Differential Impact of Index Stroke on Dementia Risk in African-Americans Compared to Whites

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Objective: To compare whites and African-Americans in terms of dementia risk following index stroke. *Methods:* The data consisted of billing and International Classification of Diseases, Ninth Revision diagnosis codes from the South Carolina Revenue and Fiscal Affairs office on all hospital discharges within the state between 2000 and 2012. The sample consisted of 68,758 individuals with a diagnosis of ischemic stroke prior to 2010 (49,262 white [71.65%] and 19,496 African-Americans [28.35%]). We identified individuals in the dataset who were subsequently diagnosed with any of 5 categories of dementia and evaluated time to dementia diagnosis in Cox Proportional Hazards models. We plotted cumulative hazard curves to illustrate the effect of race on dementia risk after controlling for age, sex, and occurrence of intervening stroke. *Results:* Age at index stroke was significantly different between the 2 groups, with African-Americans being younger on average (70.0 [SD 12.5] in whites versus 64.5 [SD 14.1] in African-Americans, $P < .0001$). Adjusted hazard ratios revealed that African-American race increased risk for all 5 categories of dementia following incident stroke, ranging from 1.37 for AD to 1.95 for vascular dementia. Age, female sex, and intervening stroke likewise increased risk for dementia. *Conclusions:* African-Americans are at higher risk for dementia than whites within 5 years of ischemic stroke, regardless of dementia subtype. Incident strokes may have a greater likelihood of precipitating dementia in African-Americans due to higher prevalence of nonstroke cerebrovascular disease or other metabolic or vascular factors that contribute to cognitive impairment.

Key Words: Alzheimer's disease—stroke—dementia—MCI (mild cognitive impairment)—survival analysis

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Introduction

Stroke and dementia share a number of risk factors, including hypertension and diabetes,[1-4] and stroke approximately quadruples the risk of dementia.[5,6] Prevalence of dementia among those with stroke is approximately equal to that in individuals without stroke who are 10 years older.[5] Cerebrovascular disease contributes to a majority of cases of dementia evaluated with autopsy.[7-9] These observations suggest that the burden of common forms of dementia may be mitigated by aggressive stroke prevention measures.

Both stroke and dementia are leading causes of serious disability, and spare no age, sex, or ethnic origin. However, African-Americans are more impacted by stroke than any other racial group.[10] In addition, African-Americans are at higher risk than whites for dementia.[11,12]

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Hypertension and other vascular risk factors likely underlie both of these disparities. Racial differences in the incidence of dementia among people with established cerebrovascular disease have not been well studied, especially in the highly stroke-prone southeastern US region. Such an investigation could lead to clinical research that informs the most appropriate treatment regimes, including modifications of recommendations based on physiological or behavioral differences.

Methods

Statewide encounter-level data were obtained from the South Carolina Revenue and Fiscal Affairs Office, which monitors all uniformed billing data for emergency department (ED) and inpatient discharges in the state, with the exception of Veterans Affairs or military health systems. Death certificate information, provided by the state Department of Health and Environment Control were linked to the discharge database. Individuals at least 18 years old with a primary diagnosis of ischemic stroke (*International Classification of Diseases, Ninth Revision (ICD-9), Clinical Modification* 433.00-434.91 and 436) between 2000 and 2010 were identified. For individuals meeting criteria, data on all other inpatient and ED encounters from 2000 to 2012 regardless of diagnosis were obtained.

Analyses were limited to non-Hispanic African-American/black and white subjects as other race groups composed <2% of the sample. The final sample included 68,758 individuals, of whom 49,262 (71.65%) were white and 19,496 (28.35%) were African-American.

As a first analysis step, index (initial) strokes were identified. Individuals with transient ischemic attack or hemorrhagic stroke were not excluded, but these diagnoses were not considered index strokes (4511 individuals with previous events in these categories). Data following index strokes occurring prior to 2008 were censored at 5 years (1825 days) or at the date of death if it occurred within 5 years of discharge. Those occurring during or after 2008 were censored at December 31st, 2012 or at the time of death if it occurred prior to that date. Individuals with any dementia diagnosis prior to index stroke were excluded, but those with initial dementia diagnosis coincident with index stroke were retained and time to diagnosis was set at 0 days. Case fatalities at time of index stroke were excluded from analyses.

Second, dementia diagnoses were identified and sorted into codes representing Alzheimer disease (AD—8 ICD-9 codes), vascular dementia (4 ICD-9 codes), Alzheimer disease-related dementias (ADRD—13 additional codes distinct from the AD and vascular dementia codes), and non-ADRD (10 other ICD-9 dementia codes). We defined the outcome of "all-type" dementia as any dementia diagnosis code. We excluded diagnosis codes for neurodegenerative diseases that do not entail dementia, such as amyotrophic lateral sclerosis and Parkinson's disease. Codes used for each category are listed in the Supplementary data. "Cases" were defined (for each analysis) as individuals who never received any dementia diagnosis prior to index stroke, but at some point subsequently received a dementia diagnosis code (respectively, any code for all-type dementia, ADRD, AD, non-ADRD, or vascular dementia).

Time to dementia diagnosis was entered as the dependent variable into Cox Proportional Hazards (CPH) regression models. For each dementia diagnosis type, we assessed the racial composition of the sample in unadjusted analysis. Predictor variables in the adjusted CPH models included age, sex, race, intervening stroke, and the interaction of race and intervening stroke, where intervening stroke was defined as the presence of any stroke after the index stroke but prior to dementia diagnosis, death, or censoring. Cumulative hazard plots were generated to illustrate differences in dementia risk by race over 5 years of follow up, after adjusting for the other predictors. Stepwise selection was used to determine significant risk factors for each dementia diagnosis type via adjusted CPH models stratified by intervening stroke status. All analyses were performed using SAS v9.4 (SAS Institute, Inc., Cary, NC). All P values were 2-sided and considered significant at $P < .05$. This study was approved by the Medical University of South Carolina's Institutional Review Board.

Results

The analytic sample included 68,758 nondemented individuals with ischemic stroke, of whom 71.65% were white and 28.35% black or African-American, 49% male, with

Table 1. *Unadjusted racial comparison of dementia within 5 years of index stroke by subtype*

Dementia sub type, n (%)	Total (n = 68,758)	White (n = 49,262)	African-American (n = 19,496)	Unadjusted HR (95% CI)	P value
All-cause	9,163 (13.33)	6,240 (12.67)	2,923 (14.99)	1.22 (1.17, 1.28)	<.0001
ADRD	8350 (12.14)	5694 (11.56)	2656 (13.62)	1.21 (1.16, 1.27)	<.0001
Alzheimer's disease	4604 (6.70)	3320 (6.74)	1284 (6.59)	.99 (.93, 1.06)	.8649
Vascular dementia	3340 (4.86)	2021 (4.10)	1319 (6.77)	1.69 (1.58, 1.82)	<.0001
Non-ADRD	4182 (6.08)	2982 (6.05)	1200 (6.16)	1.04 (.97, 1.11)	.2832

ADRD, Alzheimer disease-related dementias; CI, confidence interval; HR, hazard ratios.