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**Complications after surgery for mesial temporal lobe epilepsy associated with hippocampal sclerosis**

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**ABSTRACT**

*Background.* Hippocampal sclerosis is the most common cause of drug-resistant epilepsy amenable for surgical treatment and seizure control. This study aimed to analyze morbidities related to surgery of mesial temporal lobe epilepsy associated with hippocampal sclerosis and to identify possible risk factors for complications.

*Methods.* A retrospective analysis of postoperative complications was made for 389 operations performed between 1990 and 2015 on patients aged 15 to 67 years (mean 36.8). Three surgical approaches were used: anterior temporal lobectomy (ATL) (n=209), transcortical selective amygdalohippocampectomy (SAH) (n=144) and transylvian SAH (n=36). Complications were classified as minor, or major if there was a neurological impairment or if further surgical or medical treatment was needed.

*Results.* Complications followed 15.4% of operations. They were classed as major for 4.1% of patients, but there were no mortalities. Persistent neurological deficits occurred in 0.5% of patients. In 3 cases (0.8%) additional surgery was needed to treat an intracranial hematoma, a delayed hydrocephalus and a subdural empyema. Symptomatic visual field defects (VFDs) were frequent and included contralateral superior quadrantanopia (8.2%) or hemianopia (1.3%). Overall complications ( $P=0.04$ ) and symptomatic VFDs ( $P=0.04$ ) were most frequent in operations on men. Major complications occurred most often with the ATL surgical approach than with transcortical SAH ( $P=0.03$ ).

*Conclusions.* Major complications occur rarely after mesial temporal surgery on epileptic patients. They occur more often following ATL than transcortical SAH approach. Complications tend to be temporary with symptoms of limited duration for surgery performed by experienced teams on carefully selected and evaluated patients.

## **INTRODUCTION**

Mesial temporal lobe epilepsy (MTLE) associated with hippocampal sclerosis (HS) is the most common focal, intractable epilepsy.<sup>1</sup> Mesial temporal lobe surgery, the standard treatment for this syndrome, has been widely evaluated.<sup>2</sup> Diverse surgical approaches ensure a reduced seizure frequency. They include a selective transylvian or transcortical amygdalohippocampectomy (SAH) and an anterior temporal lobectomy (ATL).<sup>1,2</sup>

While these surgical approaches are safe, possible morbidities and even mortality must be discussed with patients before surgery. Few studies have focused on adverse events after MTLE surgery.<sup>3</sup> Accurate data on outcomes and complications would aid presurgical discussions with patients and also permit a useful comparative evaluation of different surgical approaches. We therefore conducted a 25-year retrospective study on the morbidity and mortality of MTLE-HS surgery in all patients operated in our institution. Mesial temporal lobe surgery has evolved over the duration of this retrospective study so that we could compare different surgical approaches for mesial temporal lobe resection. Each approach had its own advantages and consequences.

The primary aim of this report is therefore to describe, analyze and discuss the complications related to MTLE-HS surgery. A secondary endpoint was to search for factors that might increase the possibility of post-operative complications.

## **METHODS**

### **Patients**

We analyzed retrospectively the after-effects of surgery for MTLE-HS in all adult and teenagers (over 15 years) patients treated in our institution between November 1990 and December 2015, and who were followed for at least 6 months. This study was approved by the French National Technologies and Civil Liberties Commission, which ensures the protection of personal data.

Patients were selected for surgery after medical management of seizures had failed. Standardized, non-invasive presurgical evaluation included: complete neurological, neuropsychological and psychiatric examinations, scalp video-EEG recording of seizures, brain MRI, and when needed subtraction ictal single photon emission computed tomography co-aligned with MRI and interictal positron emission tomography. A multidisciplinary team then analyzed data from these investigations to decide if surgical treatment was indicated and if localization of the focus was clear. If so, strict selection criteria were used to define a single-stage surgical resection, avoiding further intracranial EEG recordings whenever possible. Selection criteria for surgery included the presence of typical partial seizures, epileptiform activity originating from the temporal lobe and unilateral hippocampal atrophy with or without a T2 hyperintense signal, all features of a classical MTLE-HS syndrome.

We collected data on age, gender, medical history, seizure semiology, electrophysiological findings including invasive recordings if applicable, preoperative brain MRI images, side and approach of surgery and histological findings. Any adverse event during the postoperative period was considered as a complication and documented from neurological examinations, postoperative scans and formal visual field testing.

### **Surgical methodology**

Three surgical approaches were used: (1) Spencer's ATL;<sup>4</sup> or (2) SAH via transylvian approach;<sup>5</sup> and (3) SAH via transcortical trans-STG approach.<sup>6</sup> ATL was used between 1990 and 2010, and transylvian SAH between 1994 and 2000. SAH with a transcortical approach was first used in 2000. The senior author (S.C.) performed all surgeries. The decision to perform an ATL or an SAH was first based on timing, and then on the results of the presurgical evaluation. Before 1994, patients who underwent surgery for MTLE-HS received an ATL, as this was the practice at our center. Between 1994 and 2010, SAH was used for patients with a high risk of postoperative cognitive deterioration. In 2010, the transcortical SAH was definitively adopted as the standard operation for MTLE-HS.

## Postoperative management

Patients were monitored in the recovery unit after surgery. A CT scan was done within 24 hours to exclude immediate complications, before transfer to the Neurosurgery unit. All patients were followed at regular intervals after surgery. At 6-9 months after surgery, complete neurological and ophthalmological assessments were made and a follow-up brain MRI was obtained.

## Classification of complications

Two severity scales for postoperative complications after MTLE surgery were designed to permit comparison with previous studies: (1) a binary major/minor scale: a complication was defined as major if medical or surgical treatment was needed and/or if there was a persistent neurologic impairment. Other complications, including UTI and DVT, were classed as minor. (2) A graded scale, as follows, with composite items including a prevailing surgical component:<sup>7,8</sup>

- Grade 0: no complication.
- Grade 1: a transient complication not needing treatment; or non-invalidating homonymous contralateral superior quadrantanopia.
- Grade 2: a transient complication that resolved completely but required surgical or medical treatment.
- Grade 3: a persistent neurological or visual deficit that affected daily activities for more than 6 months
- Grade 4: death linked to the surgery.

Other adverse events after surgery, such as meningeal syndrome, low-grade fever, headaches, pneumocephalus, were considered as mild functional disturbances rather than complications.

## Statistical analysis

Statistical analysis was performed with version 21 of SPSS (IBM; Armonk, NY, USA). Simultaneous binary logistic regression models were used to evaluate the ability of independent variables to predict complications. Exploratory univariate analysis was performed using the t-test of Student for quantitative variables (age at surgery, epilepsy duration) and the chi-square or Fisher exact test for dichotomous variables (gender, preoperative data, surgical approach, side of surgery and HS histological type). Independent variables correlating with complication variables at the 20% level or less ( $P < 0.2$ ) were considered for entry into the model. Independent variables without significant predictive value at the 5% level ( $P \leq 0.05$ ) were then eliminated, and final analysis carried out.

## RESULTS

### Patient demographics, surgery and seizure outcome

This analysis is based on 389 patients with severe and/or disabling drug-resistant epilepsy who underwent mesial temporal lobe resection for MTLE-HS. Their age at surgery was  $36.8 \pm 10.5$  years (range, 15.4–67.9); the male/female ratio was 0.90. The first seizure for these patients occurred at  $12.0 \pm 9.1$  years (range, 0.0–47.4) and the mean seizure frequency was  $6 \pm 5$  seizures per month (range 0.5–100). Surgical approaches for these patients were ATL in 209 cases (53.7%), trans-STG SAH for 144 patients (37.0%) and transylvian SAH for 36 cases (9.3%). 206 patients (53.0%) were operated on the left hemisphere, and 183 (47.0%) on the right. Histological examination performed according to ILAE classification<sup>9</sup> found a type 1 HS for 189 patients (75.3%), a type 2 HS for 47 patients (18.7%), a type 3 HS for 3 patients (1.2%) and no sclerosis was detected for 12 patients (type no-HS, 4.8%).

Seizure outcome was defined as follow up at a time point  $> 1$  year after surgery in 361 patients. The mean duration of follow-up for the cohort was  $8.7 \pm 5.8$  years (range, 1.0 to 25.2 years). Three hundred two patients (83.7 %) were free from



seizures (Engel class I) at the latest follow-up evaluation after surgery ( $8.7 \pm 5.8$  years) and 206 patients (57.1%) had a class Ia outcome.<sup>10</sup>

### Overall complications

For 329 patients (84.6 %) recovery from surgery was uneventful. Table 1 and Fig. 1A summarize complications of the other 60 patients (15.4%). For 44 patients (11.3 %) they were minor. Major complications followed 16 operations (4.1 %) and led to a prolonged hospitalization for 9 patients (2.3 %; Fig. 1B). On the graded scale described in the Methods, 44 patients (11.3 %) had a grade 1 complication, 8 (2.1%) a grade 2 complication and a more severe grade 3 complication occurred for 8 patients (2.1 %; Table 1 and Fig. 1C). There were no deaths after surgery. A further surgical intervention was needed for 3 of the 60 patients with complications (0.8%).

Only one parameter was significantly associated with complications. They occurred more often in male than in female patients (18.5% versus 12.7%,  $P = 0.04$ ; OR = 2.1; IC<sub>95%</sub> = [1.0-4.1]). Table 2 compares groups with and without complications. In terms of the surgical approach, Table 3 shows that ATL was more often associated with major complications than transcortical SAH (5.7% versus 2.1% respectively,  $P = 0.03$ ; OR = 4.4; IC<sub>95%</sub> = [1.1-17.2]).

### Surgical complications

Complications for 7 patients (1.8 %) were classed as surgical. They were meningitis in 4 cases (1.0%) and 1 case each of subdural empyema, intracranial hemorrhage and delayed hydrocephalus (Table 1 and Fig. 1A). Antibiotic treatment was effective for all patients with meningitis. Surgical intervention was needed in the other 3 cases (0.8 %), all after ATL.

One of these cases was a 52-year old woman, where a CT scan on the 7th day after the operation in response to hyperthermia and subcutaneous abscesses near the wound, revealed a subdural temporal empyema (pathogenic agent *Aureus staphylococcus*), which required surgical drainage and antibiotic therapy. At 2 years after the operation in a 21-year old woman, we detected a hydrocephalus by cystic

compartmentalization of the ventricular temporal horn, requiring a ventriculo-peritoneal shunt. Lastly, a 57-year old man developed an acute intracerebral hemorrhage with mass effect at the surgical site. Surgical intervention was followed by intensive care. All these patients recovered totally from surgical complications, which were classed as grade 2. A similar comparison for surgical complications as in Table 3 was made but there were no differences between patients with and without surgical complications (Supplementary Table 1).

### **Neurological complications**

For 15 patients (3.9%) complications were neurological (Table 1 and Fig. 1A). Deficits were transient in 11 cases (2.8%), but damage was persistent for 1 patient with hemiplegia and 1 with hemiparesis (0.5%). Two patients (0.6%) had a cerebral venous sinus thrombosis diagnosed from severe headaches and managed by anticoagulation. Patients who suffered a transient aphasia or hemiparesis typically recovered fully within days (grade 1 complication). A 40-year old man experienced a postoperative oculomotor nerve paralysis, which resolved completely by the follow-up evaluation at 9 months (grade 3 complication). The two persistent neurological impairments occurred after ATL.

While neurological complications occurred more frequently after ATL (5.3%) than after transcortical SAH (1.4%), the difference was not statistically significant ( $P = 0.08$ ). No significant differences were evident in groups with or without neurological complications (Table 4).

### **Visual field defects**

Postoperative Goldmann visual field testing of 323 patients revealed deficits in 125 cases (38.7%; Fig. 1D). Only 9.5% of the 389 patients had a symptomatic deficit; a homonymous superior contralateral quadrantanopia in 32 cases (8.2%) and a homonymous contralateral hemianopia in 5 cases (1.3%) (Table 1 and Fig. 1A, D). Quadrantic VFD after the operation never affected daily life. Symptomatic VFD

occurred more frequently in male than female patients ( $P = 0.04$ ;  $OR = 2.2$ ;  $IC_{95\%} = [1.0-4.6]$ , Table 5).

## **DISCUSSION**

### **Overall complications**

This study on adverse events after operations for MTLE-HS conducted over 25 years in a tertiary French center, revealed an overall rate of complications of 15.4 %. This value is close to previous reports for adults, of 5.5% - 19.0 % (Table 6).<sup>3, 11-20</sup> Major complications, which require further medical or surgical treatment or result in a persistent deficit, occur rarely after this operation.<sup>1, 2</sup> We found a rate of 4.1 %, compared to previous reports of 1.8% to 13.4% (Table 6).<sup>3, 12-18, 21</sup> There are significant differences in how different studies have classified major complications. Here we analyzed each complication using two severity scales to allow objective comparison with previous work. Retrospective studies might misjudge incidence of UTIs, DVT and VFDs. We recommend that new studies of complications after epilepsy surgery standardize severity of outcome and tests of visual deficit.

Persistent neurological deficits occurred in very few, 0.5%, operations. Reported frequencies vary from 0 to 3.1% (Table 6).<sup>3, 12-15, 17, 18, 20</sup> Hemiparesis, the most common serious neurological impairment, is typically triggered by an injury to the anterior choroidal artery<sup>22</sup> or by cerebral swelling. Another risks during resection of mesial structures are to damage the motor pathways or provoke a cerebral vasospasm, resulting in stroke.<sup>23</sup> Mortality after MTLE-HS surgery is very rare (< 0.5%)<sup>24</sup> and was null in our series.

Changes in MTLE-HS surgery represent an evolution of neurosurgical techniques. The large cohort studied here let us compare different surgical approaches used over 25 years on a homogenous group of patients with MTLE-HS. Worldwide, there has been a strong trend to reduce the extent of resections.<sup>25</sup> The SAH approach aims to spare cerebral tissue that does not contribute to seizure generation, although the volume of temporal lobe that should be resected is still debated.<sup>2</sup> In our series,

ATL was associated with major complications more often than transcortical SAH (5.7% versus 2.1%). Neurological complications also occurred more frequently after ATL (5.3%) than after transcortical SAH (1.4%), although this difference was not statistically significant ( $P = 0.08$ ). Possibly the larger surgical cavity made during ATL enhances bleeding, infection, and even hydrocephalus.<sup>26</sup> We note that comparisons of transylvian SAH with the other two surgical approaches possess less weight since surgery with this procedure was done in only 36 patients. The literature suggests a higher risk of cerebral vasospasm with transylvian SAH perhaps because this approach necessitates manipulation of the middle cerebral artery branches in the Sylvian fissure. Different mechanisms have been proposed to explain the pathophysiology of cerebral vasospasm.<sup>23</sup> None of the patients in this study experienced symptomatic cerebral vasospasm. Different surgical centers suggest that one advantage of transcortical SAH is to minimize the need to divide vascular adhesions which is tedious, time consuming, and which sometimes provokes a degree of cerebral swelling.<sup>25</sup> A multicenter randomized trial might usefully compare the safety profile of different approaches in MTLE surgery.

This study found significantly more postoperative complications for male than for female patients. Otherwise we did not identify preoperative clinical, radiological and electrophysiological data that could predict postsurgical complications. Neither the cerebral hemisphere involved (left or right) nor the histopathology of the sclerosis provided indications on adverse post-operative events. Some authors suggest that age at surgery may be linked to complications,<sup>3, 11</sup> but our data did not support such a link, even if the age range of patients in this work was relatively small. Attention to these factors together with a detailed knowledge of mesial temporal lobe microsurgical anatomy may help reduce postsurgical complications.<sup>6</sup>

### **Visual field defects**

Visual field deficits often occur after MTLE surgery. Typically they consist of a contralateral superior quadrantanopia due to injury of Meyer's Loop during access to mesial temporal structures. Standard Goldmann perimetry revealed VFDs in 38.7% of this cohort of which only 9.5% were symptomatic. These deficits rarely affect daily life after surgery. The literature reports very heterogeneous rates of VFD, between

15% and 100% (Table 7),<sup>27-35</sup> with severe deficits after 2%–35% of operations.<sup>11, 33, 35</sup>

However, visual fields were not formally tested in several of these studies, and the delay between the operation and post-surgical follow-up was variable. This delay influences visual deficit. In the study of Yam et al.,<sup>35</sup> 38% of the patients with severe VFD just after their operation report improvement with time.

Male patients were significantly more likely to report VFD symptoms. This could be related to earlier return to work in males or participating in driving or other visual coordination tasks compared to female patients. We found no difference in post-operative symptomatic VFD frequency after surgery involving SAH or ATL. In contrast, Mengesha et al.<sup>33</sup> report VFDs were more evident after ATL than transcortical SAH, where the visual field close to the horizontal meridian was relatively spared.

Surgical approaches to minimize subsequent visual deficits can be envisioned. To protect fibers of Meyer's loop, we recommend to open the ventricle anteriorly through the floor and not to resect tissue posterosuperior to the temporal horn. Excessive posterolateral opening of the ventricle wall should also be avoided to protect optic radiations.<sup>6</sup> Preoperative tractographic data on Meyer's loop, especially for left-side temporal lobe epilepsies, can also help reduce to optic radiation injury.<sup>36</sup>

### **Comparison to other surgical techniques for MTLE-HS treatment**

MTLE-HS surgery has also been made using stereotaxic radiosurgery. The most frequent adverse event after stereotaxic radiosurgery is headache (70%). Further 50 - 62.5% of patients experience a contralateral superior quadrantanopia, fairly similar to the rate described after open surgery.<sup>37, 38</sup> Adverse events occurring more rarely include brain edema, intracranial hypertension and transient increase of seizure frequency. There are reports of tumor genesis and progressive cognitive disorders.<sup>39</sup>

Amygdalohippocampal stimulation shows some therapeutic promise for MTLE. Studies on the safety of the procedure suffer from small sample sizes and short follow-up times. However, surgical practices used to implant deep brain electrodes for movement disorders are relevant. The risk of hemorrhage is about 5%.

This includes intracerebral hemorrhage along the course of the stimulating electrode, and potential postoperative subdural or epidural hematoma.<sup>21</sup> Infections also occur with a risk of at least 5% and require removal of stimulating electrode.<sup>40</sup>

### **Limitations of the study**

This study was based on a large, homogeneous, representative cohort of patients with MTLE-HS and allowed the direct comparison between three surgical approaches. However, it was a retrospective study that concerned just one center. Patients were not randomized to the distinct surgical approaches. Cognitive complications, which certainly affect the quality of life after surgery, were not considered. Our findings might usefully be re-examined in further large-scale, randomized studies.

### **CONCLUSIONS**

This retrospective study revealed a low rate of complications after surgical resections for MTLE-HS. The rate of mortality was zero, 0.5% of patients (2 of 389) suffered persistent neurological deficits, and, mainly with ATL, major events occurred after only 4.1 % of operations. The risk of complications has decreased with improved surgical techniques, anesthesia, and postoperative management. The low complication rate contributes to an acceptable surgical treatment, which can be accurately described in discussions of benefits and risks with patients who are considering treatment options for a pharmaco-resistant MTLE epileptic syndrome.

Debate persists on the optimal extent and surgical procedure for temporal lobe resections. Our data suggest that transcortical SAH is the preferred approach to minimize complications of MTLE-HS surgery. This conclusion should be confirmed in a randomized comparison of SAH and ATL. Further reductions in post-operative complications will result from an improved understanding of temporal lobe anatomy and especially from technical enhancements in MTLE-HS surgical procedures.

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## **CONFLICTS OF INTEREST**

None of the authors has any conflict of interest to disclose.

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**FIGURE LEGEND**

**Fig. 1** Quantification of different postoperative complications. A, Frequency of complications. B, Pie chart of the frequency of complication according to the class of complication. C, Pie chart of the frequency of complication according to the grade of complication. D, Pie chart of the frequency of visual field defects.

VFD, visual field defect.

<b>Symptomatic complications</b>	<b>% (n/N)</b>	<b>Class – grade of complications</b>
Transient hemiparesis	1.3% (5/389)	Minor – Grade 1
Transient aphasia	1.3% (5/389)	Minor – Grade 1
Definitive hemiparesis	0.3% (1/389)	Major – Grade 3
Definitive hemiplegia	0.3% (1/389)	Major – Grade 3
Cerebral venous sinus thrombosis	0.5% (2/389)	Major – Grade 2/3
Transient oculomotor nerve paralysis	0.3% (1/389)	Major – Grade 3
<b>Neurological complications (total)</b>	<b>3.9% (15/389)</b>	
Meningitis	1.0% (4/389)	Major – Grade 2
Subdural empyema	0.3% (1/389)	Major – Grade 2
Intracerebral hemorrhage	0.3% (1/389)	Major – Grade 2
Hydrocephalus	0.3% (1/389)	Major – Grade 2
<b>Surgical complications (total)</b>	<b>1.8% (7/389)</b>	
Homonymous quadrantanopia	8.2% (32/389)	Minor – Grade 1
Homonymous hemianopia	1.3% (5/389)	Major – Grade 3
<b>Visual complications (total)</b>	<b>9.5% (37/389)</b>	
Urinary tract infection	1.0% (4/389)	Minor – Grade 1
Deep venous thrombosis	0.5% (2/389)	Minor – Grade 1
<b>Other complications (total)</b>	<b>1.5% (6/389)</b>	
<b>Overall complications</b>	<b>15.4% (60/389)</b>	

**Table 1. Complications associated with mesial temporal lobe resection.**

Variables n/N (%) or mean $\pm$ SD	No complication	Complication	Univariate <i>P</i> -value	Multivariate <i>P</i> -value
Age at surgery, y, mean $\pm$ SD	36.8 $\pm$ 10.6	37.1 $\pm$ 9.9	0.88	
Duration of epilepsy, y, mean $\pm$ SD	24.8 $\pm$ 11.6	25.8 $\pm$ 10.5	0.54	
Seizure frequency / m, mean $\pm$ SD	11.1 $\pm$ 14.4	8.3 $\pm$ 9.1	<b>0.17</b>	0.24
Gender				
Male	150/184 (81.5%)	<b>34/184 (18.5%)</b>	<b>0.12</b>	<b>0.04 *</b>
Female	179/205 (87.3%)	<b>26/205 (12.7%)</b>		
Dominant hand				
Right	281/331 (84.9%)	50/331 (15.1%)		
Left	39/46 (84.8%)	7/46 (15.2%)	0.33	
Ambidextrous	6/9 (66.7%)	3/9 (33.3%)		
Associated disease				
Yes	32/35 (91.4%)	3/35 (8.6%)	0.33	
No	287/342 (83.9%)	55/342 (16.1%)		
Preoperative MRI				
HS pattern	260/306 (85.0%)	46/306 (15.0%)	> 0.99	
Normal	14/16 (87.5%)	2/16 (12.5%)		
EEG: bitemporal abnormalities				
Yes	76/84 (90.5%)	8/84 (9.5%)	<b>0.15</b>	0.24
No	181/217 (83.4%)	36/217 (16.6%)		
Extratemporal ictal abnormalities				
Yes	84/97 (86.6%)	13/97 (13.4%)	0.73	
No	173/204 (84.8%)	31/204 (15.2%)		
Preoperative iEEG				
Yes	37/43 (86.0%)	6/43 (14.0%)	> 0.99	
No	292/346 (84.4%)	54/346 (15.6%)		
Preoperative psychiatric disease				
Yes	78/94 (83.0%)	16/94 (17.0%)	0.61	
No	194/227 (85.5%)	33/227 (14.5%)		
Preoperative cognitive disorders				
No	27/29 (93.1%)	2/29 (6.9%)	0.28	
Yes	250/299 (83.6%)	49/299 (16.4%)		
Side of surgery				
Right	157/183 (85.8%)	26/183 (14.2%)	0.57	
Left	172/206 (83.5%)	34/206 (16.5%)		
Surgical approach				
Transylvian SAH	30/36 (83.3%)	6/36 (16.7%)		
Transcortical SAH	126/144 (87.5%)	18/144 (12.5%)	0.47	
ATL	173/209 (82.8%)	36/209 (17.2%)		
Histology of HS				
HS ILAE type 1	161/189 (85.2%)	28/189 (14.8%)		
HS ILAE type 2	41/47 (87.2%)	6/47 (12.8%)	0.88	
HS ILAE type 3	3/3 (100.0%)	0/3 (0.0%)		
No-HS	10/12 (83.3%)	2/12 (16.7%)		

**Table 2. Predictors of overall complications.**

Characteristics significant in univariate analysis are shown in bold. All variables significant in univariate analysis ( $P < 0.20$ ) were used in multivariate analysis.

\* Significant multivariate  $P$ -value ( $P < 0.05$ ).

Variables n/N (%) or mean $\pm$ SD	No major complication	Major complication	Univariate <i>P</i> -value	Multivariate <i>P</i> -value
Age at surgery, y, mean $\pm$ SD	36.9 $\pm$ 10.5	36.8 $\pm$ 10.5	0.98	
Duration of epilepsy, y, mean $\pm$ SD	24.8 $\pm$ 11.5	27.0 $\pm$ 8.6	0.45	
Seizure frequency / m, mean $\pm$ SD	10.9 $\pm$ 13.9	5.3 $\pm$ 3.2	<b>0.12</b>	0.12
Gender				
Male	175/184 (95.1%)	9/184 (4.9%)	0.61	
Female	198/205 (96.6%)	7/205 (3.4%)		
Dominant hand				
Right	317/331 (95.8%)	14/331 (4.2%)		
Left	45/46 (97.8%)	1/46 (2.2%)	0.46	
Ambidextrous	8/9 (88.9%)	1/9 (11.1%)		
Associated disease				
Yes	33/35 (94.3%)	2/35 (5.7%)	0.65	
No	328/342 (95.9%)	14/342 (4.1%)		
Preoperative MRI				
HS pattern	293/306 (95.8%)	13/306 (4.2%)	0.52	
Normal	15/16 (93.8%)	1/16 (6.2%)		
EEG: bitemporal abnormalities				
Yes	83/84 (98.8%)	1/84 (1.2%)	<b>0.12</b>	0.99
No	205/217 (94.5%)	12/217 (5.5%)		
Extratemporal ictal abnormalities				
Yes	94/97 (96.9%)	3/97 (3.1%)	0.56	
No	194/204 (95.1%)	10/204 (4.9%)		
Preoperative iEEG				
Yes	41/43 (95.3%)	2/43 (4.7%)	0.69	
No	332/346 (96.0%)	14/346 (4.0%)		
Preoperative psychiatric disease				
Yes	90/94 (95.7%)	4/94 (4.3%)	> 0.99	
No	218/227 (96.0%)	9/227 (4.0%)		
Preoperative cognitive disorders				
No	29/29 (100.0%)	0/29 (0.0%)	0.62	
Yes	285/299 (95.3%)	14/299 (4.7%)		
Side of surgery				
Right	175/183 (95.6%)	8/183 (4.4%)	> 0.99	
Left	198/206 (96.1%)	8/206 (3.9%)		
Surgical approach				
Transylvian SAH	35/36 (97.2%)	1/36 (2.8%)		
Transcortical SAH	141/144 (97.9%)	3/144 (2.1%)	0.30	
ATL	197/209 (94.3%)	12/209 (5.7%)		
Surgical approach				
Transcortical SAH	141/144 (97.9%)	<b>3/144 (2.1%)</b>	<b>0.11</b>	<b>0.03 *</b>
ATL	197/209 (94.3%)	<b>12/209 (5.7%)</b>		
Histology of HS				
HS ILAE type 1	179/189 (94.7%)	10/189 (5.3%)		
HS ILAE type 2	47/47 (100.0%)	0/47 (0.0%)	0.37	
HS ILAE type 3	3/3 (100.0%)	0/3 (0.0%)		
No-HS	11/12 (91.7%)	1/12 (8.3%)		

**Table 3. Predictors of major complications.**

Characteristics significant in univariate analysis are shown in bold. All variables significant in univariate analysis ( $P < 0.20$ ) were used in multivariate analysis.

\* Significant multivariate  $P$ -value ( $P < 0.05$ ).



Variables n/N (%) or mean $\pm$ SD	No neurological complication	Neurological complication	Univariate <i>P</i> -value	Multivariate <i>P</i> -value
Age at surgery, y, mean $\pm$ SD	36.9 $\pm$ 10.5	35.8 $\pm$ 10.2	0.70	
Duration of epilepsy, y, mean $\pm$ SD	25.0 $\pm$ 11.5	23.8 $\pm$ 7.7	0.71	
Seizure frequency / m, mean $\pm$ SD	10.6 $\pm$ 13.7	12.1 $\pm$ 14.4	0.69	
Gender				
Male	177/184 (96.2%)	7/184 (3.8%)	> 0.99	
Female	197/205 (96.1%)	8/205 (3.9%)		
Dominant hand				
Right	321/331 (97.0%)	10/331 (3.0%)	<b>0.008</b>	0.13
Left	43/46 (93.5%)	3/46 (6.5%)		
Ambidextrous	7/9 (77.8%)	2/9 (22.2%)		
Associated disease				
Yes	34/35 (97.1%)	1/35 (2.9%)	> 0.99	
No	329/342 (96.2%)	13/342 (3.8%)		
Preoperative MRI				
HS pattern	297/306 (97.1%)	9/306 (2.9%)	0.40	
Normal	15/16 (93.8%)	1/16 (6.2%)		
Extratemporal ictal abnormalities				
Yes	82/84 (97.6%)	2/84 (2.4%)	> 0.99	
No	210/217 (96.8%)	7/217 (3.2%)		
Atypical ictal EEG				
Yes	94/97 (96.9%)	3/97 (3.1%)	> 0.99	
No	198/204 (97.1%)	6/204 (2.9%)		
Preoperative iEEG				
Yes	40/43 (93.0%)	3/43 (7.0%)	0.22	
No	334/346 (96.5%)	12/346 (3.5%)		
Preoperative psychiatric disease				
Yes	92/94 (97.9%)	2/94 (2.1%)	0.73	
No	219/227 (96.5%)	8/227 (3.5%)		
Preoperative cognitive disorders				
No	28/29 (96.6%)	1/29 (3.4%)	> 0.99	
Yes	288/299 (96.3%)	11/299 (3.7%)		
Side of surgery				
Right	178/183 (97.3%)	5/183 (2.7%)	0.30	
Left	196/206 (95.1%)	10/206 (4.9%)		
Surgical approach				
Transylvian SAH	34/36 (94.4%)	2/36 (5.6%)	<b>0.15</b>	NA
Transcortical SAH	142/144 (98.6%)	2/144 (1.4%)		
ATL	198/209 (94.7%)	11/209 (5.3%)		
Surgical approach				
Transcortical SAH	142/144 (98.6%)	2/144 (1.4%)	<b>0.08</b>	0.08
ATL	198/209 (94.7%)	11/209 (5.3%)		
Histology of HS				
HS ILAE type 1	181/189 (95.8%)	8/189 (4.2%)	0.41	
HS ILAE type 2	47/47 (100.0%)	0/47 (0.0%)		
HS ILAE type 3	3/3 (100.0%)	0/3 (0.0%)		
No-HS	11/12 (91.7%)	1/12 (8.3%)		

**Table 4. Predictors of neurological complications.**

Characteristics significant in univariate analysis are shown in bold. All variables significant in univariate analysis ( $P < 0.20$ ) were used in multivariate analysis.

NA, not available.

Variables n/N (%) or mean $\pm$ SD	No symptomatic visual field defect	Symptomatic visual field defect	Univariate <i>P</i> -value	Multivariate <i>P</i> -value
Age at surgery, y, mean $\pm$ SD	36.9 $\pm$ 10.6	36.7 $\pm$ 10.1	0.90	
Duration of epilepsy, y, mean $\pm$ SD	24.7 $\pm$ 11.4	26.7 $\pm$ 11.3	0.32	
Seizure frequency / m, mean $\pm$ SD	10.9 $\pm$ 14.2	7.7 $\pm$ 6.4	<b>0.19</b>	
Gender				
Male	162/184 (88.0%)	<b>22/184 (12.0%)</b>	<b>0.12</b>	<b>0.04 *</b>
Female	190/205 (92.7%)	<b>15/205 (7.3%)</b>		
Dominant hand				
Right	300/331 (90.6%)	31/331 (9.4%)	0.94	
Left	41/46 (89.1%)	5/46 (10.9%)		
Ambidextrous	8/9 (88.9%)	1/9 (11.1%)		
Associated disease				
Yes	34/35 (97.1%)	1/35 (2.9%)	0.23	
No	307/342 (89.8%)	35/342 (10.2%)		
Preoperative MRI				
HS pattern	279/306 (91.2%)	27/306 (8.8%)	> 0.99	
Normal	15/16 (93.8%)	1/16 (6.2%)		
EEG: bitemporal abnormalities				
Yes	79/84 (94.0%)	5/84 (6.0%)	0.49	
No	197/217 (90.8%)	20/217 (9.2%)		
Extratemporal ictal abnormalities				
Yes	88/97 (90.7%)	9/97 (9.3%)	0.66	
No	188/204 (92.2%)	16/204 (7.8%)		
Preoperative iEEG				
Yes	40/43 (93.0%)	3/43 (7.0%)	0.78	
No	312/346 (90.2%)	34/346 (9.8%)		
Preoperative psychiatric disease				
Yes	82/94 (87.2%)	12/94 (12.8%)	0.22	
No	208/227 (91.6%)	19/227 (8.4%)		
Preoperative cognitive disorders				
No	28/29 (96.6%)	1/29 (3.4%)	0.33	
Yes	267/299 (89.3%)	32/299 (10.7%)		
Side of surgery				
Right	166/183 (90.7%)	17/183 (9.3%)	> 0.99	
Left	186/206 (90.3%)	20/206 (9.7%)		
Surgical approach				
Transylvian SAH	32/36 (88.9%)	4/36 (11.1%)	0.81	
Transcortical SAH	132/144 (91.7%)	12/144 (8.3%)		
ATL	188/209 (90.0%)	21/209 (10.0%)		
Histology of HS				
HS ILAE type 1	172/189 (91.0%)	17/189 (9.0%)	0.93	
HS ILAE type 2	42/47 (89.4%)	5/47 (10.6%)		
HS ILAE type 3	3/3 (100.0%)	0/3 (0.0%)		
No-HS	11/12 (91.7%)	1/12 (8.3%)		

**Table 5. Predictors of symptomatic visual field defects.**

Characteristics significant in univariate analysis are shown in bold.

\* Significant multivariate *P*-value ( $P < 0.05$ ).

Reference (period)	Institution	Surgical approach	n	Complications overall/major/permanent	Death
Rydenhag <sup>10</sup> (1990-1995)	Swedish National Epilepsy Surgery Register, Sweden	ATL	168	12.4%/2.9%/?	0%
Behrens <sup>11</sup> (1987-1997)	University of Bonn Bonn, Germany	ts SAH	279	?/4.7%/2.3%	0%
Salanova <sup>12</sup> (1984-1999)	Indiana University Indianapolis, Indiana, USA	?	104	9.5%/5.8%/1.3%	0%
Sindou <sup>13</sup> (1994-2003)	Pierre Wertheimer Hospital Lyon, France	ATL, ts SAH	100	19.0%/7.0%/2.0%	0%
Bate <sup>14</sup> (1996-2004)	Walton Centre Liverpool, GB	SAH, ATL	114	10.5%/6.1%/2.6%	0%
Tanriverdi <sup>15</sup> (1976-2006)	MNI Montreal, Canada	?	1232	5.5%/2.8%/?	0%
Bandt <sup>16</sup> (1997-2007)	Washington University St Louis, MO, USA	tcT2 SAH	76	?/3.0%/0.0%	0%
Iachinski <sup>17</sup> (1998-2010)	Curitiba institute Curitiba, Brazil	ATL	67	17.9%/13.4%/0.0%	0%
Vale <sup>3</sup> (1998-2012)	University of South Florida Tampa, Florida, USA	tcT3 SAH	483	?/2.7%/0.2%	0%
Yang <sup>18</sup> (2004-2012)	Fuzhou General Hospital Fuzhou, China	CAH	683	?/1.8%/ ?	0%
Josephson <sup>19</sup> (1997-2012)	Meta-analysis (5 studies)	SAH ATL	309 392	?/ ?/0.0-3.1% ?/ ?/0.0-2.4%	?
<b>Current series</b> (1990-2015)	<b>La Pitié-Salpêtrière University Hospital</b> <b>Paris, France</b>	<b>Total</b> tcT1 SAH ts SAH ATL	<b>389</b> 144 36 209	<b>15.4%/4.1%/0.5%</b> 12.5%/2.1%/0.0% 16.7%/2.8%/0.0% 17.2%/5.7%/1.0%	<b>0%</b>

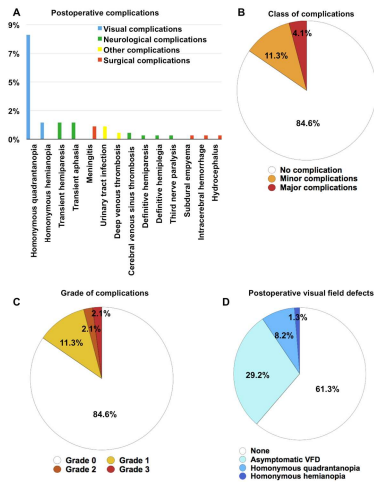
**Table 6. Morbidity and mortality of MTL surgery: Literature review.**

CAH, cortico-amygdalohippocampectomy; ts, transylvian; tc, transcortical; T1, superior temporal gyrus; T2, middle temporal gyrus; T3, inferior temporal gyrus.

References (period or publication)	Institution	Surgical approach	n	Symptomatic and asymptomatic visual field defects
<b>Egan</b> <sup>25</sup> (2000)	Casey Eye Institute, Portland, ME, USA	ATL	15	73%
		tcT2 SAH	14	79%
<b>Hervas-Navidad</b> <sup>26</sup> (1995-1998)	Virgen de las Nieves Hospital, Grenada, Spain	ATL	30	90%
<b>Pathak-Ray</b> <sup>27</sup> (2002)	University Hospital of Wales, Cardiff, GB	ATL	14	64%
<b>Nilsson</b> <sup>28</sup> (1987-1999)	Sahlgrenska University Hospital, Goteborg, Sweden	ATL	50	50%
<b>Barton</b> <sup>29</sup> (2005)	Beth Israel Deaconess Medical Center, Boston, MA, USA	ATL	29	100%
<b>Yeni</b> <sup>30</sup> (2008)	Istanbul University, Istanbul, Turkey	ts SAH	30	37%
<b>Mengesha</b> <sup>31</sup> (1990-2006)	Vanderbilt University Medical Center, Nashville, TN, USA	tcT2 SAH	18	89%
		ATL	33	91%
<b>Jeelani</b> <sup>32</sup> (1984-2004)	Great Ormond Street Hospital, London, GB	ATL	105	15%
<b>Yam</b> <sup>33</sup> (1991-2007)	London Health Sciences Centre, London, Ontario, Canada	ATL	75	65%
<b>Current series</b> (1990-2015)	<b>La Pitié-Salpêtrière</b> <b>University Hospital</b> <b>Paris, France</b>	<b>Total</b>	<b>323</b>	<b>39%</b>
		tcT1 SAH	140	34%
		ts SAH	13	46%
		ATL	170	43%

**Table 7. Visual field defects related to MTL surgery: Literature review.**

ts, transylvian; tc, transcortical; T1, superior temporal gyrus; T2, middle temporal gyrus.



**HIGHLIGHTS**

- The overall rate of complications was 15.4%.
- Persistent neurological deficits occurred in 0.5% of the patients.
- VFDs occurred in 38.7% of the patients, but only 9.5% were symptomatic.
- ATL was associated with major complications more often than transcortical SAH.
- Transcortical SAH is the preferred approach to minimize complications of HS surgery.

Variables n/N (%) or mean $\pm$ SD	No surgical complication	Surgical complication	Univariate <i>P</i> -value	Multivariate <i>P</i> -value
Age at surgery, y, mean $\pm$ SD	36.8 $\pm$ 10.5	40.9 $\pm$ 12.1	0.30	
Duration of epilepsy, y, mean $\pm$ SD	24.9 $\pm$ 11.4	28.1 $\pm$ 10.2	0.46	
Seizure frequency / m, mean $\pm$ SD	10.8 $\pm$ 13.8	4.0 $\pm$ 1.9	<b>0.19</b>	NA
Gender				
Male	180/184 (97.8%)	4/184 (2.2%)	0.71	
Female	202/205 (98.5%)	3/205 (1.5%)		
Dominant hand				
Right	324/331 (97.9%)	7/331 (2.1%)		
Left	46/46 (100.0%)	0/46 (0.0%)	0.55	
Ambidextrous	9/9 (88.9%)	0/9 (0.0%)		
Associated disease				
Yes	34/35 (97.1%)	1/35 (2.9%)	0.50	
No	336/342 (98.2%)	6/342 (1.8%)		
Preoperative MRI				
HS pattern	299/306 (97.7%)	7/306 (2.3%)	> 0.99	
Normal	16/16 (93.8%)	0/16 (6.2%)		
EEG: bitemporal abnormalities				
Yes	83/84 (98.8%)	1/84 (1.2%)	0.68	
No	211/217 (97.2%)	6/217 (2.8%)		
Extratemporal ictal abnormalities				
Yes	96/97 (99.0%)	1/97 (1.0%)	0.43	
No	198/204 (97.1%)	6/204 (2.9%)		
Preoperative iEEG				
Yes	42/43 (97.7%)	1/43 (2.3%)	0.56	
No	340/346 (98.3%)	6/346 (1.7%)		
Preoperative psychiatric disease				
Yes	91/94 (96.8%)	2/94 (3.2%)	0.42	
No	223/227 (98.2%)	4/227 (1.8%)		
Preoperative cognitive disorders				
No	29/29 (100.0%)	0/29 (0.0%)	> 0.99	
Yes	293/299 (98.0%)	6/299 (2.0%)		
Side of surgery				
Right	181/183 (98.9%)	2/183 (1.1%)	0.45	
Left	201/206 (97.6%)	5/204 (2.4%)		
Surgical approach				
Transylvian SAH	35/36 (97.2%)	1/36 (2.8%)		
Transcortical SAH	142/144 (98.6%)	2/144 (1.4%)	0.84	
ATL	205/209 (98.1%)	4/209 (1.9%)		
Histology of HS				
HS ILAE type 1	186/189 (98.4%)	3/189 (1.6%)		
HS ILAE type 2	47/47 (100.0%)	0/47 (0.0%)	0.80	
HS ILAE type 3	3/3 (100.0%)	0/3 (0.0%)		
No-HS	12/12 (100.0%)	0/12 (0.0%)		

Supplementary Table 1. Predictors of surgical complications.

Characteristics significant in univariate analysis are shown in bold. Because only 1 variable was found to be statistically significant after univariate analysis ( $P < 0.20$ ), we did not perform multivariate analysis.

NA, not available.

**Abbreviations**

ATL, anterior temporal lobectomy

CT, computerized tomography

DVT, deep venous thrombosis

EEG, electroencephalogram

HS, hippocampal sclerosis

ILAE, international league against epilepsy

MRI, magnetic resonance imaging

MTLE, mesial temporal lobe epilepsy

MTLE-HS, mesial temporal lobe epilepsy associated with hippocampal sclerosis

SAH, selective amygdalohippocampectomy

STG, superior temporal gyrus

UTI, urinary tract infection

VFD, visual field defect



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