

Vascular events after transylvian selective amygdalohippocampectomy and impact on epilepsy outcome

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SUMMARY

Objective: Epilepsy surgery is a standard treatment option for medically intractable temporal lobe epilepsy. Selective amygdalohippocampectomy (SAH) and anterior temporal lobectomy (ATL) are two of the standard surgical procedures in these cases. We conducted a retrospective analysis of patients treated with SAH via a modified transylvian approach in our epilepsy center between 2008 and 2011, and we analyzed the impact of adjacent procedure-related infarctions on seizure outcome in these patients.

Methods: Infarctions were detected by magnetic resonance imaging (MRI) within the first week postoperatively and by a second MRI 9 months after surgical intervention. Neuropsychological testing was performed preoperatively. Evaluation of seizure outcome and postoperative neuropsychological testing were conducted approximately 1 year after epilepsy surgery. Correlative clinical data were analyzed by retrospective chart review.

Results: The postoperative MRI revealed temporal infarctions in 47.9% ($n = 23/48$) and frontal infarctions in 10.4% ($n = 5/48$) of the patients. These vascular events were asymptomatic in terms of focal neurologic deficits. Of the patients, 68.5% ($n = 37/54$) were free of disabling seizures (Engel class I) 1 year after the procedure. Patients with temporal infarctions were significantly more often free of disabling seizures (Engel class I, $p = 0.046$) than patients without temporal infarctions. Neuropsychological testing indicated a deterioration in verbal memory after SAH in patients with infarctions on the language-lateralized hemisphere compared to patients without infarction ($p = 0.01$). All other tested neuropsychological categories showed no significant differences between patients with or without infarctions.

Significance: Our results indicate a surprisingly high number of procedure-related temporal infarctions after transylvian SAH. Hence, the volume of nonfunctional “eliminated” tissue is enlarged unintentionally, which is a possible explanation for better seizure outcome in these patients. This result supports the notion that ATL is the favorable procedure for temporal lobe epilepsy compared to SAH in the nondominant hemisphere, as neuropsychological deficits are rarely to be expected.

KEY WORDS: Epilepsy surgery, Infarction, Neuropsychology, MRI.



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Temporal lobe epilepsy is the most common cause of drug-resistant focal epilepsy.¹ This type of epilepsy is clearly linked to hippocampal sclerosis or gliosis, whereas the underlying nature for this pathology still remains an object of research.² Epilepsy surgery is accepted as the standard treatment in patients with longstanding, medically intractable temporal lobe epilepsy, showing good results in long-term follow-up.^{3,4} In a recently published, randomized controlled trial, there is even evidence of the benefit of

surgical treatment in patients with mesial temporal lobe epilepsy and seizures for no more than 2 years after failure of two antiepileptic drugs.⁵

Selective amygdalohippocampectomy (SAH), with its different approaches, and anterior temporal lobectomy (ATL) constitute the conventional surgical procedures. The technique of SAH was established to prevent destruction of temporal neocortical structures and is performed by using a transylvian, transcortical, or subtemporal approach with the aim of reducing neuropsychological deficits.^{6,7} There are various series reporting rates of 62–74% of freedom from disabling seizures for both surgical techniques in patients with temporal lobe epilepsy.^{8–11} However, recently, a meta-analysis of standard versus selective temporal lobe epilepsy surgery was published, suggesting the superiority of ATL with respect to seizure freedom.¹² An evaluation of neuropsychological deficits could not be undertaken in this analysis due to the different tests used, but other studies failed to demonstrate a clear reduction of neuropsychological deficits in patients who received SAH compared to those who received ATL.¹⁰ However, there are other series showing that a deterioration in neuropsychological testing is more likely after the resection of the anterior temporal lobe than after SAH.¹³

A known disadvantage of the transylvian approach in SAH, which was performed in the presented study, is the use of retraction devices to gain the desired access to the amygdalohippocampal structures. The use of such devices in some cases leads to damage of neocortical tissue, visible on postoperative magnetic resonance imaging (MRI) as areas of hyperintensity in T₂-weighted images, resulting in a decline in neuropsychological postoperative testing.¹⁴ However, even permanent infarction of adjacent brain tissue is not an unusual postoperative finding in these patients.

Therefore, we evaluated whether there is a correlation to seizure control and neuropsychological testing in patients with persisting vascular lesions 1 year after SAH.

METHODS

Patient characteristics and study design

Patients were selected for epilepsy surgery for medical refractory temporal lobe epilepsy after presurgical evaluation, which included video-electroencephalography (EEG) monitoring, 1.5- or 3-Tesla MRI, and presurgical neuropsychological testing at the Epilepsy Center Hamburg-Alsterdorf from January 2008 to March 2011. Hemispheric language lateralization was determined by functional transcranial Doppler sonography (fTCD) as described previously.^{15–17} All patients received an SAH via a transylvian approach in the Department of Neurosurgery at the University Medical Center Hamburg-Eppendorf. An early MRI was performed within the first days postoperatively, and a follow-up MRI was performed after an interval of 3–10 months.

Neuropsychological testing and evaluation of epilepsy outcome were performed in the same department where the preoperative testing was performed 1 year after epilepsy surgery. Seizure outcome was assessed according to the Engel classification system. Analysis of correlative clinical data was conducted retrospectively by chart review. Informed consent for clinical data evaluation was provided by all patients.

Technique of SAH

To achieve an anterior–posterior axis, a frontobasolateral approach was used with a pterional craniotomy distributed one third temporal and two thirds frontal to the sphenoid wing. The sphenoid wing was resected using a high-speed drill to gain anterior access to the sylvian fissure and to minimize brain retraction.

After elevating the frontal lobe with a self-retaining retractor, arachnoidal membranes were dissected sharply and the internal carotid artery, oculomotor nerve, and sylvian fissure were exposed. Due to subsequent spontaneous drainage of cerebrospinal fluid (CSF), retraction of the frontal lobe was reduced gradually. The M1 complex of the middle cerebral artery and its branches were mobilized, and subsequently, the temporal stem connecting the temporal and the frontal lobe and the mesial temporal structures were identified. Two self-retaining retractors were used intermittently to retain the surgical trajectory open. A subpial resection using an ultrasonic surgical aspirator device was performed in the anterior–posterior direction beginning at the uncus region until the temporal horn of the lateral ventricle was opened and the underlying hippocampus was exposed. The pial/arachnoidal membrane and the underlying perforating branches of the posterior cerebral artery and the medial located brainstem were carefully respected. By following the anterior–posterior trajectory, the hippocampus was resected in fragments for histologic evaluation. The dorsal border of the hippocampal resection was identified either with neuronavigation or by using the beginning of the choroid plexus as identified preoperatively by MRI as a landmark. After meticulous hemostasis, the resection cavity was lined with hemostatic material. By using this anterior–posterior approach, the temporal stem is left intact and not dissected. A characteristic example for the performed resections is given in Figure 1.

Imaging

MRI scans were initially acquired on a Siemens 1.5-Tesla MR system (Skyra; Siemens, Erlangen, Germany), changing to a 3-Tesla MR system in 2010. The MR protocol for the preoperative and the follow-up imaging involved a T₂-weighted space dark fluid and a T₁-weighted magnetization-prepared rapid gradient-echo (MP-RAGE) volume dataset. Likewise, a T₂-weighted turbo spin echo (TSE) coronal, T₁-weighted turbo inversion recovery (TIR)

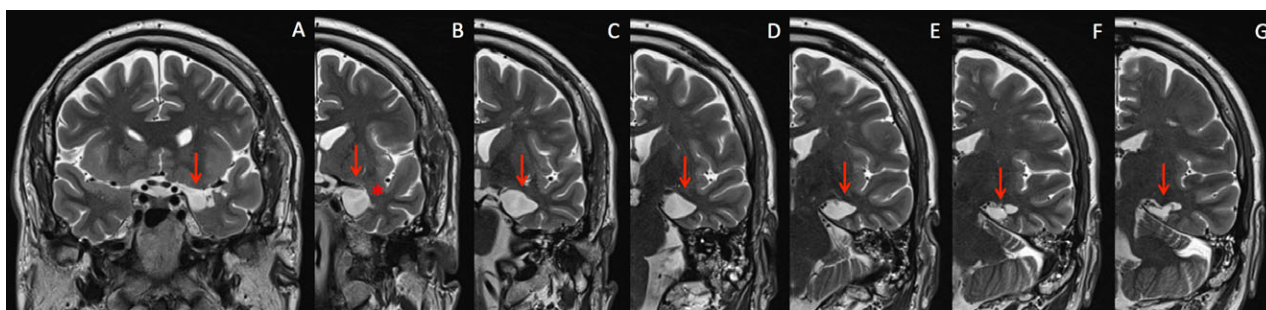


Figure 1.

Characteristic example for the extent of resection showing the resection cavity (arrows, **A–G**) and the intact temporal stem (star, **B**) in subsequent coronal plane sections of a T₂-weighted MRI scan in the anterior–posterior direction 6 months postoperatively.

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coronal, and proton density (PD)/T₂-weighted axial dataset were acquired.

The first postoperative imaging was completed using additional diffusion-weighted imaging (DWI), an apparent diffusion coefficient (ADC) map, and hemosensitive sequences.

Cerebral infarctions on the postoperative MRI were defined as circumscribed hyperintensity on the DWI and a correlating hypointense area on the ADC map. Furthermore, verification was performed by checking for residual changes on the follow-up MRI.

Neuropsychological evaluation

Cognitive assessments that are particularly sensitive to patients with epilepsy were selected. All patients underwent a neuropsychological examination preoperatively and 12 months postoperatively. The testing contained measurements of verbal and nonverbal memory functions, including the German version of the Rey Auditory-Verbal Learning Test (Verbaler Lern- und Merkfähigkeitstest, VLMT),¹⁸ a test of memory for narrative information (Logical Memory subtest of the revised Wechsler Memory Scale),¹⁹ a figural learning and memory test (Diagnosticum für Cerebralschädigung, DCS-II),²⁰ and a face recognition test (Alsterdorfer Gesichtertest, AGT).²¹ Further tests of verbal functions such as verbal fluency (Regensburger Wortfluesigkeitstest, RWT),²² speech comprehension (Token Test; subtest of the Aachener Aphasietest)²³ and naming (60-item Boston Naming Test),²⁴ and a test of visuoconstructive ability (Mosaiktest; subtest of the German adaptation of the Wechsler Adult Intelligence Scale, Wechsler Intelligenztest für Erwachsene, WIE)²⁵ were administered. The assessment also included an estimate for crystallized verbal intelligence (Wortschatztest, WST),²⁶ tests for concentration and working memory (Digit Span subtest of the revised Wechsler Memory Scale),¹⁹ and tests for attention and speed performance (various subtests of the Testbatterie zur Aufmerksamkeitsprüfung, TAP).²⁷ Test results were categorized, with respect to hemispheric language lateralization, as “average,” “lower than average,” and “much lower than average” by experienced neuropsychologists.

Statistical analyses

The correlations of infarction and seizure outcome and neuropsychological testing were assessed by using a chi-square test. Fisher’s exact test was used in the case of inappropriate small subgroup size. A 5% significance level (two-tailed) was accepted for hypothesis testing. All analyses were performed using IBM SPSS Statistics 21 (SPSS Inc., Chicago, IL, U.S.A.).

RESULTS

Fifty-six patients with medically refractory temporal lobe epilepsy were evaluated; the mean age was 40.8 years (median age 42.4 years) with the following gender distribution: male 57.1% (n = 32/56), female 42.9% (n = 24/56). Fifty percent (n = 28/56) of the patients were operated on the left hemisphere and 50% on the right hemisphere, resulting in resections in the dominant hemisphere in 39.3% (n = 22/56) and in the nondominant hemisphere in 60.7% (n = 34/56). A second surgery undertaken to treat persistent epilepsy was performed in two cases (3.6%), due to residual tumor (ganglioglioma) in one case and remaining parts of the hippocampus in the other case. Both reoperations were performed after the initial 1-year follow-up and had therefore no influence on data evaluation. Three-fourths of the histologic specimens were classified as hippocampal sclerosis (76.8%, n = 43/56). In 5.4% (n = 3/56) of the cases a ganglioglioma was diagnosed, in 3.6% (n = 2/56) a dysembryoplastic neuroepithelial tumor, in 5.4% (n = 3/56) a cavernoma, in 1.8% (n = 1/56) a pilocytic astrocytoma, and in 7.2% (n = 4/56) no specific histopathologic findings were detected. The lesions were located within the hippocampus. Therefore, an SAH was selected as the surgical procedure. Temporal infarctions occurred in patients with hippocampal sclerosis (n = 18/23 temporal infarctions) and in patients with tumor (n = 5/23).

Early postoperative MRI was performed 1–6 days after surgery (mean 3.6 days, standard deviation [SD] 2.9, n = 53), and follow-up MRI was performed after a 3- to 10-month interval (mean 279.4 days, SD 146.8, n = 45). Signs

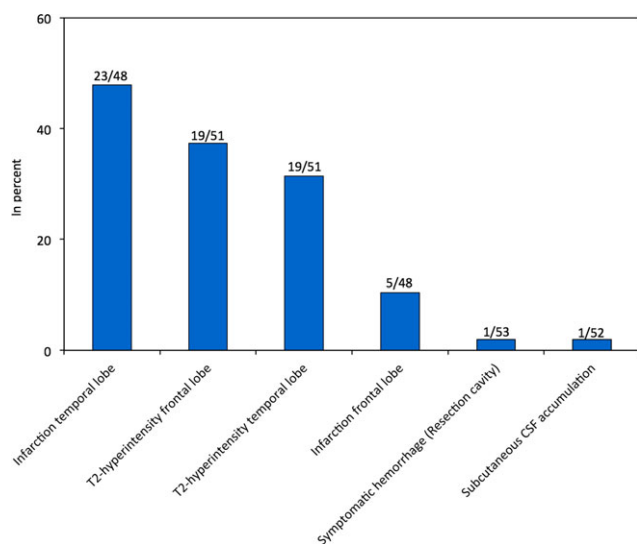


Figure 2. Summary of abnormal MRI results in percentages. *Epilepsia* © ILAE

of ischemia were observed in the frontal lobe in 10.4% ($n = 5/48$) of the patients, with a mean volume of 0.73 cm^3 (SD 0.43), and in the temporal lobe in 47.9% ($n = 23/48$) of the patients, with a mean volume of 3.19 cm^3 (SD 4.12, Fig. 2). All temporal infarctions were located adjacent to the resection cavity. There were no distant infarctions suggesting an embolic origin. According to this result, changes in the same areas were observed in the follow-up MRI, demonstrating a residual state of an infarction adjacent to the resection cavity in these patients. Hereby, the diagnosis of a manifest infarction as sequela of the procedure was confirmed.

Further frequent findings in the early postoperative MRI were hyperintense areas in the frontal and temporal lobe in the T_2 sequences, which were absent in the follow-up MRI. None of the described MRI findings led to the clinical development of persistent focal neurologic deficits such as dysphasia, pareses, or cranial nerve palsies. An example for an adjacent temporal infarction close to the resection cavity is presented in Figure 3.

The outcome according to the Engel classification system was analyzed 385.1 days (SD 113.3) postsurgery ($n = 54$, two patients lost to follow-up). Of the patients, 68.5% ($n = 37/54$)

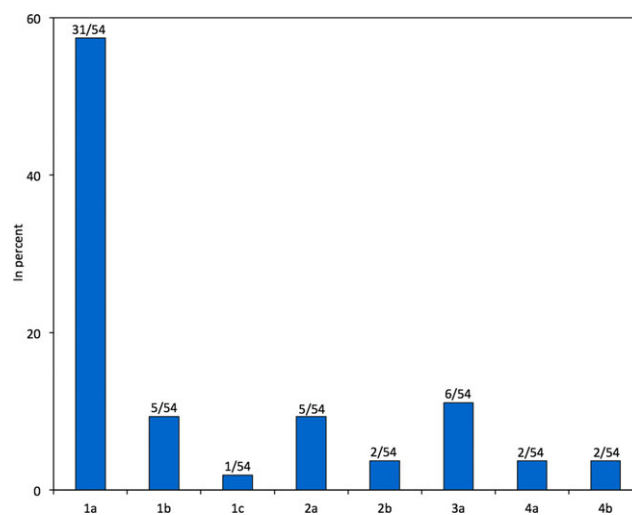


Figure 4. Epilepsy outcome in percent, 1 year after surgery according to Engel classification. *Epilepsia* © ILAE

were free of disabling seizures (Engel class I) and 13% ($n = 7/54$) were almost seizure-free (Engel class II), thus resulting in a favorable outcome in 81.5% ($n = 44/54$) of patients (Fig. 4).

Epilepsy outcome was not significantly affected by frontal lobe infarction (Fisher's exact test, $p > 0.999$), but the likelihood of being free of disabling seizures (Engel class I) was significantly increased in patients with temporal infarction (chi-square test, $p = 0.046$). The risk for not becoming seizure free was 3.8-fold higher for patients without temporal infarction (95% confidence interval [CI] 0.99–14.67). Epilepsy outcome data are shown in Figure 5.

Neuropsychological assessment at follow-up showed no significant deterioration of the verbal memory in patients who had surgery on the dominant side (4 patients improved, 4 patients deteriorated, and 11 patients unchanged). In addition, the other tested abilities were not negatively affected by surgical interventions on the dominant hemisphere. Details are given in Table 1.

However, neuropsychological testing revealed a significant correlation between verbal memory and temporal lobe infarction in patients with epilepsy surgery on the dominant hemisphere. There was no difference in verbal memory

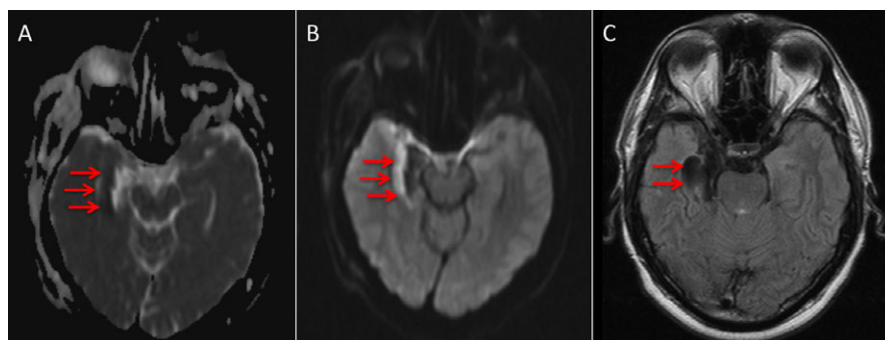


Figure 3. Patient with postoperative temporal lobe infarction evident from hypointense area lateral to the resection cavity on the ADC map (A), hyperintensity on the DWI (B), and residual changes on the follow-up MRI (C). *Epilepsia* © ILAE

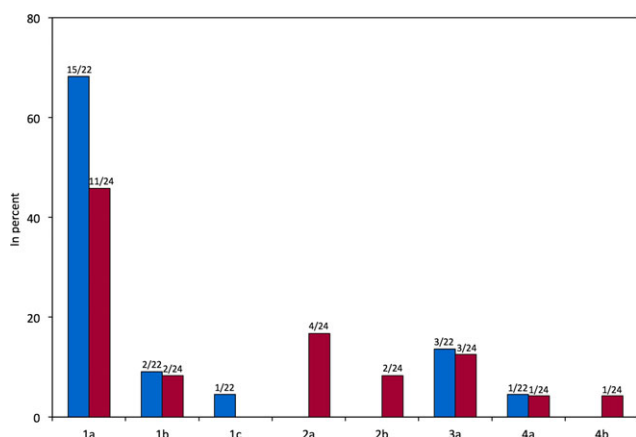


Figure 5.

Engel classification in percent according to temporal lobe ischemia (blue column: with temporal lobe infarction, red column: without temporal lobe infarction).

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between patients with and without temporal infarction preoperatively (chi-square test, $p = 0.166$). Comparing these groups postoperatively, the results of verbal memory testing were significantly inferior in patients with an infarction in the temporal lobe of the language-dominant hemisphere (chi-square test, $p = 0.011$, Fig. 6). However, verbal fluency and speech comprehension were not affected significantly by temporal infarctions on the dominant side (chi-square test, $p = 0.456$ and Fisher's exact test, $p > 0.999$).

Epilepsy surgery on the nondominant side had no negative effect on figural memory, too (9 patients improved, 5 deteriorated, and 10 unchanged, Table 1). In addition, temporal infarctions after surgery on the nondominant hemisphere had no significant impact on the tested abilities. The results for figural memory (chi-square test, $p = 0.751$), as well as for visuoconstructive abilities (chi-square test, $p = 0.543$), were postoperatively not significantly worse than those of patients of the same group without temporal lobe infarction.

DISCUSSION

Epilepsy surgery has been shown to be superior to medical treatment in pharmacologically resistant temporal lobe

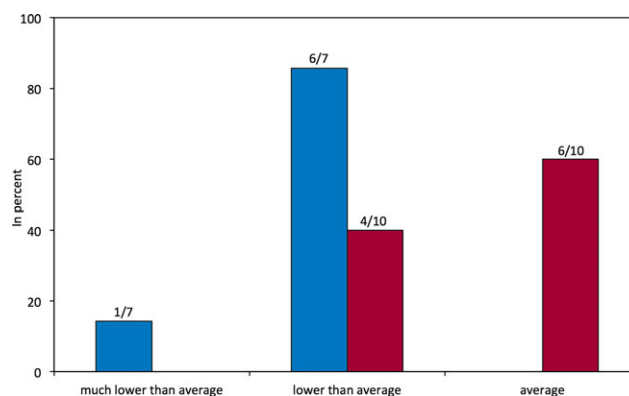


Figure 6.

Verbal memory after surgery on language-dominant hemisphere with (blue column) and without (red column) temporal lobe infarction.

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epilepsy. Wiebe et al. demonstrated in a prospective randomized trial that patients who underwent anterior temporal lobectomy were more often free of disabling seizures than patients who received the best medical care (64% vs. 8%). Moreover, quality of life was better in the operated patients than in the patients who underwent conservative treatment.³

Over the last decades, more selective resections have been performed to spare neocortical brain tissue not involved in epilepsy pathology. Subtemporal, transcortical, and transylvian approaches are used for SAH.^{7,28-31} The rates of seizure freedom are reported to be between 62% and 78% in different series.^{9,10,13,32-34} Because these results are similar to those of anterior temporal lobectomy, SAH is in many centers the preferred procedure for temporal lobe epilepsy.

In this study, we used a modified transylvian approach for SAH. To protect the temporal stem to the extent possible, a fragmented resection of the hippocampus in the anterior-posterior direction was performed. Despite seeking to reduce the application of self-retaining retractors, this technique requires some brain retraction to gain sufficient space for hippocampal resection. Therefore, the risk for retraction-related hyperintensities on the T₂-weighted images or

Table 1. Results of neuropsychological testing postoperatively compared to preoperative assessment

Tested ability	n	No. of patients (%)					
		Surgery on dominant side			Surgery on nondominant side		
		Improved	Deteriorated	Equal	Improved	Deteriorated	Equal
Verbal memory	40	4/19 (21.1)	4/19 (21.1)	11/19 (57.8)	6/21 (28.6)	2/21 (9.5)	13/21 (61.9)
Verbal fluency	41	6/19 (31.6)	3/19 (15.8)	10/19 (52.6)	7/22 (31.8)	5/22 (22.7)	10/22 (45.5)
Speech comprehension	21	0/11 (0)	0/11 (0)	11/11 (100)	1/10 (10)	0/10 (0)	9/10 (90)
Figural memory	43	5/19 (26.3)	4/19 (21.1)	10/19 (52.6)	9/24 (37.5)	5/24 (20.8)	10/24 (41.6)
Visuoconstructive abilities	39	6/17 (35.3)	1/17 (5.9)	10/17 (58.8)	5/22 (22.7)	3/22 (13.6)	14/22 (63.6)

n, number of preoperatively and postoperatively examined patients.

even infarction might be elevated, which is underscored by almost 50% of the patients with temporal infarctions postoperatively. By contrast, the pure T₂ hyperintense areas in the early postoperative MRI were no longer detectable in the follow-up MRI, showing the transient character of these findings.

Additional reasons for ischemic events associated with the vascular territory of the middle cerebral artery include the use of the transylvian approach. This approach requires a wide opening of the sylvian fissure with a preparation of small perforating branches of the artery. Subsequently the risk of vasospasm or liberation of arteriosclerotic plaques might be elevated, although distant embolic infarctions have not been detected in this study.

However, none of the patients in this study, including those with infarctions, had focal neurologic deficits at follow-up. Neither pareses nor cranial nerve palsies were detectable 1 year postoperatively.

Epilepsy outcome in the presented cohort was favorable and in agreement with the results reported in the literature,¹² with 68.5% (n = 37/54) of the patients free of disabling seizures (Engel class I) and 13% (n = 7/54) almost free of seizures (Engel class II). Surprisingly, patients with temporal infarctions were significantly more frequently free of disabling seizures (Engel class I) than patients without temporal infarctions postoperatively. Considering that infarcted and therefore nonfunctional brain tissue is equivalent to an enlargement of resection volume, patients with a larger resection or nonfunctioning volume had a better seizure outcome.

We analyzed whether patients with temporal infarctions showed a significant decline in neuropsychological testing and found that only patients with temporal infarctions on the language-dominant hemisphere were affected in terms of verbal memory. All other tested neuropsychological abilities were unchanged compared to patients without infarctions, including figural memory on the nondominant hemisphere in patients who underwent epilepsy surgery on that side. Furthermore, frontal infarctions induced no impairment of neuropsychological testing results.

Surgery for medically refractory epilepsy must generally strike a balance between the amount of resected tissue to remove from the epileptogenic region and the induction of neurologic or neuropsychological deficits by removing or disrupting functionally important neuronal networks. In particular, in temporal lobe epilepsy, saving temporal neocortical tissue and temporofrontal connections may be crucial for good neuropsychological outcomes after amygdalohippocampectomy.

There are inconsistent data regarding neuropsychological deficits in ATL compared to those in SAH.^{10,13,35,36} Whereas some authors report a deterioration in various abilities after ATL, others have failed to demonstrate differences between ATL and SAH. The consequences of SAH for memory and other neuropsychological abilities are also

discussed inconsistently in literature. Some authors have shown a persisting decline in postoperative memory after left-sided surgery in patients who underwent SAH.³⁷ By contrast, Morino et al.³⁸ demonstrated, in a retrospective series, an improvement of verbal memory function particularly after right-sided SAH, but also with marginal significance after left-sided procedures.

Recently, radiosurgery and laser-induced thermal ablation has been reported to be effective with reasonable side effects in temporal lobe epilepsy.^{39,40} However, further research is required to determine the role of these techniques in medically refractory epilepsy.

Our results indicate a risk for impairment of verbal memory when performing an ATL, which is functionally comparable to an SAH with an adjacent temporal infarction, on the language-lateralized hemisphere. Because the mean volume of the infarctions was only 3.19 mL and therefore much smaller than the volume of ATL, these results must be interpreted with caution. On the other hand, it can be speculated that “tissue does matter” in the sense that “more is better,” and therefore, supraselective resections for temporal lobe epilepsy need to be discussed and evaluated further.

CONCLUSIONS

In the present study, patients with temporal infarctions after SAH were more often free of disabling seizures (Engel class I) than were patients without infarctions. In cases in which these temporal infarctions were located on the language-dominant hemisphere, a decline in verbal memory compared to patients without infarctions was detected. Based on these results, it must be discussed whether SAH on the non-language-dominant hemisphere should be replaced by ATL. On the dominant hemisphere larger resections bear the risk of verbal memory deterioration. Therefore, SAH should be the primary surgical procedure.

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DISCLOSURE OR CONFLICT OF INTEREST

T.M. and O.H. served as paid consultants for Cyberonics, Inc., Houston, TX, U.S.A. The remaining authors have no potential conflicts of interest to report. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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