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What's in Your Nomogram? Personalized Prognostication of Verbal Memory Decline after Temporal Lobe Resection in Adults With Epilepsy

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Abstract

Objective: This study aims to develop and externally validate models to predict the probability of postoperative verbal memory decline in adults following temporal lobe resection (TLR) for epilepsy using easily accessible preoperative clinical predictors.

Methods: Multivariable models were developed to predict delayed verbal memory outcome on 3 commonly used measures: Rey Auditory Verbal Learning Test (RAVLT), and Logical Memory (LM), and Verbal Paired Associates (VPA) subtests from Wechsler Memory Scale-Third Edition. Using Harrell's step-down procedure for variable selection, models were developed in 359 adults who underwent TLR at Cleveland Clinic and validated in 290 adults at 1 of 5 epilepsy surgery centers in the United States or Canada.

Results: Twenty-nine percent of the development cohort and 26% of the validation cohort demonstrated significant decline on at least 1 verbal memory measure. Initial models had good-to-excellent predictive accuracy (calibration (c) statistic range = .77–.80) in identifying patients with memory decline; however, models slightly underestimated decline in the validation cohort. Model coefficients were updated using data from both cohorts to improve stability. The model for RAVLT included surgery side, baseline memory score, and hippocampal resection. The models for LM and VPA included surgery side, baseline score, and education. Updated model performance was good to excellent (RAVLT c = .81, LM c = .76, VPA c = .78). Model calibration was very good, indicating no systematic over- or under-estimation of risk.

Conclusions: Nomograms are provided in 2 easy-to-use formats to assist clinicians in estimating the probability of verbal memory decline in adults considering TLR for treatment of epilepsy.

Classification of Evidence

This study provides Class II evidence that multivariable prediction models accurately predict verbal memory decline after temporal lobe resection for epilepsy in adults.

"I don't remember things."[1]

Up to 30% of adults may experience verbal memory decline after epilepsy surgery. Predicting verbal memory decline after temporal lobe resection in adults with epilepsy is a foundational aspect of the decision to both offer and undergo surgery. The authors of "Nomograms to predict verbal memory decline after temporal lobe resection in adults with epilepsy"[2] have provided us with a new tool to use in making this decision.

In the quest to improve seizure control and cure epilepsy, surgical resection can be the key destination. However, with surgery comes risk. One of the most consequential risks is loss of verbal memory. The loss of memory after epilepsy surgery was most dramatic in the case of Henry Molaison (a.k.a. H.M.). Mr Molaison had epilepsy surgery that removed both hippocampi, and he was left with devastating short-term memory loss that included verbal memory loss.[3] His is a dramatic example of how epilepsy surgery can result in neuropsychological deficits. In the modern evaluation of memory prior to epilepsy surgery, neuropsychological testing, fMRI, and Wada testing can all be employed to document pre-surgical memory and attempt to predict risk of memory loss after surgery.[4] Verbal memory, the ability to recall what is read or heard, is tested in all patients prior to surgery. The potential worsening of verbal memory is one of the reasons neuropsychological testing before and after epilepsy surgery is standard of care. Patient counseling regarding risk of verbal memory deficits as a consequence of surgery is an important element of risk vs benefit and the shared decision-making process.

The ability to use data to inform patients about risk in a way that is personalized, valid, reliable, and easy to understand is critically important. The development of these statistical prediction models is one of the goals in modern medicine. One of these predictive tools is the nomogram. Although nomograms have been described as a "medical relic"[5] compared to the use of a slide-ruler rather than the use of a software program, they are widely used and found to be helpful by both physicians and patients. Nomograms are a simple graphical representation of

statistically predictive models and merge the data into a single numerical estimate of the probability of a clinical event. This estimate is tailored to the profile of an individual patient. The equations used in the nomograms can be translated into web-based applications for physicians and patients to better inform them about the risks of various decisions. A review of any nomogram should analyze the steps taken to develop and validate the nomogram, including the patient population, outcome, identification of important covariates, specification of the statistical model, and validation of its performance.

Busch and colleagues have developed nomograms for use in adults with epilepsy considering temporal lobe resection. They clearly describe the process in their article[2] using easily available neuropsychological tests to predict risk of verbal memory loss after temporal lobectomy. These nomograms use only clinical data and do not include neuroimaging data or Wada testing. The authors developed 3 nomograms that use results of specific neuropsychological tests: the Rey Auditory Verbal Learning Test (RAVLT), or subtests from the Wechsler Memory Scale-Third Edition (WMS-III) Logical Memory (LM) or Verbal Paired Associates (VPA). They examined eight other possible data points for inclusion: sex, education, age at epilepsy onset, duration of epilepsy, age at surgery, side of surgery, preoperative MRI findings, and hippocampal resection (resected or spared). The nomograms ended up including surgery side, hippocampal resection, and, in the case of LM and VPA, education. The models were developed in 359 adults who underwent temporal lobe resection at the Cleveland Clinic and validated in 290 adults at Columbia University Medical Center New York, NY; University of California, San Diego, CA; University of Washington, Seattle, WA; Emory University School of Medicine, Atlanta, GA; and almost half of the 290 adults were from University Health Network, Toronto, Ontario, Canada (n = 140). They used rigorous statistical models and showed good-to-excellent discriminatory ability (*c* statistic > .8) in identifying at-risk patients. The models were adjusted after the initial model was found to underestimate the probability of decline.

This study presents a helpful tool for discussing risk of memory loss in patients who are similar to the patient population used to develop the nomogram. In the future, more widespread use of this nomogram to refine its predictive power could help our patients with epilepsy know what their risk to verbal memory is with temporal lobe resection. This study did not include patients undergoing other temporal lobe procedures, such as selective amygdalohippocampectomy or laser ablation. A nomogram in the future that specifies the type of temporal lobe intervention would be helpful in further counseling patients. Also important to patient counseling regarding verbal memory decline is information regarding the risk to verbal memory decline without surgery as long-term effects of refractory temporal lobe epilepsy include cognitive decline.[6] The implications of memory loss in quality of life and other functional outcomes is not examined and will still require the use of additional data and the art of personalized medicine. We must continue to work with our patients and our patient data. As H.M. said about his doctors, "…what they find out about me helps them to help other people."

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