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Accuracy of expert predictions of seizure freedom after epilepsy surgery

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ABSTRACT

Purpose: To evaluate the accuracy of expert estimations of achieving seizure freedom after epilepsy surgery in the context of presurgical patient counseling.
Method: The retrospective study comprised a random sample of 200 patients who underwent any type of resective epilepsy surgery at the University of Bonn Epilepsy Center and the routine 1-year postoperative control visit in the years from 2008–2016. The prediction by a team of epileptologists and the actual seizure outcome were extracted from the pre- and postsurgical medical files, respectively. A deviation of > 10% was a priori defined as a relevant discrepancy.
Results: Estimated chances of achieving seizure freedom ranged from 30 to 90% (mean: 67%). The actual seizure freedom rate was 66% (Engel Ia/ ILAE 1a). Nine of 12 estimation categories showed a tolerable deviation of ≤10%, none of these with a worse than expected outcome. Two estimation categories (40–50%, and 80%) showed a worse actual seizure outcome with deviations of −40% (n = 3); and −17% (n = 30), respectively. All in all, for 83% of the patients a correct prediction was provided.
Conclusions: For the vast majority of surgical patients, the expert prediction of postsurgical seizure freedom at the 1-year follow-up was accurate despite the heterogeneity of patients and surgical procedures.

1. Introduction

Epilepsy surgery is an efficacious elective treatment for pharmacoresistant epilepsies [1,2]. Following comprehensive presurgical evaluation [3], patients are counseled with regard to the chances and risks of surgical treatment. This is essential for informed decision making [1]. At the University of Bonn Epilepsy Center, which has been conducting up to 120 epilepsy surgeries per year since 1988 [4], a team of trained epileptologists explicitly estimates the individual chances of getting seizure free after surgery. This prediction is communicated to the patient (e.g. a 70% chance of becoming seizure free) and stated in the medical report. The expert judgement is derived from the constellation of diagnostic findings obtained during presurgical work-up and under consideration of past personal and institutional experience with similar cases and published outcome series.

A key issue in personalized outcome predictions is that the accuracy of the estimation cannot be evaluated in individual surgical patients. The actual outcome is binary, i.e. after surgery the patient will become seizure free or not. Thus, the prediction cannot be confirmed or proven wrong in an individual case. The accuracy of the presurgical prediction can only be judged on a group level by analyzing a cohort of surgical cases. By choosing this approach, the current study evaluated the accuracy of the presurgically estimated chances of getting seizure free after epilepsy surgery.

2. Methods

We retrospectively analyzed a random sample of 200 patients who underwent elective epilepsy surgery at the University of Bonn Epilepsy Center and the routine 1-year postoperative control visit in the years from 2008–2016. This approach was chosen to avoid a potential bias due to cohort effects when solely enrolling consecutive patients from a specific time period. Data on the estimated chances of becoming seizure free and the actually achieved seizure freedom one year after surgery were extracted from the respective pre- and postsurgical medical reports and anonymized for the subsequent evaluation. Ethical approval for local data collection as part of a registry was given by the ethic committee of the University Bonn Medical Center (#002/17). The major demographic and clinical characteristics of the sample are presented in Table 1.

For the different outcome categories, deviations of actual outcome from estimated seizure freedom rates were quantified. A deviation of

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Table 1
Demographic and clinical characteristics of the random sample of 200 patients who underwent epilepsy surgery.

	N = 200
Sex	
female	102 (51%)
male	98 (49%)
Age at surgery [years]	
M (SD)	36.3 (14.6)
range	3-72
Onset of epilepsy [age in years]	
M (SD)	16.0 (11.9)
range	0–62
Duration of epilepsy [years]	
M (SD)	20.3 (15.1)
range	0-65
Postsurgical seizure freedom	
Engel Ia/ILAE Ia	132 (66%)
Presurgical invasive EEG	
yes	64 (32%)
Surgical site	
temporal	152 (76%)
frontal	25 (13%)
posterior	12 (6%)
multilobar	1 (< 1%)
hemispheric	8 (4%)
insular	2 (1%)
Side of surgery	
left	101 (50%)
right	99 (50%)
Surgical procedure	
SAH	98 (49%)
extended lesionectomy	70 (35%)
standard ATLR	12 (6%)
extended lesionectomy + AHE	10 (5%)
functional hemispherectomy	8 (4%)
topectomy	1 (< 1%)
partial resection + AHE	1 (< 1%)
Histopathology[a]	
hippocampal sclerosis	96 (47%)
FCD IIb	23 (11%)
gliosis	21 (10%)
ganglioglioma (WHO I)	19 (9%)
cavernoma	11 (5%)
DNT	11 (5%)
FCD IIa	8 (4%)
encephalitis	4 (2%)
oligodendroglioma (WHO II)	4 (2%)
loss of gray-white-matter differentiation	3 (1%)
astrocytoma (WHO II)	2 (1%)
astrocytoma (WHO I)	1 (< 1%)
meningioma	1 (< 1%)
tissue defect	1 (< 1%)

[a] Due to dual pathologies, the total number is higher than the total sample size M, mean; SD, standard deviation; SAH, selective amygdalohippocampectomy; AHE, amygdalohippocampectomy; LE, lesionectomy; FCD, focal cortical dysplasia; DNT, dysembryoplastic neuroepithelial tumor.

more than 10% was a priori considered as a relevant discrepancy. Actual seizure freedom was defined as no seizures since the neurosurgical intervention (ILAE Ia, Engel Ia).

3. Results

In the analyzed random sample of 200 patients, 76% had undergone epilepsy surgery for treatment of temporal lobe epilepsy, 13% for frontal lobe and 6% for posterior epilepsies (Table 1). The surgical site was hemispheric in 4% and insular in 1%. In one patient (< 1%) seizures originated from the temporal and the occipital lobe. The most frequent surgical procedure was selective amygdalohippocampectomy in 49% of the patients, followed by extended temporal or extratemporal lesionectomies in 35%. Further surgeries were standard anterior temporal lobe resections (6%), extended lesionectomy in combination with amygdalohippocampectomy (5%), and functional hemispherectomy (4%). Topectomy (< 1%) and partial resection plus amygdalohippocampectomy (< 1%) were performed in one patient each (Table 1). The three most frequent histopathological findings were hippocampal sclerosis (47%), focal cortical dysplasia (FCD) type IIb (11%), and astrogliosis (10%) (Table 1).

The estimated chances of achieving seizure freedom after resective surgery ranged from 30 to 90%, and were either given as fixed percentages in 117 patients (59%), e.g. a 70% probability of becoming seizure free, or as a limited range in 83 patients (42%), e.g. a chance ranging between 70–80%.

As depicted in Fig. 1a, the most frequently predicted seizure freedom rate was 70% (n = 44, 22%) followed by the 60–70% (n = 40, 20%) and the 80% (n = 30, 15%) estimation categories. The least represented categories with less than 5 patients each were the 30% (n = 1, < 1%), 40% (n = 2, 1%), 40–50% (n = 3, 2%), 80–90% (n = 3, 2%), and 90% (n = 2, 1%) chance categories.

The mean estimated chance of getting seizure free[1] and its standard deviation was 67 ± 10%, the actual seizure freedom rate at the 1-year postsurgical follow-up was 66%.

Fig. 1b depicts the predicted versus actual seizure outcome.

Fig. 1c shows the major results, i.e. the deviations of the actual seizure outcome for each estimation category. In general the estimation was quite accurate with 9 of 12 categories showing a deviation within a range of ± 10%. The two categories with the largest sample sizes (60–70%, n = 40, and 70%, n = 44) showed no or a small deviation of +5%, respectively. A perfect prediction was observed for the 50–60% estimation category (n = 16). The largest deviation was seen for the one patient with a 30% chance of getting seizure free who actually became seizure free (i.e. a +70% deviation). For most estimation categories the actual outcome tended to be better than the prediction. The two exceptions were the 40–50% (n = 3) and the 80% (n = 30) estimation categories with deviations of −40% and −17%, respectively.

All in all, for 83% of the patients a correct presurgical prediction was provided.

4. Discussion

The current study was set up to evaluate the accuracy of expert predictions of achieving seizure freedom after resective epilepsy surgery. The prediction which is communicated to the patient before an offered surgical treatment was accurate for the vast majority (83%) of surgical patients with 9 of 12 estimation categories showing an excellent match or a minor deviation of up to 10%. Most of the surgical patients tended to have a better seizure outcome than expected. The largest deviation was seen for the one patient with a 30% chance of becoming seizure free who actually became seizure free, i.e. a +70% deviation. Two further categories with significant deviations showed a worse seizure outcome than predicted: In a small group of 3 patients with an estimated chance of 40–50% nobody achieved seizure freedom, and in a relatively larger group of 30 patients with a predicted 80% chance the actual seizure freedom rate was 63%. The 80% prediction category was obviously too optimistic. Interestingly, this category also deviates from an anticipated normal distribution displayed in Fig. 1a.

The match of predictions and outcome is considerable taking into account the heterogeneity of patients (although mostly patients with

[1] If the estimation category was a range, the median of the range was used to calculate the mean estimated chance of getting seizure free, e.g. in case of 70-80% → 75%.

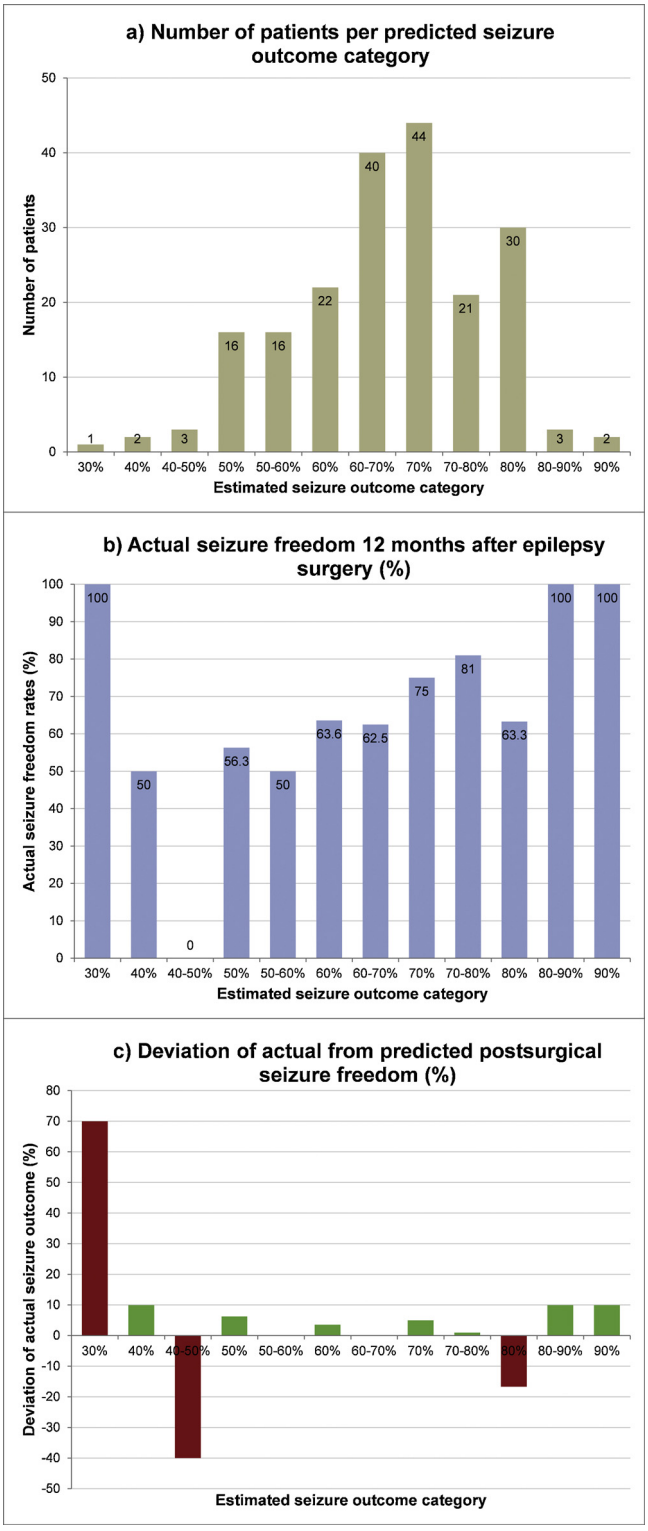

Fig. 1. a) Number of patients per predicted seizure outcome category; b) Actual seizure freedom 12 months after epilepsy surgery; c) Deviation of actual from predicted postsurgical seizure freedom; deviations larger than 10% are displayed as red bars.

temporal lobe epilepsy) and procedures (Table 1) and that the predictions were based on subjective expert ratings grounded on information which cannot be retrieved post hoc. But is it better or worse than formalized approaches which predict seizure outcome based on multiple predefined variables, including age, sex, history of febrile convulsion, age at habitual seizure onset, concordant semiology, pathological cause, results from structural MRI, duration of epilepsy, seizure frequency, secondary seizure generalization, type and site of surgery, invasive EEG, and/or deficits in conscious long-term memory? These approaches comprise nomograms (with a concordance statistic of 0.60 for postoperative seizure freedom) [5], 4–6 item scales (with no reported information regarding their accuracy) [6], or a statistical approach via logistic regression analysis [7]. The regression approach showed that only one of six considered variables contributed significantly to the prediction of the postsurgical seizure outcome, i.e. the need for invasive EEG that was associated with a worse outcome. However, that logistic regression model had a poor predictive accuracy (Nagelkerke $R^2 = 0.11$; note: $R^2 = 1.0$ would indicate a perfect prediction). A very recent head-to-head study [8] in 20 patients who underwent epilepsy surgery compared the accuracy of seizure outcome estimations by experts from various comprehensive epilepsy surgery centers with predictions based on the nomograms (the Epilepsy Surgery Nomogram; ESN) and a 6-item scale (modified Seizure-Freedom score; m-SFS). Results indicated that there was no statistically significant difference regarding the accuracy of the three different approaches. However, there was a large variance regarding the individual predictions by the 20 epilepsy experts with concordance indices ranging from 0.275 to 0.742. Thus, some experts were superior to the formalized approaches with concordance indices below 0.540. It is important to note that the epilepsy experts were not involved in the actual presurgical diagnostics of the evaluated cases and that there was no possibility for discussion among the experts. This is a major difference to the present study.

At present most formalized approaches of seizure outcome prediction appear inferior to the expert estimation given to patients in a highly specialized epilepsy center with a long history of epilepsy surgery and many surgeries per year.

The major limitation of the present study is its retrospective nature with all associated limitations.

The expert prediction was good for the outcome one year after surgery. However, this does not cover patients with a late seizure relapse or late seizure freedom in the time after [9–11]. But if epileptologists would systematically assess the long term outcomes beyond the 1–2 year standard follow-up intervals, they might develop the expertise for long-term predictions as well.

A question which cannot be answered by this study is how much the epileptologists' individual training and clinical experience makes a difference. As mentioned above, patients are counseled on the basis of the judgement of a team of epileptologists with varying clinical experience. Prospective studies should evaluate the experience of the center, years of epileptological training, numbers of surgeries, and also interrater agreement among team members. Future studies should also investigate the decision process in individual surgical patients with the question of whether this can be formalized and transferred into a transparent decision tree.

5. Conclusion

All in all, expert judgements regarding the individual chances of getting seizure free after epilepsy surgery are reliable allowing patients to make an informed decision whether to accede to a proposed surgical procedure. This is at least valid for the first year after surgery and seems superior to formalized decision making. This does not disqualify approaches using scales and multiple regression analyses which in the future, with big data available, may represent a promising complementary and more transparent approach to provide an accurate prediction.

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