Racial differences in recurrent ischemic stroke risk and recurrent stroke case fatality

Karen C. Albright, DO, MPH, Lei Huang, PhD, Justin Blackburn, PhD, George Howard, DrPH, Michael Mullen, MD, Vera Bittner, MD, MSPH, Paul Muntner, PhD, and Virginia Howard, PhD

Neurology® 2018;91:e1741-e1750. doi:10.1212/WNL.0000000000006467

Correspondence

Dr. Albright
albrighk@upstate.edu

Abstract

Objective

To determine black-white differences in 1-year recurrent stroke and 30-day case fatality after a recurrent stroke in older US adults.

Methods

We conducted a retrospective cohort study using a 5% random sample of Medicare beneficiaries with fee-for-service health insurance coverage who were hospitalized for ischemic stroke between 1999 and 2013. Hazard ratios for recurrent ischemic stroke and risk ratios for 30-day case fatality comparing blacks to whites were calculated with adjustment for demographics, risk factors, and competing risk of death when appropriate.

Results

Among 128,789 Medicare beneficiaries having an ischemic stroke (mean age 80 years [SD 8 years], 60.4% male), 11.1% were black. The incidence rate of recurrent ischemic stroke per 1,000 person-years for whites and blacks was 108 (95% confidence interval [CI], 106–111) and 154 (95% CI 147–162), respectively. The multivariable-adjusted hazard ratio for recurrent stroke among blacks compared with whites was 1.36 (95% CI 1.29–1.44). The case fatality after recurrent stroke for blacks and whites was 21% (95% CI 21%–22%) and 16% (95% CI 15%–18%), respectively. The multivariable-adjusted relative risk for mortality within 30 days of a recurrent stroke among blacks compared with whites was 0.82 (95% CI 0.73–0.93).

Conclusion

The risk of stroke recurrence among older Americans hospitalized for ischemic stroke is higher for blacks compared to whites, while 30-day case fatality after recurrent stroke remains lower for blacks.

From the Departments of Epidemiology (K.C.A., L.H., P.M., V.H.), Health Care Organization and Policy (J.B.), Biostatistics (G.H.), and Medicine (V.B.), University of Alabama at Birmingham; Geriatric Research, Education and Clinical Center (K.C.A.), Birmingham VA Medical Center, AL; and Department of Neurology (M.M.), University of Pennsylvania, Philadelphia.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

CI = confidence interval; **HR** = hazard ratio; **ICD-9-CM** = *International Classification of Diseases, 9th edition, clinical modification*; **NOMAS** = Northern Manhattan Study; **PROFESS** = Prevention Regimen for Effectively Avoiding Second Strokes; **PROGRESS** = Perindopril Protection Against Recurrent Stroke Study; **REGARDS** = Reasons for Geographic and Racial Differences in Stroke; **RR** = relative risk; **SPARCL** = Stroke Prevention by Aggressive Reduction in Cholesterol Levels; **VISP** = Vitamin Intervention for Stroke Prevention.

As a leading cause of disability¹ and the fifth leading cause of death,² stroke is considered a substantial public health concern in the United States.³ Each year, ≈610,000 US adults experience their first stroke, and despite secondary stroke prevention, 185,000 US adults experience a recurrent stroke.⁴ An analysis of Medicare beneficiaries found that recurrent stroke is more disabling and costly than a first stroke.⁵

Compared to whites, surveillance and longitudinal cohort studies have shown that blacks have a 1.5 to >3 times higher incidence rate of ischemic stroke.^{6–10} While a higher incidence rate of stroke has been consistently reported for blacks compared with whites, studies on racial differences in recurrent stroke have produced conflicting results. The scientific statement from the American Heart Association/American Stroke Association on racial-ethnic disparities in stroke care¹¹ reported 2 studies that suggest that recurrent stroke risk is higher among blacks than whites: a prospective cohort from a single New York hospital¹² and a retrospective cohort created from California administrative data.¹³ However, the evidence that blacks have a higher risk of recurrent stroke than whites was not present in 2 hospital-based prospective cohort studies,^{14,15} 1 national cohort study,¹⁶ and a secondary data analysis of a randomized trial.¹⁷

While data on black-white differences in recurrent stroke rate are conflicting, there are few data on black-white differences in 30-day case fatality after recurrent ischemic stroke. Although studies suggest that the 30-day case fatality rate after recurrent stroke may be as high as 4 times the rate after incident stroke,^{8,18} few data are available on racial differences in case fatality. The purpose of this analysis is to determine whether black-white differences exist in recurrent stroke and 30-day case fatality after a recurrent stroke in older US adults. In addition, we evaluated black-white differences in recurrent stroke in calendar periods reflecting the use of antithrombotic agents,^{19–23} angiotensin-converting enzyme inhibitors and diuretics,²⁴ and statins²⁵ in an effort to determine whether advances in secondary stroke prevention medications are broadening or closing racial disparities.

Methods

Study cohort

We conducted a retrospective cohort study of a 5% sample of white and black Medicare beneficiaries hospitalized with an overnight stay for an ischemic stroke with an admission date

on or after January 1, 1999, and a discharge date on or before December 31, 2012. Medicare is a US government program that provides health insurance for adults ≥65 years of age and younger adults with end-stage renal disease or who are disabled. The Medicare Master Beneficiary Summary File and fee-for-service Part A (inpatient) and B (outpatient) claims were used for the current analyses. Beneficiaries enrolled in Medicare Advantage plans (Medicare Part C coverage) were excluded because complete claims data were not available for these beneficiaries. Data were obtained from the Centers for Medicare & Medicaid Services data warehouse.

Index stroke events were identified by an ICD-9-CM code of 433.x1, 434.x1, or 436 in any discharge diagnosis position in an inpatient file claim. We excluded beneficiaries if their index stroke hospitalization duration was >30 days, if they died in the hospital, or if they were discharged to hospice. Patients with hospital a length of stay >30 days were excluded because they have been shown to differ from patients with shorter length of stay in terms of severity of current illness, as well as the presence and control of medical comorbid conditions.²⁶ Patients who were discharged to hospice were excluded because their treatment plan often differs from those placed on intensive medical therapy. Additional eligibility for the current analysis included (1) age ≥66 years but <110 years at the time of hospital admission for the index stroke event; (2) black or white race; (3) continuous fee-for-service coverage, defined as Medicare Parts A and B for the 182 days before the index stroke hospitalization (i.e., the “look-back period”) to identify the presence of comorbid conditions; (4) living in the United States during the entire look-back period; and (5) no hospitalizations for ischemic stroke during the look-back period.^{5,27–29} We restricted the analysis to participants ≥66 years of age (i.e., ≥65 years of age at the start of the look-back period) because Medicare beneficiaries <65 years of age are not representative of the general population. If a Medicare beneficiary had >1 hospitalization for ischemic stroke meeting the above criteria, only the earliest eligible hospitalization was included, resulting in a final cohort of 128,789 Medicare beneficiaries (figure 1).

Exposure/covariates

Information on age, sex, and race was obtained from the Master Beneficiary Summary File. Race was self-reported by beneficiaries when they first applied for Medicare coverage. We used dual eligibility for Medicare and Medicaid (i.e., dual-eligible status or state buy-in from the entitlement variable) at

Figure 1 Exclusion cascade

HMO = health maintenance organization; ICD-9 = *International Classification of Diseases, 9th edition*.

any time during the look-back period, identified in the Master Beneficiary Summary File, as a proxy of low socioeconomic status. Comorbid conditions, including atrial fibrillation, hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, heart failure, dementia, depression, and chronic kidney disease, were defined from claims during the look-back period and previously published algorithms (data available from Dryad, table e-1, doi.org/10.5061/dryad.9f646f2).^{30,31} Hospitalizations during the look-back period were identified from Part A claims. The presence of a skilled nursing facility stay on hospital discharge for the index stroke event was determined with Part A claims.

Outcomes

Recurrent ischemic strokes were defined by an overnight hospitalization for ischemic stroke, ICD-9-CM code 433.x1, 434.x1, or 436 in any discharge diagnosis position in an inpatient file, within the 365 days after hospital discharge for the index stroke. A sensitivity analysis was done using ischemic

stroke ICD-9-CM codes only in the primary discharge diagnosis position. Thirty-day case fatality was defined as a death within 30 days of hospital admission for recurrent stroke. Deaths were identified with the Master Beneficiary Summary File.

Time periods

We studied event rates for index strokes occurring during 3 calendar periods: 1999 to 2001, 2002 to 2006, and 2007 to 2013 (data available from Dryad, figure e-1, doi.org/10.5061/dryad.9f646f2). The first calendar period (1999–2001) was selected to represent the time period before publication of the Perindopril Protection Against Recurrent Stroke Study (PROGRESS), which was published on September 29, 2001.³² PROGRESS was a randomized clinical trial that confirmed the efficacy of an angiotensin-converting-enzyme inhibitor (perindopril) and a diuretic (indapamide) in preventing recurrent stroke. The second calendar period (2002–2006) was selected to begin the calendar year after

PROGRESS was published, allowing for dissemination of results, through the year that the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial was published (publication date August 10, 2006).²⁵ SPARCL was a randomized clinical trial that demonstrated the efficacy of a statin (atorvastatin) in preventing recurrent stroke. The third calendar period (2007–2013) was chosen to begin the calendar year after the publication of SPARCL and to include the remaining years for which we had Medicare data.

Statistical analysis

Characteristics of Medicare beneficiaries hospitalized for ischemic stroke were calculated by race. The cumulative incidence and recurrent ischemic stroke rate within 1 year after hospital discharge for the index stroke were determined for whites and blacks separately for each of the calendar periods. Hazard ratios (HRs) for recurrent stroke comparing blacks and whites were calculated with the extension of the Cox regression accounting for the competing risk for mortality.^{33,34} HRs were adjusted for age, sex, dual eligibility, Charlson score, hospitalization for any cause during the look-

back period, length of stay for the index stroke, being discharged home after the index stroke, skilled nursing facility stay, and previously described comorbid conditions. The statistical significance of differences in the black-white recurrent stroke rates and HR for recurrent stroke between calendar periods was assessed with multiplicative interaction terms (e.g., race × calendar period).

The proportion of Medicare beneficiaries dying within 30 days of their recurrent ischemic stroke (i.e., 30-day case fatality) was calculated for blacks and whites separately. Relative risks (RRs) for 30-day case fatality comparing blacks to whites were calculated with generalized linear models with a Poisson distribution, a log link, and a robust variance estimator.³⁵ This model included adjustment for the same covariates used in the HR calculations described above. The statistical significance of differences in 30-day case fatality and the black-white RR between calendar periods was assessed with multiplicative interaction terms (e.g., race × calendar period). Evidence of interaction was determined by an a priori 2-sided alpha level of 0.10. In

Table 1 Characteristics of black and white Medicare beneficiaries hospitalized for ischemic stroke between 1999 and 2013

Characteristic	White (n = 114,453)	Black (n = 14,336)
Age, y	80.3 (7.8)	77.9 (8.1)
Women, n (%)	68,626 (60.0)	9,115 (63.6)
Low-income subsidy, n (%)	16,006 (14.0)	6,143 (42.9)
Charlson score categories, n (%)		
0–1	44,085 (38.5)	4,912 (34.3)
2–3	28,944 (25.3)	3,161 (22.0)
≥4	41,424 (36.2)	6,263 (43.7)
History of atrial fibrillation, n (%)	22,140 (19.3)	1,492 (10.4)
History of hypertension, n (%)	53,110 (46.4)	8,229 (57.4)
History of hyperlipidemia, n (%)	11,178 (9.8)	1,220 (8.5)
History of diabetes mellitus, n (%)	22,292 (19.5)	4,520 (31.5)
History of coronary heart disease, n (%)	33,823 (29.6)	3,532 (24.6)
History of heart failure, n (%)	14,937 (13.1)	2,180 (15.2)
History of chronic kidney disease, n (%)	13,104 (11.4)	2,682 (18.7)
History of dementia, n (%)	14,385 (12.6)	2,296 (16.0)
History of depression, n (%)	6,214 (5.4)	570 (4.0)
Hospitalization for any cause during baseline period, n (%)	28,842 (25.2)	4,033 (28.1)
Length of stay, d	8.9 (6.8)	10.3 (7.3)
Discharged home, n (%)	61,961 (54.1)	8,224 (57.4)
Skilled nursing facility stay, n (%)	39,140 (34.2)	4,714 (32.9)

Age and length of stay are expressed as mean (SD).

Figure 2 Cumulative incidence of 1-year recurrent ischemic stroke in blacks and whites over time, accounting for the competing risk of death

a final analysis, the black-white HR of 1-year recurrent ischemic stroke and the black-white RR for case fatality were evaluated in subgroups defined by each of the covariates in the multivariable-adjusted models. In the sensitivity analyses, we calculated the recurrent ischemic stroke rate within 1 year after hospital discharge for the index stroke for whites and blacks as previously described, first restricting our definition of ischemic stroke to those with a primary diagnosis code for ischemic stroke and then restricting our sample to individuals with a 2-year look-back period.

All analyses were conducted with SAS 9.4 (SAS Institute, Research Triangle Park, NC). The institutional review board at the University of Alabama at Birmingham and Centers for Medicare & Medicaid Services approved the study.

Data availability

The data used in this analysis include restricted Medicare claims data and therefore cannot be made publicly available because of ethical/legal restrictions.

Results

Of 128,789 Medicare beneficiaries having an ischemic stroke (mean age 80 years [SD 8 years], 11.1% black, 60.4% male), blacks ($n = 14,336$) were younger, more frequently received a low-income subsidy, and had a lower prevalence of atrial fibrillation and a higher prevalence of hypertension, diabetes mellitus, and chronic kidney disease when compared to whites ($n = 114,453$, table 1).

Risk of 1-year recurrent ischemic stroke in whites and blacks

There were 10,450 recurrent ischemic strokes over the 1 year after hospital discharge for the index stroke. The cumulative incidence of recurrent ischemic stroke was higher for blacks compared with whites for each calendar period (figure 2). The incidence rates of recurrent ischemic stroke for whites and blacks were 108 and 154 per 1,000 person-years, respectively (table 2). Recurrent ischemic stroke rates declined over the calendar periods for both whites (p for trend < 0.001) and blacks (p for trend $= 0.009$). There was no difference in the decline in recurrent ischemic stroke rates between blacks and whites (p for interaction $= 0.484$). Blacks had a higher risk for recurrent ischemic stroke compared to whites during the overall study period (adjusted HR 1.36, 95% confidence interval [CI] 1.29–1.44) and within each of the 3 calendar periods. The adjusted black-white HR for recurrent stroke was 1.38 (95% CI 1.29–1.47) when outcomes were restricted to

Table 2 Incidence rates and HRs for 1-year recurrent ischemic stroke in black compared to white Medicare beneficiaries

	1999–2013 (all years)		1999–2001		2002–2006		2007–2013	
	Whites ($n = 114,453$)	Blacks ($n = 14,336$)	Whites ($n = 24,164$)	Blacks ($n = 3,014$)	Whites ($n = 42,012$)	Blacks ($n = 5,423$)	Whites ($n = 48,277$)	Blacks ($n = 5,899$)
No. of recurrent ischemic strokes/No. at risk	8,876	1,574	2,094	375	3,371	587	3,411	612
Incidence rates (95% CI) for recurrent ischemic stroke	108 ^a (106–111)	154 ^a (147–162)	117 (112–122)	170 (153–187)	109 (105–113)	147 (135–159)	103 (100–106)	153 (141–165)
HR (95% CI)	1 (Referent)	1.36 ^b (1.29–1.44)	1 (Referent)	1.39 (1.24–1.55)	1 (Referent)	1.30 (1.19–1.42)	1 (Referent)	1.41 (1.29–1.54)

Abbreviations: CI = confidence interval; HR = hazard ratio.

Values are expressed as counts, incidence rates (per 1,000 person-years), and HRs with 95% CIs. Adjusted for age; sex; low-income subsidy; Charlson score; history of atrial fibrillation, hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, heart failure, chronic kidney disease, dementia, or depression; hospitalization for any cause during the baseline period; length of stay; discharged home after the index hospitalization; and skilled nursing facility stay after the index hospitalization, accounting for the competing risk of death.

^a Recurrent ischemic stroke rates declined over the calendar periods for both whites (p for trend < 0.001) and blacks (p for trend $= 0.009$).

^b The black-white HR did not change over the calendar period (p for interaction $= 0.484$).

hospitalizations with a primary diagnosis code for ischemic stroke (data available from Dryad, table e-2, doi.org/10.5061/dryad.9f646f2) and 1.36 (95% CI 1.28–1.45) when the look-back period was expanded to 2 years (data available from Dryad, table e-3).

The race-specific recurrent ischemic stroke rate within subgroups is shown in data available from Dryad (table e-4, doi.org/10.5061/dryad.9f646f2). After multivariable adjustment, blacks had a higher risk of recurrent ischemic stroke compared to whites in all subgroups investigated (figure 3) except

Figure 3 Forest plot for adjusted hazard ratios and 95% confidence intervals for 1-year recurrent ischemic stroke among patients hospitalized with index ischemic stroke

AF = atrial fibrillation; CHD = coronary heart disease; CKD = chronic kidney disease; HF = heart failure; SNF = skilled nursing facility.

for those with a history of depression. Among those with a history of depression, the HR for recurrent stroke comparing blacks and whites was 1.26 (95% CI 0.94–1.68). The black-white HR for recurrent ischemic stroke differed by length of stay for the index hospitalization (p for interaction = 0.016). The black-white HR for recurrent stroke was 1.47 (95% CI 1.33–1.61), 1.35 (95% CI 1.22–1.50), and 1.26 (95% CI 1.14–1.39) for those with a length of stay for their index stroke hospitalization ≤ 5 , 6 to 9, and ≥ 10 days, respectively.

Thirty-day case fatality in whites and blacks

Between 1999 and 2013, 21% of whites died within 30 days of their recurrent stroke compared to 16% of blacks (table 3). Case fatality was lower in blacks compared with whites in each of the study periods. The 30-day case fatality did not change over time for whites (p for trend = 0.845) or blacks (p for trend = 0.459). After multivariable adjustment, blacks had a lower risk of 30-day case fatality after their recurrent stroke compared with whites during the overall study period (RR 0.82, 95% CI 0.73–0.93). There was no difference in the change in 30-day case fatality between blacks and whites over time (p for interaction = 0.7089). The adjusted black-white RR of 30-day case fatality after recurrent stroke was 0.79 (95% CI 0.67–0.92) when recurrent strokes were restricted to those with a primary diagnosis code for ischemic stroke (data available from Dryad, table e-5, doi.org/10.5061/dryad.9f646f2) and 0.80 (95% CI 0.69–0.91) when the look-back period was expanded to 2 years (data available from Dryad, table e-6).

Race-specific 30-day case fatality rates are presented for subgroups in data available from Dryad (table e-7, doi.org/10.5061/dryad.9f646f2). A lower 30-day case fatality was present among blacks compared with whites in most subgroups (figure 4). Black race was not associated with lower case-

fatality among beneficiaries with a Charlson score of ≤ 1 (HR 1.09, 95% CI 0.88–1.35), with a history of chronic kidney disease (HR 1.00, 95% CI 0.79–1.26), without a history of hypertension (HR 0.96, 95% CI 0.81–1.15), or without a history of dementia (HR 0.89, 95% CI 0.78–1.01).

Discussion

There are several important findings from this study. First, blacks had a higher 1-year risk for recurrent stroke compared with whites. This increased risk was present in the overall population and the majority of subgroups investigated. Second, recurrent ischemic stroke rates decreased over time for whites and blacks, with no difference in the rate of decline by race. In the most recent time period, blacks still had a 41% higher risk than whites. Third, blacks had a lower 30-day case fatality after hospitalization for recurrent ischemic stroke in the overall population and in the majority of the subgroups investigated. Fourth, 30-day case fatality did not change over time for whites or blacks.

In an analysis of older stroke patients discharged from California hospitals, blacks were found to have a higher risk of recurrent stroke than whites.¹³ This increased risk in blacks was not present in the South London Stroke Register³⁶ or the Northern Manhattan Study (NOMAS),^{14,15} perhaps due to the small number of recurrent stroke events and sampling from a single geographic area. However, the Prevention Regimen for Effectively Avoiding Second Strokes (PROFESS) trial, which enrolled 20,232 patients at 695 centers in 35 countries from North America, Latin America, Occidental and Eastern Europe, Africa, and Australasia, also did not find a significant difference in recurrent stroke among ethnicities (Hispanics, Asian, white, black).³⁷ Although it did not reach statistical significance, a potentially

Table 3 Rate and RR of 30-day case fatality after recurrent ischemic stroke among black compared to white Medicare beneficiaries with recurrent ischemic stroke, fully adjusted

	1999–2013 (all years)		1999–2001		2002–2006		2007–2013	
	Whites (n = 8,876)	Blacks (n = 1,574)	Whites (n = 2,094)	Blacks (n = 375)	Whites (n = 3,371)	Blacks (n = 587)	Whites (n = 3,411)	Blacks (n = 612)
No. of deaths within 30 d of recurrent ischemic stroke	1,900	256	427	68	762	91	711	97
Case fatality rate (95% CI) among those with recurrent ischemic stroke	0.21 ^a (0.21–0.22)	0.16 ^a (0.15–0.18)	0.20 (0.19–0.22)	0.18 (0.15–0.22)	0.23 (0.21–0.24)	0.16 (0.13–0.19)	0.21 (0.20–0.22)	0.16 (0.13–0.19)
Adjusted black-white RR (95% CI)^b	1 (Referent)	0.82 ^b (0.73–0.93)	1 (Referent)	0.93 (0.74–1.17)	1 (Referent)	0.74 (0.61–0.91)	1 (Referent)	0.83 (0.69–1.01)

Abbreviations: CI = confidence interval; RR = relative risk.

Values are expressed as counts and RR with 95% CI. Adjusted for age; sex; low-income subsidy; Charlson score; history of atrial fibrillation, hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, heart failure, chronic kidney disease, dementia, or depression; hospitalization for any cause during baseline period; length of stay; discharged home after the index hospitalization; and skilled nursing facility stay after the index hospitalization.

^a Case fatality did not decline over the calendar periods for whites (p for trend = 0.8450) or blacks (p for trend = 0.4589).

^b The black-white RR did not change over calendar period (p for interaction = 0.7089).

Figure 4 Forest plot for adjusted hazard ratios and 95% confidence intervals for 30-day case fatality after hospitalization for ischemic stroke

higher risk of recurrent stroke was identified in blacks compared to whites in the secondary analysis of the Vitamin Intervention for Stroke Prevention (VISP) trial, which was performed at 56 centers across the United States, Canada, and Scotland.¹⁷ However, this analysis did not study recurrent strokes after a cardioembolic stroke, raising concern about the generalizability of its findings to the older population. The current findings differ from those of the Reasons for Geographic and Racial Differences in Stroke

(REGARDS) study, in which blacks did not have a higher recurrent stroke risk than whites.¹⁶ While the current analysis and that of California hospital discharges focused on short-term stroke recurrence (≤ 1 year), REGARDS examined recurrent stroke over a longer time horizon (average 6.8 years). The current study focused on older Americans who experienced their index stroke at an average age of 80 years. The average stroke survivor in REGARDS was 69 years old and reported a prior stroke at an average age of

55 years. The effect of this difference in age is not known. However, given that the risk of recurrent stroke is highest in the first 6 months after stroke,³⁸ it is possible that the recent temporal proximity of the prior stroke is a contributing factor to stroke risk.

The key finding is that recurrent ischemic stroke incidence rates have declined over time for both whites and blacks. This decline in recurrent ischemic stroke may be a function of improved risk factor control and improved selection of agents shown to be efficacious at reducing recurrent stroke risk. However, blacks still have a higher risk compared to whites. In fact, the risk of recurrent stroke for blacks in the most recent period (2007–2013) is greater than the risk for whites in the earliest period (1999–2001). Further efforts are needed to reduce the risk of recurrent stroke and to eliminate this racial disparity.

The lower 30-day case fatality observed in blacks may be a function of racial differences in the subtype of ischemic stroke. Whites have a higher incidence of atrial fibrillation,^{39,40} with cardioembolic stroke having the highest mortality.⁴¹ It is possible that older black Americans are having strokes due to atherosclerosis, which have the highest risk of recurrent stroke⁴¹; conversely, older white Americans are having cardioembolic strokes, which have the highest mortality.⁴¹ It is less likely that blacks are experiencing lower 30-day case fatality and higher stroke recurrence due to lacunar infarcts, given that lacunar infarcts have been shown to have the lowest 1-year recurrence.^{41,42} The use of administrative data limits our access to granular clinical data that would allow us to explore these issues. The lower 30-day case fatality in blacks may also be a function of patient/family preferences regarding end-of-life care. Compared to whites, black patients less frequently have a living will and more frequently desire the use of life-sustaining measures.⁴³ Investigating end-of-life preferences was beyond the scope of the current analysis.

The 30-day case fatality after recurrent stroke was estimated at 41% in a 1990s Australian cohort.¹⁸ The 30-day case fatality after recurrent stroke was approximately half of that in the current study, which may reflect differences in study populations or geographic locations or the more contemporary nature of the current study. Despite advances in acute stroke care and critical care, there was no statistically significant change over time in the 30-day case fatality after recurrent stroke in blacks or whites. These data emphasize the need to reduce case fatality after ischemic stroke.

There are important clinical implications for the current findings. Clinicians should be cognizant that blacks ≥ 65 years of age with ischemic stroke are more likely than whites to have recurrent ischemic stroke in the year after stroke. Efforts should be made to raise awareness, treat, and maximize risk factor control in older black stroke survivors during the first year after ischemic stroke. In addition to risk factor modification, providers need to eliminate disparities in intravenous tissue plasminogen administration, deep vein thrombosis

prophylaxis, and smoking cessation counseling⁴⁴; ensure that blacks are being treated with the appropriate secondary stroke prevention medications⁴⁵; provide adequate access to care⁴⁶; and encourage adherence to treatment plans.^{46,47}

The current study has many strengths. Using Medicare, we were able to study a large population that has a high degree of generalizability to older US adults.⁴⁸ With 128,789 stroke survivors and 10,450 recurrent strokes in the current analyses, we had statistical power to detect a small difference between groups. The current findings should be interpreted in the context of the known and potential limitations of the current study. We used ICD-9-CM codes to identify ischemic stroke admissions. Although a systematic review found the positive predictive value of 433, 434, and 436 combined to be $>77\%$ in 12 of the 19 studies, the positive predictive value ranged from 46% to 94%.⁴⁹ We focused on older individuals, limiting the ability to generalize these findings to patients <65 years of age. In addition, a recent study investigating the effect of varying look-back periods on the ascertainment of incident and recurrent stroke suggests that just over 10% of strokes classified as incident using a 1-year look-back period are actually prevalent when the administrative data look-back period is expanded to 12 years.⁵⁰ We used ICD-9-CM codes to identify comorbid conditions and crude proxies to estimate socioeconomic status and functional outcome at the time of hospital discharge, making residual confounding a possibility. Furthermore, several potentially relevant variables (e.g., trust in the medical system, perceived discrimination, stroke severity) that may explain racial differences in recurrent stroke are not available in Medicare claims.

In the current nationwide study of Medicare beneficiaries, the risk for recurrent stroke was substantially higher for blacks compared with whites. Despite the decline in recurrent stroke rates for both blacks and whites, racial disparities remain present. Although case fatality was lower in blacks, it was high in both groups and did not decline over the study period. Approaches are needed to eliminate racial disparities in recurrent stroke risk and to reduce case fatality.

Author contributions

K.C. Albright participated in the design or conceptualization of the study, interpretation of data, and drafted the manuscript. L. Huang performed the analysis and participated in revision of the manuscript. J. Blackburn and G. Howard participated in the design or conceptualization of the study, interpretation of data, and revision of the manuscript. M. Mullen and V. Bittner participated in the design or conceptualization of the study and revision of the manuscript. P. Muntner and V. Howard participated in the design or conceptualization of the study, interpretation of data, and revision of the manuscript.

Study funding

Supported by the American Heart Association (14CRP20380256).

Disclosure

K.C. Albright, L. Huang, J. Blackburn, G. Howard, M. Mullen, and V. Bittner report no disclosures relevant to the manuscript. P. Muntner receives research support from Amgen Inc. V. Howard reports no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* January 27, 2018. Accepted in final form July 26, 2018.

References

- Centers for Disease Control and Prevention (CDC). Prevalence and most common causes of disability among adults—United States, 2005. *MMWR Morb Mortal Wkly Rep* 2009;58:421–426.
- Kochanek K, Xu J, Murphy S, Arias E. Mortality in the United States, 2013 [online]. Available at: cdc.gov/nchs/products/databriefs/db178.htm. Accessed October 5, 2016.
- Pahigiannis K, Waddy SP, Koroshetz W. Toward solutions for minimizing disparities in stroke: National Institute of Neurological Disorders and Stroke update. *Stroke* 2013;44:e129–e130.
- Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–e360.
- Samsa GP, Bian J, Lipscomb J, Matchar DB. Epidemiology of recurrent cerebral infarction: a Medicare claims-based comparison of first and recurrent strokes on 2-year survival and cost. *Stroke* 1999;30:338–349.
- Rosamond WD, Folsom AR, Chambless LE, et al. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke* 1999;30:736–743.
- White H, Boden-Albala B, Wang C, et al. Ischemic stroke subtype incidence among whites, blacks, and Hispanics: the Northern Manhattan Study. *Circulation* 2005;111:1327–1331.
- Kleindorfer DO, Khoury J, Moomaw CJ, et al. Stroke incidence is decreasing in whites but not in blacks: a population-based estimate of temporal trends in stroke incidence from the Greater Cincinnati/Northern Kentucky Stroke Study. *Stroke* 2010;41:1326–1331.
- Howard VJ, Kleindorfer DO, Judd SE, et al. Disparities in stroke incidence contributing to disparities in stroke mortality. *Ann Neurol* 2011;69:619–627.
- Sacco RL, Boden-Albala B, Gan R, et al. Stroke incidence among white, black, and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. *Am J Epidemiol* 1998;147:259–268.
- Cruz-Flores S, Rabinstein A, Biller J, et al. Racial-ethnic disparities in stroke care: the American experience: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011;42:2091–2116.
- Sheinart KF, Tuhim S, Horowitz DR, Weinberger J, Goldman M, Godbold JH. Stroke recurrence is more frequent in blacks and Hispanics. *Neuroepidemiology* 1998;17:188–198.
- Kennedy BS. Does race predict stroke readmission? An analysis using the truncated negative binomial model. *J Natl Med Assoc* 2005;97:699–713.
- Sacco RL, Hauser WA, Mohr JP, Foulkes MA. One-year outcome after cerebral infarction in whites, blacks, and Hispanics. *Stroke* 1991;22:305–311.
- Dhamoon MS, Sciacca RR, Rundek T, Sacco RL, Elkind MS. Recurrent stroke and cardiac risks after first ischemic stroke: the Northern Manhattan Study. *Neurology* 2006;66:641–646.
- Howard G, Kissela BM, Kleindorfer DO, et al. Differences in the role of black race and stroke risk factors for first vs. recurrent stroke. *Neurology* 2016;86:637–642.
- Park JH, Ovbiagele B. Association of black race with recurrent stroke risk. *J Neurol Sci* 2016;365:203–206.
- Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke* 2004;35:731–735.
- Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;146:857–867.
- CAPRIE Steering Committee. A randomised, blinded, trial of Clopidogrel Versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE). *Lancet* 1996;348:1329–1339.
- Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study, 2: dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci* 1996;143:1–13.
- Halkes PH, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. *Lancet* 2006;367:1665–1673.
- Sacco RL, Diener HC, Yusuf S, et al. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med* 2008;359:1238–1251.
- Arima H, Chalmers J. PROGRESS: prevention of recurrent stroke. *J Clin Hypertens* 2011;13:693–702.
- Amarencu P, Bogousslavsky J, Callahan A III, et al. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* 2006;355:549–559.
- Kim SM, Hwang SW, Oh EH, Kang JK. Determinants of the length of stay in stroke patients. *Osong Public Health Res Perspect* 2013;4:329–341.
- Brown DL, Lisabeth LD, Roychoudhury C, Ye Y, Morgenstern LB. Recurrent stroke risk is higher than cardiac event risk after initial stroke/transient ischemic attack. *Stroke* 2005;36:1285–1287.
- Allen NB, Holford TR, Bracken MB, et al. Trends in one-year recurrent ischemic stroke among the elderly in the USA: 1994–2002. *Cerebrovasc Dis* 2010;30:525–532.
- Feng W, Hendry RM, Adams RJ. Risk of recurrent stroke, myocardial infarction, or death in hospitalized stroke patients. *Neurology* 2010;74:588–593.
- Romano PS, Roos LL, Jollis JG. Presentation adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epidemiol* 1993;46:1075–1079.
- Noyes K, Liu H, Lyness JM, Friedman B. Medicare beneficiaries with depression: comparing diagnoses in claims data with the results of screening. *Psychiatr Serv* 2011;62:1159–1166.
- PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001;358:1033–1041.
- So Y, Lin G, Johnston G, SAS Institute Inc. Using the PHREG procedure to analyze competing-risks data [online]. Available at: support.sas.com/rnd/app/stat/papers/2014/competingrisk2014.pdf. Accessed March 12, 2016.
- Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat* 1988;16:1141–1154.
- Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;159:702–706.
- Mohan KM, Crichton SL, Grieve AP, Rudd AG, Wolfe CD, Heuschmann PU. Frequency and predictors for the risk of stroke recurrence up to 10 years after stroke: the South London Stroke Register. *J Neurol Neurosurg Psychiatry* 2009;80:1012–1018.
- Estol CJ, Bath PM, Gorelick PB, Cotton D, Martin RH. Differences in ischemic and hemorrhagic recurrence rates among race-ethnic groups in the ProFESS secondary stroke prevention trial. *Int J Stroke* 2014;9(suppl A100):43–47.
- Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. *Stroke* 1998;29:2491–2500.
- Alonso A, Agarwal SK, Soliman EZ, et al. Incidence of atrial fibrillation in whites and African-Americans: the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J* 2009;158:111–117.
- Howard G, Safford MM, Moy CS, et al. Racial differences in the incidence of cardiovascular risk factors in older black and white adults. *J Am Geriatr Soc* 2016;65:83–90.
- Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of functional outcome, survival, and recurrence. *Stroke* 2000;31:1062–1068.
- Moroney JT, Bagiella E, Paik MC, Sacco RL, Desmond DW. Risk factors for early recurrence after ischemic stroke: the role of stroke syndrome and subtype. *Stroke* 1998;29:2118–2124.
- Phipps E, True G, Harris D, et al. Approaching the end of life: attitudes, preferences, and behaviors of African-American and white patients and their family caregivers. *J Clin Oncol* 2003;21:549–554.
- Schwamm LH, Reeves MJ, Pan W, et al. Race/ethnicity, quality of care, and outcomes in ischemic stroke. *Circulation* 2010;121:1492–1501.
- Tuhim S, Cooperman A, Rojas M, et al. The association of race and sex with the underuse of stroke prevention measures. *J Stroke Cerebrovasc Dis* 2008;17:226–234.
- Levine DA, Neidecker MV, Kiefe CI, Karve S, Williams LS, Allison JJ. Racial/ethnic disparities in access to physician care and medications among US stroke survivors. *Neurology* 2011;76:53–61.
- Levine DA, Kiefe CI, Howard G, Howard VJ, Williams OD, Allison JJ. Reduced medication access: a marker for vulnerability in US stroke survivors. *Stroke* 2007;38:1557–1564.
- Virgig B. Strengths and limitations of CMS administrative data in research [online]. Available at: resdac.org/resconnect/articles/156. Accessed April 4, 2017.
- McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. *PLoS One* 2015;10:e0135834.
- Worthington JM, Gattellari M, Goumas C, Jalaludin B. Differentiating incident from recurrent stroke using administrative data: the impact of varying lengths of look-back periods on the risk of misclassification. *Neuroepidemiology* 2017;48:111–118.