Antecedent Aspirin Use Is Associated with Less Severe Symptoms on Admission for Ischemic Stroke

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Background: Aspirin is known to reduce stroke risk; however, its role in reducing severity of ischemic syndrome is not clear. We sought to investigate the relationship between antecedent aspirin use and stroke severity in patients presenting with acute ischemic stroke (AIS). *Methods:* We retrospectively analyzed a prospectively collected database of consecutive AIS patients presenting to our center. Clinical characteristics (including antecedent aspirin use), imaging findings, and laboratory data were assessed in association with presenting stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS). Logistic regression models were used to determine univariate and multivariate predictors of baseline NIHSS. *Results:* Of the 610 AIS patients with admission brain magnetic resonance imaging available for volumetric analysis of acute infarct size, 241 (39.5%) used aspirin prior to stroke onset. Antecedent aspirin use ($P = .0005$), history of atrial fibrillation ($P < .0001$), acute infarct volume ($P < .0001$), initial systolic blood pressure ($P = .041$), admission glucose level ($P = .0027$), and stroke subtype ($P < .0001$) were associated with presenting stroke severity in univariate analysis. Antecedent aspirin use ($P < .0001$), history of atrial fibrillation ($P < .0002$), acute infarct volume ($P < .0001$), systolic blood pressure ($P = .038$), and glucose level ($P = .0095$) remained independent predictors of NIHSS in multivariable analysis. *Conclusions:* Antecedent aspirin use was independently associated with milder presenting stroke severity, even after accounting for acute infarct volume. While the underlying biology of this apparent protective relationship requires further study, patients at high risk of stroke may benefit from routine aspirin use. **Key Words:** Brain infarction—aspirin—glucose—atrial fibrillation—blood pressure.

Introduction

Aspirin reduces serious vascular events as a primary prevention agent,[1-3] and data for its role in the secondary prevention of ischemic stroke are even stronger.[4,5] However, studies on aspirin's effect on stroke severity have been conflicting. Some literature suggests no change in, or greater, presenting National Institutes of Health Stroke Scale (NIHSS) in antecedent aspirin users,[6-8] whereas others link prestroke aspirin use to milder initial stroke severity.[9,10]

Several studies have shown that infarct volume affects baseline NIHSS,[11-13] and thus, it is possible that antecedent aspirin use could influence NIHSS by its effect on

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infarct size. However, there are clinical factors that are known to correlate with the severity of clinical stroke syndrome besides the size of acute infarction.[14,15] Because prior studies showing the benefit of antecedent aspirin use on initial NIHSS have not accounted for acute infarct volume, they could not address the link between severity of clinical syndrome and radiographic extent of acute injury.[9,10] We hypothesized that, in acute ischemic stroke (AIS) patients, presenting stroke severity as measured by baseline NIHSS is affected by antecedent aspirin use independent of acute infarct size on diffusion-weighted MRI (DWI).

Materials and Methods

Patient Selection

We conducted a retrospective analysis of a prospectively ascertained hospital-based cohort of ischemic stroke subjects aged 18 years or older admitted to a large academic medical center through the emergency department (ED) from February 2002 to February 2012. Informed consent was obtained from all subjects, and the study was conducted under the approval of our Institutional Review Board. Demographic, clinical, and laboratory data were collected on admission. Inclusion criteria were as follows: (1) diagnosis of ischemic stroke confirmed by radiographic (computed tomography [CT] or MRI) evidence of cerebral infarct; (2) availability of brain MRI within 48 hours of symptom onset; and (3) absence of diagnoses that could interfere with MRI interpretation including intracranial hemorrhage, neoplasms, and demyelinating diseases. Only subjects with MRI available for volumetric assessment of acute infarct size were included in this study.

Data Collection and Outcome Definitions

All patients were evaluated by a neurologist in the ED, where the NIHSS score was determined. Clinical information, prestroke medication use, and vascular risk factors were collected by patient or proxy interview and supplemented by medical record review. To ascertain medication use, all data regarding prescribed and over-the-counter medications used prior to stroke onset were collected; however, no information on the duration of and compliance to use was available. Aspirin use was also not confirmed by sources other than those mentioned above. Aspirin users included all patients on aspirin regardless of dose, and patients on nonsteroidal anti-inflammatory drugs, anticoagulants, and other antiplatelets but not on aspirin were not considered aspirin users. The initial venous blood draw and all clinical measurements (systolic blood pressure [SBP] and diastolic blood pressure [DBP]) were completed on admission to the ED. TOAST (Trial of Org 10172 in Acute Stroke Treatment) stroke subtype was assigned by a trained vascular neurologist (K.L.F.) prospectively as part of an independent research project.

Neuroimaging Analysis

MR images were performed using 1.5-Tesla Signa scanners (GE Medical Systems, Boston, MA). MRIcro software (University of Nottingham School of Psychology, Nottingham, UK; www.mricro.com) was used to convert images from DICOM to Analyze format for computer-assisted measurement of DWI volume (DWIv). Analysis of DWIv was performed on DWI sequences using a previously validated semiautomated method with high inter-rater reliability, adapted to the measurement of hyperintensity due to diffusion restriction.[16-18] Total DWIv was calculated using coregistered apparent diffusion coefficient sequences for lesion outline validation and following adjustment for intracranial area based on a previously validated protocol.[19] All MRI measurements were acquired prospectively by qualified readers (A.S.K., K.M.F., K.I.S., A.S.P.) blinded to clinical data.

Statistical Analysis

Statistical analyses were performed using SAS software (SAS 9.2, SAS Institute, Cary, NC). Continuous variables were expressed as mean ± standard deviation except for DWIv, which was expressed as median (interquartile range, IQR). Student's *t*-test, Wilcoxon rank-sum test, Fisher's exact test, and chi-square test were used in comparison of aspirin users versus nonusers, as appropriate. Quartiles of NIHSS scores (NIHSSq; Q1: 0-1, Q2: 2-3, Q3: 4-6, Q4: 7-36) were derived using a standard statistical approach and used in ordinal regression modeling of baseline stroke severity with prespecified P value < .05 for all association analyses. Multivariable model included variables associated with NIHSSq in the univariate analysis with a P value < .05.

Results

Six hundred ten patients with MRI available for acute infarct size analysis were included in this analysis. Of these patients, 241 (39.5%) used aspirin prior to their stroke onset. Patient demographics, clinical characteristics, and laboratory and imaging data categorized by aspirin users versus nonusers are summarized in Table 1.

Three hundred eighty-three (62.8%) patients were male, and distribution of sex was not statistically significant between patients who used aspirin prior to incident stroke and those who did not. Antecedent aspirin users were older (mean 68.3 ± 13.2 versus 62.6 ± 16.2 years; $P < .0001$). Vascular risk factors were frequent in our dataset, but hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, prior ischemic stroke, and prior transient ischemic attack (TIA) were significantly more common in aspirin users than nonusers (all $P < .05$). Use of tobacco and alcohol was not significantly different between aspirin users and nonusers. Median NIHSS was 2 in aspirin users and 3 in aspirin nonusers ($P = .16$). There