

# Vascular risk linked to long-term antiepileptic drug therapy

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New research reveals that patients with epilepsy who were treated for extended periods with older generation antiepileptic drugs (AEDs) may be at increased risk for developing atherosclerosis, a common disorder known as hardening of the arteries. According to the findings now available in *Epilepsia*, the journal of the International League Against Epilepsy (ILAE), the vascular risk is significantly associated with the duration of AED monotherapy.

While the majority of [epilepsy patients](#) have good results with treatment, more than 30% of patients continue to have seizures even with AED therapy. In these cases of refractory epilepsy, long-term or lifelong AED therapy is needed. Prolonged treatment can lead to diabetes, thyroid issues, psychiatric problems and [adverse drug reactions](#). Prior studies suggest that older-generation AEDs such as phenytoin, carbamazepine, phenobarbital, and [valproic acid](#) may alter [metabolic pathways](#), contributing to increased vascular risks.

Lead author, Dr. Yao-Chung Chuang from Kaohsiung Chang Gung Memorial Hospital in Taiwan, and colleagues compared the long-term impact of different categories of AED monotherapy on atherosclerosis development. The team recruited 160 [adult patients](#) with epilepsy who had received AED [monotherapy](#) for more than 2 years, along with 60 healthy controls. Ultrasonography was used to measure participants' common carotid artery (CCA) intima media thickness (IMT) -- a measurement used to assess the extent of atherosclerosis.

"Our study found patients with epilepsy who were under long-term monotherapy with phenytoin, carbamazepine and valproic acid displayed significantly increased CCA IMT measurements," said Dr. Chuang.

"These altered circulatory markers from prolonged AED therapy may accelerate the atherosclerotic process." Analysis showed that CCA IMT is positively correlated with the duration of AED therapy.

Researchers also investigated specific [vascular risk factors](#) associated with the type of AED therapy. Epilepsy patients taking carbamazepine or phenytoin for long periods exhibited increased levels of cholesterol and of the amino acid, total homocysteine (tHcy), and lower levels of folate, all of which increase risk of adverse cardiovascular and cerebrovascular events. Patients who were treated with valproic acid displayed elevated levels of uric acid, tHcy, and thiobarbituric acid reactive substances (TBARS), increasing atherosclerosis risk which the authors believe is based on oxidative mechanisms.

The authors argue that drug choice should be carefully selected for epilepsy patients requiring long-term AED treatment, particularly in elderly or individuals at high-risk of vascular events. Dr. Chuang concluded, "Our findings suggest that newer AEDs, such as lamotrigine, may minimize metabolic disturbances, and therefore reduce the risk of atherosclerosis brought on by long-term AED therapy."

**More information:** "Effects of Long-Term Antiepileptic Drug Monotherapy on Vascular Risk Factors and Atherosclerosis." Yao-Chung Chuang, Hung-Yi Chuang, Tsu-Kung Lin, Chiung-Chih Chang, Cheng-Hsien Lu, Wen-Neng Chang, Shang-Der Chen, Teng-Yeow Tan, Chi-Ren Huang, and Samuel H.H. Chan. *Epilepsia*; November 15, 2011 ([DOI: 10.1111/j.1528-1167.2011.03316.x](https://doi.org/10.1111/j.1528-1167.2011.03316.x)).

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