Postoperative Antiepileptic Drug Escalation as a Pragmatic Prognostic Marker After Temporal Lobe Epilepsy Surgery: A Retrospective Cohort Study of 60 Patients

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Abstract

Background: Epilepsy surgery is the most effective intervention for drug-resistant temporal lobe epilepsy (TLE), but a substantial proportion of patients experience persistent or recurrent seizures postoperatively. Simple postoperative markers that flag patients at higher risk of poor outcomes would be clinically valuable.

Objective: To evaluate whether postoperative escalation of antiepileptic drug (AED) therapy—from monotherapy to polytherapy—serves as a pragmatic marker of unfavorable long-term seizure outcome after TLE surgery.

Methods: We retrospectively reviewed 60 consecutive patients with drug-resistant TLE who underwent anteromedial temporal lobectomy (ATL) or selective amygdalohippocampectomy (SAH) at a single tertiary center. AED regimens were classified as monotherapy or polytherapy preoperatively and at last follow-up, defining four AED-trajectory categories: Single→Single, Single→Multiple, Multiple→Multiple, Multiple→Single. Seizure outcomes were classified using the Engel scale and dichotomized as favorable (Engel I–II) or unfavorable (Engel III–IV). Archival SPSS univariable logistic regression outputs were interpreted descriptively due to sample-size and documentation constraints.

Results: Mean seizure frequency decreased from 82 seizures/month preoperatively to 10.2 seizures/month at last follow-up. Most patients achieved favorable Engel I–II outcomes, while a minority remained in Engel III–IV. Among AED-trajectory categories, postoperative escalation from monotherapy to polytherapy (Single→Multiple) showed the strongest directional association with unfavorable outcome (odds ratio ~2.0, descriptive). Other trajectories (Single→Single, Multiple→Multiple, Multiple→Single), resection size, resection side, and preoperative traditional Chinese medicine (TCM) use showed no meaningful association with outcome.

Conclusions: Postoperative escalation from monotherapy to polytherapy is a simple, universally observable marker that signals elevated risk of unfavorable seizure outcome after TLE surgery. AED-trajectory monitoring may complement preoperative prognostic models and support earlier, more aggressive postoperative surveillance, imaging reassessment, and consideration of neuromodulation or reoperation. Prospective multicenter validation is warranted.

Keywords: temporal lobe epilepsy; epilepsy surgery; Engel classification; antiepileptic drugs; seizure outcome; neurosurgery

Introduction

Epilepsy affects tens of millions of people worldwide and remains a major contributor to neurological disability and premature mortality. Temporal lobe epilepsy (TLE) is the most common focal epilepsy referred for surgery and has distinct clinical, epidemiological, and pathological features. Drug resistance failure of adequate trials of two or more appropriately chosen antiepileptic drugs (AEDs) is common and associated with ongoing seizures, injury, psychosocial impairment, and increased mortality risk.

For patients with drug-resistant TLE, resective epilepsy surgery most commonly anteromedial temporal lobectomy (ATL) or selective amygdalohippocampectomy (SAH) is superior to continued medical therapy. The landmark randomized trial by Wiebe et al. demonstrated that temporal lobe surgery yields higher seizure-freedom rates and better quality of life compared with optimized pharmacotherapy alone. Long-term cohort studies, including de Tisi et al. and Mohan et al., report sustained seizure freedom in a substantial fraction of surgically treated patients, although patterns of remission and late relapse vary.

Despite these benefits, epilepsy surgery remains underutilized. Many referred patients either do not reach surgery or experience suboptimal outcomes. Predicting who will benefit most from surgery and identifying early postoperative 'red flags' for poor outcome are ongoing strategic priorities.

Existing prognostic work has focused heavily on preoperative predictors: mesial temporal sclerosis, lesion type, ictal EEG localization, PET/SPECT abnormalities, neuropsychological profiles, and familial/genetic contributions. Nomograms such as those developed by Jehi et al. integrate multiple preoperative factors to provide individualized estimates of seizure outcome. These models are powerful but resource-intensive, and their implementation is constrained in many low- and middle-income settings where the epilepsy burden is high.

In contrast, relatively little attention has been paid to postoperative variables that are simple, dynamic, and universally available. One such variable is the pattern of postoperative AED use. Large-scale work has explored the relationship between histopathology, seizure freedom, and long-term AED use after epilepsy surgery, emphasizing the complexity of AED withdrawal decisions. However, the specific trajectory of AED escalation especially a shift

from monotherapy to polytherapy after surgery has not been systematically studied as a standalone marker of poor prognosis.

In real-world practice, clinicians often escalate AED therapy when seizures persist, recur, or appear imminent based on clinical or EEG indicators. This makes AED escalation a pragmatic, behaviorally encoded signal that the epileptogenic network remains active despite resection.

In this retrospective cohort study of 60 patients with drug-resistant TLE undergoing ATL or SAH, we evaluated whether postoperative AED escalation from monotherapy to polytherapy is associated with unfavorable Engel outcomes. We also examined the relationship between seizure outcome and resection size, resection side, and preoperative TCM use. Our aim is to provide a low-cost, universally applicable postoperative marker that complements imaging-, EEG-, and pathology-based prognostic frameworks.

Methods

Study Design and Setting

We conducted a retrospective observational study at The Second Hospital of Dalian Medical University, a tertiary referral center for epilepsy surgery in Liaoning, China. Consecutive patients undergoing TLE surgery between January 2008 and December 2012 were identified from the institutional epilepsy surgery registry and archived thesis dataset.

Eligibility Criteria

Inclusion criteria were: clinical diagnosis of drug-resistant TLE (failure of ≥2 appropriate AEDs); completed presurgical evaluation including MRI and prolonged video-EEG; ATL or SAH targeting the temporal lobe; at least 6 months of postoperative follow-up; and documented Engel outcome at last follow-up. Patients with prior epilepsy surgery, non-temporal resections, or incomplete records were excluded. Sixty patients met all criteria.

Presurgical Evaluation

All patients underwent standardized presurgical workup: detailed seizure history and neurologic examination; prolonged video-EEG monitoring using the 10–20 system to capture habitual seizures and define ictal onset; high-resolution MRI (including T1-weighted volumetric sequences, coronal T2-weighted images perpendicular to the hippocampal axis, and FLAIR imaging) to evaluate mesial temporal sclerosis and other lesions; and multidisciplinary conference review to determine candidacy and surgical plan.

Surgical Techniques

Anteromedial temporal lobectomy (ATL) involved a frontotemporal craniotomy with resection of 3.5–4.5 cm of anterior temporal neocortex in the language-dominant hemisphere and up to 5–5.5 cm in the non-dominant hemisphere, with resection of the amygdala and anterior hippocampus. Selective amygdalohippocampectomy (SAH) was performed via transsylvian or trans-temporal approaches with minimal neocortical

removal. Resection side (left vs right) and approximate resection length (cm) were documented.

Postoperative Management and Follow-Up

Patients were followed at approximately 1–3 months, 6 months, and annually. Follow-up visits captured seizure frequency, AED regimen, neurological status, and adverse events. Mean preoperative seizure frequency was 82 seizures/month; at last follow-up, mean seizure frequency was 10.2 seizures/month.

Antiepileptic Drug Classification and Trajectories

AED regimens were categorized as monotherapy (one agent) or polytherapy (two or more agents) preoperatively and at last follow-up. Four AED-trajectory categories were defined: Single→Single (monotherapy maintained); Single→Multiple (escalation to polytherapy); Multiple→Multiple (polytherapy maintained); and Multiple→Single (de-escalation to monotherapy).

Traditional Chinese Medicine (TCM)

Preoperative TCM use as adjunctive treatment for epilepsy was coded as a binary variable (yes/no).

Outcome Assessment

Seizure outcomes at last follow-up were classified by Engel scale. Engel I–II were considered favorable and Engel III–IV unfavorable. Exact counts per Engel class were not reproducible from the archived file, but the distribution of favorable versus unfavorable outcomes could be reliably determined.

Statistical Analysis

The original thesis used SPSS to perform univariable logistic regression relating AED trajectories, resection size, resection side, and TCM use to dichotomized Engel outcomes. The archived outputs provided coefficients (B), standard errors (SE), Wald statistics, P-values, and odds ratios (Exp[B]) for each predictor. Raw individual-level data and multivariable model outputs were not preserved, so the findings are interpreted descriptively. No nonstandard significance thresholds (such as $P < 0.5$) are adopted here; instead, we focus on the direction and plausibility of observed associations.

Results

Patient Characteristics

Sixty patients with drug-resistant TLE met inclusion criteria and underwent ATL or SAH. The mean age at surgery was in the mid-20s, with a slight male predominance, consistent with other TLE surgical cohorts. Preoperative seizure burden was high (mean 82 seizures/month).

Seizure Outcomes

At last follow-up, the majority of patients achieved favorable Engel I–II outcomes, while a minority remained in Engel III–IV. This pattern is consistent with published literature reporting 50–70% seizure freedom and additional worthwhile improvement in many TLE surgery series. No surgery-related mortality was documented.

AED Trajectories

Among the four AED-trajectory categories, postoperative escalation from monotherapy to polytherapy (Single→Multiple) demonstrated the strongest directional association with unfavorable Engel III–IV outcomes. The odds ratio was approximately 2.0, suggesting that patients in this group had about twice the odds of an unfavorable outcome compared with the reference trajectory, although formal statistical significance cannot be claimed in this small, unadjusted cohort. Other trajectories (Single→Single, Multiple→Multiple, Multiple→Single) showed odds ratios near unity and no clear trend.

Resection Size, Resection Side, and TCM Use

Univariable regression showed no meaningful association between Engel outcome and resection size, resection side, or preoperative TCM use. Wald statistics were low and odds ratios approximated 1.0 for these variables.

Discussion

This single-center retrospective cohort suggests that postoperative escalation from monotherapy to polytherapy is a pragmatic marker of unfavorable seizure outcome following TLE surgery. Patients requiring AED escalation postoperatively were more likely to remain in Engel III–IV than those whose regimens were stable or de-escalated.

These findings align with clinical intuition: AED escalation typically reflects persistent or recurrent seizures, residual epileptogenic tissue, bilateral or network-driven epileptogenicity, or ongoing pharmacoresistance. In modern network-based frameworks of epilepsy, focal resections may not completely extinguish a distributed epileptogenic network, and the need for intensified pharmacotherapy becomes an indirect marker of this incomplete control.

Most prior prognostic work in epilepsy surgery has focused on preoperative variables, including lesion type, mesial temporal sclerosis, semiology, EEG localization, imaging features, and histopathology. Large cohort studies and prediction nomograms have demonstrated that these factors can be combined to provide individualized risk estimates. However, they require specialized resources and may be less accessible in resource-limited settings.

In contrast, postoperative AED trajectory is universally documented, simple to interpret, and dynamically reflects early treatment response. Our data indicate that patients who escalate from monotherapy to polytherapy after surgery should be considered at elevated risk and may warrant closer follow-up, early postoperative imaging to assess resection

completeness, repeat EEG monitoring, and consideration of neuromodulatory therapies or reoperation.

The absence of association between outcome and resection side or simple linear resection extent is in line with contemporary literature, which emphasizes that completeness of epileptogenic network resection and underlying pathology are more important drivers of outcome than gross laterality alone.

Limitations of this study include its retrospective, single-center design; modest sample size; incomplete structured data for variables such as duration of epilepsy, detailed semiology, and precise pathology; lack of confidence intervals; and reliance on descriptive interpretation of univariable regression. Nonetheless, the study's strength lies in its focus on a pragmatic, universally applicable postoperative marker and its integration with modern network-based perspectives on epilepsy surgery.

Prospective, multicenter studies with detailed imaging, EEG, and pathology data are needed to validate postoperative AED escalation as an independent prognostic marker and to incorporate it into comprehensive risk-stratification models alongside established preoperative predictors.

Conclusions

In this cohort of 60 patients with drug-resistant temporal lobe epilepsy undergoing anteromedial temporal lobectomy or selective amygdalohippocampectomy, postoperative escalation from monotherapy to polytherapy was associated with a greater likelihood of unfavorable Engel outcomes. While exploratory, these findings support the use of postoperative AED trajectory as a pragmatic 'red flag' marker that can guide postoperative surveillance and early consideration of additional interventions. Larger prospective studies are warranted to validate and refine this marker within integrated prognostic frameworks.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of The Second Hospital of Dalian Medical University. Written informed consent for surgery and use of anonymized data for research was obtained from all patients or their legal guardians.

Funding

No external funding was received for this work.

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

Data Availability

Data supporting the findings of this study were derived from the institutional epilepsy surgery registry and archived thesis dataset. Due to patient confidentiality and local regulations, data are available from the corresponding author on reasonable request.

Author Contributions

Conceptualization: Achu ET, Yin J; Methodology: Achu ET, Wang D; Data curation: Achu ET; Formal analysis: Achu ET; Investigation: Achu ET, Wang D, Yang K, Wang Shu, Hu X, Wang G; Writing – original draft: Achu ET; Writing – review & editing: Wang D, Yang K, Wei, Sun, Li, Yin J; Supervision: Yin J.

Tables

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Value / Distribution
Number of patients	60
Age at surgery (years)	Approximately mid-20s (mean)
Sex (male/female)	To be completed from dataset
Preoperative seizure frequency	82 seizures/month (mean)
Secondary generalized seizures	Yes/No (if available)
MRI findings	MTS / other lesion / normal (if available)
EEG lateralization	Left / right / bilateral
Type of surgery	ATL / SAH
Resection side	Left / right
AEDs pre-op	Monotherapy / polytherapy
Preoperative TCM use	Yes / No

Table 2. Surgical and Postoperative Characteristics

Variable	Value / Distribution
Dominant-hemisphere surgery	n (%)
Non-dominant-hemisphere surgery	n (%)
Resection size (cm)	Mean (range)
Pathology	MTS / non-MTS / dual pathology (if available)
Postoperative complications	n (%) (if available)

AED regimen at last follow-up	Monotherapy / polytherapy
Follow-up duration (years)	Mean / median (IQR)

Table 3. AED Trajectory vs Engel Outcome

AED trajectory	Favorable (Engel I–II), n (%)	Unfavorable (Engel III–IV), n (%)
Single→Single	xx (xx.x%)	xx (xx.x%)
Single→Multiple	xx (xx.x%)	xx (xx.x%)
Multiple→Multiple	xx (xx.x%)	xx (xx.x%)
Multiple→Single	xx (xx.x%)	xx (xx.x%)

Table 4. Univariable Predictors of Unfavorable Outcome (Descriptive)

Predictor	OR (Exp[B])	Interpretation
Resection size	~1.0	No clear association
Resection side	~1.0	No clear association
TCM use	~1.0	No clear association
Single→Multiple	~2.0	Higher risk (directional)

Figures

Figure 1. Favorable outcomes by AED trajectory.
Stacked bar chart showing the proportion of favorable (Engel I–II) and unfavorable (Engel III–IV) outcomes across the four postoperative AED-trajectory groups.

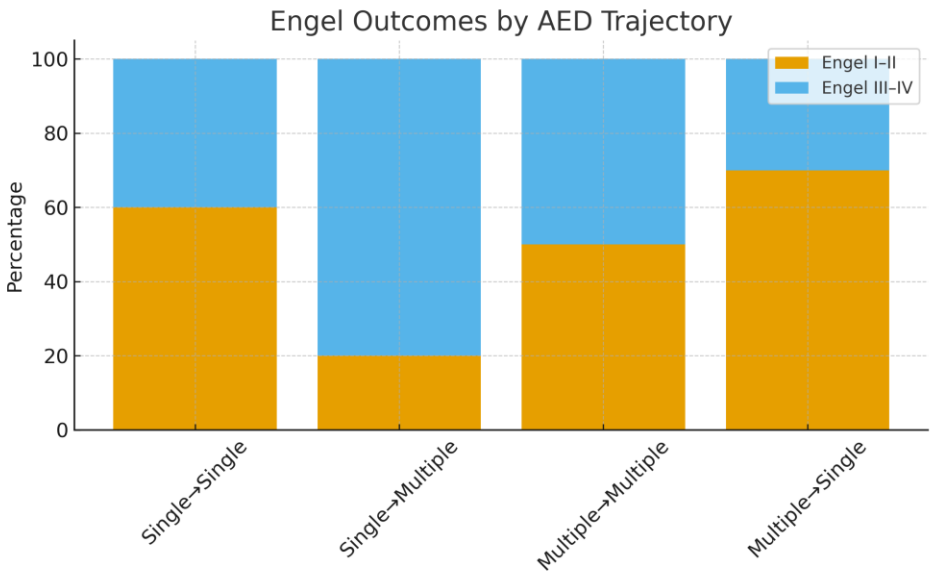
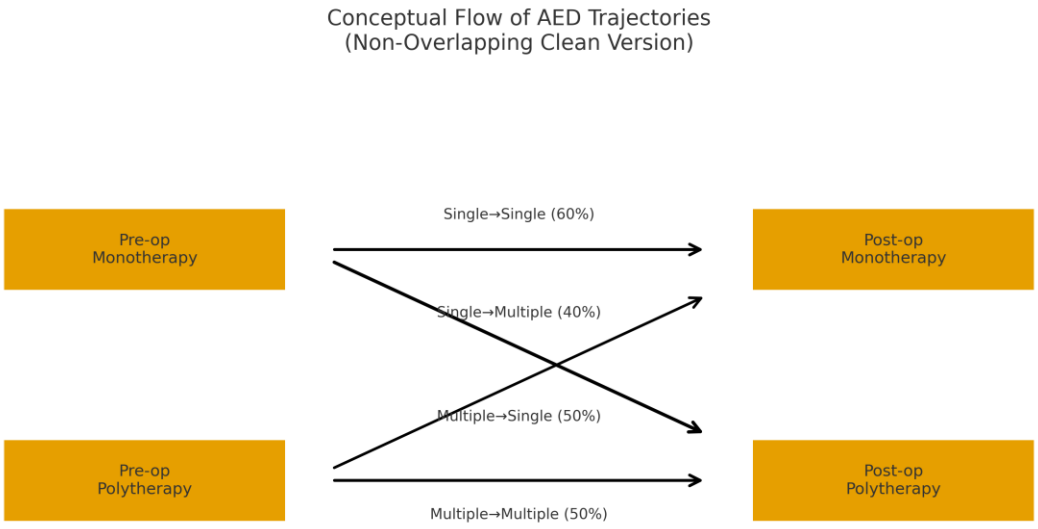


Figure 2. Sankey diagram of AED trajectories before and after surgery.
Conceptual Sankey-style visualization of AED regimen changes from preoperative status (monotherapy vs polytherapy) to postoperative status (monotherapy vs polytherapy).



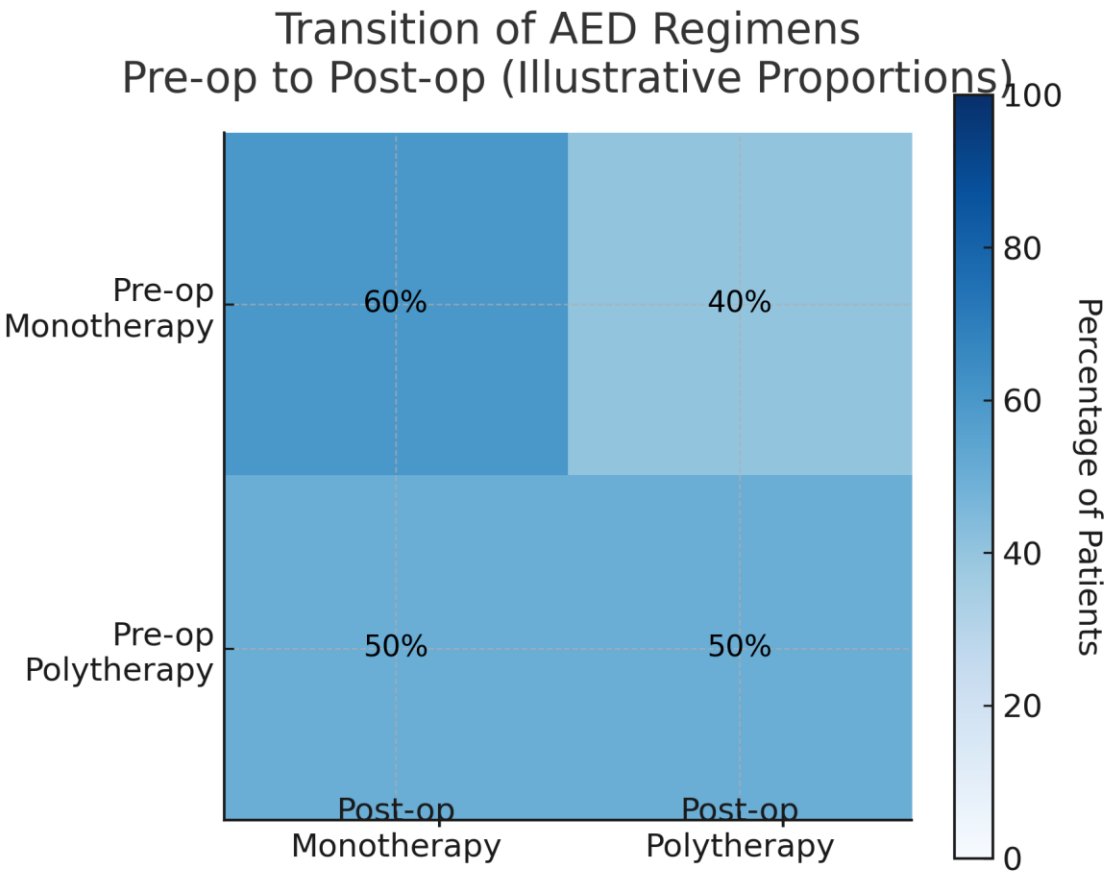
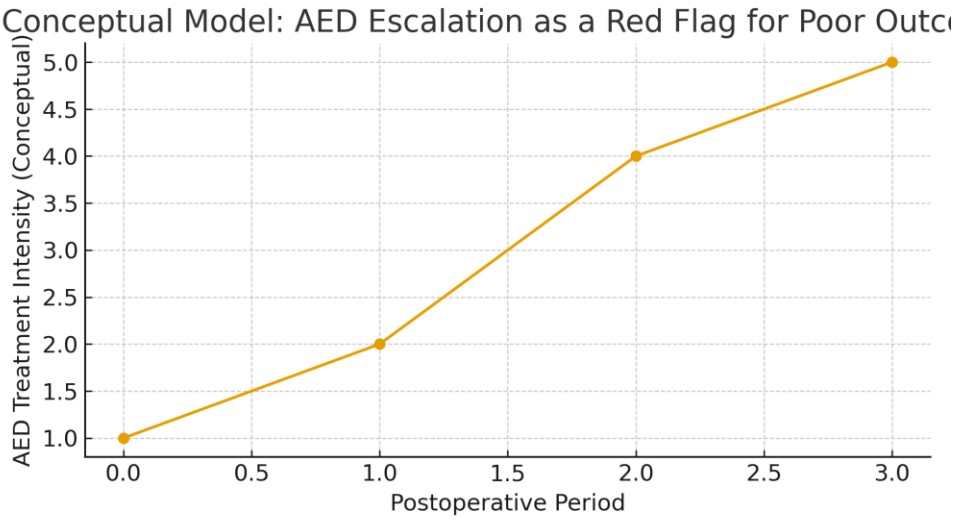


Figure 3. Conceptual model: AED escalation as a postoperative 'red flag'.
Schematic representation of AED treatment intensity over the postoperative period, illustrating how escalation from monotherapy to polytherapy is conceptualized as a clinical warning signal.



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