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Systematic Review

Safety and Efficacy of Stereoelectroencephalography-guided Resection and Responsive Neurostimulation in Drug-resistant Temporal Lobe Epilepsy: A Systematic Review

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Abstract

Background and objectives: Temporal lobe epilepsy (TLE) is the most common focal epilepsy, with many patients developing drug-resistant epilepsy. Surgical interventions, including stereoelectroencephalography (SEEG)-guided temporal lobe resection (TLR) and SEEG-guided responsive neurostimulation (RNS), are key treatment options. This systematic review compares the efficacy and safety of these interventions in drug-resistant TLE.

Methods: A systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines. A comprehensive search of multiple databases was performed (January 23–February 14, 2025). Eligible studies included adult patients with drug-resistant TLE undergoing SEEG-guided TLR or RNS (where SEEG was used pre-implant for localization). Primary outcomes assessed included seizure freedom, seizure reduction, adverse events, and quality of life (QoL) improvements. Quality assessments were performed using appropriate tools for randomized and observational studies.

Results: Fifteen studies met the inclusion criteria, with sample sizes ranging from 10 to 440 participants. SEEG-guided TLR achieved an average seizure freedom rate of 58.5% (range: 32–85%) and a mean seizure reduction of 75% (range: 60–90%). SEEG-guided RNS resulted in an average seizure freedom rate of 12.85% and seizure reduction of 63.2%, with variability across studies. QoL improvements were reported in 80–82% of patients. Adverse events were infrequent but varied between interventions.

Conclusions: This review highlights the effectiveness of SEEG-guided TLR and RNS in managing drug-resistant TLE. While both interventions reduce seizure burden and improve QoL, seizure freedom rates are higher with resection. However, gaps remain in understanding long-term cognitive outcomes and demographic influences on treatment response. Future research should address these factors to refine patient selection and optimize epilepsy care.

Keywords: Temporal lobe epilepsy; Stereoelectroencephalography; SEEG; Drug-resistant epilepsy; Resection; Responsive neurostimulation; Systematic review.

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Introduction

Temporal lobe epilepsy (TLE) is the most common focal epilepsy syndrome, accounting for approximately 60% of focal epilepsy cases. It is characterized by recurrent, unprovoked seizures originating in the temporal lobe, which plays a critical role in memory, language, and emotion. The prevalence of epilepsy in developed countries ranges from four to ten cases per 1,000 individuals, with TLE being the most frequently encountered focal epilepsy subtype.[1]

Drug-resistant epilepsy is the failure of adequate trials of two

appropriately chosen and tolerated antiseizure medications to achieve sustained seizure freedom.[2] Approximately 30–50% of individuals with TLE develop drug resistance, necessitating surgical intervention.[3]

Stereoelectroencephalography (SEEG) is an essential tool in the presurgical evaluation of drug-resistant epilepsy, enabling precise localization of epileptogenic zones and guiding treatment selection between SEEG-guided resection and SEEG-guided responsive neurostimulation (RNS). While resective surgery has traditionally been associated with higher seizure freedom rates, RNS has emerged as an alternative, particularly for patients with dominant hemisphere involvement, bilateral seizure onset, or high risks for memory and language deficits.[4–6]

SEEG has refined epilepsy surgery by facilitating three-dimensional mapping of epileptic networks, particularly in magnetic resonance imaging-negative cases or those with widespread epileptogenic zones.[7] SEEG-guided resection has been reported to achieve seizure freedom in up to approximately 85% of patients.[8] In contrast, SEEG-guided RNS therapy provides a median seizure reduction of 70%, with sustained long-term benefits.[9,10] RNS has also been associated with cognitive preservation, making it a valuable option for patients at risk of neuropsychological decline.[11] While RNS effectively reduces seizure burden, direct comparisons with SEEG-guided resections in strictly TLE cases remain limited.[12–14] SEEG has further demonstrated utility in guiding re-evaluations and reoperations in cases where initial surgery fails to achieve seizure freedom.[15] Moreover, recent evidence suggests that patients undergoing RNS experience fewer cognitive declines compared to those undergoing resection.[16] Patient-reported outcomes, including quality of life (QoL) and mood improvements, further support the role of neuromodulation in optimizing patient-centered care.[16]

This systematic review aims to compare the clinical efficacy and safety of SEEG-guided temporal lobe resection (TLR) and RNS in patients with drug-resistant TLE. The findings will have significant implications for clinical decision-making, aiding neurologists and neurosurgeons in selecting optimal treatment strategies to enhance patient outcomes and QoL.

Materials and methods

Search strategy

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[17] The study aimed to evaluate the clinical efficacy, safety, and QoL outcomes associated with SEEG-guided TLR and SEEG-guided RNS in patients with drug-resistant TLE, where SEEG was used preoperatively to inform lead placement; it did not imply that stimulation itself was guided by SEEG. The comprehensive literature survey was conducted from January 23 to February 14, 2025, utilizing multiple databases, including PubMed, Europe PMC, ScienceDirect, EBSCO Open Dissertations, Cochrane Library (CENTRAL), Google Scholar, and ClinicalTrials.gov. The search strategy employed a combination of MeSH terms and keywords, using Boolean operators (AND/OR) to refine the results. The search terms included "stereoelectroencephalography", "SEEG", "temporal lobe epilepsy", "TLE", "drug-resistant epilepsy", "intractable epilepsy", "resection", "responsive neurostimulation", and "RNS" (Table 1).

Study selection and eligibility criteria

Studies were included if they met the following eligibility criteria. Eligible studies focused on adult patients (≥18 years) diagnosed with drug-resistant TLE, defined as the failure of at least two appropriate antiepileptic medications. Only studies in which patients underwent SEEG-guided TLR or SEEG-guided RNS were considered. Additionally, included studies had to report at least one relevant outcome, such as seizure freedom rates, seizure reduction, neuropsychological outcomes, adverse events, or QoL improvements. Accepted study designs included randomized controlled trials (RCTs), controlled clinical trials, observational studies (prospective or retrospective cohorts, case-control studies), or case series with at least 10 patients. Only studies published in peer-reviewed journals in English within the past 10 years were included. Studies were excluded if they focused solely on pediatric patients (≤18 years) or investigated only non-TLE epilepsy syndromes, such as frontal, parietal, or occipital epilepsy. Additionally, case reports with fewer than 10 patients per intervention group, reviews, conference abstracts, editorials, expert opinions, or non-English publications were not considered for inclusion.

Data extraction and synthesis

Two independent reviewers screened titles, abstracts, and full texts, with data extracted using a structured form. Extracted variables included study and patient characteristics, interventions (SEEG-guided TLR vs. SEEG-guided RNS), seizure outcomes, neuropsychological measures, QoL measures, and adverse events. We required a follow-up period of at least six months, prioritizing outcomes within the first twelve months. To harmonize reporting, Engel I/ILAE 1 were classified as seizure freedom, Engel II/ILAE 2 as seizure reduction, and Engel III–IV/ILAE 3–5 as persistent seizures; percentage reductions were aligned with the ≥50% responder threshold. QoL was synthesized qualitatively by direction of change (improved, stable, declined). Given the heterogeneity of outcome definitions, variable follow-up windows, and frequent absence of variance data, a quantitative meta-analysis was not feasible. We therefore conducted a qualitative synthesis with descriptive statistics. Outcome data were extracted as mean, median, interquartile range, and percentage.

Quality assessment

Risk of bias was assessed using appropriate tools based on study design. The Cochrane Risk of Bias Tool (RoB 2) was used for randomized studies,[18] while the Newcastle-Ottawa Scale was applied for observational studies.[19] Two independent reviewers performed bias assessments, with disagreements resolved by a third reviewer.

Results

Study selection and characteristics

Following our inclusion criteria and screening process, 260 studies were transferred to Rayyan for further evaluation.[20] During this process, four studies were identified as duplicates and subsequently removed. After the initial screening, 94 studies were excluded based on title and abstract review. A total of 162 studies were then assessed for eligibility through full-text review. Ultimately, four studies met all inclusion criteria. Additionally, on February 10, 2024, we conducted a manual search on Google Scholar and performed citation searching. This process led to the inclusion of 11 additional studies, resulting in a total of 15 studies for the final analysis, as illustrated in the PRISMA flow diagram (Fig. 1).

Results of quality appraisal

The quality appraisal of the included cohort studies was conducted

Table 1. Search strategy

Database/ Register	Search strategy	Filters	Results
PubMed	(“SEEG-guided surgery” OR “SEEG-guided resection” OR “stereoelectroencephalography-guided surgery” OR “stereoelectroencephalography-guided resection” OR “Temporal lobe surgery” OR “Temporal lobe resection” OR “Surgical treatment of epilepsy” OR “Epilepsy/surgery”[Mesh] OR “Electroencephalography/adverse effects”[Mesh] OR “Electroencephalography/classification”[Mesh] OR “Electroencephalography/mortality”[Mesh] OR “Electroencephalography/statistics and numerical data”[Mesh] OR “Electrodes, Implanted”[Mesh]) OR “Electrodes, Implanted/adverse effects”[Mesh] OR “Electrodes, Implanted/statistics and numerical data”[Mesh]) AND (“SEEG-guided responsive neurostimulation” OR “SEEG-guided RNS” OR “Stereoelectroencephalography-guided RNS” OR “SEEG-based RNS” OR “SEEG-informed responsive neurostimulation” OR “Electric Stimulation Therapy”[Mesh] OR “Electric Stimulation Therapy/adverse effects”[Mesh] OR “Electric Stimulation Therapy/classification”[Mesh] OR “Electric Stimulation Therapy/economics”[Mesh] OR “Electric Stimulation Therapy/instrumentation”[Mesh] OR “Electric Stimulation Therapy/methods”[Mesh] OR “Electric Stimulation Therapy/mortality”[Mesh] OR “Electric Stimulation Therapy/standards”[Mesh] OR “Electric Stimulation Therapy/statistics and numerical data”[Mesh] OR “Neurosurgical Procedures”[Mesh] OR “Neurosurgical Procedures/adverse effects”[Mesh] OR “Neurosurgical Procedures/classification”[Mesh] OR “Neurosurgical Procedures/instrumentation”[Mesh] OR “Neurosurgical Procedures/methods”[Mesh] OR “Neurosurgical Procedures/mortality”[Mesh] OR “Neurosurgical Procedures/statistics and numerical data”[Mesh]) AND (“Drug-resistant epilepsy” OR “refractory epilepsy” OR “intractable epilepsy” OR “Temporal lobe epilepsy” OR “TLE” OR “Drug-resistant temporal lobe epilepsy” OR “refractory temporal lobe epilepsy” OR “Epilepsy, Temporal Lobe”[MeSH] OR “Drug Resistant Epilepsy”[Mesh] OR “Epilepsy”[Mesh]) AND (“Seizure freedom” OR “seizure reduction” OR “clinical efficacy” OR “Adverse events” OR “complications” OR “treatment safety” OR “Quality of life” OR “QoL outcomes” OR “Cognitive outcomes” OR “neuropsychological effects” OR “treatment outcome”[MeSH] OR “adverse effects” [Subheading] OR “Quality of Life”[Mesh])	Adaptive Clinical Trial Clinical Trial Pragmatic Clinical Trial Controlled Clinical Trial Equivalence Trial Randomized Controlled Trial Clinical Study Multicenter Study Observational Study Comparative Study	139
Europe PMC	(SEEG-guided surgery OR SEEG-guided resection OR stereoelectroencephalography-guided surgery OR stereoelectroencephalography-guided resection OR Temporal lobe surgery OR Temporal lobe resection OR Surgical treatment of epilepsy OR Epilepsy surgery) AND (SEEG-guided responsive neurostimulation OR SEEG-guided RNS OR Stereoelectroencephalography-guided RNS OR SEEG-based RNS OR SEEG-informed responsive neurostimulation OR Electric Stimulation Therapy OR Electric Stimulation Therapy adverse effects OR Electric Stimulation Therapy methods) AND (Drug-resistant epilepsy OR refractory epilepsy OR intractable epilepsy OR Temporal lobe epilepsy OR TLE OR Drug-resistant temporal lobe epilepsy OR refractory temporal lobe epilepsy OR Epilepsy) AND (Seizure freedom OR seizure reduction OR clinical efficacy OR Adverse events OR treatment safety OR Quality of life OR Cognitive outcomes OR neuropsychological effects) (SEEG-guided surgery OR SEEG-guided RNS OR Temporal lobe surgery OR Surgical treatment of epilepsy) AND (Drug-resistant epilepsy OR refractory epilepsy OR Temporal lobe epilepsy) AND (clinical efficacy OR Quality of life) AND (((SRC:MED OR SRC:PMC OR SRC:AGR OR SRC:CBA) NOT (PUB_TYPE: “Review”))) AND (HAS_FT:Y) AND (FIRST_PDATE:[2015 TO 2025]) AND (HAS_FT:Y) AND (((SRC:MED OR SRC:PMC OR SRC:AGR OR SRC:CBA) NOT (PUB_TYPE: “Review”))) AND (FIRST_PDATE:[2015 TO 2025])	Full text, Research Articles Last 10 years	23
Science Direct	(“SEEG-guided surgery” OR “SEEG-guided RNS” OR “Temporal lobe surgery” OR “Surgical treatment of epilepsy”) AND (“Drug-resistant epilepsy” OR “refractory epilepsy” OR “Temporal lobe epilepsy”) AND (“clinical efficacy” OR “Quality of life”)	Research articles English 2015–2025	90

(continued)

Table 1. *(continued)*

Database/ Register	Search strategy	Filters	Results
EBSCO Open Dissertations	(“SEEG-guided surgery” OR “SEEG-guided resection” OR “stereoelectroencephalography-guided surgery” OR “stereoelectroencephalography-guided resection” OR “Temporal lobe surgery” OR “Temporal lobe resection” OR “Surgical treatment of epilepsy” OR “Epilepsy surgery”) AND (“SEEG-guided responsive neurostimulation” OR “SEEG-guided RNS” OR “Stereoelectroencephalography-guided RNS” OR “SEEG-based RNS” OR “SEEG-informed responsive neurostimulation” OR “Electric Stimulation Therapy” OR “Electric Stimulation Therapy adverse effects” OR “Electric Stimulation Therapy methods”) AND (“Drug-resistant epilepsy” OR “refractory epilepsy” OR “intractable epilepsy” OR “Temporal lobe epilepsy” OR “TLE” OR “Drug-resistant temporal lobe epilepsy” OR “refractory temporal lobe epilepsy” OR “Epilepsy”) AND (“Seizure freedom” OR “seizure reduction” OR “clinical efficacy” OR “Adverse events” OR “treatment safety” OR “Quality of life” OR “Cognitive outcomes” OR “neuropsychological effects”)	English 2015–2025	0
Clinical. Trials.Gov	Condition/Disease: “Drug-resistant epilepsy” OR “refractory epilepsy” OR “intractable epilepsy” “Temporal lobe epilepsy” OR “TLE” “Drug-resistant temporal lobe epilepsy” OR “refractory temporal lobe epilepsy” Intervention/Treatment: “SEEG-guided surgery” OR “SEEG-guided resection” OR “stereoelectroencephalography-guided surgery” OR “stereoelectroencephalography-guided resection” OR “Temporal lobe surgery” OR “Temporal lobe resection” OR “Surgical treatment of epilepsy”	Interventional Observational studies Completed, with results	0
Cochrane Library	#1 “SEEG-guided surgery” OR “SEEG-guided resection” OR “stereoelectroencephalography-guided surgery” OR “stereoelectroencephalography-guided resection” OR “Temporal lobe surgery” OR “Temporal lobe resection” OR “Surgical treatment of epilepsy” 38 #2 MeSH descriptor: [Electrocorticography] explode all trees 17 #3 #1 OR #2 54 #4 “SEEG-guided responsive neurostimulation” OR “SEEG-guided RNS” “Stereoelectroencephalography-guided RNS” “SEEG-based RNS” OR “SEEG-informed responsive neurostimulation” 0 #5 MeSH descriptor: [Implantable Neurostimulators] explode all trees 344 #6 #4 OR #5 344 #7 #3 OR #6 396 #8 “Drug-resistant epilepsy” OR “refractory epilepsy” OR “intractable epilepsy” “Temporal lobe epilepsy” OR “TLE” “Drug-resistant temporal lobe epilepsy” OR “refractory temporal lobe epilepsy” 1020 #9 MeSH descriptor: [Epilepsy, Temporal Lobe] explode all trees 230 #10 #8 OR #9 1212 #11 “Seizure freedom” OR “seizure reduction” OR “clinical efficacy” “Adverse events” OR “complications” OR “treatment safety” “Quality of life” OR “QoL outcomes” “Cognitive outcomes” OR “neuropsychological effects” 221507 #12 MeSH descriptor: [Treatment Outcome] this term only 197835 #13 #11 OR #12 373953 #14 #7 AND #10 AND #13 21	Trials English 2015–2025	8

RNS, responsive neurostimulation; SEEG, stereoelectroencephalography; TLE, temporal lobe epilepsy.

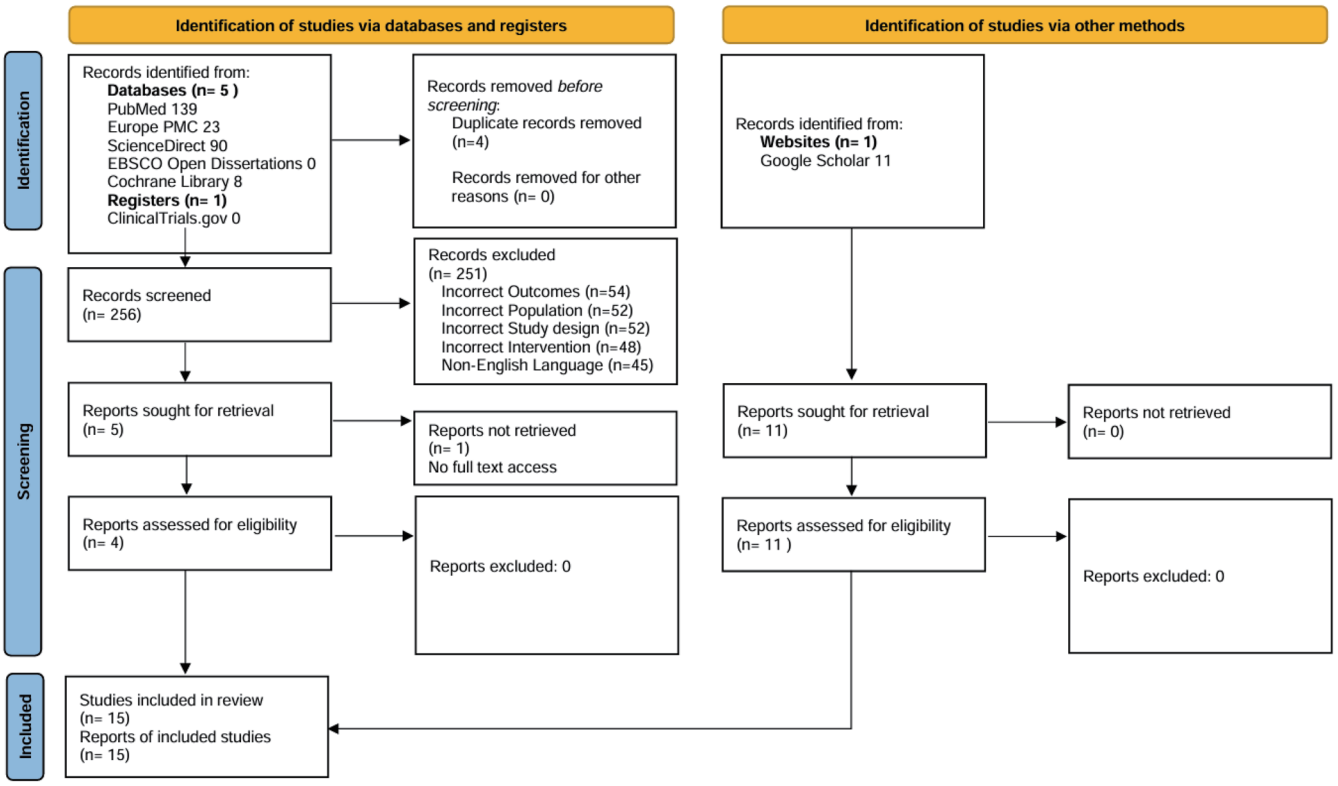

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

using the Newcastle-Ottawa Scale.[19] The scores for the studies ranged from seven to nine, indicating varying levels of quality (Table 2).[8,11–13,15,21–28]

Table 3 below summarizes the quality assessment of RCTs,[16,29] showing that all included RCTs demonstrated a low risk of bias across all domains evaluated by the Cochrane RoB 2 tool.[18]

Summary of included studies on epilepsy intervention

This systematic review analyzed a total of 15 studies focusing on the efficacy and safety of SEEG-guided TLR and RNS in patients

Table 2. Quality appraisal of included observational cohort studies using NOS for cohort design

Study	Selection	Comparability	Outcome	Overall
Busch RM[8]	★★★	★★	★★★	8 out of 9
Owens MR[21]	★★★	★	★★★	7 out of 9
Kobayashi K[11]	★★★	★	★★★	7 out of 9
Weiss SA[22]	★★★★	★★	★★★	9 out of 9
Tran DK[12]	★★★	★	★★★	7 out of 9
Roa JA[13]	★★★	★★	★★★	8 out of 9
Bulacio JC[15]	★★★★	★	★★★	8 out of 9
McGovern R[23]	★★★	★	★★★	7 out of 9
Scheid B[24]	★★★	★	★★★	7 out of 9
Dührsen L[25]	★★★	★	★★★	7 out of 9
Steriade C[26]	★★★	★	★★★	7 out of 9
González-Martínez J[27]	★★★	★	★★★	7 out of 9
You L[28]	★★★	★★	★★	7 out of 9

NOS permits four stars for selection, two for comparability, and three for outcome. Total scores range between zero and nine. A total score of seven or above is specified as "Good Quality". NOS, Newcastle-Ottawa Scale.

Table 3. Quality appraisal of included randomized clinical trials using Cochrane RoB 2

Study	D1	D2	D3	D4	D5	Overall
Loring DW[16]	2	2	1	1	1	2
Meador KJ[29]	2	2	1	1	1	2

Cochrane RoB 2 Tool assesses five domains: Domain 1: Bias arising from the randomization process; Domain 2: Bias due to deviations from intended interventions; Domain 3: Bias due to missing outcome data; Domain 4: Bias in measurement of the outcome; Domain 5: Bias in selection of the reported result(s). Each domain is scored as follows: low risk = 1, intermediate risk = 2, and high risk = 3.

with drug-resistant TLE. The sample sizes across these studies varied significantly, ranging from 10 to 440 participants, with a median age of participants typically between 31 and 38 years. The studies included adult patients, with some studies noting a male-to-female ratio reflective of typical epilepsy demographics. The interventions assessed included SEEG-guided TLR and RNS, with several studies employing SEEG as a preoperative evaluation tool to enhance surgical planning. Some studies utilized RNS following SEEG to improve seizure localization before device implantation. Comparisons were primarily made between outcomes of patients undergoing SEEG-guided TLR and RNS. A few studies also included simulations of surgical outcomes based on SEEG data, contrasting these with actual clinical results. Outcomes measured across the studies included seizure freedom rates, seizure reduction percentages, neuropsychological outcomes, adverse events, and QoL improvements. Most studies reported seizure freedom rates, often classified using the Engel classification system*, with varying success rates (Table 4).[8,11-13,15,16,21–29]

Seizure freedom rate by intervention

In analyzing the seizure freedom rates reported in various studies, a notable distinction emerges between interventions. Among the seven studies that employed SEEG-guided TLR, the seizure freedom rates ranged from 32% to 85%, yielding an overall average of approximately 58.5% (Fig. 2). This variability highlights the effectiveness of SEEG-guided TLR in achieving seizure freedom, with some studies demonstrating particularly high success rates. Conversely, the five studies utilizing SEEG-guided RNS reported seizure freedom rates ranging between 6.7% and 19%, resulting in an overall average of 12.85% (Fig. 3). Given this substantial difference, the two intervention types do not exhibit comparable overall averages. The markedly lower seizure freedom rates associated with SEEG-guided RNS highlight the need for further refinement in neuromodulation-based interventions. While SEEG remains instrumental in surgical planning, its application in optimizing RNS outcomes may benefit from enhanced patient selection criteria and stimulation strategies. This analysis emphasizes the necessity of a tailored, patient-centered approach to maximize seizure control in drug-resistant TLE.

Seizure reduction rate by intervention

In examining the seizure reduction rates across various studies, a distinct trend emerges between SEEG-guided TLR and SEEG-guided RNS. The studies reporting on SEEG-guided TLR demonstrated seizure reduction rates ranging from 60% to 90%, with an overall average reduction of approximately 75% (Fig. 4). This strong efficacy underscores the reliability of SEEG-guided TLR in significantly lowering seizure frequency among patients with drug-resistant TLE. Conversely, the SEEG-guided RNS studies presented more variable outcomes, with seizure reduction rates spanning from 40% to 86.4%, resulting in an overall average reduction of 63.2% (Fig. 5). While SEEG-guided RNS offers notable seizure reduction benefits, its effectiveness is generally less consistent compared to resective approaches, potentially due to patient selection factors and variability in neuromodulation response. Although the difference in average seizure reduction between the two interventions is 12.3%, the higher consistency and superior percentage outcomes associated with SEEG-guided TLR reinforce its role as the most effective intervention for reducing seizure burden in drug-resistant TLE.

Combined SEEG-guided TLR and RNS outcomes

A study by Tran *et al*.[14] highlighted the effectiveness of combining SEEG-guided TLR with RNS for drug-resistant TLE. Their findings demonstrated an average seizure reduction of 81% at six months post-surgery, with 40% achieving complete seizure freedom at one year (Fig. 6).

QoL by intervention

Quantitative data from included studies indicated QoL improvements ranging from 44% to 82%. SEEG-guided TLR demonstrated consistently high improvements (72–82%), while SEEG-guided RNS showed a lower but notable 44% improvement in the study by Meador *et al*. (Fig. 7).[29]

Safety outcomes

SEEG-guided TLR and RNS exhibited strong safety profiles with no major complications. However, minor complications varied. TLR was associated with transient memory deficits (12%) and mild infections (8%). RNS had higher device-related issues, with 10% requiring lead revisions and 4% experiencing minor infections. Neuropsychologically, TLR had a 12% cognitive decline, whereas RNS preserved or improved cognition. Additionally, RNS had positive mood effects, with no increase in depression or suicidality.

SEEG itself had minor surgical risks, with a 4.8% intracerebral hemorrhage rate. No major infections, hardware failures, or electrode misplacements were reported, reinforcing SEEG's role in enhancing surgical precision.

Discussion

In this systematic review, we evaluated the clinical efficacy and safety of SEEG-guided TLR compared to SEEG-guided RNS for the treatment of drug-resistant TLE. Our findings indicate that both interventions provide substantial benefits in seizure control, with SEEG-guided resection demonstrating higher seizure freedom rates. However, treatment decisions must consider individual patient characteristics, including seizure type, anatomical factors, and cognitive risks. The variability in patient responses underscores the need for tailored strategies prioritizing both efficacy and QoL.

Across SEEG-guided resections, reported seizure-freedom rates range from approximately 32% overall to as high as 85% in series of left temporal lobe resections,[8,26] underscoring SEEG-guided surgery as a powerful option for appropriately selected patients with well-localized epileptogenic zones. However, potential cognitive decline, particularly in memory and language functions, is a critical consideration, especially in dominant hemisphere cases. In our review, transient memory deficits were observed in 12% of patients,[8] highlighting the importance of preoperative cognitive assessments. SEEG-guided RNS demonstrated an average seizure reduction of 63.2% and a seizure freedom rate of approximately

Table 4. Characteristics of included studies

First author	Population characteristics	Intervention	Comparison	Efficacy results	Safety results	Outcomes related to QoL	Duration of follow-up
Busch RM[8]	152 adults Median Age: 36.8 years (18–65) Condition: Drug-resistant (TLE) MTS	TLR after SEEG	Direct TLR without SEEG	Seizure Freedom 85% (Engel I) Seizure Reduction 20% (Engel II) Persistent Seizures 15% (Engel III-IV)	No major complications reported 3 patients had transient memory deficits post-TLR Neuropsychological decline was observed in 12% of patients	80% of Engel I-II patients reported improved QoL	Mean follow-up time: 3.8 years
Owens MR[21]	30 adults Median Age: 31.1 years (18–55) Male-to-Female Ratio: 60% male, 40% female Condition: (MTLE): 67% Multiple Seizure Foci: 43.3% Prior (SEEG): 57%	RNS implantation after SEEG	No direct comparison group (Single-arm study)	(≥50% seizure reduction): 70% Seizure Freedom 6.7%	Lead revisions in 3 patients No major infections or intracranial hemorrhages reported No device-related deaths	Not directly assessed in this study	Mean follow-up: 3.0 years (range: 6 months – 5 years)
Kobayashi K[11]	12 adults Median Age 26 years (18–60) Male-to-Female Ratio: 6 females, 6 males Condition: 3 MTLE 7 neocortical TLE 2 extratemporal	RNS implantation after SEEG	No direct comparison group (Single-arm study)	Seizure Freedom: Not reported as a primary outcome Better seizure reduction with higher in-degree CCEPs near RNS contacts	No major infections, intracranial hemorrhages, or permanent neurological deficits No reported deaths or cases of suicide	Not directly assessed in this study	Median follow-up: 2.7 years (range: 1.3–4.8 years)
Weiss SA[22]	28 adults (18 patients with epilepsy surgery; 10 patients with RNS Median Age: 34.5 years (18–55) Condition: MRFE with mesial temporal, neocortical, and insular involvement	Resection after SEEG RNS implantation after SEEG	No direct control group; simulated resection & RNS placement were compared with actual clinical outcomes	Seizure Freedom: 50% for TLR Seizure Reduction overall: 77.5% for both TLR and RNS	No major complications with RNS or resections No deaths reported	Not directly assessed in this study	Surgical patients: minimum of 18 months postoperatively RNS patients: minimum of 4 years post-implantation
Tran DK[12]	10 adults Median Age: 38.6 years (27–53) Condition: MRFE includes bilateral temporal, frontal, and insular SOZ	Resection with RNS implantation after SEEG	No direct comparison group (Single-arm study)	Seizure Reduction at 6 months: 81% Seizure Freedom at 1 Year: 40%	1 Epidural hematoma 1 CSF leak No major infections or permanent deficits	Not directly assessed in this study	Mean follow-up: 1–2 years

(continued)

Table 4. *(continued)*

First author	Population characteristics	Intervention	Comparison	Efficacy results	Safety results	Outcomes related to QoL	Duration of follow-up
Roa JA[13]	70 adults Median Age: 31.9 years (18–68) DRE Common Etiologies: Idiopathic 50% Syndromic 27% Traumatic 13% Infectious 10%	RNS implantation after SEEG	No direct comparison group (Single-arm study)	Seizure Freedom: 19% Seizure Reduction: 69.2%	No major complications 4 patients had mild infections that resolved with antibiotics 2 patients required RNS lead repositioning	78% of Engel I-II patients reported improved QoL	Mean follow-up time: 3.9 years
Bulacio JC[15]	440 adults Median Age: 29 years (18–69) Condition: MRFE HS Gliosis	Resection after SEEG	Surgical vs Non-Surgical Patients	Seizure Freedom: 55–58% Seizure Reduction overall: 60%	No major intraoperative hemorrhages or strokes No significant differences in surgical complications between temporal and frontal resections	No significant cognitive decline in 82% of patients Better seizure control correlated with improved postictal states	Mean follow-up: 2 years
Loring DW[16]	175 adults Median Age: 34.3 years (18–66) Male-to-Female Ratio 1:1 (48% female) Epilepsy Subtypes: (MTLE) 49% Neocortical 43% Mixed 8%	RNS implantation after SEEG	Patients with MTLE vs. Neocortical Seizure Onset	Seizure Freedom: 6.7% Seizure Reduction overall: 66%	No reported infections or device failures	No significant cognitive decline MTLE patients improved in verbal learning	Mean follow-up: 2 years (long-term follow-up available for up to 6 years)
Meador KJ[29]	191 adults Median Age: 32.6 years (18–66) Male-to-Female Ratio: 48% female MTL 50% Neocortical 42% Mixed 8%	RNS implantation after SEEG	RNS Treatment Group vs. Sham Group (Blinded Phase)	No data regarding seizure freedom and seizure reduction were reported	No significant worsening of depression or suicidality Two patients died by suicide (both had prior depression histories; one received active RNS, the other did not)	QoL improved at 1–2 years 44% reported meaningful improvement	Mean Follow-Up: 2 years
McGovern R[23]	12 Adult patients Median Age: 36.5 (18–54) SEEG was used for pre-surgical evaluation in all cases	Robot-assisted RNS placement (ROSA) after SEEG	Robotic-assisted RNS placement vs. standard stereotactic placement	Seizure Reduction: 40% No data regarding seizure freedom was reported	2 wound infections (MSSA/MRSA) No neurological complications	Not directly assessed in this study	Mean follow-up: 2 years

(continued)

Table 4. *(continued)*

First author	Population characteristics	Intervention	Comparison	Efficacy results	Safety results	Outcomes related to QoL	Duration of follow-up
Scheid B[24]	30 adults Median Age: 31.1 years (18–55)	RNS implantation after SEEG	Responders (≥50% seizure reduction) vs. Non-Responders (<50% seizure reduction)	Overall Seizure reduction: 61.5% No data regarding seizure freedom was reported	No direct report on complications such as infections, hemorrhages, or deaths in this study Prior studies cited a small risk of infections and hardware-related issues with RNS implants	Not directly assessed in this study	Mean follow-up: 2 years
Dührsen L[25]	21 adults with drug-resistant TLE Median Age: 32.7 years (18–50.8)	Resection after SEEG	Bilateral vs unilateral SEEG	Overall seizure freedom 57%	1 Intracerebral hemorrhage post-SEEG explant	Not directly assessed in this study	Mean follow-up: 18 months
Steriade C[26]	160 adults Median Age: 34.7 years (18–59.6) Some patients had previously failed resections	Resection after SEEG RNS implantation after SEEG	Adult vs pediatric cohort	SEEG-Guided TLR Overall Seizure freedom: 32% Overall Seizure reduction: 80% SEEG-Guided RNS Overall Seizure freedom: 10% Overall Seizure reduction: 80%	No major surgical complications were reported	QoL improved in 72%	Mean follow-up time: 3.8 years
González-Martínez J[27]	86 adults Median Age: 31.6 years (18–67) Drug-Resistant TLE	Resection after SEEG	Resective vs non-resective management	Overall Seizure freedom: 66.2% Overall Seizure reduction: 90%	4 Intracranial hematomas (3 minor, 1 major requiring surgery → poor outcome) No infections or hardware failures	82% of Engel I-II patients reported improved QoL	Mean follow-up: 3.5 years
You L[28]	40 adults Median Age: 32 years (20–64) Drug-Resistant TLE	Resection after SEEG	No comparison	Overall Seizure freedom: 67.5% Overall Seizure reduction: 80%	No major postoperative complications reported	78% Patients who underwent ATLR reported improved QoL	Mean follow-up: 26 months

*Engel classification system is a widely used scale to assess seizure outcomes after epilepsy surgery, categorizing results into four classes: Class I (seizure freedom), Class II (rare disabling seizures), Class III (worthwhile improvement), and Class IV (no worthwhile improvement). ATLR, anterior temporal lobe resection; CCEPs, cortico-cortical evoked potentials; CSF, cerebrospinal fluid; DRE, drug resistant epilepsy; HS, hippocampal sclerosis; MRFE, medically refractory focal epilepsy; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus; MTL, mesial temporal lobe; MTLE, mesial temporal lobe epilepsy; MTS, mesial temporal sclerosis; QoL, quality of life; RNS, responsive neurostimulation; ROSA, robotic surgical assistant; SEEG, stereo-electroencephalography; SOZ, seizure onset zone; TLE, temporal lobe epilepsy; TLR, temporal lobe resection.

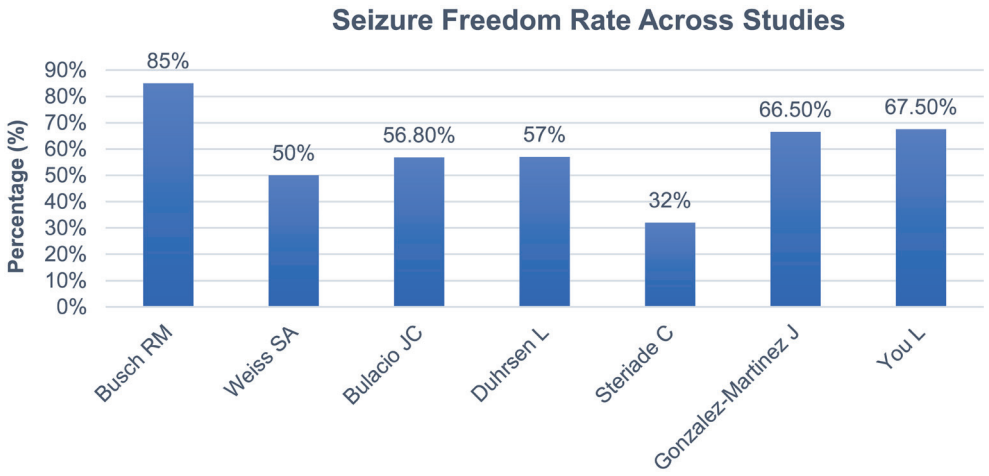

Fig. 2. Seizure freedom rate by stereoelectroencephalography (SEEG)-guided temporal lobe resection (TLR) for drug-resistant temporal lobe epilepsy.

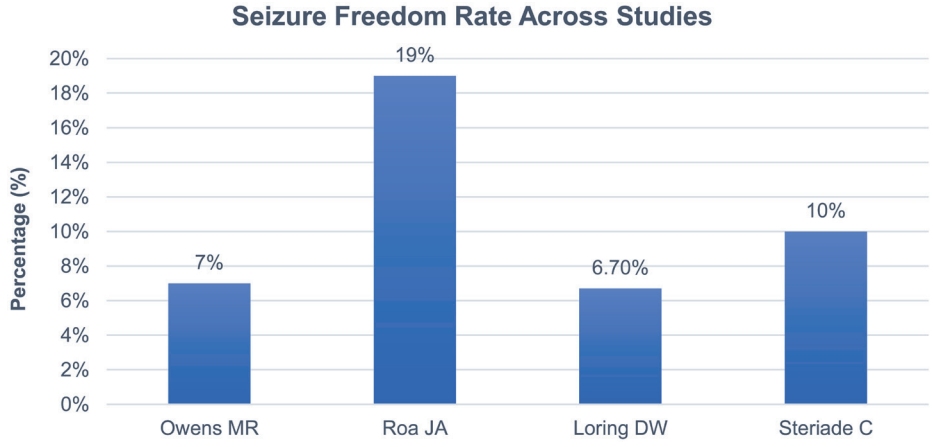

Fig. 3. Seizure freedom rate by stereoelectroencephalography (SEEG)-guided responsive neurostimulation (RNS) for drug-resistant temporal lobe epilepsy.

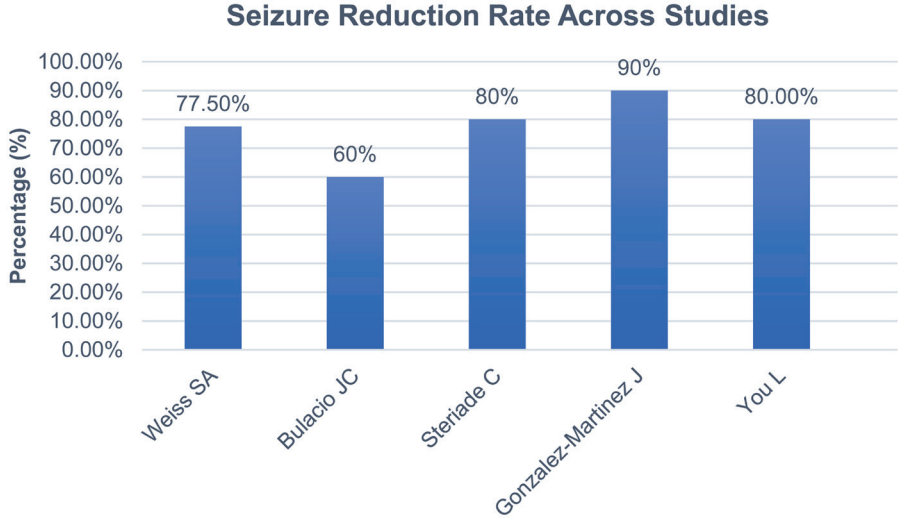

Fig. 4. Seizure reduction rate by stereoelectroencephalography (SEEG)-guided temporal lobe resection (TLR) for drug-resistant temporal lobe epilepsy. Seizure reduction rate by stereoelectroencephalography (SEEG)-guided responsive neurostimulation (RNS) for drug-resistant temporal lobe epilepsy.

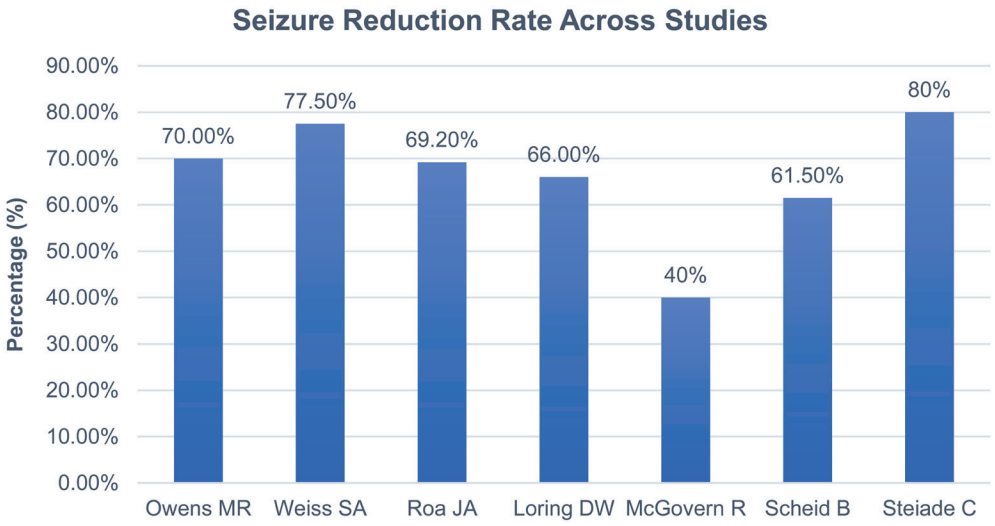

Fig. 5. Seizure reduction rate by stereoelectroencephalography (SEEG)-guided responsive neurostimulation (RNS) for drug-resistant temporal lobe epilepsy.

12.85%. While the reduction in seizure frequency is significant, outcome variability raises questions about consistency in efficacy. Notably, RNS offers cognitive preservation benefits, making it a viable alternative for patients at risk of neuropsychological decline.[16] Device-related complications, including lead revisions in 10% of RNS patients,[21] emphasize the need for close monitoring and management. It is also important to recognize that the patient populations undergoing SEEG-guided resection and SEEG-guided RNS differ substantially, which limits direct comparability of outcomes. RNS cohorts frequently include patients with bilateral seizure onset zones, seizure foci in eloquent cortex, or prior failed resections, all of which are inherently biased against seizure freedom. In contrast, candidates for resection typically present with well-localized, surgically accessible seizure foci. These baseline differences likely account for part of the disparity in seizure freedom rates and should be considered when interpreting efficacy comparisons between the two interventions. Both interventions demonstrated a favorable safety profile, with major complications reported infrequently. In studies evaluating TLR, minor complications were relatively uncommon. Transient memory deficits occurred in approximately 12% of patients, particularly when resections involved the dominant temporal lobe.[8] Mild postoperative infections were reported in around 5–8% of cases and were typically managed conservatively. Major intraoperative complications, such as significant hemorrhage or stroke, were not consistently observed across studies. In contrast, complications associated with RNS were more often device-related. Lead revisions were required in 10–15% of patients, usually due to lead migration or fracture.[21,13] Minor infections at the implant site occurred in 4–6% of cases and were generally resolved without removal of the

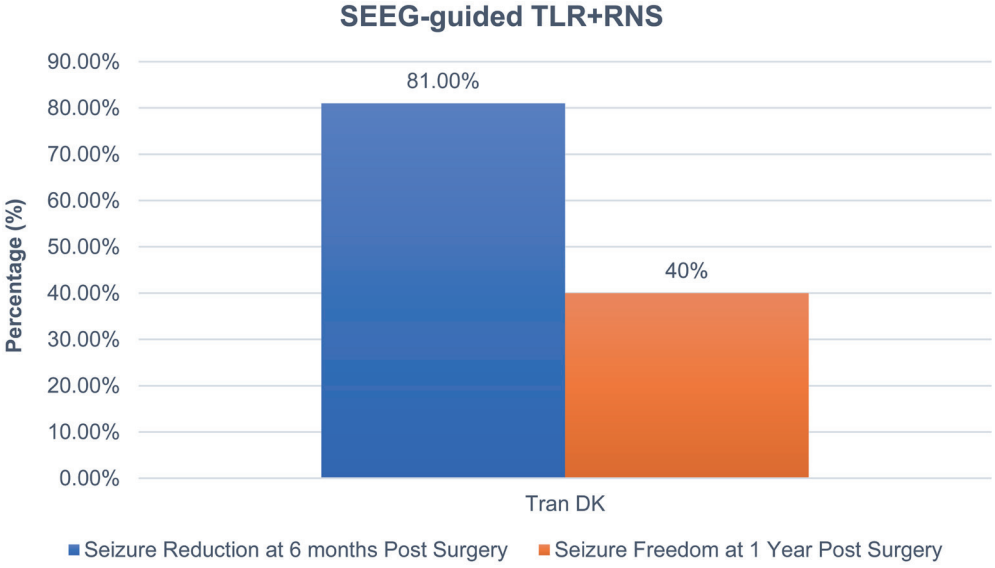

Fig. 6. Seizure reduction and freedom rate by combined stereoelectroencephalography (SEEG)-guided temporal lobe resection (TLR) and responsive neurostimulation (RNS) for drug-resistant temporal lobe epilepsy.

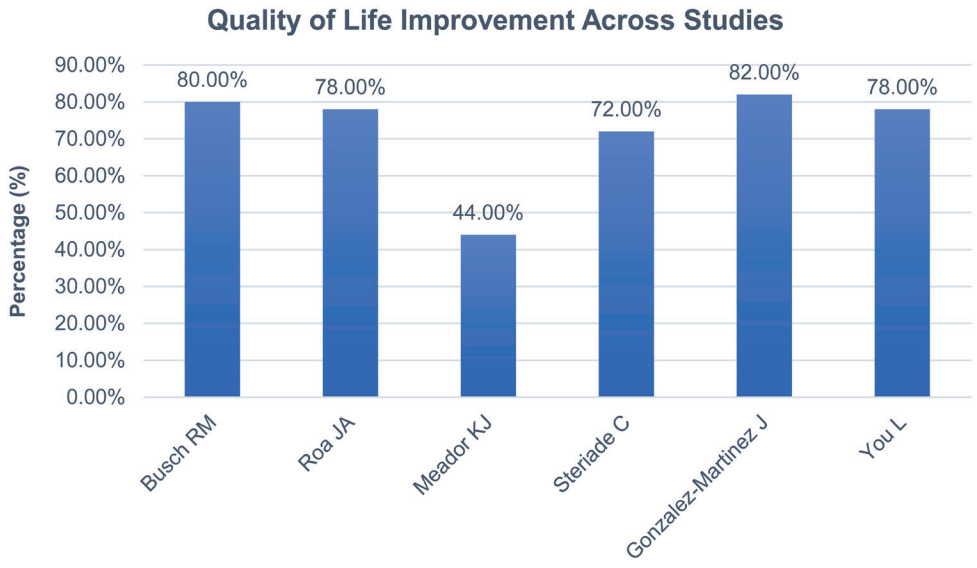

Fig. 7. Quality of life by intervention.

device.[13] Some rare complications observed included cerebrospinal fluid leaks and one isolated case of a superficial epidural hematoma.[12] Notably, no studies reported intracranial hemorrhage or device-related mortality. Cognitive outcomes following RNS were consistently positive, with 85–90% of patients maintaining or even demonstrating improvements in neuropsychological function after implantation.[16]

From a patient-centered perspective, RNS was consistently associated with the preservation of cognitive function, with some patients even experiencing improvements in neuropsychological performance after implantation.[16] Additionally, individuals treated with RNS often reported better mood, improved emotional regulation, and increased energy levels. These benefits are likely attributable to both seizure reduction and the neuromodulatory effects on cortical networks.[13,16] These outcomes were particularly meaningful for patients who were not suitable candidates for resective surgery, such as those with bilateral seizure onset or seizure foci in the dominant hemisphere.[12] In contrast, patients who achieved seizure freedom following SEEG-guided TLR often reported substantial improvements in day-to-day functioning, social engagement, and overall independence, and many were able to reduce or completely discontinue antiepileptic medications, further enhancing their overall quality of life.[26] Both interventions reported no major complications, such as severe infections or intracranial hemorrhages, reinforcing their overall safety. However, the differences in adverse events highlight the importance of individualized treatment strategies. Patients with drug-resistant TLE require comprehensive evaluations balancing seizure control benefits with cognitive and device-related risk.

Our findings align with prior studies, reinforcing established outcomes in SEEG-guided interventions for drug-resistant TLE. Inaji *et al*.[30] reported an RNS seizure freedom rate of 18%, i.e., 5.15% higher than our findings. Kusyk *et al*.[31] documented a slightly higher seizure reduction rate (68%) than our 63.2%, but their reported RNS complication rate (18.9%) exceeded ours (10%). Remick *et al*.[32] found a seizure freedom rate of 76% for SEEG-guided resection, compared to our review's estimate of 58.5%. Our review uniquely highlights the safety profile and QoL outcomes, emphasizing long-term treatment considerations that have received limited attention in prior studies. By incorporating diverse patient-centered metrics, our findings contribute to a more holistic understanding of epilepsy management. The included studies, primarily cohort-based, provide a comprehensive evaluation of SEEG-guided interventions. Large sample sizes (some exceeding 400 patients) enhance statistical power and generalizability. Rigorous quality assessments strengthen methodological reliability, and the assessment of multiple outcomes, including cognitive effects, reinforces a patient-centered approach.

Our findings emphasize the necessity of individualized treatment plans for drug-resistant TLE. SEEG-guided resection offers superior seizure freedom rates but carries cognitive risks, particularly for dominant hemisphere cases. RNS provides an alternative with cognitive preservation benefits but presents higher device-related complications. Treatment decisions should balance these factors, ensuring that both seizure control and QoL considerations are prioritized in clinical decision-making. QoL assessments should be integrated alongside seizure outcomes to provide a comprehensive evaluation of treatment success. The lack of standardized QoL measures highlights the need for further research in this domain. Clinicians should incorporate long-term QoL assessments into patient follow-up protocols.

This systematic review exhibits several strengths that enhance its credibility and transparency. It utilized multiple databases, dissertation searches, and registries, following PRISMA 2020 guidelines to ensure reproducibility.[17] The review included a comprehensive quality appraisal of studies and clearly presented search strategies for all databases. With a sufficient number of included studies, it analyzed multiple outcomes, effectively visualizing results in charts. Additionally, the protocol was registered on PROSPERO, further supporting transparency. Several limitations should be acknowledged. Most included studies were observational cohorts, with only two RCTs, limiting the strength of comparative conclusions. Outcome definitions for seizure freedom and QoL varied considerably, complicating synthesis across studies. Selection bias is also likely, as patients undergoing SEEG-guided resection generally had well-localized, surgically accessible seizure foci, whereas those selected for RNS often had bilateral onset zones, involvement of eloquent cortex, or prior failed resections. These baseline differences inherently favor better outcomes in the resection group. Reporting bias

may further influence findings, as cognitive and QoL outcomes were inconsistently measured and, at times, selectively reported. The review also did not include pediatric populations, which restricts applicability to younger patients. In addition, most study populations were relatively homogeneous, further limiting generalizability. A formal meta-analysis was not feasible given the heterogeneity of study designs, outcome measures, and follow-up durations.

Future directions

Several critical gaps warrant further investigation. Large prospective registries with harmonized outcome definitions would provide more robust data than is feasible through RCTs in this space. Standardization of seizure outcome metrics (Engel, ILAE, responder rates) and epilepsy-specific QoL instruments would enable more meaningful comparisons across studies. Long-term prospective tracking of cognition and psychiatric comorbidities is especially important, as these outcomes are central to patient QoL but remain underreported. Greater attention should also be given to demographic variability, including age, sex, and socio-economic factors, to better understand differential treatment responses. Finally, systematic reporting of device-related complications, such as lead revisions and infections, will help refine clinical guidelines and improve patient care.

Conclusions

This systematic review highlights the comparative efficacy and safety of SEEG-guided TLR and RNS in drug-resistant TLE. While SEEG-guided resection achieves higher seizure freedom rates, RNS provides cognitive preservation benefits. Treatment decisions should be individualized, balancing seizure control, cognitive risks, and QoL considerations. Future research should focus on long-term QoL outcomes, cognitive assessments, and refining intervention selection criteria to optimize patient care.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

Study conception and design (MA, AM, JM, ST, VYMR, NJ, IM), material preparation, data screening, data extraction (MA, AM, JM), manuscript drafting (MA, ST), and manuscript revision (AM, JM, VYMR, NJ, IM). All authors read and approved the final manuscript.

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