

The impact of epilepsy surgery on seizure among adults; A systematic review

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Abstract

Background: Epilepsy is a chronic neurological illness that has deleterious impacts on vocational, physical, social, and psychological well-being. Epileptic patients are at increased risk of experiencing unprovoked seizures which are the primary cause of epilepsy-related disability, mortality, and morbidity. Epilepsy surgery is the alternative approach for the management of seizures in case of failure of antiseizure medications. The primary goal of epilepsy surgery is seizure freedom.

Aim: To assess the impact of epilepsy surgery on seizure outcomes among adult patients by reviewing the previous original literature that evaluated such a subject.

Methods: Exploration of PubMed, Springer, Scopus, Science Direct, and Google Scholar was done to obtain related studies. Studies published between 2015 and 2024 were eligible. Original English articles that reported seizure outcomes following surgical management of epilepsy and focused on the adult population were considered eligible articles and included in the review.

Results: Eight studies were included in agreement with eligible criteria; they included 1422 patients with an age range of 17-70 years duration of epilepsy ranged between zero to 59 years and follow-up duration ranged between one year and 27 years.

Conclusion: Epilepsy surgery is a good approach for the management of epilepsy with the achievement of seizure-free under the condition of an appropriate selection of patients and an appropriate selection of surgical approach as well as precise pre-surgical evaluation.

Keywords: Epilepsy, Seizures, Outcomes, Adults.

Introduction:

Epilepsy is a chronic neurological illness that is characterized by recurrent episodes of disorientation, tonic, convulsions, and spasms [1] that affect individuals of any ethnicity and age [2]. Epilepsy affects more than 70 million individuals globally [3] and it has deleterious impacts on vocational, physical, social, and psychological wellbeing [2]. Epileptic patients are at increased risk of experiencing unprovoked seizures [3]. Seizures are the primary cause of epilepsy-related disability, mortality, reduced quality of life (QOL), and morbidity [4, 5]. The first line of treatment for seizures is antiseizure medications (ASMs); however, one-third of the patients are resistant to drugs and they are drug-resistant epilepsy (DRE) individuals [6], and they experience ongoing seizures [3]. DRE is defined as the failure of adequate trials of two tolerated and appropriately chosen antiepileptic drug schedules to achieve sustained seizure freedom [7]. Drug resistance epilepsy and ASM fail to control seizures among 30% of patients with epilepsy [8]. Furthermore, the development of more than 20 novel ASMs over the past three decades hasn't had a considerable impact on the rate of DRE [9, 10]. Therefore, surgical management can be implemented; epilepsy surgery involves resection or less commonly destruction or disconnection of epileptic tissue and it is the most effective strategy for selected epileptic patients with DRE [2]. Various surgical approaches may be adopted for individuals with DRE. Resective epilepsy surgery is considered a definitive management option for certain focal DREs and achieves almost 50%-70% change of post-surgical seizure freedom in

well-selected individuals [11, 12]. This type of surgery is generally effective and safe; however, it is underutilized [13]. Epilepsy surgery is commonly performed in children and younger adults; however, there is an increasing number of studies reporting epilepsy among older adults [14]. So, this systematic review was performed to identify the outcomes of seizures after performing epilepsy surgery by examining the previous studies reported on this subject.

Method and Search strategy:

This review was written in agreement with the PRISMA statement for systematic review [15]. The databases of PubMed, Springer, Scopus, Science Direct, and Google Scholar were explored to obtain related articles published in a duration of ten years between 2015 and 2024. Different terms were used as search keywords, including "Epilepsy surgery, Resection, Operation, Surgical management, Impact, Effect, Influence, Outcomes, Seizure, Frequency, and Rate." All the titles of the findings from this primary exploration were revised thoroughly to prevent missing potential studies.

Eligibility criteria:

The findings were then explored to exclude duplicate articles, those reporting non-surgical management of epilepsy, and those published before 2015. Also, irrelevant articles that didn't report seizure outcomes or reported other focused on other subjects and appeared coincidentally were excluded. The remaining articles were checked to include English articles and exclude those written in non-English languages. Then, only original articles were defined as eligible articles whereas other types of articles were excluded. The articles that provided overlapped data, those available for abstracts only and aren't available for full-text, or those reported outcomes of adult patients and pediatric patients or pediatric patients only were excluded. The description of the determined criteria is illustrated in Figure 1.

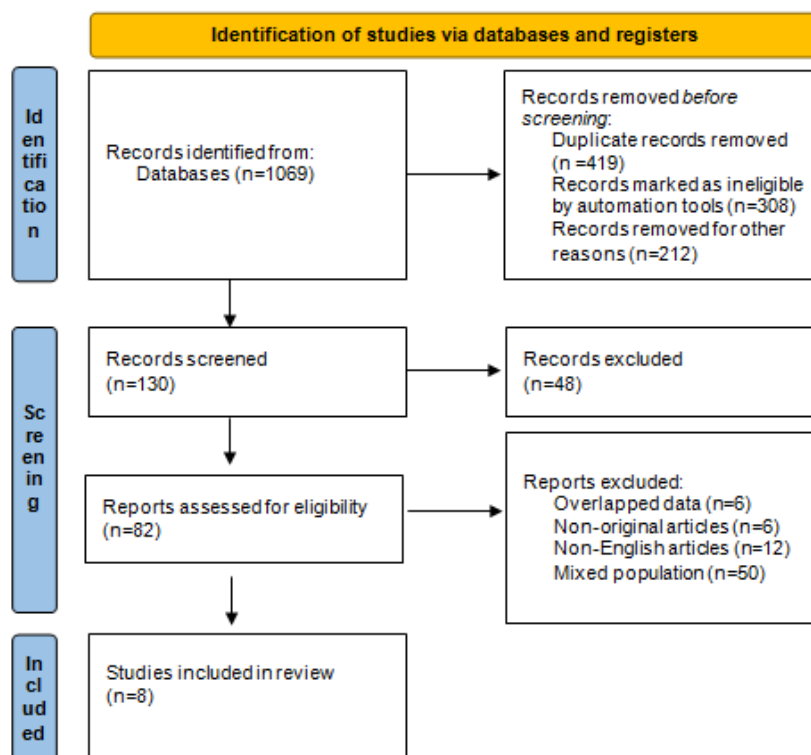


Fig1: Criteria of the included articles

Data review and analysis:

Reviewing of data started with a preliminary review of the abstract of each included article to determine the data of interest for data collection, including design, demographics, surgery, complaint, seizure outcomes, recurrence, and associated factors. The full-text articles were then

reviewed for data extraction. The extracted data were revised via the Excel sheet and then transferred to a pre-designed table for summarization.

Results:

In agreement with the inclusion criteria, a total of eight studies [16-23] were included in this systematic review, (Table 1). The studies were published from 2016 to 2023 with retrospective design as the major study design of all studies, while there were two studies reported longitudinal retrospective [18], and retrospective analysis of prospective data [20]. The complaints of patients included drug-resistant frontal lobe epilepsy [16], temporal lobe epilepsy associated with structural lesions [17], drug-resistant temporal lobe epilepsy associated with hippocampal sclerosis [18], intractable focal epilepsy [19], refractory focal epilepsy [20], temporal, frontal and occipital epilepsy [21], drug-resistant focal epilepsy [22], and temporal lobe epilepsy with mesial temporal sclerosis [23]. The surgical approaches performed for patients, included frontal lobe epilepsy surgery [16], anterior structural lesions lobectomy and lesionectomy [17], temporal lobectomy [18], resective focal epilepsy surgery [19], and anterior temporal lobectomy [23], whereas the remaining three studies reported various approaches. One study reported epilepsy surgery without determination of the approach [21], and the remaining two studies reported more than one approach [20, 22].

The total number of patients was 1422 patients with an age range of 17-70 years, but two studies reported the mean age of patients [20, 23]. The duration of epilepsy ranged between zero to 59 years, whereas two studies reported the mean duration of epilepsy [20, 23]. The follow-up duration ranged between one and 27 years.

The studies reported freedom seizure and/ or disabling seizure at various periods based on the follow-up duration. Generally, the free seizure rate at the first follow-up ranged between 47% [20] and 92.3% [17], whereas free seizure at the last follow-up ranged between 38% [20] and 80.8% [17]. Due to the high variations in follow-up durations among the included studies, the rates of free seizure post-surgery will be arranged in a descending manner. There were two studies reported the rates of seizure freedom at one period, one study reported the rate of seizure-free at the last follow-up (2 years) to be 78% [22], and the other study reported free disabling seizure among 66.4% and sustained seizure freedom among 48.4% after one year as the follow-up duration was only one year [23].

The remaining studies reported free seizures at two periods, at the first follow-up and the last follow-up of median follow-up. The highest rate of seizure freedom in the first year was 92.3% which declined in the second year to 80.8% [17]. Free disabling seizure was achieved among 73.6% of patients and maintained among 65% up to 23 years post-surgery [18]. There 68% of cases were free of seizures, then the proportion declined to 58% at two years. Additionally, at a median of 4.7 years, 65% of cases were free of disabling seizure and 46% remained seizure-free [21]. Seizure-free at three years was 53.2% which declined to 42.42 after five years among those who continued follow-up [16]. Seizure freedom was achieved among 47.5% in the first year then reduced to 42.5% in the second year and 37.5% in the third year [19]. Seizure-free was detected among 47% at five years and declined to 38% at ten years after surgery [20].

One study reported repeating surgery among 3.7% of cases and of them, 52.2% achieved seizure-free [18]. Another study reported discontinuation of medication among 9% of cases post-surgery [21].

The predictors of seizure outcomes were reported in six studies [16, 18, 19, 20, 22, 23] and they were either predictors or factors associated with favorable outcomes or factors associated with poor outcomes. Good outcomes of seizure were associated with history of febrile seizure ($P=0.04$), undergoing ATL ($P=0.002$) [18], and hippocampal sclerosis [20]. Also, a good prognosis was associated with localized PET, having no aura ($P=0.04$) and clear ictal onset on EEG ($P<0.002$) [19].

Poor outcomes of seizures included recurrence of seizures after five years which was significantly associated with partial resection ($P < 0.01$) [16]. Also, the recurrent seizure was associated with amygdalo-hippocampectomy compared to resection of the anterior temporal lobe ($P = 0.006$) and temporal lesionectomy ($P = 0.02$) [20], history with tonic-clonic seizures in the year preceding surgery (OR 2.4, $P = 0.01$) [23]. Worse seizure outcomes were associated with the presence of dysmnestic aura ($P = 0.02$), olfactory aura ($P = 0.03$) [18], frequency of pre-surgical daily seizure ($P = 0.004$), and histological diagnosis of LEAT ($P = 0.02$) [22].

Table 1: Summary of the extracted data

Author and Publication year	Study design	Condition/ Surgery	Patient characteristics and follow-up	Results and main findings
Giampiccolo et al 2023 [16]	Retrospective case collection	-Drug-resistant frontal lobe epilepsy -Frontal lobe epilepsy surgery	-N=47 patients -Age: 17-60 years -Epilepsy duration:3-50 years -FU:3-5 years [16]	*53.2% were seizure-free at 3 years after surgery. *Of 33 patients who continued follow-up for five years, 14 (42.42%) were still seizure-free. *Histology was not associated with seizure outcome at 3 or 5 years. *There was no relationship between the history of focal-to-bilateral tonic-clonic seizures and seizure outcome at any time point. *There was no correlation between resection volume and seizure outcome [at 3 years, P = 0.865; at 5 years, P = 0.162], nor between epilepsy duration and seizure outcome [3 years: P = 0.755; 5 years: P = 0.762]. *Partial resection was not associated with a worse seizure outcome 3 years after surgery [P=0.344]; however, it was significantly associated with seizure recurrence after 5 years [P < 0.017].
Demir et al 2023 [17]	Retrospective	-Temporal lobe epilepsy associated with structural lesions -Anterior temporal lobectomy and lesionectomy	-N=26 patients -Age:18-48 years -Epilepsy duration:4-38 years -FU:2 years [17]	*The rate of seizure freedom in the first year was 92.3% and 80.8% in the second year. *At the 2nd year postoperatively, demographic parameters(age, gender, age of onset), disease duration before surgery, presence of focus to bilateral tonic-clonic seizure, EEG, video EEG monitoring, clinical lateralization, scanning results, surgical technique, and histopathological diagnosis did not demonstrate a significant difference between the seizure-free and non-seizure-free groups (p>0.05).
Pereira Dalio et al 2022 [18]	Longitudinal retrospective	-Drug resistant-temporal lobe epilepsy associated with hippocampal sclerosis -Temporal lobectomy	-N=621 patients -Age:18.6-70 years -Epilepsy duration:0.7-57.3 years -FU:1-23 years [18]	*73.6% of the patients were free from disabling seizures, which were maintained over time among 65% of patients followed up to 23 years post-surgery. *3.7% (23 cases) underwent reoperation and of them, 52.2% were seizure free.

					<p>*The presence of dysmnestic and olfactory aura predicted less favorable outcomes; cases with dysmnestic (P=0.02) or olfactory auras (P=0.03) had worse seizure outcomes</p> <p>*The history of febrile seizure and the surgical technique predicted a good outcome; cases with febrile seizures displayed significantly better seizure outcomes (79.4%, P=0.047) and those who underwent standard ATL led significantly better outcomes</p>
Alsumaili et al 2021 [19]	Retrospective	-Intractable epilepsy -Resective epilepsy surgery	focal focal	-N=40 patients -Age:17-59 years -Epilepsy duration:0-8 years -FU:1-3 years [19]	<p>*Seizure freedom was detected among 47.5 % in the first year, among 42.5 % of patients in the second year, and among 37.5% in the third year in non-lesion cases.</p> <p>*Based on surgery type, temporal love surgery achieved seizure freedom among 50% in the first year and persisted 50% in the second year.</p> <p>*Frontal lobe surgery achieved seizure freedom among 15% in the first year and 0% in the second year.</p> <p>*Multilobe surgery achieved 60%seziure free in the first year and 20% seizure-free in the second year.</p> <p>*Predictors of good prognosis were found among cases with localized PET, had no aura (P=0.04), and had a clear ictal onset on scalp EEG (P<0.002).</p>
Mohan et al 2018 [20]	Retrospective analysis of prospective data	-Refractory epilepsy -Epilepsy surgery *Anterior lobe resection *Selective amygdalo-hippocampectomy *Temporal lesionectomy *Extratemporal lesionectomy	focal	-N=284 patients -Age: mean=33 years -Epilepsy duration: mean=19.6 years -FU:1-27 years [20]	<p>*47% of cases remained seizure-free at 5 years and 38% at 10 years post-surgery.</p> <p>*Patients who had an amygdalo-hippocampectomy were more Prone to have recurrent seizures compared to those who had an anterior temporal lobe resection (P = 0.006) and temporal lesionectomy (P= 0.029).</p> <p>*There was no significant difference between extra-temporal and temporal lesionectomies.</p> <p>*Hippocampal sclerosis was associated with a good outcome but declined in relative frequency over the years.</p>

Lang et al 2018 [21]	Retrospective	-Temporal, frontal, and occipital epilepsy -Epilepsy surgery	-N=79 patients -Age:50-67 years -Epilepsy duration:<1-57 years -FU:2-16 years [21]	* 68% of cases were free of seizures (75% of them aged ≥ 60 years) and 58% were seizure-free (70% of them ≥ 60 years) at two years. *After a median follow-up of 4.7 years, 65% of all patients were free of disabling seizures and 46% remained seizure-free. *9% discontinued or reduced their medication.
D' Orio et al 2017 [22]	Retrospective	-Drug-resistant focal epilepsy -Temporal surgeries *Antero-mesial temporal lobectomy *Disconnection *Lesionectomy + cortectomy *Lesionectomy	-N=50 patients -Age:50-62 years -Epilepsy duration:2-59 years -FU:2 years [22]	*78% of patients were seizure-free at last FU. *Poorer seizure outcomes were associated with pre-surgical daily seizure frequency (P= 0.004) and the histological diagnosis of LEAT (P= 0.0233).
Adadi-Pooya et al 2016 [23]	Retrospective	-Temporal lobe epilepsy with mesial temporal sclerosis -Anterior temporal lobectomy	-N=275 patients -Age: mean=37 -Epilepsy duration: mean 22 and 23 years among those without and with postoperative seizure respectively -FU: one year. [23]	*66.4% of patients were free of disabling seizure and 48.4% had sustained seizure freedom. *Cases with a history of tonic-clonic seizures in the year preceding surgery were more prone to experience recurrent seizure (OR 2.4; P= 0.01). *Gender, family history of epilepsy, race, history of febrile seizure, status epilepticus, duration of disease before operation, intelligence quotient, and seizure frequency were not predictors of outcome.

FU; Follow-up, EEG; Electroencephalopathy, ATL; Anteromesial temporal lobectomy, PET; Positron emission tomography, LEAT; Long-term epilepsy associated tumor.

Discussion:

Epilepsy surgery can be beneficial for epileptic patients who have drug-resistant disease [14]. This review was conducted to identify the impact of epilepsy surgery on seizure outcomes among adults as there is no focus on the adult population as previous analysis focused on the older population [14] or included a mixed population of children and adults [24]. Epilepsy should be classified based on the type of seizure, type of epilepsy, and etiology of epileptic syndrome when it is possible [2]. The present review included studies that were conducted on many types of epilepsy. The assessment of long-term outcomes in epilepsy surgery is essential as it is a chronic disease and the impact of its surgical intervention isn't reversible [25]. In the present review, the studies assessed the outcomes at long-term which reached 27 years; however four studies assessed outcomes at short-term of one to three years only [17, 19, 22, 23].

Seizure freedom is the primary goal of resective epilepsy surgery [26]. Therefore, the seizure outcome was the major focus of this review; however, there were variations in studies regarding reporting seizure outcomes as some studies reported disabling seizure-free and others reported seizure freedom. Also, some studies reported the rate of seizure-free at first and last follow-up, whereas others reported one rate along the study duration. Despite such variations, we could find that the rate of free seizure ranged between 47% and 92.3% at the first follow-up, but such rates were reduced at the last follow-up and reached 38% to 80.8%. The reduction in rates of free seizure in the last follow-up revealed that the proportions of patients who experienced recurrence and those who persisted in free seizure reduced over time.

In contrast to our findings, a previous review involving high-quality studies revealed that 40–50% of patients had been continuously free from seizures after resective surgery, with a higher proportion seizure-free at each annual follow-up [27]. Such findings were different from ours as we found higher rates of free seizure achieved after surgery. Additionally, there was a decline in the rate of free seizures over time.

Earlier systematic review and meta-analysis involved 76 studies of patients aged 20 years and older who underwent resective and non-resective surgery. The review reported different epilepsy surgeries, including temporal lobe surgery, temporal and extratemporal surgery, frontal surgery, extratemporal surgery, hemispherectomy, and partial and occipital surgery [25]. This was similar to our review, as there were various surgical approaches performed for epileptic patients.

Patients who underwent surgical management of epilepsy hope to gain seizure remission; however, surgery might not be effective for some patients experience and some patients may experience even worse outcomes and be classified as Engel class III or IV [28, 29]. Recurrence of seizures was a poor outcome of epilepsy surgery and it included recurrence of seizures after five years of surgery and worse seizure outcomes. Worse seizure outcomes and recurrent seizures were found to be associated with certain factors, including the surgery itself, and type of surgery, the type and frequency of seizure pre-operatively, and the histological diagnosis of LEAT. However, such factors need strong evidence as such factors were reported by studies that reported different periods for follow-up and performed different surgical interventions. Additionally, few studies reported such factors.

Worse outcomes or ineffective surgery could be due to wrong localization or incomplete resection of the epileptogenic zone. In both cases, reoperation may be beneficial for the patients who didn't improve [30]. In our analysis, only one study reported reoperation of patients with more than fifty percent achieved seizure-free after reoperation [18]. Also, it was demonstrated that the proportion of seizure-free adults in whom AEDs have been withdrawn differed widely across studies and ranged between 19% and 63% after almost five years of seizure freedom [27]. Only one study in this review reported discontinuation of medication after surgery and it was achieved among only 9% of the cases [21].

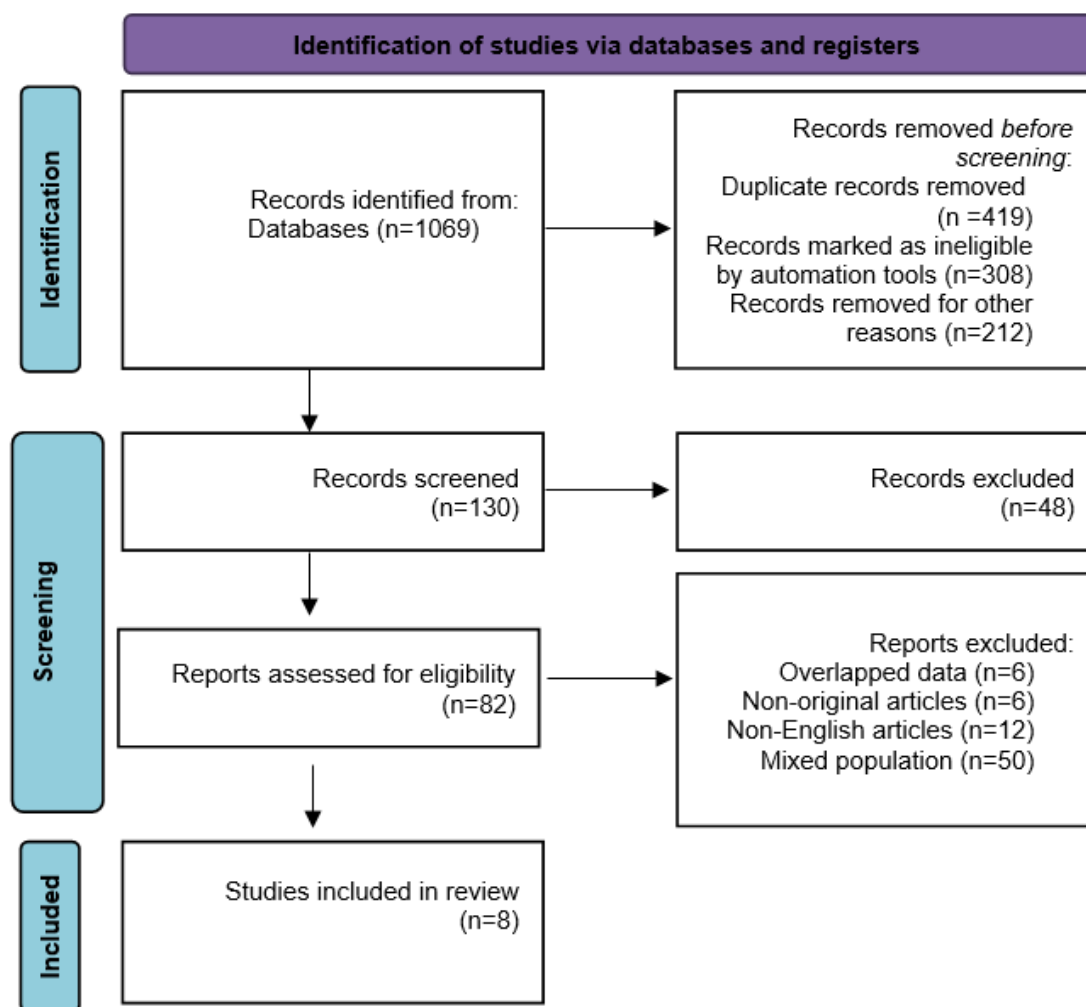
The probability of seizure freedom following epilepsy surgery is dependent on several factors including the type of epilepsy, the findings of pre-surgical investigations and evaluations, the extent of resection, pathology, and duration of follow-up [31].

A previous analysis reported that the rate of disabling seizure-free was reported regarding non-resective intervention. However, it was stated that long-term seizure freedom was lower following extratemporal surgery, and the long-term seizure-free rate at five years or longer following temporal lobe resective operation was similar to that reported in short-term controlled studies. The outcomes of patients were strongly associated with year of operation, duration of follow-up, and classification system of outcomes. The analysis reported many sources of heterogeneity among studies such as outcome definition and methodology [25]. In our analysis, we found that seizure outcomes were associated with the history of seizure, frequency, and types, the presence and type of aura, and type of surgery.

In a previous analysis including 12 studies, it was deduced that individuals with shorter epilepsy duration were more prone to be seizure-free at follow-up. Additionally, a positive association was found between shorter duration and seizure freedom for very long epilepsy durations [24]. The current review didn't identify the duration of seizure as an associated factor with seizure outcomes. We found that epilepsy duration had no significant association with outcomes in three studies [16, 17, 23].

Resective surgical approaches for epilepsy were reported to result in seizure freedom in almost two-thirds of patients with intractable temporal lobe epilepsy and almost one-half of those with focal neocortical epilepsy [32]. Another review reported that seizure freedom resulted for at least one year among 53-84% of patients following anteromesial temporal lobe resections for mesial temporal lobe sclerosis; however such rates were reported in adults and children [33]. In the present analysis, we found that the type of surgery affected the outcomes, but we couldn't determine the rate of seizure-free regarding each type due to the variations of the performed approaches.

A previous systematic review focused on adults older than 50 years old including 11 case series and 14 cohort studies with a total number of 1111 older adults who underwent epilepsy surgery along with 4111 younger adults as a control group. It was found that the pooled cumulative incidence of achieving seizure freedom after surgical resection among older adults was 70.1% with no evident variation in the incidence of seizure freedom among older and younger adults [14]. This indicates that age may be a non-effective factor or a non-predictor of seizure outcomes. This was in agreement with our findings revealed that there was no difference between seizure-free and non-seizure-free patients regarding age as reported in one of the included studies [17]. Another study of the included studies in this review conducted on older patients revealed that free seizure was equal to or even higher among older patients compared to younger ones [21].



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/register).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

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Conclusion:

This review revealed that the epilepsy surgery resulted in promising rates of free seizure, but such rates declined over time reflecting the occurrence of recurrent seizures. Many factors affected seizure outcomes, including history of seizure, frequency, and types, the presence and type of aura, and type of surgery. Hence, epilepsy surgery is a good approach for the management of epilepsy with the achievement of seizure-free under the condition of an appropriate selection of patients and an appropriate selection of surgical approach as well as a skillful neurosurgeon and precise pre-surgical evaluation.

Limitations and strengths:

The limitations in this review are related to heterogeneity across the included studies regarding different follow-up durations, some patients missed follow-up, variations in surgical approach, variation in epilepsy type, predictors of seizure outcomes; studies reported the associated

factors, not the predictors, some studies reported the mean age of the patients and didn't report the inclusion of adults only or children and adults. The strength of this study is the focus on the adult population as there were no systematic reviews focused on seizure outcomes after epilepsy surgery among adults.

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