Influence of Antithrombotics on the Etiology of Intracerebral Hemorrhage

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Background: To determine the influence of antithrombotic use on the etiology of primary intracerebral hemorrhage (ICH). *Methods:* We conducted a retrospective review of consecutive patients admitted with primary ICH from 2009 to 2012. Data recorded included age, history of hypertension, and use of antithrombotic medications. Imaging was reviewed to determine hemorrhage location and the presence and the location of any microhemorrhages. Etiologies were classified using a predetermined algorithm, which was based on existing literature. *Results:* In total, 292 patients were included. Median age was 74 years (range, 18-101), and 52% were male (n = 151). Hemorrhage etiology was hypertension in 50.6% (n = 148), indeterminate in 29.5% (n = 86), and cerebral amyloid angiopathy (CAA) in 19.9% (n = 58). Most patients were on antithrombotics (61.3%, n = 179). Nearly half of the patients (49%) were 75 years of age or older, and the most common etiology in this group was hypertension (n = 77, 53%). There was a nonsignificant trend toward older age and CAA–ICH (median age, 77 years; interquartile range [IQR], 70-82 years) compared with other causes (median age, 74 years; IQR, 61-82 years; $P = .07$). There was no difference between CAA–ICH and other-cause ICH with respect to proportion of patients on antithrombotics in general (67% versus 60%; $P = .367$) or anticoagulants in particular (24% versus 25%; $P = 1.000$). *Conclusions:* The most common ICH etiology in this study was hypertension, regardless of age. Our findings do not suggest that the higher occurrence of ICH in older patients or in patients with CAA-associated ICH is because of a higher frequency of anticoagulant use. **Key Words:** Intracerebral hemorrhage—etiology—antithrombotics—anticoagulation—antiplatelet.

Introduction

Intracerebral hemorrhages (ICHs) can be devastating events that leave survivors with significant disability. Hypertension has historically been considered the main risk factor for primary ICH.[1,2] With improved treatment of hypertension, the incidence of ICH was expected to decrease. Unfortunately, recent studies have demonstrated that the incidence of ICH has remained unchanged.[3-5] However, the demographics of patients experiencing ICH have shifted, with a decrease in hemorrhages occurring in younger patients (<60 years) and an increase in patients 75 years of age or older.[3]

Cerebral amyloid angiopathy (CAA) has been recognized as a major risk factor for ICH, and the prevalence of CAA increases with age.[6,7] Several, recent, large population-based studies showed an increase in the use of antithrombotic medications over the last 3 decades.[3,8] Based on these findings, the shift in ICH demographics is thought to be secondary to a combination of CAA and increased use of antithrombotic medications.[3,8]

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Determining the etiology of a patient's ICH may identify specific risk factors for a given patient population and help clinicians guide treatment options in an effort to reduce the incidence of ICH.

In this study, we aimed to evaluate the influence of antithrombotic medication use on the etiology of ICH in a tertiary referral center over a 4-year period. We hypothesized that the use of antithrombotic medications would be higher in CAA–ICH as compared with other causes of ICH.

Materials and Methods

All patients admitted to Mayo Clinic Hospital, St. Mary's Campus in Rochester, Minnesota, with a primary ICH from 2009 to 2012 were screened for inclusion in this study. We excluded patients younger than 18 years of age, those with a known underlying vascular lesion or tumor, hemorrhagic conversion of ischemic stroke, or hemorrhage secondary to trauma. We reviewed the comprehensive medical record retrospectively and recorded demographic data, including gender, age, and use of any antiplatelet or anticoagulant medication. A patient was considered hypertensive if they had a prior diagnosis of hypertension in the medical record, were taking antihypertensive medications, or had evidence of left ventricular hypertrophy on their admission electrocardiogram (as determined by the official interpretation by the cardiologist). Available imaging studies, including computed tomography and magnetic resonance imaging (MRI), obtained after the ICH were reviewed. Hemorrhage location and the presence and the location of microhemorrhages by susceptibility-weighted or gradient-echo imaging on MRI were recorded when available. In patients who underwent surgical evacuation, the presence of pathologically confirmed amyloid angiopathy was recorded.

Algorithms to determine hemorrhage etiology were created using existing diagnostic criteria (including the Boston criteria for CAA) and published literature regarding imaging characteristics of various hemorrhage etiologies.[2,7,9-11] These algorithms were applied to our patient cohort to determine ICH etiology and are shown in Figures 1 and 2.

This study was approved by the Mayo Foundation Institutional Review Board. As this was a retrospective chart review, patient consent was not required.

Statistical Analysis

Categorical variables are presented as counts and frequencies. Continuous variables are described with means or medians as appropriate, given the distribution of data.

Univariate comparisons between dichotomous subgroups were carried out with the chi-square test or 2-sided Fisher exact test. Probability (*P*) values less

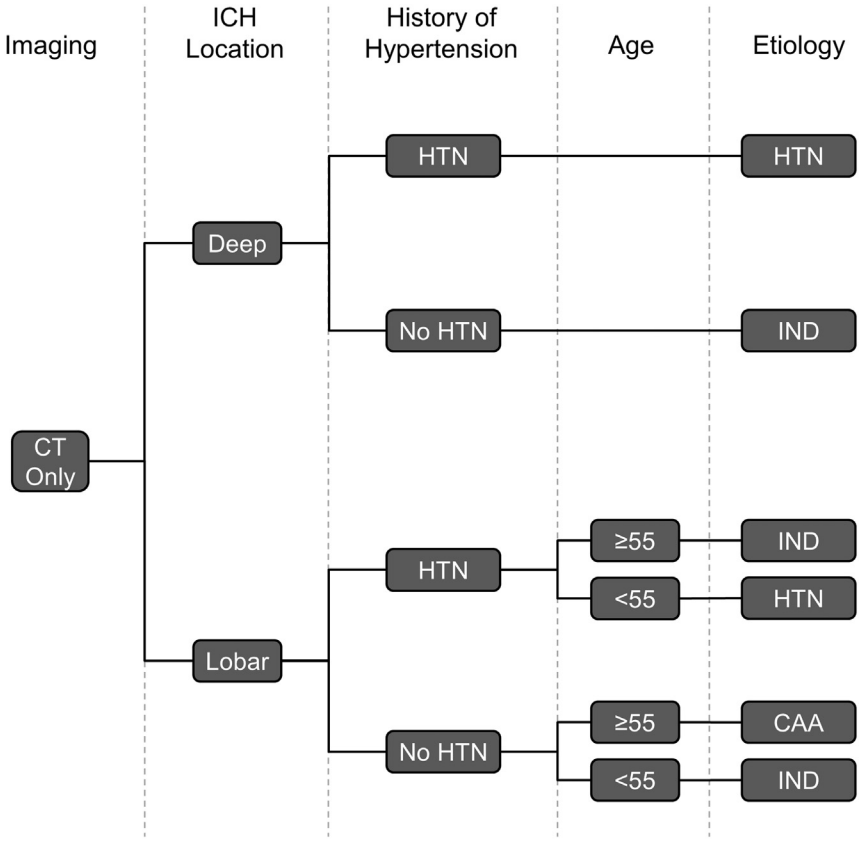

Figure 1. *Algorithm for patients without MRI. Abbreviations: CAA, cerebral amyloid angiopathy; CT, computed tomography; HTN, hypertension; ICH, intracerebral hemorrhage; IND, indeterminate; MRI, magnetic resonance imaging.*