

# Epidemiology of Acquired Immune Deficiency Syndrome and Cerebrovascular Disease in a Post Antiretroviral Era

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*Background:* People with acquired immune deficiency syndrome (AIDS) develop ischemic stroke through distinct mechanisms. These include infections such as syphilis, tuberculosis, varicella, and other conditions such as cocaine abuse, endocarditis, and hypercoagulability. The effect of improved awareness, detection, and treatment with highly active antiretroviral therapy (HAART) on the incidence and outcome of AIDS patients with stroke is unknown. *Methods:* Data from the Nationwide Inpatient Sample from 1995 to 2010 were analyzed. Patients with ischemic stroke and AIDS were identified using ICD-9 (International Classification of Diseases) codes. Time trends for demographics, survival, and frequency of AIDS-associated conditions were analyzed. *Results:* Proportion of AIDS among stroke patients increased significantly during the study. Median age of all strokes decreased from 75 years in 1995 to 72 years in 2010. Conversely, median age for men with stroke and AIDS increased from 43 years to 53 years; and for women with stroke and AIDS, from 41 years to 51 years. Death rates from stroke in the AIDS patients declined. In recent years, the death rates from stroke are similar to patients without HIV/AIDS. Stroke patients with AIDS had increased odds of syphilis (odds ratio [OR]: 33.50), varicella (OR: 48.34), tuberculosis (OR: 137.48), endocarditis (OR: 5.19), cocaine abuse (OR: 26.05), and hypercoagulability (OR: 4.82). *Conclusions:* In the HAART era, the median age of incident stroke in AIDS has increased and the mortality from stroke has improved. Research should focus on optimal management of dyslipidemia while on HAART. Whether HAART can reduce the incidence and improve survival of stroke needs to be explored. **Key Words:** Ischemic stroke—AIDS—HAART—trends—epidemiology.

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## Introduction

HIV/AIDS is an established risk factor for stroke. The risk of ischemic stroke for people with AIDS is increased severalfold.<sup>1</sup> People with HIV/AIDS develop ischemic stroke through a variety of unique mechanisms.

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HIV vasculopathy, infectious vasculitides secondary to tuberculosis, varicella zoster and syphilis, hypercoagulability, and cardiac embolism are some consequences of HIV infection that could result in ischemic stroke.<sup>2,3</sup> On the other hand, with increasing utilization of protease inhibitors in highly active antiretroviral therapy (HAART) regimens, severe dyslipidemia and premature atherosclerosis have increased in this population, further increasing the stroke risk.<sup>4</sup>

Over the last 2 decades, there have been major advances in the treatment of ischemic stroke and HIV/AIDS. Therapies such as tissue plasminogen activator (tPA), mechanical thrombectomy, and organization of stroke systems of care have successfully reduced disability and mortality from ischemic stroke. Development of new, highly effective HAART regimens has resulted in aging of the HIV population. Therefore, it is likely that there has been a significant shift in the demographics of people with HIV

who develop ischemic stroke as well as improvement in their mortality rates.

The objective of the study was to analyze the trends in the incidence and outcome of ischemic stroke among people with HIV/AIDS in different demographic groups, and changes in prevalence of AIDS-related conditions in people with stroke from 1995 to 2010.

## Methods

The Nationwide Inpatient Sample (NIS) is the largest all-payer inpatient care database in the United States. It was developed as part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality. It is a nationally representative database of a 20% sampling of inpatient hospitalizations across the country. It includes data from 19 states in the year 1995, expanding annually to include 45 states in 2010. The database serves as a powerful tool to detect trends in disease incidence, comorbidities, and outcomes of inpatient hospitalizations.

Data from 1995 to 2010 were included in the study. Patient hospitalization records with primary or secondary diagnosis of ischemic stroke were identified using ICD-9 (International Classification of Diseases) codes (Table 1). Patients with HIV/AIDS were identified using the ICD-9 codes 042 (HIV disease, including AIDS, AIDS-like syndrome, AIDS-related complex, symptomatic HIV infection, and HIV-1), 079.53 (HIV-2), and V08 (asymptomatic HIV).

**Table 1.** ICD-9 codes used to identify acute ischemic stroke discharges and the subset of patients carrying a diagnosis of HIV/AIDS

Primary and secondary diagnostic codes	
Ischemic stroke	
433.11	Occlusion and stenosis of the carotid artery with cerebral infarction
433.31	Occlusion and stenosis of multiple and bilateral precerebral arteries with cerebral infarction
433.81	Occlusion and stenosis of other specified precerebral artery with cerebral infarction
433.91	Occlusion and stenosis of unspecified precerebral artery with cerebral infarction
434.01	Cerebral thrombosis with cerebral infarction
434.11	Cerebral embolism with cerebral infarction
434.91	Cerebral artery occlusion unspecified with cerebral infarction
436	Acute but ill-defined cerebrovascular disease
HIV/AIDS	
042	HIV disease, including AIDS, AIDS-like syndrome, AIDS-related complex, symptomatic HIV infection, and HIV-1
79.53	HIV-2 infection
V08	Asymptomatic HIV infection

Abbreviation: ICD-9, International Classification of Diseases.

As HIV/AIDS would not be the primary admitting diagnosis in the subset of patients under study, including all 3 codes would improve the sensitivity of detecting patients with an HIV diagnosis. We also identified certain AIDS-related conditions relevant to ischemic stroke using ICD-9 codes. These included varicella zoster, syphilis, central nervous system (CNS) tuberculosis, cocaine abuse, infective endocarditis, and hypercoagulable states.

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC). Age trends were compared between stroke patients with and without HIV/AIDS. In both subsets, the analysis was repeated for gender (male versus female) subgroups. Mortality rates from stroke over time were compared between the HIV/AIDS and non-HIV/AIDS groups, and between gender and race subgroups. Home discharge (versus discharge to a rehabilitation setting/nursing home) was used as a surrogate for good recovery from stroke. The rates of home discharge over time were compared between the 2 groups. Assuming a priori that the subset of patients with HIV/AIDS would be younger than the non-HIV group, comparison of outcomes (mortality and home discharge) between the groups was repeated among young stroke patients (<50 years of age) to exclude the influence of age on the outcome from stroke. Finally, trends in the proportions of patients with certain AIDS-related conditions relevant to stroke were examined. The Cochran Armitage test was used to evaluate all time trends.

The study was conducted using a pre-existing database with deidentified patient information. Therefore, it received an exemption from review by the Wayne State University Institutional Review Board. The investigator analyzing the data (P.B.) completed the data use agreement training, required by the HCUP.

## Results

Over the 16 years of analyzed data, there were 1,874,067 hospitalizations for ischemic stroke. The number of stroke hospitalizations has decreased over time. Stroke admissions decreased from 124,925 in 1995 to 105,639 in 2007 (the year with the lowest stroke hospitalizations) and 114,477 in 2010 (trend  $P$  value < .0001).

The proportion of people living with HIV/AIDS has increased in the stroke population (Fig 1). The number of stroke patients carrying a diagnosis of HIV/AIDS rose from 272 hospitalizations in 1995 (.22% of all ischemic strokes) to 462 hospitalizations in 2010 (.4% of all ischemic strokes); trend  $P$  < .0001. This trend was true for both men and women. The proportion of stroke hospitalizations with HIV/AIDS diagnosis increased from .35% in 1995 to .59% in 2010 among men; and from .11% in 1995 to .24% in 2010 among women. For each year during the study period, the proportion of stroke patients with HIV/AIDS was significantly higher among men than women (Table 2). A significantly higher proportion of persons with

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