows satisfactory results for the purpose of treatment. In these patients, there is a decrease in the frequency of seizures and improved quality of life[4,32].
The materials needed to perform a callosotomy can be found in all hospitals and include a simple headlight and binocular loupes or microscope, self-retention brain retractor, bipolar cauterization, and simple micro instruments[58].

Casuistry and Methods

It was performed bibliographical consultation, using the databases MEDLINE, LILACS, SciELO, utilizing language as selection criteria, choosing preferably recent articles in portuguese, spanish or english, with publication year higher than 2000.

Anatomy of callosum body

The corpus callosum is the principal interhemispheric commissure. Embryologically, it arises in the brain of placental mammals as an elongated midline structure composed of 2-3 x 108 fibers horizontal interconnecting homotopical and heterotopical cortical areas[2,23,24].
The mature corpus callosum contains myelinated (70%) and unmyelinated fibers (30%), glial cells (astrocytes and oligodendrocytes), and neurons[5,31,43-45] and normally the callosum body has 7.5 - 9 cm in length and 2.5 - 3 in height and the 2/3 that we need to perform callosotomy is almost five to six centimeters[21].

Regions

By means studies with diffusion tensor magnetic resonance imaging (dt-MRI) and fiber tractography, Hoffer and Frahm[23] showed the trajectory of the fiber, and concluded that the corpus callosum may be classified in five portions from anterior to posterior, which have different fiber compositions:
Region 1: Anterior portion or genu;
Region 2: Anterior portion of the middle third;
Region 3: Posterior portion of the middle third;
Region 4: Isthmus of corpus callosum
Region 5: Splenium.

There are two types of fibers in the corpus callosum: small fibers, mainly connecting association cortical areas, found in the rostrum, genu and anterior body and large diameter fibers in the posterior part of the splenium and in the body, where interhemispheric sensory fibers cross the commissure and exchange information at high speed[1,2].

Vascularization

Over the inner ependymal surface, the drainage veins are spreaded, which drains posteriorly to basal vein of Rosenthal and internal cerebral veins[59].
The arterial vascularization comes from pericallosal, callosomarginal and fronto polar arteries by perforating arteries

Callosum fibers

There are two enlargement of fibers that forms the forceps: posteriorly this enlargement of white fibers forms the forceps major and at the anterior portion there is a continuous enlargement laterally to the forceps minor.
The fibers of callosum body are associative white fibers with connections with striatum in inferior middle anterior portion, limbic system, and between the motor fibers of the two hemispheres. They are parallel to coronal plane and

perpendicular to sagittal plane. In the posterior portion of the corpus callosum there are interhemispheric connecting fibers related to motor function, speech, visual and interactive memory and in istmus related to visual function. In the upper part of the medial wall of ventricular carrefour, the forceps major produces a prominence named bulbo of callosum body. Another fiber tract in the posterior part of body and splenium is the tapetum, that sweeps laterally and inferiorly to integrate the roof and lateral wall of atrium and temporal as well the occipital horn (Figure 1)[46].

The classical division of the corpus callosum proposed by Witelson in 1989, has not been used for be not practical[57]. Fabri et al 2014 showed a specific correspondence with sensorial, motor functions are related to corpus callosum (Figure 2)[19].

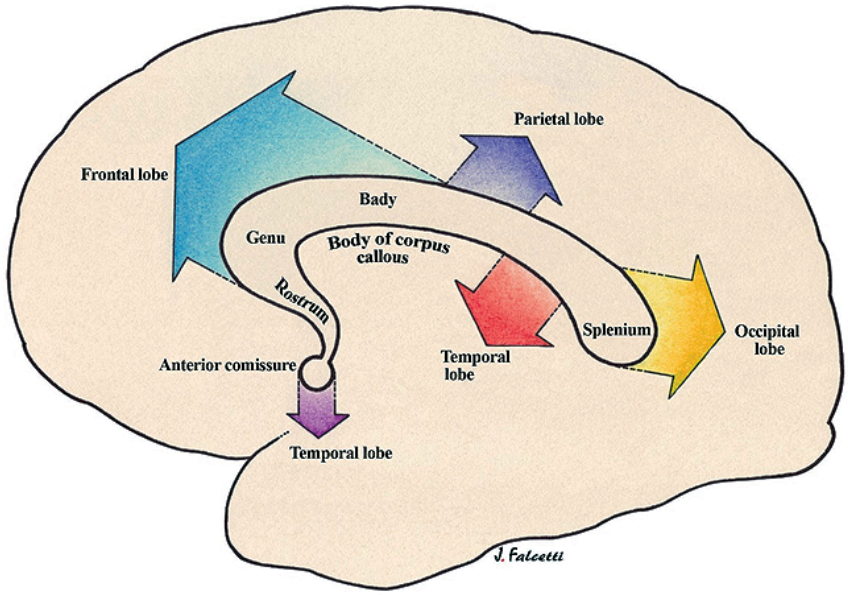

Figure 1. Connections flow of corpus callosum with adjacent structures.

Technical details

Under general anesthesia, the patient is placed in lateral or supine position with the right hemisphere turned down. With the aid of a neuronavigator, avoiding mistakes of extension of resection, showing the genus of callosum body, and the posterior point representing the 2/3 of body, the incision is marked in curvilinear shape turned anteriorly, surpassing the midline and posteriorly enough to reach the posterior third of corpus callosum[26, 55]. The incision may be bicoronal or in horseshoe bifronto-parietal centered in the coronal suture unilaterally or bilaterally. The authors of this paper prefer the curvilinear right side, in neutrum position of head fixed by head fix of Mayfield or Sugita type, ¾ prone may be used for two stage posteriorly resection[25] and lateral position of head, with the right side turned down. Some authors use ¾ of resection of callosum body[55]. Nonetheless, the side to be approchead may be determined by preoperative tests studies, including MRI angiography, in order to ensure the veins dominance of Trollárd vein complex[26].

To identify the sagittal sinus and allow retraction of the right hemisphere, the craniotomy has to be as large as possible (Figure 3)[15].The dura-mater is opened in arch turned to the sagittal sinus. In lateral position, the right hemisphere drops through the gravity and the left is hanged by the middle sagittal falx

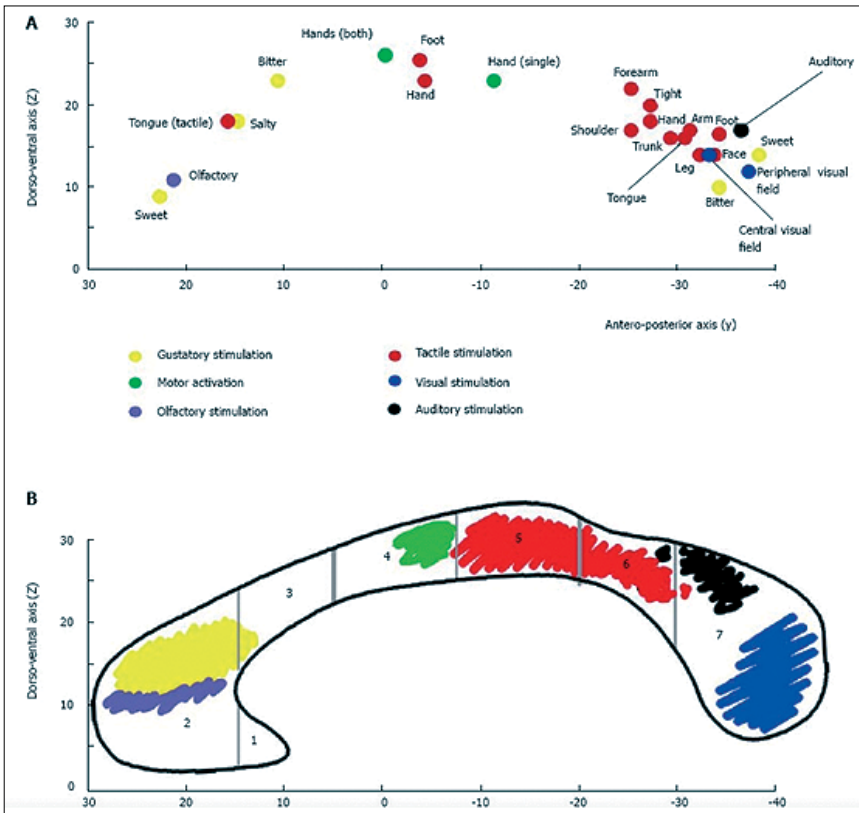

Figure 2. (From Fabri et al, 2014) Callosal activation and callosal fibers topography. **A:** Summary diagram showing the distribution of the callosal foci evoked by different stimuli in control subjects. Each dot represents the "mean" value of the y and z Talairach coordinates (reported on the respective Cartesian axes) of the foci evoked by different stimuli. Yellow: Foci by gustatory stimuli; violet: Olfactory stimuli; green: Hand motor tasks; red: Tactile stimuli; black: Auditory stimuli; blue: Visual stimuli; **B:** Shows the crossing sites of interhemispheric fibers interconnecting the sensory and motor cortical areas activated by the specific peripheral stimuli. Vertical gray lines mark the seven CC regions according to Witelson classification.

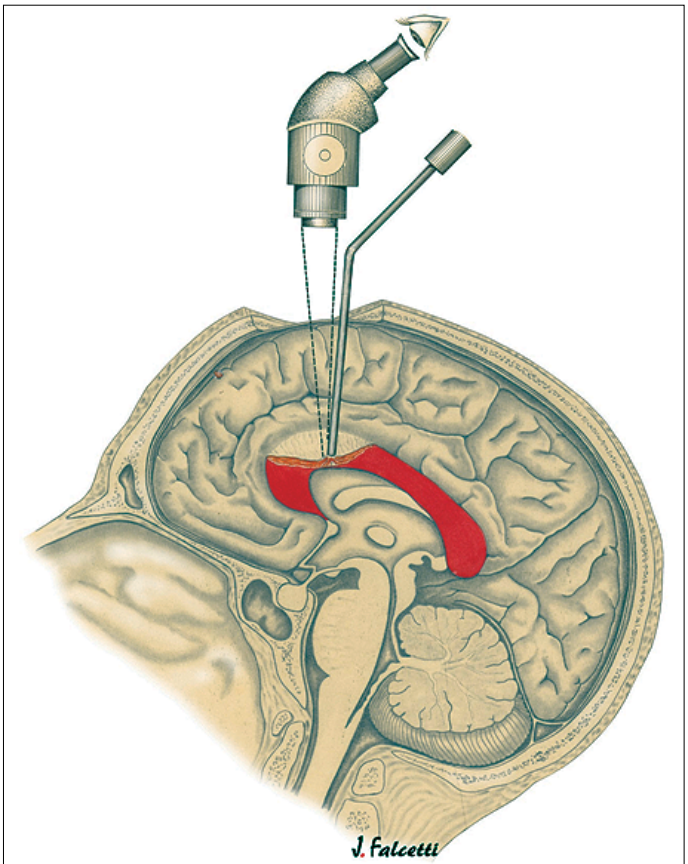

Figure 3. View of the surgical field craniotomy to access the anterior two thirds of the corpus callosum.

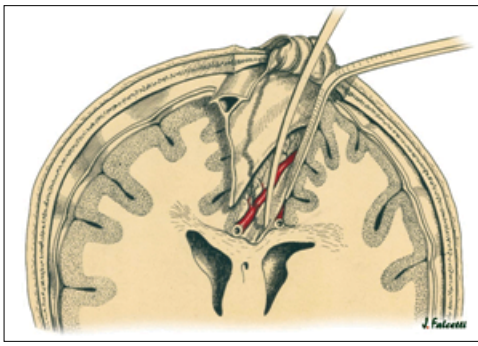

Figure 4. Unilateral inter hemispheric space access using a spatula to displace the ipsilateral hemisphere and the falx cerebral to hold the contralateral hemisphere.

(Figure 4). Only few authors emphasize the use of two steps to reach the posterior part of the corpus callosum[25,49,50,51]. The microscopical magnification may be employed to meticulous dissection of interhemisferic fissure, taking care with the fronto parietal veins. The falx covers the left hemisphere and with retractor of Leila or Greenberg we gently push the mesial surface of frontal and parietal lobe. The bipolar coagulation of pia-mater is necessary in few points, due to bleedings of pia-mater during the dissection. If the coagulation does not solve the bleeding could be used simple tamponament with cotton and oxcell. The both cingullum gyri might be attached with hudge adhesion, and dificulting the dissection, that must be sharp and with microdissector. After the separation of the two cingulate gyri, we may identify the pericallosal artery running over a white shining structure that is the corpus callosum (Figure 5). Most of the times the pericallosal artery from one side is larger than the other. We go on further in dissection, with the aid of neuronavigator, showing the callosum body since the genus until two thirds posteriorly. Near the genus, the pericallosal artery may be followed until the bifurcation with de callosum marginal artery and fronto polar artery. The surface of callosum body may be coagulated if the variation is azigos or hemiazigos between the pericallosal arteries, and opened with blade of knife. After that with enlargement using suction with gentile movement in order to open the corpus callosum from posteriorly untill anteriorly, showing two important landmarks: posteriorly with open the roof of third ventricle medially to fornice column bilaterally and anteriorly the A2 of anterior cerebral artery after the aspirate and remove the anterior portion of callosum body and genus. In order to avoid bleeding into ventricle cavity or accumulation of clots it is necessary careful hemostasis. The dura-mater suture could be done with separated suture or continually with silk or prolene, 4-0, water tightly. Mini plates and mini screws could be used for osteosynthesis.

Stereotatic callosotomy using radiosurgery

In the study of Pedl et all the authors described good results with doses near 150 Gy in three patient, that had intractable epilepsy (One had multifocal epilepsy with atonic, tonicoclonic, and atypical absence seizures and two had Lennox-Gastaut syndrome) treated by means of Gama Knife, from 1992 to 1995, showing that radiosurgery would be an promising method[40].

A case of a 17 year old male patient underwent corpus callosotomy conformal SRS using a dedicated linear accelerator with dynamic arcs technique, was described by Cellis et al, using the dose of 36 Gy at the periphery of the rostrum, genu and a half of the body of the corpus callosum (CCA). In this case, the patient evolved with a significant brain edema and moderate transitory motor deficit at eight months after surgery, which were controlled with steroids[14]. The authors of these study observed that there was an improvement of 84% on drop attacks and generalized tonic-clonic seizures after 32 months follow-

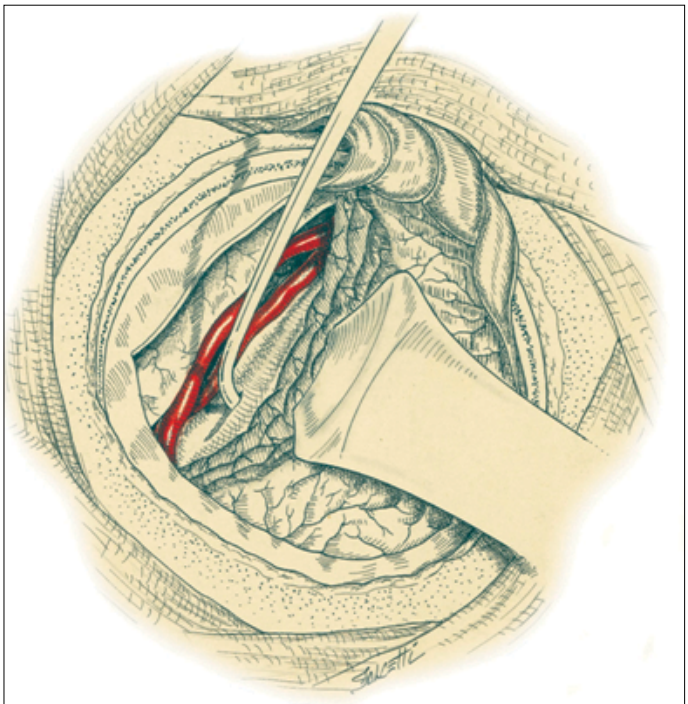

Figure 5. Inter hemispheric fissure space's view with pericallosal arteries displacement using a spatula.

up[14], nevertheless in our opinion is not a method well established in the literature for routine use.

We must take into consideration that most patients subject to callosotomy are young and the radiation dose to which they will be exposed is high, which may increase the rates of malignant changes over the decades. After hemispherotomy, a radiosurgical callosotomy could be indicated, to complete the callosal resection[18].

Selection of patients

Most patients eligible for callosotomy are children between the age of 11[11,12,13]. Some criteria may select patients eligible for surgery callosotomy:

- Patients with drug refractory epilepsy, include atonic, clonic, myoclonic, absence, tonic clonic seizures, after two years treatment with at least two anticonvulsive drugs[15,37,38,49,50,51];
- Patients with partial complex epilepsy or sensorio motor with generalization can be also treated with callosotomy;
- Patients who did not achieve complete seizures control after VNS, principally atonic[17];
- Patients with uncontrollable seizures with a potential of severe injury due to falls (collapse into the floor).

Epileptogenic evaluation for surgery

Some items should be included in the evaluation of epileptogenic activity for surgery, including interictal electroencephalogram (iEEG), interictal spect, magnetic resonance imaging (MRI) and age-appropriate neuropsychological/developmental assessment. Some exams, like the intracranial EEG, could indicate a complementar surgery after a callosotomy, because it provides the localization of the correct focus of seizure[53]. Other exams may be useful on this avaliation and should be included in the protocols of seizures foci investigation, like functional MRI and EEG[33].

Risks of callosotomy surgery

Although lasting complications of corpus callosotomy are very rare on this type of epilepsy surgery, it is known that impaired language skills, calossum mutism (temporary loss of speech) and damage to the frontal lobe due to the procedure that may lead to changes in behavior are risks to be considered during the surgical act.

In the literature has been described that cerebellar mutism is very similar to the calossum mutism, insofar as there be damage of dentate thalamus cortical pathway[35]. However, others authors indicated the transient disconnection syndrome as a cause of this side effect[13]. It should be emphasized that in spite of the complete syndrome of disconnection described, it is more common when the section of callosum body is posterior.

Regarding to the risk of meningitis, in spite of it is rare, when happened it is a difficult complication to treat because may there is a difficult to differentiate symptoms from the caused purely by the callostomy disconnection and the symptoms induced by the inflammation and fever associated cognitive symptoms.

The risk of bleeding, it is uncommon, but acumulus of clots third ventricule and in lateral ventricule may be observed in few cases. However, in spite of its rare, arterial lesions may a possibility of side effect of this surgery with a high mortality and morbidity.

Combined approaches

Regarding to choose of the surgical combined approaches of callosum body, it is depending on the kind of pre-operative electrographic, neuropsychological, image evaluation the callosotomy may associated with anterior, posterior comissurotomy, hippocampectomy, hemispherotomy and others[11,12,13].

Results

In the literature there are many types of approaches and procedures for epilepsy, so that the result after corpus callosotomy surgery is difficult to summarize, because of the many variations, according to the authors in his critical review of literature, of the definition of a good or poor seizure outcome[22]. Authors concluded that the best reduction in seizure frequency is archived in patients with atonic and estimated ranging 65% to 85% of them[22].

In a clinical study constituted by group of 9 women and 24 men, whose age at surgery ranged from 5 months to

19 years, was performed the corpus callosotomy, lesionectomy, temporal lobectomy, multiple subpial transections and VNS and analyzed the QOL and Engels cale of seizure in the post-operative period, with mean follow-up of 11,9 months[30]. In this study the results of all the groups showed that there weren't patients with worse and stabling QOL status. So that the group treated with callosotomy showed the considerable improvement in QOL estimated in 36,4% of the cases[30]. Furthermore, in more than 43% of patients observed there weren't seizures after the surgery and in more than 95% of cases showed the reduction in seizures frequency was greater than 75%[30].

From 1981 to 2001 was developed a study constituted by group of 95 patients treated by callosotomy at Montreal Neurological Institute[52]. In this essay was confirmed that the rate of complications are mild and transient and the presents a 0% of mortality, so that concluded that the extent of the callosal sections is correlated with favorable seizure outcome. Ranging to the patient's seizure, this paper concluded that their patients had more than on type of seizure so that the majority showed generalized tonic-clonic and drop attacks seizures. In their opinion based in clinical and surgical experience the disabling seizure type harboring the patients in this group was drop attacks, followed by generalized tonic-clonic seizures. After the callosotomy was observed the improvement in several seizure types and mainly for drop attacks (77.2%) and tonic-clonic seizures (77.3%), so that this paper concluded that the anterior callosotomy also benefited the generalized, simple partial and myoclonic seizures.

Another important paper that should be mentioned because it compare total callosotomy with anterior callosotomy and also a two stage callosotomy[49]. In this essay the patients were divided into 3 groups constituted by 42 patients after anterior callosotomy (first group), 22 after total callosotomy (second group) and 14 patients of second group was underwent a two-stage procedure (third group). The results showed important diminution and some cases cure of seizures was most significant for tonic-clonic and tonic seizures in the first group (83% and 100%, respectively), in the means that in the second group was for tonic and tonic-clonic (57% and 68%). Important incremental results were showed for all seizure types, in spite of the results in the third group showed failure to improve after anterior section and after that they were underwent total section total section. More than two seizure types was identified, so that were significantly more common in the first group the diffuse ictal EEG patterns and verbal IQ<80. With the anterior callosotomy failure, the total callosotomy was then indicated by the authors, mainly due to the persistence of tonic and tonic-clonic seizures.

In a study from 2007 constituted by 37 pediatric patients, it was found a similar result[42]. This study showed bigger or equal reduction of 75% of seizures in 75% underwent a total callosotomy and 55% underwent a partial one. Nonetheless, in this paper was showed an important matter in the reference of the family's satisfaction that commonly is slighted in the pre-operative period due to excessive number of caily seizures. So that the family's rate of satisfaction was 73% and 89% in the partial callosotomy and total respectively.

Complications of callosotomy surgery

About the consequences of callosotomy surgery, many complications may be listed like an occiptal and cingular contusion due to a posterior interhemispheric approach, ischemia in the pericallosal territory in the anterior communicating artery territory, bilateral mesiofrontal damage and venous infarct from bridging vein damage, so that all of them are transient or permanent[20].

Among of the concerns on the surgical act of callosotomy, an important matter to be considered is about destruction of the patient's social and professional activities due to the lesions in the dominant left hemisphere, consequence similar to Gerstmann syndrome[9].

In spite of the complications for both VNS and corpus callosotomy are rarely permanent, the VNS's complication rate is lower (8%; none permanent) than that for corpus callosotomy (21% all complications; 3.8% permanent)[36].

In the literature has been observed a low rate of morbidity and mortality associated a callosotomy surgery, ranging from 3.6% to 5.6%[48,58] and 1.3%[48], respectively. However, a morbidity rate of 37% was described in 1991; this is being related to probably an intraoperative technology of the period inferior to modern era[37]. So that, the most frequent of all the complications in the callosotomy surgery were epidural bleeding, subdural collections, hydrocephalus, disconnection syndrome was observed in a rate from 6% to 89%[15,27,54] in the means that permanent disconnection syndrome was observed in 3%[15].

Future on callosotomy

In the literature there are studies suggesting that surgical approach of callosum body by endoscopy are controversial and initial, so that in our opinion it does not will to decrease the complications[13]. Furthermore, in the literature showed that there was 90% of satisfaction after a parental questionnaire attributed to the control of drop attacks when associated the posterior, anterior and hippocampal commissurotomy[11,12].

Conclusions

According to author's experience and references, callosotomy is a safe procedure when indicated to selected cases and the success rate is proportional to the extent of callosal resection[15,30,37,38,48,54]. A greater resection can reduce the seizure frequency; however, the morbidity may also be larger. In the author's opinion, the neuronavigation is important for the purpose and one stage resection is more comfortable for patient.

The VNS allows the control of seizures in 60% of cases, with minor complications and no mortality[41]. However if we use the same patient selection criteria to indicate the VNS it is possible to select more restrictively patients who have indication for callosotomy.

The callosotomy show better result in control of seizures (Control of generalized tonic clonic seizures rate of 79.5%) when compared to VNS (50% control), however with higher rate or permanent complications (2.8% callosotomy, 0% VNS)[36]. There is no important study comparing VNS *versus* callosotomy versus VNS plus callosostomy, what would be for future necessary for an important source of data about this topic.

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