

Discontinuation of antiepileptic drugs after successful surgery: who and when?

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ABSTRACT – Surgery is a highly effective treatment for some specific types of refractory epilepsy and once seizure freedom is achieved many patients and clinicians have to ponder whether to taper or discontinue antiepileptic drugs (AEDs). However, there is no standard practice or guidelines and practices vary widely. The few studies that have addressed this question are retrospective and lack randomised, controlled comparisons, making it difficult to draw any solid inferences. This review examines this topic by analysing key data based on the following: controlled studies which compare outcomes in patients with either withdrawn or unmodified AEDs after epilepsy surgery, non-controlled studies, information from meta-analyses and systematic reviews, surveys of clinical practice, and other relevant reviews. Between 12 and 32% of patients had seizure relapse following tapering or discontinuation of AEDs, which was not significantly different from 7 to 45% in patients without AED modification. In the event of seizure relapse upon tapering of AEDs, 45-92.3% restarted AED treatment and regained seizure freedom. The most consistent risk factors for seizure relapse were: age older than 30 years at the time of surgery, persistent auras, early drug tapering, seizure recurrence before a reduction of drugs, normal MRI, a longer period with epilepsy, absence of hippocampal sclerosis, and the presence of interictal discharges on EEG after surgery.

Key words: epilepsy, discontinuation, withdrawal, AED, successful epilepsy surgery

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Surgery is a highly effective and durable treatment for specific types of refractory epilepsy, such as temporal lobe epilepsy (Wiebe *et al.*, 2001; Engel *et al.*, 2003; Spencer and Huh, 2008; de Tisi *et al.*, 2011). Once seizure freedom is achieved with surgery, patients and clinicians must

carefully ponder whether to taper or discontinue antiepileptic drugs (AEDs) (Berg, 2004). Unfortunately, there is no solid evidence to guide this decision. Clinicians often either resort to local practices which are highly variable or the latest trend espoused by others. In the last few

years, more reports of non-surgical outcomes have been published and we therefore have a better picture of the prognosis of patients after epilepsy surgery.

In this review, we have included studies that focus mainly on adult subjects in the literature from 1992 to 2011, which investigated the management of AEDs after epilepsy surgery as the main outcome. We excluded reports of patients in the general paediatric population and studies where the main outcome was not the management of AEDs after epilepsy surgery.

Regarding AED withdrawal after successful epilepsy surgery, the published information can be divided into the following groups:

1) *Controlled studies*. These compare outcomes between patients with withdrawn and unmodified AEDs following epilepsy surgery. These are the most useful studies and provide the best evidence in the field (see table 1);

2) *Non-controlled studies*. These only report outcomes in patients where medications were modified after surgery. Although these studies provide useful information, some outcomes may have been overestimated (see table 2);

3) *Systematic reviews and meta-analyses*. These provide pooled information regarding the number of patients who are rendered free of seizures and medication after epilepsy surgery. Some reviews from experts are also discussed in this section; although this evidence is relevant, it may be biased, according to the opinion of a particular expert or centre of research;

4) *Surveys*. These provide useful information about the potential practice of epileptologists in North America.

Controlled studies assessing discontinuation of AEDs after surgery

The most useful information regarding the management of AEDs after successful epilepsy surgery is provided by studies where a comparison has been made between patients who have reduced or stopped medications and patients who continued with the same treatment. The majority of the studies are not randomised clinical trials, although they provide critical information (see table 1 for details of the studies).

Berg *et al.* (2006) studied 301 patients who attained at least one year of seizure remission after surgery. Of these, a reduction from two to one or from one to no AEDs was observed in 129 patients and no drug reduction was observed in 162 patients. The relapse rate was 32% in the reduction group and 45% in the non-reduction group. The difference between groups was not statistically significant. In this study, those with immediate remission were much more likely to attempt AED reduction than those who had delayed remission. Following a relapse, remission was achieved in 63% with a reduction of AEDs and 51% despite maintaining unmodified AEDs. The authors concluded that the risk of seizure relapse was similar in patients whether medications were tapered or not. The authors

Table 1. Controlled studies assessing discontinuation of AEDs after epilepsy surgery.

Reference	Study type	Total no. of patients available for study	No. of patients eligible for study	No. patients with AED taper and/or cessation/no change	Relapse rate or other outcome	Type of surgery
Berg <i>et al.</i> (2006)	prospective	301	291	taper: 129 no change: 162	taper: 32% no change: 45%	temporal: 264 (91%) extratemporal: 27 (9%)
Schiller <i>et al.</i> (2000)	retrospective	493	210	taper: 96 cessation: 84 no change: 20	taper: 12% cessation: 26% no change: 7%	temporal: 188 (90%) extratemporal: 22 (10%)
Kuzniecky <i>et al.</i> (1992)	open label randomised trial	not specified	40	no change: 20 monotherapy with carbamazepine: 20	no change: 20% monotherapy with carbamazepine: 30%	temporal: 100%
Kerling <i>et al.</i> (2009)	prospective pilot study	73	60	taper: 34 no change: 26	taper: 23.5% no change: 38.5%	temporal: 54 (90%) extratemporal: 6 (10%)

Table 2. Non-controlled studies assessing discontinuation of AEDs after epilepsy surgery.

Reference	Study type	Total no. of patients available for study	No. of patients eligible for study	No. patients with AED taper and/or cessation	Relapse rate	Type of surgery
Lee <i>et al.</i> (2008)	prospective	171	124	taper: 124 cessation: 79	taper: 40.3% cessation: 19%	anterior temporal lobectomy: 100%
Kim <i>et al.</i> (2005)	retrospective	100	60	taper: 60	taper: 22%	temporal lobectomy: 100%
Park <i>et al.</i> (2010)	retrospective	223	147	taper or cessation: 147	taper or cessation: 53%	temporal: 100 (45%) extratemporal: (55%)
Griffin <i>et al.</i> (2004)	retrospective	30	22	taper: 22	taper: 27%	anterior temporal lobectomy: 100%
Rathore <i>et al.</i> (2011)	prospective	310	258	taper: 258	taper: 24.8%	anterior temporal lobectomy: 100%

also suggested that future randomised clinical trials are needed to assess the impact of drug reduction in seizure-free postsurgical patients.

Schiller *et al.* (2000) performed a retrospective study of 210 patients who were rendered seizure- and aura-free for more than one year after surgical treatment for intractable partial epilepsy. Patients with auras were not included in this study. Eighty-nine per cent of patients had temporal epilepsy and the rest had extratemporal epilepsy. All the patients were followed for more than three years to assess outcome. Of the 210 patients, AED treatment was modified after surgery in 180 patients, reduced but not withdrawn in 96 patients (46%), tapered and discontinued in 84 patients (40%), and unchanged in 30 patients. The seizure relapse rate was 7% in the group with unmodified treatment, 26% in the group with tapered and discontinued treatment, and 14% in the group with reduced but not withdrawn treatment. The authors reported that 90% of patients who had recurrence of seizures after AEDs were withdrawn reached a seizure-free status by re-initiating the medication. The rest of the patients had intractable epilepsy. The authors concluded that AED withdrawal was associated with seizure recurrence in a significant proportion of patients who were rendered seizure-free after epilepsy surgery, suggesting the importance of careful selection of candidates and proper counselling with regards to AED withdrawal following surgery.

Kuzniecky *et al.* (1992) performed a randomised clinical trial in patients with intractable temporal lobe epilepsy who had surgery for the treatment of seizures. In this study, 40 patients were randomised; 20 patients had carbamazepine as monotherapy and 20 continued

with polytherapy. Patients in the former group had been converted to monotherapy in the post-operative period. In the latter group, for some patients, AEDs were tapered from three to two AEDs. Patients were followed for 52 weeks. In the group with carbamazepine, 70% of patients were seizure-free and 30% reported seizures. In the group with polytherapy, 80% of patients were seizure-free and 20% had recurrence. Seizure recurrence between groups was not statistically significant. The authors concluded that patients can be safely treated with carbamazepine and that the treatment with polytherapy is not necessary.

Kerling *et al.* (2009) performed a prospective pilot study of AED withdrawal in patients who had epilepsy surgery. Sixty patients who reached seizure freedom for one year were included in the study. Patients were stratified into two cohorts; a withdrawal group ($n=34$) and a control group ($n=26$). The majority of patients had temporal epilepsy. Discontinuation was carried out by moderate tapering over one year with yearly follow-up visits. Withdrawal was stopped when seizures recurred. Twenty-six of 34 (76.5%) patients in the withdrawal group and 16 of 26 (61.5%) patients in the control group were seizure-free five years after surgery. In addition, in the withdrawal group, 5 of 8 patients with seizure relapse became seizure-free for at least one year after adjusting the antiseizure medications. However, in the control group, only 1 of 10 patients with relapse entered one-year remission with adjustment of medication. The authors concluded that postsurgical reduction is safe and is not associated with a higher risk of seizure recurrence, relative to controls.

Non-controlled studies (see *table 2*)

Lee *et al.* (2008) investigated the outcome of AED treatment in 171 patients following anterior temporal lobectomy for mesial temporal epilepsy. The mean postoperative follow-up period was 69 months and 124 (72.5%) patients achieved seizure-free status. Of the 171 patients, AEDs were tapered in 124 patients and discontinued in 79. The recurrence rate was 40.3% for tapered AEDs and 19% for discontinued AEDs. Seizure recurrence occurred during hospitalisation in 23% of patients, and thereafter in 44% in the first year, 14% in the second year, 7.1% in the third year, and 11% after three years. The authors concluded that tapering of AEDs should be performed at least 10 months after surgery. They suggested that longer periods are required before any changes in the doses of AEDs are implemented, due to the possibility of seizure recurrence.

Kim *et al.* (2005) performed a retrospective study to investigate the prognosis related to AED discontinuation after successful epilepsy surgery. In this study, the reports of 100 patients, who had had surgery for temporal lobe epilepsy, were reviewed. Sixty-six patients achieved complete seizure freedom for more than one year. In this group, AED discontinuation was attempted in 90% of patients with a successful outcome. In 22% of patients, seizure relapse developed during AED reduction and in 12% after discontinuation of AEDs. Among patients with seizure recurrence, 45% regained seizure freedom after reinstitution of AED treatment. The authors suggested that seizure freedom without auras for more than one year is a potential indication to taper or withdraw medications after successful epilepsy surgery. The authors also suggested that subsequent control of recurrent seizures was excellent (45%), especially if seizures relapsed after the complete discontinuation of AEDs (85.7%).

Park *et al.* (2010) performed a retrospective study including 223 patients who underwent epilepsy surgery. This study included patients with temporal and extratemporal epilepsy. AED reduction was attempted in 147 patients (65.9%). Fifty-three percent of patients had seizure recurrence after initial reduction. The authors reported complete discontinuation of AEDs in 32.7% of patients and 80% remained seizure-free until the last follow-up visit. The main conclusion of this study was that the rate of completely successful treatment of previously intractable neocortical epilepsy by resectional surgery was 27.4%.

Griffin *et al.* (2004) performed a retrospective study of 30 patients who underwent anterior temporal lobectomy. Twenty-four (80%) of the 30 patients became seizure-free. AEDs were reduced in 22 patients. Patients were followed for an average of 3.4 ± 2.7 years. AED reduction was initiated at 4.6 ± 7.2 months (range:

0-27 months) after surgery. Seizures recurred in 6 patients (27%) and 3 became seizure-free after adjustment of AEDs. The authors concluded that reduction of AEDs after successful epilepsy surgery should be performed with an individualised approach in order to decrease the risk of seizure recurrence.

Rathore *et al.* (2011) performed a prospective study to investigate the feasibility of AED withdrawal following anterior temporal lobectomy. The authors followed 310 consecutive patients for a minimum of five years. In seizure-free patients, AED tapering was performed at three months in patients on duotherapy/polytherapy and at one year in patients on monotherapy. AED withdrawal was performed in 258 patients (83.2%). Sixty-four patients (24.8%) had seizure recurrence during tapering of AEDs. Of the 26 patients who had seizure relapse after complete AED withdrawal, 24 (92.3%) regained seizure-free status after restarting AEDs. The cumulative probability of achieving AED-free status among patients in whom AED withdrawal was attempted was 44% at year 4, 65% at year 6, 71% at year 8, and 77% at year 10. The authors concluded that AED withdrawal can be safely attempted following successful epilepsy surgery in patients with temporal epilepsy and that seizure recurrence is scarce and can be managed easily.

Information from meta-analyses and expert reviews

Current meta-analyses focus on calculating estimates of patients who are rendered seizure-free and AED-free after successful epilepsy surgery. Schmidt *et al.* (2004) performed a non-systematic review of the use of AEDs after temporal lobe epilepsy surgery with short-term and long-term follow-up studies, emphasizing the proportion of "cured" patients (seizure-free and AED-free after surgery). Following temporal lobe epilepsy, approximately 1 in 4 patients were shown to be seizure-free for five years without AEDs. Fifty-five percent of patients who were free of disabling seizures preferred not to discontinue their medication completely, as late as five years after surgery. The study concluded that a randomised controlled trial is needed to confirm whether in fact only 1 in 4 patients with temporal lobe epilepsy are considered cured following surgery. In another non-systematic review, Schmidt and Loscher (2003) analysed six retrospective clinical studies in order to assess seizure recurrence after planned discontinuation of AEDs in patients who were rendered seizure-free after temporal lobe epilepsy surgery; the mean percentage recurrence rate in adults in four studies was 33.8% (95% CI: 32.4-35.2%), with maximum follow-up ranging from one to five years. Seizure recurrence increased during the follow-up

period of one to three years and occurred within three years of AED discontinuation. In one study of children with temporal lobe epilepsy, the recurrence rate was 20%. More than 90% of adult patients with seizure recurrence regained seizure control with reinstitution of previous AED therapy.

Tellez-Zenteno *et al.* (2007) performed a meta-analysis of long-term surgical outcomes, investigating the use of AEDs after epilepsy surgery. For all types of surgery, in the long term, 22% (95% CI: 18-23%) were cured and 20% (95% CI: 18-23%) were not taking AEDs (with or without seizures); 41% (95% CI: 37-45%) were on monotherapy and 31% (95% CI: 27-35%) on polytherapy. Outcomes with regards to AEDs varied according to type of surgery; after temporal lobe surgery, 20% (95% CI: 17-23%) were cured, 14% (95% CI: 11-17%) were free of AEDs, 50% (95% CI: 45-55%) were on monotherapy, and 33% (95% CI: 29-38%) were on polytherapy. In the subgroup of studies reporting results of controls (possible surgical candidates who did not have surgery), 0% of patients were free of AEDs or cured, 24% (95% CI: 15-32%) were on monotherapy, and 75% (95% CI: 66-83%) were on polytherapy.

A review by McLachlan and Maher (2000) discussed different aspects of discontinuation of AEDs. Recommendations were made in the review with regards to the management of AEDs after successful epilepsy surgery of which some may still be applicable, considering the lack of information derived from randomised clinical trials. The recommendations were as follows:

- 1) an early goal of resective epilepsy surgery to reduce treatment from polytherapy to monotherapy;
- 2) if monotherapy is used preoperatively, either there should be no change of treatment or in some cases, a slight reduction of dose may be initiated five or six days after surgery and prior to discharge from hospital;
- 3) if monotherapy is not achieved at the time of discharge, a gradual reduction in medication may be started six months postoperation until this goal is reached or a seizure occurs;
- 4) patients on monotherapy who are seizure-free for one or preferably two years may be offered the opportunity to withdraw medications based on published guidelines for drug withdrawal and medical management; and
- 5) for extratemporal resections and other procedures, such as corpus callosotomy, a more cautious approach to reduce AEDs is required since complete seizure control is less likely to be achieved compared to temporal lobectomy. With the information that has been published in the last few years, some of these recommendations may be controversial, such as the reduction of AEDs in the first days or in the first year after epilepsy surgery. The majority of recent studies report discontinuation when patients complete one year of seizure freedom, although some studies still report discontinuation in the first months after surgery and the surveys performed in the US

and Canada indicate that some physicians (although not frequently) discontinue treatment very early after surgery. On the other hand, there are fewer studies that report discontinuation of AEDs a few days after surgery, which may be controversial considering the results of recent studies. The remaining recommendations may still be followed.

Surveys

Two surveys have addressed the potential management of AEDs after successful epilepsy surgery. Berg *et al.* (2007) performed a survey based on 151 neurologists from epilepsy centres in the US to assess the range of self-reported practices concerning AED discontinuation after successful epilepsy surgery. The survey included which factors influenced their decisions and whether each factor supported the decision to continue or discontinue AED treatment. In this study, 62% of neurologists stated that patients should wait for at least two years with seizure freedom before stopping medications. Seventy-one percent of respondents indicated that they would obtain an EEG most or all the time. MRI and AED levels were infrequently examined before stopping AEDs. The best candidates for successful reduction of AEDs were those with focal pathology and candidates considered least appropriate were those with persistent auras.

The second study was performed by Tellez-Zenteno *et al.* (2012) and comprised a survey in which 82 (80.5%) epileptologists from all the Canadian provinces participated. The minimum seizure-free period after epilepsy surgery before withdrawing AEDs varied substantially among responders: <6 months in 10%, 6-11 months in 21%, >2 years in 3%, and >1 year in 50%. The most important factors influencing the decision to withdraw AEDs were a negative EEG before discontinuation (71%), patients' preferences (78%), and the presence of unilateral mesial temporal sclerosis (70%). The most important factors influencing the decision not to reduce AEDs were the following: a desire to resume driving (67%), focal (65%) or generalised epileptiform activity after epilepsy surgery (81%), and presurgical multifocal/bilateral/diffuse findings (78%). This study reported other potential indications identified by open questioning by epileptologists, including the desire of women to become pregnant and some contraindications such as prior history of status epilepticus, mental retardation, and prior failed epilepsy surgery. Canadian epileptologists indicated that MRI, EEG, and examination of AED levels are typically performed before discontinuing AEDs.

Overall, both studies identified the same factors as being important with regards to the decision to alter

medication after successful epilepsy surgery. In general, physicians stated that a good candidate for the withdrawal of AEDs should have focal pathology, be completely seizure-free, and have had anterior temporal lobe resection and no epileptiform discharges on EEG after surgery. The majority of US and Canadian epileptologists prefer to wait for more than one year before any change in medication. It is important to note that the perceived practice identified in both studies does not necessarily represent the actual practice of physicians, although both studies provide useful information to guide medical decisions.

Timing of postoperative AED modification

Reduction and eventual withdrawal of AEDs is one of the expected outcomes after successful epilepsy surgery. There is no specific recommendation when these changes should occur, although more information has been published in the last few years giving rise to potential recommendations. The controlled studies showed a variety of ranges. In the studies of Berg *et al.* (2006), Schiller *et al.* (2000), and Kerling *et al.* (2009), patients had at least one year of seizure freedom before treatment was modified. In the randomised clinical trial of Kuzniecky *et al.* (1992), drugs were withdrawn in the immediate postoperative period (*refer to tables 1 and 2 for details of the studied cohorts*).

In the non-controlled studies, the timing of reduction was also variable. Lee *et al.* (2008) reported that the mean time to initial reduction after surgery was 7.6 ± 6.42 months and mean for discontinuation was 22.7 ± 13.8 months. In the studies of Kim *et al.* (2005) and Park *et al.* (2010), medications were withdrawn after one year of seizure freedom as well as absence of auras. In the study of Griffin *et al.* (2004), AED reduction was initiated after 4.6 ± 7.2 months with a range between 0 and 27 months. In the study of Rathore *et al.* (2011), the median time interval for complete AED discontinuation was 43 (range: 15-20) months.

The two surveys performed in the US and Canada reported variable times of initiation of AED withdrawal. The majority of physicians wait for more than one year and only some endorsed discontinuation in the immediate postoperative period or few months after surgery (Berg *et al.*, 2007; Tellez-Zenteno *et al.*, 2012).

Although it is difficult to make a recommendation with regards to AED withdrawal following surgery, additional articles concur that patients should be seizure- and aura-free for more than one year before treatment is modified. Seizure reduction in the immediate postoperative period has been performed in a few studies and the consensus does not support this strategy due to safety issues.

Risk factors associated with seizure relapse after AED withdrawal

Lee *et al.* (2008) identified that patients younger than 30 at the time of surgery had a lower rate of seizure relapse after AED withdrawal. Other factors that were investigated in this study included: postoperative duration of epilepsy, seizure frequency, history of febrile convulsions, number of medications, and presence of hippocampal sclerosis. None of these were statistically significant.

In the study of Berg *et al.* (2006), an increased rate of seizure relapse was associated with delayed remission following hospitalisation and continuous auras.

In the study of Kim *et al.* (2005), patients who had complete discontinuation of AEDs had better prognosis than patients who had only AED reduction. Seizure freedom was reached in the former group in 86% of patients compared with 23% in the latter group. The rate of seizure freedom after discontinuation was greater for patients with a younger age at the time of surgery and for those patients with shorter disease duration.

In the study of Park *et al.* (2010), a multivariate analysis revealed that early drug tapering, seizure recurrence before reduction, normal MRI, and longer epilepsy duration were associated with recurrence. The authors suggested that medication withdrawal should be performed cautiously in these groups of patients because of a potential higher risk of relapse.

Rathore *et al.* (2011) identified predictors for seizure recurrence following AED withdrawal. Based on univariate analysis, the risk factors related to seizure recurrence were: patients older than 30 at the time of surgery, duration of epilepsy >20 years, absence of hippocampal sclerosis, and the presence of interictal discharges on EEG after surgery. Based on multivariate analysis, the last two variables were statically significant.

In the study of Schiller *et al.* (2000), patients with focal pathology, identified by MRI, had a seizure relapse rate of 40% compared with 20% in patients with normal MRI. This difference did not reach clear significance ($p=0.06$), although normal MRI was identified as a potential risk factor for seizure relapse in this study.

Discussion

This review analyses the evidence for appropriate timing and criteria for tapering or discontinuing AED treatment after epilepsy surgery. The main conclusions are outlined below.

The majority of the controlled studies describe AED withdrawal in patients who remained seizure-free one-year postsurgery; between 12 and 32% of these patients

had seizure relapse following tapering or discontinuation of AEDs, which was not significantly different from 7 to 45% in patients without AED modification. The lack of difference could be a methodological bias related to the lack of randomisation or alternatively may result from a small sample size. Finally, data has mainly been described in patients with temporal lobe epilepsy, thus the results cannot be extrapolated to other types of epilepsy; a randomised clinical study is therefore required to address this issue.

Further issues are of concern with regards to controlled studies. A common factor in all these studies is the definition of "candidate for discontinuation". In order to taper or withdraw medications, the patients were required to be seizure- and aura-free, and only one study was randomised. This is an important methodological issue, because patient selection for withdrawal or tapering AEDs may be biased by the clinician treating the patient, who may select a preferred candidate. Another important aspect of these studies is the length of time before modifying the dose of AEDs. The majority of these studies included patients who were seizure-free for at least 12 months, which may be a significant obstacle for randomised clinical trials due to a potentially prolonged duration of study. In addition, no other outcomes were investigated in the studies to examine whether discontinuation has any benefit for patients, other than potential seizure recurrence. The discontinuation of AEDs may induce changes in the quality of life, including physical changes due to side effects of medications, changes in driving status, and other potential adverse outcomes for the patient.

In non-controlled studies, seizure relapse after modification of AED dose was between 22 and 53%. Overall, these studies, similar to the controlled studies, consistently showed that patients with seizure relapse easily regained seizure freedom by restarting treatment with AEDs. However, there was a significant percentage of patients who went on to develop intractable epilepsy, either related to the discontinuation of AEDs or unsuccessful epilepsy surgery. Almost all the studies considered that AED withdrawal is a safe procedure, but careful selection of patients should be made. As for the controlled studies, no other outcomes were assessed to investigate the impact of AED discontinuation on the quality of life or other factors.

The systematic and non-systematic reviews showed that between 22 and 25% of patients were seizure-free and free of AEDs after epilepsy surgery. In general, the systematic reviews and meta-analyses revealed the following methodological issues: 1) the majority of the studies investigating this topic are retrospective, and neither blinded nor controlled; 2) few studies investigated this outcome with follow-up periods of longer than five years; 3) the results were variable and difficult

to interpret; 4) few prospective studies are available and none are blinded; and finally 5) the majority of the studies are related to temporal epilepsy. On the other hand, reviews by experts can be a source of information; however, they may be biased due to specific practices in some epilepsy centres which influence training and individual experience.

Overall, the reviewed studies support one year of postsurgical seizure freedom prior to tapering or discontinuing AEDs, since safety should be the main aspect of decision-making. However, surveys generally showed a more conservative approach as they commonly recommended two years of seizure freedom prior to AED tapering. With regards to risk factors for seizure recurrence, there is agreement between the studies and surveys that normal brain MRI, absence of hippocampal sclerosis, seizure recurrence before AED reduction, and abnormal interictal EEG are important. However, some other important risk factors delineated by the reviewed studies were not considered in the surveys. These include age older than 30 years at the time of the surgery, persistent auras, and longer epilepsy. Therefore, these are important factors that need further emphasis when dealing with postsurgical patients. Although, the current published literature provides clinicians with some guidelines based on safety, the reports do not describe methods of tapering AEDs, which is an important aspect considering the tremendous variation between approaches by epileptologists to taper medications. In addition, they do not assess the effect of AED tapering on patients' quality of life. Future research in the form of randomised controlled clinical trials is needed to further delineate the best timing and method of AED modification after epilepsy surgery.

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References

- Berg AT. Stopping antiepileptic drugs after successful surgery: what do we know? And what do we still need to learn? *Epilepsia* 2004; 45: 101-2.
- Berg AT, Vickrey BG, Langfitt JT, *et al.* Reduction of AEDs in postsurgical patients who attain remission. *Epilepsia* 2006; 47: 64-71.
- Berg AT, Langfitt JT, Spencer SS, Vickrey BG. Stopping antiepileptic drugs after epilepsy surgery: a survey of US epilepsy center neurologists. *Epilepsy Behav* 2007; 10: 219-22.

- de Tisi J, Bell GS, Peacock JL, et al. The long-term outcome of adult epilepsy surgery, patterns of seizure remission, and relapse: a cohort study. *Lancet* 2011; 378: 1388-95.
- Engel J Jr, Wiebe S, French J, et al. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* 2003; 60: 538-47.
- Griffin CT, Abastillas ME, Armon C, et al. Early antiepileptic drug reduction following anterior temporal lobectomy for medically intractable complex partial epilepsy. *Seizure* 2004; 13: 434-7.
- Kerling F, Pauli E, Lorber B, Blumcke I, Buchfelder M, Stefan H. Drug withdrawal after successful epilepsy surgery: how safe is it? *Epilepsy Behav* 2009; 15: 476-80.
- Kim YD, Heo K, Park SC, et al. Antiepileptic drug withdrawal after successful surgery for intractable temporal lobe epilepsy. *Epilepsia* 2005; 46: 251-7.
- Kuzniecky R, Rubin ZK, Faught E, Morawetz R. Antiepileptic drug treatment after temporal lobe epilepsy surgery: a randomized study comparing carbamazepine and polytherapy. *Epilepsia* 1992; 33: 908-12.
- Lee SY, Lee JY, Kim DW, Lee SK, Chung CK. Factors related to successful antiepileptic drug withdrawal after anterior temporal lobectomy for medial temporal lobe epilepsy. *Seizure* 2008; 17: 11-8.
- McLachlan RS, Maher J. Management of antiepileptic drugs following epilepsy surgery: a review. *Can J Neurol Sci* 2000; 27: S106-10.
- Park KI, Lee SK, Chu K, et al. Withdrawal of antiepileptic drugs after neocortical epilepsy surgery. *Ann Neurol* 2010; 67: 230-8.
- Rathore C, Panda S, Sarma PS, Radhakrishnan K. How safe is it to withdraw antiepileptic drugs following successful surgery for mesial temporal lobe epilepsy? *Epilepsia* 2011; 52: 627-35.
- Schiller Y, Cascino GD, So EL, Marsh WR. Discontinuation of antiepileptic drugs after successful epilepsy surgery. *Neurology* 2000; 54: 346-9.
- Schmidt D, Loscher W. How effective is surgery to cure seizures in drug-resistant temporal lobe epilepsy? *Epilepsy Res* 2003; 56: 85-91.
- Schmidt D, Baumgartner C, Loscher W. The chance of cure following surgery for drug-resistant temporal lobe epilepsy. What do we know and do we need to revise our expectations? *Epilepsy Res* 2004; 60: 187-201.
- Spencer S, Huh L. Outcomes of epilepsy surgery in adults and children. *Lancet Neurol* 2008; 7: 525-37.
- Tellez-Zenteno JF, Dhar R, Hernandez-Ronquillo L, Wiebe S. Long-term outcomes in epilepsy surgery: antiepileptic drugs, mortality, cognitive and psychosocial aspects. *Brain* 2007; 130: 334-45.
- Tellez-Zenteno JF, Ronquillo LH, Jette N, et al. Discontinuation of antiepileptic drugs after successful epilepsy surgery. A Canadian survey. *Epilepsy Res* 2012. In press.
- Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal lobe epilepsy. *N Engl J Med* 2001; 345: 311-8.