

Surgery soon after failure of drug treatment for epilepsy may lower risk of seizures

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Patients with epilepsy who underwent brain surgery soon after failing to respond to drug treatment, but who also continued to receive drug therapy, had a lower risk of seizures during the 2nd year of follow-up compared to patients who received drug treatment alone, according to a study in the March 7 issue of *JAMA*.

"Epilepsy is a worldwide serious health concern, accounting for 1 percent of the global burden of disease, equivalent to [lung cancer](#) in men and [breast cancer](#) in women. The 20 percent to 40 percent of patients who have medically intractable epilepsy account for 80 percent of the cost of epilepsy. [Temporal lobe epilepsy](#) (TLE) is the most common cause of drug-resistant seizures, but it can be treated surgically," according to background information in the article. The American Academy of Neurology practice parameter recommends surgery as the treatment of choice for medically intractable TLE, but use of this treatment is delayed and underutilized. Patients who are referred for surgery have had epilepsy for an average of 22 years, more than 10 years after failure of 2 [antiepileptic drugs](#) (AEDs). Because earlier surgery could prevent significant illness and [premature death](#), it has been recommended that a [randomized controlled trial](#) be conducted to evaluate its efficacy.

Jerome Engel Jr., M.D., Ph.D., of the University of California, Los Angeles, and colleagues conducted a study to compare outcomes of surgery for epilepsy with those of continued drug treatment. The clinical trial, performed at 16 U.S. epilepsy [surgery centers](#), included 38

participants (18 men and 20 women; age 12 years or older) who had mesial temporal lobe (a section of the brain) epilepsy (MTLE) and disabling seizures for no more than 2 consecutive years following adequate trials of 2 brand-name AEDs. Planned enrollment was 200, but the trial was halted prematurely due to slow accrual. Eligibility for anteromesial temporal resection (AMTR; surgery/removal of tissue of a section of the brain) was based on a standardized presurgical evaluation protocol. Participants were randomized to continued AED treatment (n = 23) or a standardized AMTR plus AED treatment (n = 15). In the medical group, 7 participants underwent AMTR prior to the end of follow-up and 1 participant in the surgical group never received surgery. The primary outcome measure for the study was freedom from disabling seizures during year 2 of follow-up. Other outcomes included measures on health-related quality of life (QOL) and cognitive function.

In results for the primary analysis, 0 of 23 participants in the medical group and 11 of 15 in the surgical group (73 percent) were seizure free. Analysis of only those participants who provided complete data in year 2 (or reported seizures in year 2) showed that 0 of 19 in the medical group vs. 11 of 13 in the surgical group (85 percent) were seizure free. Nine of the 11 participants in the surgical group who became free of disabling seizures never experienced a seizure after surgery; the other 2 participants last reported seizures 4 and 21 days after surgery.

"In the intention-to-treat analyses, participants in the surgical group had significantly higher increases in health-related QOL than those in the medical group at months 6, 12, and 18, but not at month 24. When excluding data obtained after surgery from participants in the medical group (n = 6), the effect of surgery on overall QOL was statistically significant at month 24," the authors write.

There were no significant treatment group differences with respect to the primary memory and nonmemory measures, although participants in

the medical group tended to perform better on memory measures. A total of 13 serious adverse events (7 in the medical group and 6 in the surgical group) occurred in 9 participants (4 in the medical group, 5 in the surgical group) during the study.

"Only a small percentage of patients with medically [intractable epilepsy](#) are ever referred to an epilepsy center that offers surgery, and they are often referred too late for successful surgery to prevent serious disability. The reasons for this remain obscure. The data presented here reinforce the view that surgery soon after failure of 2 AED trials offers the best chance of preventing a lifetime of disability. The results of this study support the conclusions of the American Academy of Neurology practice parameter, namely that all patients with epilepsy should be referred to an [epilepsy](#) center as soon as trials of 2 AEDs fail, and surgery should be performed if patients meet criteria for an AMTR," the researchers conclude.

In an accompanying editorial, Donald L. Schomer, M.D., of the Beth Israel Deaconess Medical Center, Harvard University, Boston, and Roger J. Lewis, M.D., Ph.D., of the Harbor-UCLA Medical Center, Torrance, and David Geffen School of Medicine at University of California, Los Angeles, write that there are several clinically important messages from this study.

"First, the early surgical approach for patients with refractory MTLE was far superior to the medical treatment when comparing seizure freedom and QOL. Because QOL measures have a high correlation with seizure freedom, this is not surprising. Second, the surgical treatment of MTLE may lead to specific memory deficits. MTLE appears to have a progressive decline in memory tasks in some patients over the long-term course. What is not known from this study is whether the surgically induced memory decline is equal to, greater than, or less than memory decline that might occur during the long-term medical management. ...

Third, freedom from seizures and improved QOL do not predict return to work. Employment activities did not seem to show a group difference even though measures of social engagement did show a positive effect. This matter is especially troublesome in terms of the ultimate effect of either treatment approach on the total medical and social burden and costs of MTLE. Patients with MTLE need ongoing counseling and access to work-related training whether they receive [surgery](#) or not."

More information: *JAMA*. 2012;307[9]:922-930.
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