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Long-Term Outcome in Patients With Transient Global Amnesia: A Population-Based Study

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Abstract

Objective: To study the long-term risk of cerebrovascular events, seizures, and cognitive impairment in patients with transient global amnesia (TGA).

Patients and Methods: Data for all patients diagnosed with possible TGA in Olmsted County, Minnesota, between January 1, 1985, through December 31, 2010, were retrieved from the Rochester Epidemiology Project database. Transient global amnesia was defined clinically. End points were cerebrovascular event (stroke or transient ischemic attack), seizure, or cognitive impairment (mild cognitive impairment or dementia) during follow-up. End points were studied using Kaplan-Meier survival plots and log-rank test.

Results: A total of 221 patients with TGA were identified and 221 age- and sex-matched controls were included in the analysis. The mean duration of follow-up was 12 years in both groups (range, 0.07-29.93). Prevalence of vascular risk factors and history of seizures were similar between both groups. Previous migraine was more common in the TGA group (42 patients [19.1%] vs 12 patients [5.4%]; $P<.001$). There was no statistically significant difference between survival curves for the TGA group and the control group using time to any type of cerebrovascular event (log-rank $P=.30$), time to seizures event (log-rank $P=.55$), and time to cognitive impair event (log-rank $P=.88$) as end points. The TGA recurrence occurred in 5.4% of patients after a median interval of 4.21 years (interquartile range, 2.82-8.44). Modified Rankin scale and death rates at last follow-up were also similar between both groups.

Conclusion: Our findings indicate that having an episode of TGA does not increase the risk of subsequent cerebrovascular events, seizures, or cognitive impairment.

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Transient global amnesia (TGA) is characterized by the sudden onset of anterograde amnesia, generally lasting up to 24 hours.[1-4] It has an annual incidence of 3.4 to 10.4 per 100,000 people.[5-7]

The leading hypothesis on the pathogenesis of TGA is abnormal venous drainage of the temporal lobes caused by increased intrathoracic pressure resulting in jugular hypertension.[8-11] Others include arterial ischemia,[12] migraine-,[5,13,14] and epilepsy-related.[15]

The recurrence rate of TGA has been estimated to be between 2.9% and 23.8%.[13,16-19] Available studies about the long-term outcome are few and limited in scope. Acquiring information is necessary to enhance clinical practice.

Available data suggest that TGA does not put patients at a higher risk of cerebrovascular events, myocardial infarction, or peripheral artery disease.[13,16,19,20] Data on the risk of seizures after TGA are inconsistent. Studies that have suggested a higher risk of seizures concluded that at least some of the patients could have had a seizure mimicking TGA, as suggested by abnormal interictal electroencephalograms (EEGs).[5,11]

The long-term risk of cognitive decline has not been sufficiently evaluated. Complete recovery of cognitive function has been reported 5 days to 6 months after the episode.[21-24] Other investigators have found memory and visuoperceptual dysfunction.[25-30] Long-term risk was assessed in one study with an average follow-up of 82.2 months, showing no difference in the incidence of dementia (2.9%) compared with general population.[16]

We conducted a population-based, matched cohort study on patients with TGA to establish the long-term risk of cerebrovascular events, seizures, and cognitive impairment.

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PATIENTS AND METHODS

A list of all patients with a potential diagnosis of TGA among residents of Olmsted County, Minnesota, occurring from January 1, 1985, through December 31, 2010, was obtained using the resources of the Rochester Epidemiology Project[31] database. The list included patients diagnosed in both the outpatient and inpatient settings, including cases seen at Mayo Clinic, and those seen at other medical providers in Olmsted County. We reviewed electronic and paper medical records for all patients. TGA was defined clinically, and all cases were confirmed using previously proposed criteria.[1,32,33] Cases in which an alternative diagnosis was suspected or could not be ruled out were excluded from the study. Fourteen patients were excluded because of a confirmed diagnosis of seizures or stroke. The other 75 patients were excluded for suspicion of alternative diagnosis, including the classical differential diagnosis of TGA such as transient ischemic attack [TIA], seizures, and transient epileptic amnesia, with the latter consisting of focal seizures with similar clinical features, shorter duration and higher recurrence, and sometimes accompanied by other manifestations such as oral automatisms. One age- and sex-matched control for each case was selected from the same database; controls were also matched for date of assessment.

Data collected in both cases and controls included demographic characteristics, relevant cerebrovascular risk factors, and conditions reported to be associated with TGA (hypertension, dyslipidemia, diabetes mellitus, smoking history, coronary artery disease, atrial fibrillation, peripheral vascular disease, alcohol abuse, personal or familial history of stroke, personal or familial history of migraine, personal or familial history of seizures or epilepsy).

The primary end points for our analysis were cerebrovascular events (TIA or stroke), seizures, and cognitive impairment (diagnosis of mild cognitive impairment and dementia). The diagnosis of stroke or TIA was made on the basis of comprehensive data from the medical record, and using the definition on current guidelines.[34,35] The presence of seizures was recorded according to the clinical diagnosis by the treating neurologist, sometimes aided by an abnormal ictal or interictal EEG. The presence of cognitive impairment was considered to be the first time the patient was given a clinical diagnosis of mild cognitive impairment or dementia by a neurologist.[36,37] Secondary end points were death, functional outcome at last follow-up as assessed by the modified Rankin score (mRS),[38] and TGA recurrence.

Approval from the Ethics Standards Committee was obtained to conduct this retrospective study.

Statistical Analyses

Descriptive summaries were reported as mean ± SD or median and interquartile range (IQR) as appropriate. Comparisons between cases and controls for continuous variables such as body mass index (calculated as the weight in kilograms divided by the height in meters squared) and duration of follow-up were done using Wilcoxon rank sum test. Categorical variables such as relevant medical history, family history, and smoking history were performed using Fisher exact test. To account for differential follow-up and censoring, events of interest at follow-up such as death, first cerebrovascular event, seizures, or diagnosis of cognitive impairment were analyzed using Kaplan-Meier survival curves. Comparisons of curves between the cases and controls were performed using the log-rank test. All tests were 2-sided, and P values of less than .05 were considered statistically significant. All analyses were performed using SAS 9.3.

RESULTS

Two hundred twenty-one cases and the same number of matched controls were included in the study (Figure 1). Baseline data for cases and controls are presented in the Table.

Among the patients with TGA, 20 (9.0%) had experienced 1 or more previous episodes of TGA. Twelve (5.4%) patients had recurrences after the index episode; 10 had only 1 recurrence and 2 had 4 recurrences each. The median interval to the first recurrence was 4.2 years (IQR, 2.8-8.4 years). The resulting recurrence rate from the index event was 67 per 100 person-years of follow-up (95% CI, 52.3-84.5).

The mean ± SD age at onset of TGA was 65.6±12.2 years (range, 0.07-29.93 years).

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