INPLASY PROTOCOL

To cite: Guo et al. Prognosis After Surgery for Refractory Epilepsy Diagnosed by 18F-FDG PET/MRI. Inplasy protocol 2022110049. doi: 10.37766/inplasy2022.11.0049

Received: 10 November 2022

Published: 10 November 2022

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Support: **202006010928.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Prognosis After Surgery for Refractory Epilepsy Diagnosed by 18F-FDG PET/MRI

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Review question / Objective: **The purpose of this study was to examine the prognostic status of PET/MRI on surgery in patients with refractory epilepsy, and the methods chosen were randomized controlled trials, cohort studies, and case series of >15 patients.**
Condition being studied: **Medically intractable epilepsy, characterized by recurrent episodes of tonicity, disorientation, spasms, and convulsions, affects 1-2% of the population because treatment trials with 3 or more different antiepileptic drugs have failed. Patients are selected for PET mainly because other standard noninvasive tests (especially MRI and EEG) fail to provide sufficiently reliable localization to allow precise excision of the epileptogenic zone and a good prognosis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 November 2022 and was last updated on 10 November 2022 (registration number INPLASY2022110049).

INTRODUCTION

Review question / Objective: **The purpose of this study was to examine the prognostic status of PET/MRI on surgery in patients with refractory epilepsy, and the methods chosen were randomized controlled trials, cohort studies, and case series of >15 patients.**

Rationale: **When MRI fails to detect underlying epileptogenic lesions, the odds of a good prognosis after epilepsy surgery are significantly reduced (from 60-90% to 20-65%). Mixed 18F-FDG PET/MRI, provides additional information for determining epileptogenic bands. Our aim was to investigate the possible effects of introducing mixed 18F-FDG PET/MRIR into decision-making algorithms in patients with lesion and non-lesional drug-resistant**

epilepsy. Surgery for refractory epilepsy is the most successful treatment for medically unresponsive epilepsy, but carries a risk of developing it. 18F-FDG PET/MRI, is an emerging technique that increases the detection of lesions and relieves symptoms by removing them. Surgery for refractory epilepsy is based on histological diagnosis and includes patients with abnormal and normal preoperative 18F-FDG PET/MRI. However, in clinical practice, surgical patient selection is based on preoperative examination results including 18F-FDG PET/MRI, and we conducted a systematic review and meta-analysis of the literature to determine the incidence and predictors of good outcome after surgery for epilepsy found by 18F-FDG PET/MRI.

Condition being studied: Medically intractable epilepsy, characterized by recurrent episodes of tonicity, disorientation, spasms, and convulsions, affects 1-2% of the population because treatment trials with 3 or more different antiepileptic drugs have failed. Patients are selected for PET mainly because other standard noninvasive tests (especially MRI and EEG) fail to provide sufficiently reliable localization to allow precise excision of the epileptogenic zone and a good prognosis.

METHODS

Search strategy: We searched PUBMED, EMBASE, and Web of Science for 12 months ≥of postoperative follow-up of people with 18F-FDG PET/MRI/MRI detected refractory epilepsy. Random-effects meta-analyses were used to calculate the proportion of patients who had a good outcome, defined as Engel class I, International Anti-Epileptic Union grade 1 to 2, or epileptic-free status. Meta-regression was used to study sources of heterogeneity.We searched 3 electronic databases of eligible publications: Ovid PUBMED, Ovid EMBASE, and Web of Science (all databases). We removed duplicate articles and checked the bibliographies of articles included in other relevant publications. The initial search was performed on October 18, 2022, with no specified date range limit. We used the following extended search terms: epilepsy, surgery, surgery, PET/MRI, and multiple variations of the term. The full search strategy is detailed in Appendix 1. All retrieved publications are managed by Endnote 20 software.

Embase

#1 'epilepsy'/exp OR epilepsy

#2 'surgery'/exp OR surgery

#3 ('pet'/exp OR pet) AND ('mri scanner'/exp OR 'mri scanner')

Search query: #1 AND #2 AND #3. Pubmed

((((((((((((epilepsy) OR (Epilepsies)) OR (Seizure Disorder)) OR (Seizure Disorders)) OR (Awakening Epilepsy)) OR (Epilepsy, Awakening)) OR (Epilepsy, Cryptogenic)) OR (Cryptogenic Epilepsies)) OR (Cryptogenic Epilepsy)) OR (Epilepsies, Cryptogenic)) OR (Aura)) OR (Auras)) AND (("Surgical Procedures, Operative"[Mesh]) OR ((((((((((((((Operative Procedures) OR (Operative Procedure)) OR (Procedure, Operative)) OR (Procedures, Operative)) OR (Surgical Procedure, Operative)) OR (Operative Surgical Procedures)) OR (Procedure, Operative Surgical)) OR (Procedures, Operative Surgical)) OR (Surgical Procedures)) OR (Procedure, Surgical)) OR (Procedures, Surgical)) OR (Surgical Procedure)) OR (Operative Surgical Procedure)) OR (Surgery, Ghost)) OR (Ghost Surgery)))) AND ((((PET/MRI) OR (PET-MRI)) OR (MRI)) OR (PET MRI))

Web of science

#1:((((((((((ALL=(Epilepsy)) OR ALL=(Epilepsies)) OR ALL=(Seizure Disorder)) OR ALL=(Seizure Disorders)) OR ALL=(Awakening Epilepsy)) OR ALL=(Epilepsy, Awakening)) OR ALL=(Epilepsy, Cryptogenic)) OR ALL=(Cryptogenic Epilepsies)) OR ALL=(Cryptogenic Epilepsy)) OR ALL=(Epilepsies, Cryptogenic)) OR ALL=(Aura)) OR ALL=(Auras)

#2:(((((((ALL=(surgery)) OR ALL=(operative therapy)) OR ALL=(invasive procedures)) OR ALL=(operative procedures)) OR ALL=(operations)) OR ALL=(perioperative procedures)) OR ALL=(intraoperative procedures)) OR ALL=(peroperative procedures)) OR ALL=(preoperative procedures)

#3:ALL=(PET MRI)
Search query：#1 AND #2 AND #3

Participant or population: Patients with a diagnosis of refractory epilepsy who have undergone PET/MRI scans and surgical procedures with a postoperative follow-up of more than 12 months (n= 1292).

Intervention: PET/MRI scan and Surgical Procedures.

Comparator: Patients with negative MRI or PET scans individually.

Study designs to be included: RCT, Cohort studies, Case series>15 cases.

Eligibility criteria: Patients with a diagnosis of refractory epilepsy who have undergone PET/MRI scans and surgical procedures with a postoperative follow-up of more than 12 months.

Information sources: PubMed, Web of Science, Embase.

Main outcome(s): PET/MRI scans followed by surgical excision of the epileptogenic zone resulted in an overall good postoperative regression rate of 71% of patients, (95% confidence interval [CI] 63.6-74.9). There was a high degree of heterogeneity between studies. Good prognosis was associated with the location of the refractory epileptic lesion in the temporal lobe or extratemporal (risk ratio RR 1.27 [95% confidence interval CI 1.01-1.52], p = 0.0090.05) were not associated. Years of postoperative follow-up ≥40 months included in the same study accounted for 0.6% of the observed heterogeneity.

Additional outcome(s): In all 23 studies, the overall pooled proportion of people with refractory epilepsy who achieved good postoperative outcomes was 71% (95% CI 66% to 76%; There was heterogeneity between studies (I2 = 74%, p < 0.001). Stratified by age group (< 18 for children = Children; ≥18 for adult = adult; Meta-analysis of children and adults = both) showed significant differences between age groups in mixed-age studies (69% [95% CI 63% to 74%), children (72% [95% CI 58% to 86%), and adults (82% [95% CI 74% to 89%]). Heterogeneity was significantly due to mixed ages; Figure 3. In the 12 subgroups detailing actual seizure-free outcomes (Engel class IA, ILAE class 1, or absence of all seizures, including aura), the overall proportion of patients with refractory epileptic epilepsy in the epileptogenic zone detected by 18F-FDG PET/MRI, was 65% (95% confidence 57% to 74%; Figure 4). Again, there was heterogeneity between studies (I2 = 80.1%, p < 0.001).
In a subgroup analysis of specific variables, we found that one variable was significantly associated with a good prognosis after 18F-FDG PET/MRI detection of refractory epilepsy (Figure 5). Good prognosis related to the location of the lesion temporal or non-temporal lobe (hazard ratio RR 1.27 [95% confidence interval CI 1.02 to 1.58], p = 0.034). <0.05) related; The postoperative good rate of temporal lobe surgery is 1.27 times that of non-temporal lobes. Data from the seven studies included in this analysis were all homogeneous (I2 = 0%, p = 0.810); The extent of epileptogenic areas of refractory epilepsy (single-lobed vs. multilobe), and the reported direction of excision location (left vs. right) are not associated with a good postoperative epilepsy prognosis.
Meta-regression showed that the number of years of postoperative follow-up included in the same study ≥ 40 months accounted for 0.6% of the observed.

Data management: All studies were observational case series from tertiary epilepsy centres (6 in Europe, 13 in Asia and 7 in North America). The main focus of the studies varied widely, including postoperative epilepsy outcomes in people with single-lobed or multilobar refractory epilepsy (11 articles), postoperative epilepsy outcomes in patients with temporal lobe or extratemporal refractory epilepsy (7 articles), postoperative epilepsy outcomes in patients with left- or right-side refractory epilepsy (6 articles), specific preoperative tests such as ECog (4

articles), and neurodevelopmental outcomes of pediatric epilepsy surgery (4 articles).
Of the 23 included studies, four (17%) described postoperative epilepsy outcomes for children only (corresponding to 95 patients), four (17%) for adults only (156 patients), and 15 (66%) for mixed adult and pediatric cohorts (1041 patients).
Studies typically report that patients undergo a series of tests prior to epilepsy surgery, including scalp EEG, MRI, PET, SEEG (Table 1). Of these studies, six studies (26%) provided information on the location of lesions in the epileptogenic zone; Eleven studies (48%) provided information on their scope. Twenty-three studies all indicated the use of EEG before surgery, including ECoG (4 studies) and SEEG (19 studies).

Quality assessment / Risk of bias analysis: The risk of bias for each included study was assessed independently using the 23-item National Heart, Lung, and Blood Institute (NHLBI) Case Series Study Quality Assessment Tool.29 Items were rated as yes, no, inconclusive, not applicable, or not reported. These ratings were then used to guide the overall rating of each study quality as good, fair, or poor. Both authors entered their ratings in a spreadsheet. When differences arose, consensus was reached through discussion.

Strategy of data synthesis: The STATA17 software was selected for data analysis, and I2>50% and P<0.05 was considered heterogeneous, and the presence of heterogeneity was selected for random-effects combined effect sizes and the absence of heterogeneity for fixed-effects combined effect sizes. Random-effects meta-analysis was performed using the Der Simonian and Laird method and Freeman-Tukey double inverse sine transformation to calculate the combined good regression rate, and 95% confidence intervals (CI) were estimated using the exact method. Effect sizes were expressed as the percentage of patients achieving seizure freedom, and heterogeneity was assessed using Cochran Q and I2 statistics. Meta-regression was used to further explore the sources of heterogeneity.

Subgroup analysis: Stratification was performed by population age group (adult, child, or mixed age), location of the epileptogenic zone (temporal lobe vs. extratemporal), extent of lesions in the epileptogenic zone (unilobar vs. multilobar), and direction of location of lesions in the epileptogenic zone (left vs. right), followed by meta-analysis.The use of any EEG (ECoG vs SEEG), and postoperative follow-up time (12-24 months vs 25-39 months vs ≥40 months).

Sensitivity analysis: Sensitivity analysis was performed by stata17 software to reflect the sensitivity of the article by the change in effect size after the removal of one of the articles.However, the meta-analysis of single-group rate completed by metaprop in this paper cannot be used for sensitivity analysis.

Language restriction: American English.

Country(ies) involved: China.

Other relevant information: Fund project support 202006010928
Mechanism of natural truncation of NS gene in inhibition of H3N2 influenza virus proliferation
Shandong Province Medical and Health Science and Technology Development Plan Project
Contract.

Keywords: Refractory Epilepsy; 18F-FDG PET/MRI; Surgery; Prognosis; Meta-analysis.

Dissemination plans: Submit to the journal Biomolecules.

Contributions of each author:
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