Seizure outcome and complications following hypothalamic hamartoma treatment in adults: endoscopic, open, and Gamma Knife procedures

Clinical article

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Object. This study aimed at identifying outcomes with respect to seizures, morbidity, and mortality in adult patients undergoing resective or Gamma Knife surgery (GKS) to treat intractable epilepsy associated with hypothalamic hamartoma (HH).

Methods. Adult patients undergoing surgical treatment for HH-related epilepsy were prospectively monitored at a single center for complications and seizure outcome by using a proprietary database. Preintervention and postintervention data for patients 18 years of age and older, and with at least 1 year of follow-up, were analyzed, with specific attention to seizure control, complications, hormonal status, and death.

Results. Forty adult patients were found in the database (21 were women). The median HH volume was 0.54 cm3. In 70% of patients, it was located inside the third ventricle, attached unilaterally and vertically to the hypothalamus (Delalande Type II). Most patients (26) underwent an endoscopic resection, 10 patients had a transcallosal or other type of open (pterional or orbitozygomatic) resection, and 4 patients chose GKS.

Twenty-nine percent became seizure free in the long term, and overall a majority of patients (55%) reported at least >90% seizure improvement. Only 3 patients were ultimately able to discontinue anticonvulsants, whereas most patients were taking an average of 2 antiepileptic drugs pre- and postoperatively. The only factor significantly correlated with seizure-free outcome was the absence of mental retardation. The HH volume, HH type, and amount of resection or disconnection were not correlated to seizure freedom. A total of 4 patients (10%) died, 2 immediately after surgery and 2 later. All of them had undergone a resection, as opposed to GKS, and still had seizures. Postoperatively, persistent neurological deficits were seen in 1 patient; 34% of patients had mild hormonal problems; and 59% experienced weight gain of at least 6.8 kg (average gain 12.7 kg).

Conclusions. Surgical or GKS procedures in adults with HH provided seizure freedom in one-third of patients. The only significant favorable prognostic factor was the absence of mental retardation. The overall mortality rate was high, at 10%. Other important morbidities were persistent hormonal disturbances and weight gain.

Key words • hypothalamic hamartoma • gelastic seizure • outcome • epilepsy surgery

Hypothalamic hamartomas are malformations originating from the hypothalamus that are associated with seizures and hormonal and behavioral abnormalities. Most patients, particularly those with a typical syndrome characterized by gelastic seizures, precocious puberty, cognitive decline, and behavior problems, are diagnosed in childhood. However, some patients are adults when an HH is found, either incidentally or when workup is initiated because of typical, yet previously unidentified or undiagnosed symptoms. Seizures in patients with HH are usually drug resistant, but there are potentially curative treatment options, namely resection or radiosurgery (GKS). This study aimed to investigate the outcome with respect to seizures, as well as morbidity and mortality rates, following surgical procedures in adult HH patients at a single large referral hospital.

Methods

The prospective HH database at Barrow Neurologi-
cal Institute was searched for all patients in whom HH had been diagnosed and treated at the age of 18 years and older, with at least 12 months of follow-up, effectively including patients between 2003 and 2010. The database is approved by the institutional review board and prospectively enrolls and follows all patients with HH who are referred to our center for evaluation. Candidacy for surgery was decided following group consensus, including the requirement that all patients had intractable epilepsy and that at least 2 previous trials of antiepileptic medication had failed to control seizures. The prospective database was supplemented by chart review and retrospective standardized telephone interview for this study. Immediate postoperative outcome was considered to be any outcome regarding seizures, morbidity, and death occurring during the hospital stay and within 30 days postoperatively. Long-term postoperative outcome included all outcomes beyond the first 30 days postprocedure.

Preoperative data were reviewed for seizure types and frequency, antiepileptic treatment, and comorbidities. Postoperative data were analyzed for death, immediate and late postoperative complications, and hormonal abnormalities as well as seizure outcome.

Neuroimaging Studies

The MRI studies were reviewed by a single pediatric neuroradiologist (E.P.) who was blinded to the clinical outcome. The HH type according to the Delalande classification (see below), pre- and postoperative HH size, site of attachment, amount of resection, and amount of disconnection were determined. Image sequences and measurements of the area of attachment were performed as described in a previous publication."}

Hypothalamic hamartomas were classified using the Delalande system. This system divides HHs into 4 types: Type I has a horizontal implantation plane inferior to the floor of the third ventricle; Type II is within the third ventricle, with a vertical insertion plane; Type III is a combination of Types I and II; and Type IV includes all giant hamartomas.3

Evaluation of Outcomes

Seizure outcome was recorded per the patient’s or caregiver’s report and grouped into “seizure free,” isolated seizures (that is, 1–2 postoperatively), > 90% seizure reduction, 50%–90% seizure reduction, and < 50% seizure reduction, and was also categorized according to the Engel4 and ILAE19 classifications.

Statistical Analysis

Statistical analysis was performed using the program SPSS (version 16). The Kendall tau test was used to correlate nonparametric variables. Logistic regression analysis was used for multivariate assessment of seizure freedom. The following variables were included in the analysis: diagnosis of mental retardation, Delalande type of HH, side of HH attachment, size of HH before resection, percentage of HH resection, and percentage of HH disconnection. The chi-square statistic was used separately to investigate whether distributions of categorical variables (seizure freedom in relationship to 100% resection) differ from one another. In all testing, significance was established at p < 0.05.

Results

Study Population and Length of Follow-Up

Forty adult patients with HH (21 women and 19 men) were treated at Barrow Neurological Institute between April 2003 and February 2010. At the time of surgery, the age in this population ranged from 18 to 55 years. The average age was 27.6 years (median 27 years). Follow-up ranged from 12 months to more than 7 years, and the mean duration was 58 months (median 70 months, range 12–94 months).

Preoperative Clinical Profile

Characteristics of Epilepsy. The majority of patients (26 [65%]) had seizures starting in the 1st year of life. In 18 patients, the seizures began at or shortly after birth, and in 8 more patients within the first 9 months. In another 13 patients (33%), seizures started within 10 years of age. Only 1 patient (3%) had the first seizure during adulthood (age 20 years). The average duration of epilepsy was 26 years (range 9–55 years), and in many patients it was nearly identical to their age at the HH procedure.

Although epilepsy was diagnosed in most patients earlier in life, it took an average of 17 years (median 17 years, range 0–55 years; 38 patients), until the HH was identified.

Ninety percent of patients (36 of 40) had gelastic seizures or seizures with a gelastic component. However, most experienced more than 1 type, that is, 2–3 seizure types (31 patients [78%]). The second most common seizure type was complex partial seizures, experienced by 73% (29 of 40 patients). Only 5 patients experienced just 1 seizure type, and 4 patients experienced 4 or more seizure types. More than two-thirds (29 of 40 [73%]) had gelastic seizures as the most frequent type. Only 6 patients (15%) presented with complex partial seizures as the predominating type. Three patients had mainly generalized seizures (8%), whereas auras without any clinical signs dominated in 2 patients (5%), and in 1 patient (3%) myoclonic seizure was most common. Drop attacks were seen as an independent seizure type in 5 patients (13%).

Almost all of the patients (37 [93%]) had daily seizures, with an average of 5 seizures per day (range 1–20 per day). Seizures occurred at least once per month in the 3 remaining patients (8%).

At the time of the procedure, all but 1 patient were taking 1–4 different AEDs, with most being treated with 2 or 3 drugs (median 2 AEDs in 28 patients [70%]). However, on average, 8 different AEDs had been tried in the past. Fourteen patients had undergone vagal nerve stimulation treatment (35%), and 3 patients had tried a ketogenic diet (8%).

Previous EEG and Video-EEG Evaluations. Only 21 patients (53%) had previous routinely documented EEG results, of which 15 patients had abnormalities (71%). The majority of these 15 patients (11 [73%]) had focal abnormalities, although generalized epileptiform discharges or abnormal slowing were also seen.
Seizures had been investigated using video-EEG studies in 29 patients (73%). Available reports documented that seizures had a focal or lateralized onset in 17 (59%) of these 29 individuals. Four patients (14%) had nonlocalizable seizures, 3 (7%) had generalized seizure patterns, and 1 (3%) had no ictal EEG change. A more detailed description of EEG and video-EEG findings is found in the study by Troester et al.18

Comorbidities. As part of their medical history, hormonal problems were known in 16 (42%) of 38 patients, in all of whom precocious puberty had been diagnosed. Three of these patients also had hypothyroidism. Twenty-two (55%) of the 40 patients carried a diagnosis of mental retardation.

Prior Procedures. Sixteen patients (40%) had previously undergone one or more unsuccessful procedures for seizures. Three (19%) of these 16 patients had had focal resections aiming at a suspected cortical seizure focus, and one (6%) also underwent corpus callosotomy. Thirteen of these 16 patients (81%) had already had procedures targeting the HH (8 GKS procedures [once], 4 biopsy or partial resection, and 1 thermoablation).

Preoperative Imaging. Volumetric MRI analysis showed that the median HH volume was 0.54 cm³ (average 2.32 cm³; minimum 0.09 cm³, maximum 11.19 cm³). In 70% of patients (28 of 40), HH volume was < 2 cm³. The median surface area of HH attachment was 0.67 cm² (average 0.86 cm²; minimum 0.16 cm², maximum 3.36 cm²). Not surprisingly, there was a significant correlation between HH size and base of attachment (r = 0.751, p < 0.0005).

According to the Delalande classification, 8% of patients had Type I (3 of 40), 70% had Type II (28 of 40), 13% had Type III (5 of 40), and 10% had Type IV (4 of 40).

Apart from the HH, no other congenital abnormalities were seen on the MRI studies.

Procedures and Outcome

Types of Procedures. Twenty-six patients (65%) underwent an endoscopic resection of the HH, and 6 (15%) had transcortical resection. Four patients had staged, combined procedures, with interventions that either combined an endoscopic and an open procedure with a pterional or orbitozygomatic approach (3 patients [8%]), or combined an endoscopic procedure and a transcortical approach (1 patient [3%]) within 1 week. Four patients (10%) had GKS. Later, 3 patients who first had a resective surgery underwent Gamma Knife treatment—2 months, 9 months, and 12 months after the initial intervention. Dose planning for GKS was done according to previously published data by Abla et al.1 The variety of procedures was dictated by the size and location of the HH, which did not allow for a uniform approach. Larger HHs required a craniotomy to achieve a complete resection, whereas smaller lesions could be removed endoscopically or treated by GKS. There were multiple factors that determined this, including the relationship of the lesion to the optic chiasm, the size of the lesion, and its location in relation to the floor of the third ventricle.1

Postoperative Imaging. Of 36 patients who underwent endoscopic, transcortical, or other open surgeries, 31 (86%) had resection of > 50% of the HH, including 14 patients whose HH was 100% removed. Whereas 100% resection obviously equaled 100% disconnection, lesser amounts of resection were accompanied by varying degrees of disconnection, ranging from 0% to 92%.

Preoperatively, patients who had an endoscopic resection (26 individuals) had a mean HH volume of 1.77 cm³ (range 0.09–11.19 cm³), of which on average 80% was removed (range 7%–100%). Those with transcortical or combined procedures had a larger mean HH volume of 4.59 cm³ (range 0.24–10.23 cm³), of which on average 64% was resected (range 11%–100%). Patients treated with GKS had the smallest mean HH volume of 0.20 cm³ (range 0.14–0.28 cm³).

Abnormalities were seen on MRI studies obtained postoperatively in 6 patients as follows: 2 patients had an asymptomatic thalamic infarct; 1 had a symptomatic thalamic infarct; 1 had multiple symptomatic infarcts and signs of malignant edema; 1 had a right frontal subdural hematoma; and 2 had subarachnoid and intraparenchymal bleeding (1 patient had more than one finding).

Immediate Postprocedural Outcome. There were 2 deaths (5%) in the immediate postoperative period. One patient died as a result of multiple venous strokes after intraoperative injury to a large cortical vein (transcranial approach), and the other presumably died during a seizure 7 days after discharge (endoscopic surgery). Both patients had severe epilepsy and mental retardation at baseline. Immediate medical complications were observed in 19 (48%) of the 40 patients. More than half of these patients (11 of 19; 11 of 40 [28%]) had evidence of hormonal disturbance: 9 with a disturbance of sodium metabolism (either hyper- or hyponatremia), and 2 with thyroid dysfunction. Six patients (15%) experienced an intracranial hemorrhage or ischemia, 2 of whom underwent an endoscopic and 4 an open approach. One of these patients died (as mentioned above), 1 had a transient right hemiparesis and also suffered optic tract injury causing persistent hemianopia, and 4 were asymptomatic. Two patients were treated for infection postoperatively (one had Gram-positive cocci cultured from CSF; the other had persistent fever, but negative cultures).

Of the surviving patients, 11 (29%) of 38 were seizure free immediately postprocedure, but that was not a guarantee for cure, as long-term data showed (see below). Two-thirds continued to have seizures (25 [66%] of 38), including 2 patients with worsened seizures.

Long-Term Postoperative Outcome. Of 38 patients (95%) who survived the immediate postoperative period, 2 were lost to follow-up. Long-term data were therefore available for 36 patients (95%).

Two (6%) of 36 patients died during long-term follow-up, one 6 months after the last intervention without known cause, and the other 3 years later during a seizure. Neither had become seizure free. One patient had a significant persistent neurological deficit related to HH resection (hemianopia). No permanent deficits were associated with GKS.
Approximately one-third of patients had hormonal problems (11 [34%] of 32). Specific complaints and laboratory abnormalities were as follows: decreased libido in 5 patients, sodium abnormalities in 4, and temperature regulation disturbances in 2 patients, one of whom also had thyroid dysfunction.

Almost two-thirds of patients (20 [59%] of 34) experienced an average weight gain of 28.1 lbs (12.7 kg; median 22.5 lbs [10.2 kg], range 15–61 lbs [6.8–27.7 kg]). Approximately one-third of these patients (7 individuals), eventually returned to their preprocedure weight.

Long-Term Seizure Outcome. Overall, seizure frequency at last follow-up (available from 35 of 36 surviving patients), according to patient or caregiver reporting, revealed that approximately one-third (10 [29%] of 35) were seizure free or had had only isolated seizures postoperatively. Nine patients (26%) rated their seizures as > 90% improved; another 8 patients (23%) estimated them to be > 50% better. Approximately one-fourth of patients (8 [23%] of 35) judged their seizures to be < 50% improved. Four patients had either no improvement (2 [6%] of 36) or were worse (2 [6%] of 35). This implies that 51% of patients (18 of 35) reported a > 90% improvement. According to the Engel classification, 10 patients were in Engel class I, no patients were in class II, 17 patients were in class III, and 8 patients were class IV. When categorized using the ILAE classification, 10 patients were in level 1, no patients were in levels 2 or 3, 17 patients were in level 4, 8 patients were in level 5, and no patients were in level 6.

When examining the evolution of seizure activity over time postintervention, it was found that only 2 (6%) of 36 patients were immediately and permanently seizure free. However, 6 more patients (17%) reported that their seizures became less frequent and then ceased (including 2 of 4 patients who underwent GKS), and 2 more patients (6%) had only isolated seizures postoperatively. Seven patients (19%) were seizure free after surgery or had only isolated seizures postoperatively, but then saw a gradual return of seizures. One patient reported a new type of spell without EEG correlate that was judged to be nonepileptic in origin. The majority of patients (16 [44%] of 36) had immediately improved seizures after the procedure, and the frequency remained stable. One patient was immediately worse, but improved later.

At the time of their last phone interview, only 3 patients (3 of 10 seizure-free patients [30%]) were no longer receiving anticonvulsants. Long-term, 8 patients were on fewer AEDs, but 5 were on more. All others were on the same number of medications as preoperatively.

The mean percentage resection for those patients who were seizure free was 91% (range 60%–100%), compared with 75% (range 7%–100%) for those who continued to have seizures (not statistically significant). Nevertheless, of 14 patients who had a 100% resection (11 endoscopic, 3 open and/or transcallosal), 43% were seizure free, which is higher than average for the whole population (29%), but again not significant (p < 0.5, using the chi-square test). Apparently, it was difficult to resect “giant” HH lesions (Delalande Type IV), which were on average only 35% removed and 32% disconnected. Of the patients with “giant” HH (4 of 40), 1 died and none of the others was seizure free.

Kendall tau testing evaluating correlations between nonparametric variables was used to detect associations of seizure freedom and presence or absence of mental retardation, preoperative lesion size, Delalande classification, amount of resection, and degree of disconnection. Mental retardation was the only factor that was significantly correlated with continued seizures (r = 0.398, p = 0.02). Mental retardation also significantly correlated with HH volume (r = 0.384, p = 0.004).

Logistic regression was used for multivariate modeling of seizure freedom after surgery. Factors used in the model included age at surgery, HH type, and amount of resection. There were no significant associations found.

Postoperatively, almost half the patients (15 [48%] of 31) were working or actively pursuing an education. Eight patients were driving.

Key outcomes observed immediately postoperatively and long term after HH procedures are listed in Table 1. Outcomes for patients who underwent endoscopic resection (average HH size 1.77 cm³) are presented in Table 2. Outcomes for patients who had a transcallosal or other open resections (that is, pterional or orbitozygomatic approach) and bigger HH size (average 4.59 cm³) are displayed in Table 3, and those for patients who underwent GKS (average HH size 0.20 cm³) are shown in Table 4. It has to be emphasized that 12 months of follow-up is not adequate to assess the success of GKS, because improvement can be seen up to 3 years afterward.

Discussion

To our knowledge this is the largest study investigating outcome in adult patients undergoing procedures for intractable epilepsy due to HH. Specific outcome data in some patients have been summarized elsewhere. However, in these publications the focus was on outcome with one particular procedure type (GKS, transcallosal, and endoscopic approach), and adults represented only a fraction of the patient population. This study focused on an adult population that underwent treatment for HH typically at an adult age, and our observations were used to compare an adult population with HH to the mostly pediatric or adolescent populations described in the literature. The adult population seems to respond less favorably to interventions than pediatric patients, as outlined below.

Adults with HH undergoing treatment of epilepsy present with a wide spectrum of seizure severity, and their seizures are just as disabling and drug resistant as in children. However, it has to be assumed that gelastic seizures are underrecognized in adult patients. Although the majority of patients (73%) experienced daily gelastic (that is, “laughing”) seizures, which are typical for HH, there was an average delay of 17 years until diagnosis. This implies that either the seizures were not recognized as such or that the recognition did not prompt a specific search for HH, which is probably due to a lack of awareness about this rare condition.

Complicating the matter could be the fact that an HH is easy to miss. The median HH size in our patients was small, only 0.54 cm³, and the lesions were often incom-
spicuously situated next to the third ventricle (70% with Delalande Type II). If standard MRI studies are acquired as slices of 2-mm thickness with an interslice gap of 5 mm, an HH 5 mm or less in diameter may not even be demonstrated on imaging.

Obviously, the number of AEDs tried in these patients emphasizes the refractoriness of their seizures and calls for a more definitive intervention aiming to remove the HH. However, although the majority of patients reported seizure improvement after the intervention, only approximately one-third (29%) of all patients became seizure free. An additional 26% rated their seizures as > 90% improved, but only 8% of all patients were off AEDs at last follow-up. In addition, > 90% improvement in seizure frequency may continue to limit driving or pursuit of a career, because most patients had multiple daily seizures, and even a > 90% improvement may still imply weekly or monthly seizures. This is a worse outcome regarding seizure control compared with series of younger patients, which showed a seizure freedom rate of 51%–54% for transcallosal resections,7,10 49% for endoscopic resections,11,14 37.5% for interstitial radiosurgery,17 and 37%–66% for Gamma Knife procedures.1,8,15 In addition, children and adolescents were more likely to come off medication; 31%–42% were able to discontinue AEDs, and 60%–79% of seizure-free patients were off drugs.1,10 Younger patients also seemed to experience an instantaneous and lasting rate of seizure freedom of 49%,15 whereas our adult cohort saw an immediate impact, but then a tendency for seizures to recur. This difference in efficacy depending on age group may be due to “secondary epileptogenesis” induced by the HH; that is, a persistent seizure focus triggers independent epileptogenic circuitry. Alternatively, in adults the HH focus may have become more robust or better connected over time and may be more difficult to remove.

In our study, only absence of mental retardation was significantly correlated with a higher chance of becoming seizure free. Complete resection or irradiation was related to a higher chance of seizure freedom in other studies,5,8,10,12 but our data—surprisingly—did not support any significant impact of extent of resection or disconnection.

There was a high mortality rate of 10% in our series over the total observation period. However, only 1 patient (2.5%) died due to postoperative complications while still in the hospital, whereas all others who died did so after discharge, without any significant problems recovering from the surgical procedure. They had persistent

| TABLE 1: Immediate and long-term postoperative outcomes in 40 patients with HH* |
|---------------------------------|-----------------|-----------------|-----------------|
| Category                        | Preop Period    | Immediate Postop Outcome† | Long-Term Outcome |
| seizures                        | 100 (40 of 40)  | 63 (25 of 40)     | 71 (25 of 35)   |
| seizure free                    | 0               | 30 (12 of 40)     | 29 (10 of 35)   |
| avg no. of AEDs per pt          | 2               | 2                | 2               |
| pts off AEDs                    | 3 (1 of 40)     | 0                | 8 (3 of 36)     |
| stroke/permanent deficit        | 0               | acute: 15 (6 of 40) | residual: 5 (2 of 40) |
| hormonal disturbances           | 42 (16 w/ PP, of 38) | acute postop: 28 (11 of 40) | persistent postop: 34 (11 of 32) |
| weight gain                     | 0               | not measured     | 59 (20 of 34); avg gain 12.7 kg |
| death                           | 0               | 5 (2 of 40)       | 10 (4 of 40)    |

* Except when otherwise indicated, all values are expressed as the percent of patients, with the number in parentheses. Percentages that do not add up to 100% indicate that patients had died or that information was not known for all patients. Abbreviations: avg = average; PP = precocious puberty; pts = patients.
† Immediate is defined as during the hospital stay and within 30 days postoperatively.

| TABLE 2: Immediate and long-term postoperative outcomes in 26 patients who underwent endoscopic HH resection |
|---------------------------------|-----------------|-----------------|-----------------|
| Category                        | Preop Period    | Immediate Postop Outcome | Long-Term Outcome* |
| mean HH vol in cm³; range       | 1.77; 0.09–11.19 | 0.35; mean resection 80%, range 7–100% |
| seizures                        | 100 (26 of 26)  | 65 (15 of 23)    | 64 (14 of 22)   |
| seizure free                    | 0               | 35 (8 of 23)     | 36 (8 of 22)    |
| avg no. of AEDs per pt          | 2               | 2                | 2               |
| patients off AEDs               | 4 (1 of 26)     | 4 (1 of 26)      | 14 (3 of 21)    |
| stroke/postop deficit           | 0               | acute postop: 8 (2 of 26) | residual: 5 (1 of 22) |
| hormonal disturbances           | 35 (9 w/ PP, of 26) | acute: 23 (6 of 26) | persistent postop: 24 (5 of 21) |
| weight gain                     | 0               | not measured     | 59 (13 of 22)   |
| death                           | 0               | 4 (1 of 26)      | 8 (2 of 26)     |

* At last follow-up the total was 22 because 1 patient died postoperatively, 2 patients were lost to follow-up, and 1 other patient died 3 years after the procedure. A smaller denominator indicates that data were not available for all surviving patients.
seizures, which complicates a judgment as to the extent to which surgery impacted their mortality. Only patients who underwent resection died, as compared with those who underwent GKS, suggesting that GKS is safer in adult cases. In younger populations mortality rates were 0% for any type of procedure,\textsuperscript{5,10,11,14,17} suggesting that adults may have a higher risk of death, especially if they have a resection and their seizures continue.

Next to death, usually the most devastating complication after neurosurgery is stroke. In our population, 15% suffered a stroke. One died and one had lasting neurological deficits, but the remaining 4 patients were asymptomatic. This is a substantial side effect, but this high rate is similar to what was found for younger samples, between 7% and 26%\textsuperscript{7,11} with most of these strokes being clinically silent and only detected on MRI studies.\textsuperscript{11}

Mild long-term endocrinological disturbances were observed in approximately one-third of our population, which exceeds numbers in reports of younger cohorts, in which hormonal problems approached 6%–30% after transcallosal and endoscopic resections.\textsuperscript{5,10,14,17} However, just as in other reports,\textsuperscript{15} no lasting hormonal problems were seen after GKS.

Weight gain was observed in 59% of the adults in this study. This is worse than what has been described for younger groups, with weight gain in 9%–45% of patients after transcallosal, endoscopic, and interstitial radiosurgical interventions.\textsuperscript{5,9,10,14,16,17} In our study, 1 patient (25%) experienced weight gain after GKS, which matches a larger series in which 20% of patients of all ages who underwent GKS had weight gain,\textsuperscript{1} although typically no weight gain was found in younger populations.\textsuperscript{8,15}

In terms of different surgical approaches, it can be said that the adult patients undergoing GKS did not experience any immediate or long-term neurological deficits or problems, and 50% of these patients were seizure free, despite a shorter than desirable follow-up for these patients, who can experience improvement up to 3 years postoperatively. Studies on Gamma Knife treatment involving children and adults with 1- to 3-year follow-up durations reported seizure freedom rates of 37%–60%,\textsuperscript{1,8,15} with no recorded deaths. This suggests that GKS may provide a

TABLE 3: Immediate and long-term postoperative outcomes in 10 patients who underwent transcallosal, or a combined endoscopic-transcallosal, or combined endoscopic-pterional/endoscopic-orbitozygomatic approach for resection of the HH

<table>
<thead>
<tr>
<th>Category</th>
<th>Preop Period</th>
<th>Immediate Postop Outcome</th>
<th>Long-Term Outcome*</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean HH vol in cm(^3); range</td>
<td>4.59; 0.24–10.23</td>
<td>1.65; mean resection 64%, range 11–100%</td>
<td></td>
</tr>
<tr>
<td>seizures</td>
<td>100 (10 of 10)</td>
<td>70 (7 of 10)</td>
<td>100 (7 of 7)</td>
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<tr>
<td>seizure free</td>
<td>0</td>
<td>30 (3 of 10)</td>
<td>0 (0 of 7)</td>
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<tr>
<td>avg no. of AEDs per pt</td>
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<td>2</td>
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<tr>
<td>no. of pts off AEDs</td>
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<td>0</td>
</tr>
<tr>
<td>stroke/postop deficit</td>
<td>0</td>
<td>acute postop: 40 (4 of 10)</td>
<td>residual: 29 (2 of 7)</td>
</tr>
<tr>
<td>hormonal disturbance</td>
<td>70 (7 w/ PP, of 10)</td>
<td>acute: 50 (5 of 10)</td>
<td>persistent postop: 57 (4 of 7)</td>
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<td>weight gain</td>
<td>0</td>
<td>not measured</td>
<td>71 (5 of 7)</td>
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<tr>
<td>death</td>
<td>0</td>
<td>10 (1 of 10)</td>
<td>20 (2 of 10)</td>
</tr>
</tbody>
</table>

* At last follow-up the total was 7 because 1 patient died immediately postoperatively, 1 died late after surgery, and 1 was lost to follow-up.

TABLE 4: Immediate and long-term postoperative outcomes in 4 patients who underwent GKS for resection of the HH

<table>
<thead>
<tr>
<th>Category</th>
<th>Preop Period</th>
<th>Immediate Postop Outcome</th>
<th>Long-Term Outcome*</th>
</tr>
</thead>
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<tr>
<td>mean HH vol in cm(^3); range</td>
<td>0.20; 0.14–0.28</td>
<td>100 (4 of 4)</td>
<td>50 (2 of 4)</td>
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<td>seizures</td>
<td>100 (4 of 4)</td>
<td>100 (4 of 4)</td>
<td>50 (2 of 4)†</td>
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<tr>
<td>seizure free</td>
<td>0</td>
<td>0 (0 of 4)</td>
<td>50 (2 of 4)†</td>
</tr>
<tr>
<td>ave no. of AEDs per pt</td>
<td>2</td>
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<tr>
<td>no. of pts off AEDs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>stroke/postop deficit</td>
<td>0</td>
<td>acute: 0 (0 of 4)</td>
<td>residual: 0 (0 of 4)</td>
</tr>
<tr>
<td>hormonal disturbances</td>
<td>0 (0 of 4)</td>
<td>acute postop: 0 (0 of 4)</td>
<td>persistent postop: 0 (0 of 3)</td>
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<tr>
<td>weight gain</td>
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<td>not measured</td>
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<tr>
<td>death</td>
<td>0</td>
<td>0 (0 of 4)</td>
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</tbody>
</table>

* At last follow-up the total was 4. A smaller denominator indicates that data were not available for all surviving patients.
† Follow-up duration was 4 years and 2 years for the 2 seizure-free patients. One patient with ongoing seizures had only 12 months of follow-up, and the other had 27 months. Given that GKS can require up to 3 years to become effective (that is, provide seizure freedom), it cannot be definitively concluded that only 50% of this cohort would ultimately be seizure free.
favorable outcome with respect to seizures in children, and possibly even more so in adults, if the HH is small and favorably located (that is, sufficiently distant from the optic chiasm, optic tracts, fornices, or mammillary bodies). Furthermore, the patient should be stable, with a seizure burden that is tolerable in terms of frequency and severity, to accept a potentially long period (2–3 years) until seizure freedom is achieved.

Limitations of this observational study are that data collection over the years was not complete and that the Gamma Knife treatment group was too small to allow for a rigorous comparison between treatment types and outcome.

Conclusions

Surgery or Gamma Knife treatment for HH-associated epilepsy offers a chance of cure for seizures in adult patients that does not occur with medication alone but has a lower success rate than in children. A diagnosis of mental retardation was the only factor that was significantly correlated with failure to become seizure free. In light of our results, GKS may be the preferred treatment option in adults, although the number of patients in this study is insufficient to support such a recommendation conclusively. The mortality rate is higher in adults, and there is a greater chance of weight gain. Additional side effects, such as stroke, appear to be as common as in children. The overall results suggest that an earlier age at resection offers fewer complications and a greater chance of attaining seizure freedom.

Disclosure

Dr. Maganti is a consultant for Lundbeck, and he belongs to the speaker’s bureau for UCB Pharma and GlaxoSmithKline. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Drees, Kerrigan. Acquisition of data: Drees, Chapman, Prenger, Maganti, Rekate, Shetter. Analysis and interpretation of data: Drees, Prenger, Baxter, Kerrigan. Drafting the article: Drees. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Drees. Statistical analysis: Prenger, Baxter. Administrative/technical/material support: Bobrowitz. Study supervision: Kerrigan.

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