Stroke

BRIEF REPORT

Contemporary Trends in the Nationwide Incidence of Primary Intracerebral Hemorrhage

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BACKGROUND: We report contemporary trends in nationwide incidence of intracerebral hemorrhage (ICH) across demographic and regional strata over a 15-year period.

METHODS: Utilizing the Nationwide Inpatient Sample (2004–2018) and US Census Bureau data, we calculated ICH incidence rates for age, race/ethnicity, sex, and hospital region sub-cohorts across 5 consecutive 3-year periods (2004–2006 to 2016–2018). We fit Poisson and log binomial regression models to evaluate demographic and regional differences in ICH incidence and trends in prevalence of hypertension and past/current anticoagulant use among hospitalized ICH patients.

RESULTS: Overall, the annual incidence rate (95% CI) of ICH per 100 000 was 23.15 (23.10–23.20). The 3-year incidence of ICH (per 100 000) increased from 62.79 in 2004 to 2006 to 78.86 in 2016 to 2018 (adjusted incidence rate ratio, CI: 1.11 [1.02–1.20]), coinciding with increased 3-year prevalence of hypertension and anticoagulant use among hospitalized ICH patients (adjusted risk ratio, CI: hypertension—1.16 [1.15–1.17]; anticoagulant use—2.30 [2.14–2.47]). We found a significant age-time interaction, whereby ICH incidence increased significantly faster among those aged 18 to 44 years (adjusted incidence rate ratio, CI: 1.10 [1.05–1.14]) and 45 to 64 years (adjusted incidence rate ratio, CI: 1.08 [1.03–1.13]), relative to those aged ≥75 years.

CONCLUSIONS: Rising ICH incidence among young and middle-aged Americans warrants ICH prevention strategies targeting these economically productive age groups.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: anticoagulant ■ cerebral hemorrhage ■ hospital ■ hypertension ■ incidence ■ prevalence ■ stroke

Prior studies, limited to specific US regions, have provided divergent estimates of either stable,[1] declining,[2] or increasing[3] temporal trends in incidence of intracerebral hemorrhage (ICH), whereas an earlier analysis of nationwide data (2003–2012) reported hospitalization rates rather than population-level incidence.[4] Therefore, nationwide changes in ICH incidence, particularly during the contemporary decade, across various demographic subgroups and geographic regions are not known. We sought to provide nationally representative estimates of demographic and regional differences in ICH incidence between 2004 and 2018.

METHODS

Per Houston Methodist institutional review boards' policy, informed consent and board approval were not required for this study because it used de-identified and publicly available data. We followed the RECORD guidelines (Reporting of Studies Conducted Using Observational Routinely-Collected Data).

Data Source, Study Design, and Case Identification

The National Inpatient Sample (NIS) is the largest publicly available all-payer in-hospital database in the United States,

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Nonstandard Abbreviations and Acronyms

AAPI	Asian American and Pacific Islanders
aIRR	adjusted incidence rate ratio
ICD	International Classification of Diseases
ICH	intracerebral hemorrhage
IRR	crude incidence rate ratio
NHB	non-Hispanic Black
NHW	non-Hispanic White
NIS	nationwide inpatient sample

representing over 90% of US hospitalizations.[5] NIS underwent sampling redesign in 2012; consequently, trend weights for pre-2012 NIS data were used to provide estimates comparable across pre- and post-2012 NIS (Appendix S1).[5] In a repeated cross-sectional design, we identified adults (≥18 years) with principal diagnosis of ICH using validated[6] International Classification of Disease (ICD), Ninth Revision code 431 and Tenth Revision codes I61 (I61.0–I61.6 and I61.8–I61.9). We excluded hospitalizations with concurrent diagnoses of head trauma or arteriovenous malformation and records with "Other," "Native American," or "Missing" race. Census Bureau's public use microdata sample provided the time-specific denominators for ICH incidence rate calculations.

Statistical Analyses

We aggregated data into 5 consecutive 3-year time periods (P1: 2004–2006, P2: 2007–2009, P3: 2010–2012, P4: 2013–2015, and P5: 2016–2018). We used discharge and trend weights (for pre-2012 NIS) to yield nationally representative estimates of time-specific ICH incidence across various age, sex, race/ethnicity, and regional sub-cohorts. We categorized age (18–44, 45–64, 65–74, and ≥75 years) and coded race/ethnicity as non-Hispanic White (NHW); non-Hispanic Black (NHB); Asian American and Pacific Islanders (AAPI), and Hispanic. We categorized hospitals' geographic location according to the 4 US census regions: Northeast, Midwest, South, and West.

We calculated cohort-specific unadjusted ICH incidence rates (IR) using the US Census Bureau's cohort-specific mid-period population counts as denominators. We fit panel data random effects Poisson regression models with robust standard errors to provide crude and adjusted incidence rate ratio (aIRR) with 95% CIs for age, sex, race/ethnicity hospital region and time-specific differences in ICH incidence. We fit separate multivariable Poisson regression models to evaluate age/sex/race/region-time interactions (see Appendix S1). We also provide age-stratified aIRR for sex, race/ethnicity, hospital region, and time-specific differences in ICH incidence. Additionally, we fit log binomial and modified Poisson regression models to provide the crude (overall and stratified by age and race/ethnicity) and adjusted risk ratios (controlling for age, sex, race/ethnicity and hospital region) for time-specific differences in prevalence of hypertension and anticoagulant use among hospitalized ICH

Table. Crude ICH Incidence Rates (per 100 000) and 95% CI Stratified by Demographic and Hospital Characteristics and 3-Year Period

Demographic characteristics	Average incidence per period	P1	P2	P3	P4	P5	Absolute difference (P5–P1)	IRR (P5 vs P1)
Sex								
Male	72.6	64.39	63.16	73.24	76.61	83.77	19.38	1.13 (1.02–1.25)*
Female	66.72	61.31	60.56	67.83	68.55	74.22	12.91	1.09 (0.96–1.24)
Age								
18–44 y	9.45	8.13	7.77	9.36	10.28	11.57	3.44	1.38 (1.24–1.52)†
45–64 y	61.93	52.22	52.95	63.09	65.94	73.48	21.26	1.33 (1.21–1.47)†
65–74 y	145.56	142.86	140.12	146.42	143.82	151.91	9.05	1.05 (0.95–1.15)
≥75 y	362.95	376.39	337.62	373.38	361.52	366.93	−9.46	0.97 (0.85–1.10)
Race								
AAPI	66.47	59.35	67.1	65.36	64.42	73.44	14.09	1.09 (0.94–1.26)
NHW	68.71	62.43	60.55	69.09	72.49	78.48	16.05	1.10 (0.98–1.23)
NHB	103.41	87.44	85.97	111.02	108.93	118.96	31.52	1.24 (1.11–1.39)†
Hispanic	47.35	44.64	45.75	45.63	46.72	52.48	7.84	0.98 (0.89–1.08)
Hospital region								
Northeast	74.24	79.63	74.79	69.83	72.21	75.14	−4.49	0.86 (0.81–0.92)†
Midwest	55.23	38.48	36.11	58.32	64.76	76.61	38.13	1.76 (1.54–2.01)†
South	77.12	72.57	67.79	79.31	79.84	84.49	11.92	1.03 (0.92–1.14)
West	67.17	57.21	66.54	68.02	67.79	74.61	17.4	1.13 (1.04–1.24)‡
Overall	69.57	62.79	61.83	70.46	72.47	78.86	16.07	1.11 (1.02–1.20)*

AAPI indicates Asian American and Pacific Islander; and ICH, intracerebral hemorrhage.
*P<0.05, †P<0.001, ‡P<0.01.

patients. We used STATA (v.16) for analyses. Our sample of 803 230 ICH hospitalizations provides >99% power to detect 2% difference in incidence rate between AAPI and Hispanics (the 2 smallest race/ethnicity subgroups in our data),[7] (see Appendix S1).

RESULTS

Between 2004 and 2018, we analyzed a total of 803 230 adult ICH hospitalizations (mean (SD) age 68.9 (13.6) years, 49.3% females), which included 539 471 (67.1%) NHW, 142 420 (17.7%) NHB, 40 582 (5.1%) AAPI, and 80 756 (10.1%) Hispanic patients. The average annual IR (CI) of ICH per 100 000 was 23.15 (23.10–23.20). The crude nationwide 3-year ICH IR (per 100 000) significantly increased, from 62.79 in P1 to 78.86 in P5 (aIRR, CI: 1.11 [1.02–1.20]; Table S1), coinciding with an increased prevalence rate (P1% to P5% [adjusted risk ratio, CI]) of hypertension (74.5%–86.4% [1.16, 1.15–1.17]) and anticoagulant use (6.0% to 13.2% [2.30, 2.14–2.47]) among ICH patients. Age, sex, race/ethnicity, and hospital region-specific ICH IRs are provided in the Table and Figure 1. Also, age and race/ethnicity-specific prevalence rates of hypertension and anticoagulant use are reported in Table S2.

Overall, ICH incidence was higher among NHB (versus NHW) (aIRR, CI: 2.27 [1.99–2.59]) and males (versus females) (aIRR, CI: 1.43, [1.32–1.54]) (Table S1). In an age-stratified analysis, the higher ICH incidence among NHB and males was persistently observed across all age categories other than the ≥75 years age-category. For this age-category (≥75 years), the association between sex and ICH incidence was not statistically significant (Table S3).

There was also a significant age-time interaction, indicating that ICH incidence is rising significantly faster over time among those aged 18 to 44 years (aIRR, CI: 1.10 [1.05–1.14]) and 45 to 64 years (aIRR, 95% CI: 1.08, 1.03–1.13), relative to those aged ≥75 years. Also, relative to the Northeast, ICH incidence is increasing at a significantly faster rate in the Midwest (aIRR CI: 1.22 [1.18–1.27]), South (aIRR CI: 1.06 [1.03–1.09]), and West (aIRR, CI: 1.06 [1.03–1.09]). However, there was no significant interaction between sex or race with time (Figure 2; Table S4).

DISCUSSION

Our analyses indicate an 11% increase in nationwide ICH incidence during the last 15 years, which coincides

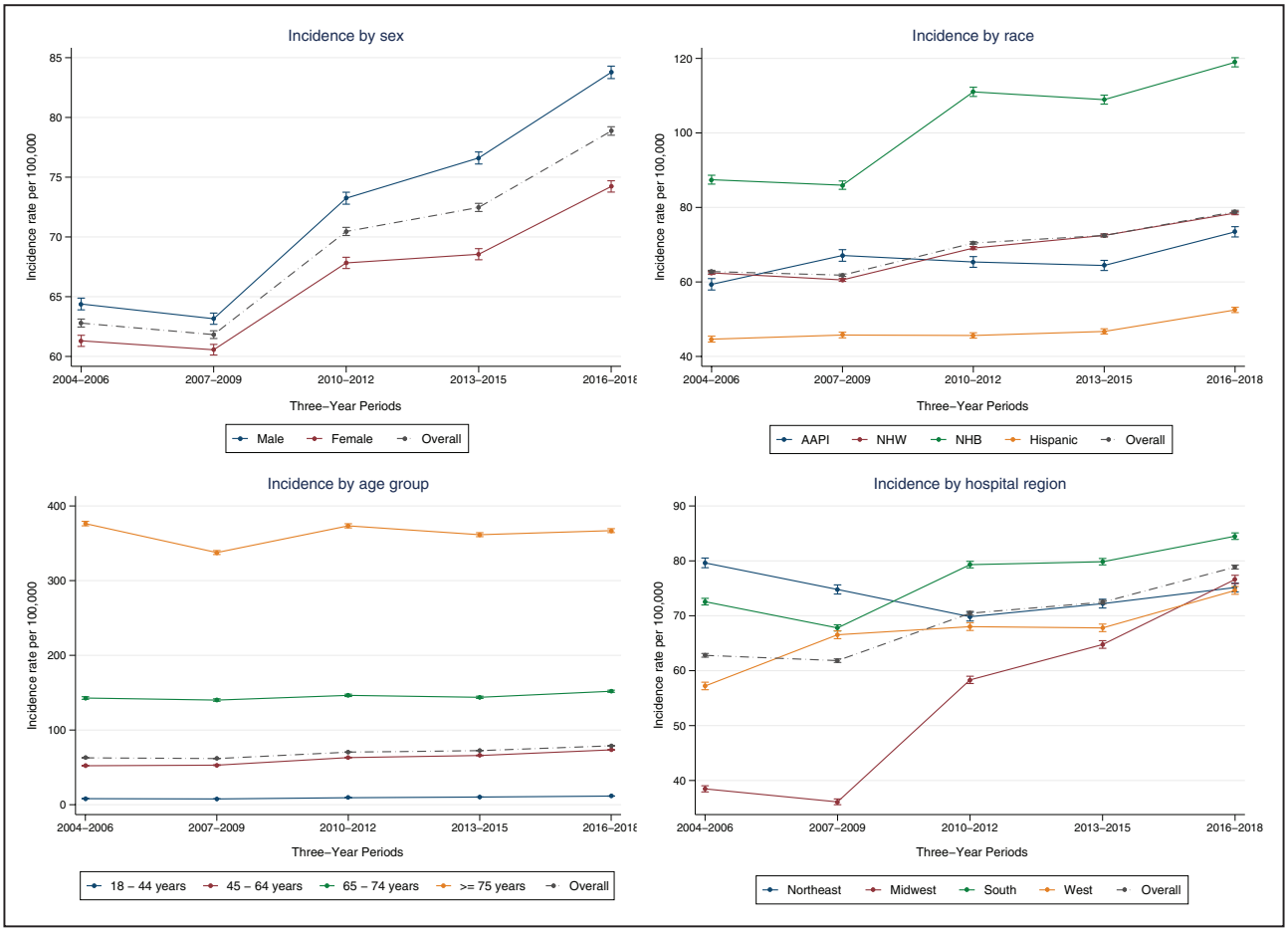

Figure 1. Crude incidence rate of intracerebral hemorrhage over 3-y period stratified by sex, age race, and hospital region.
AAPI indicates Asian American and Pacific Islander.

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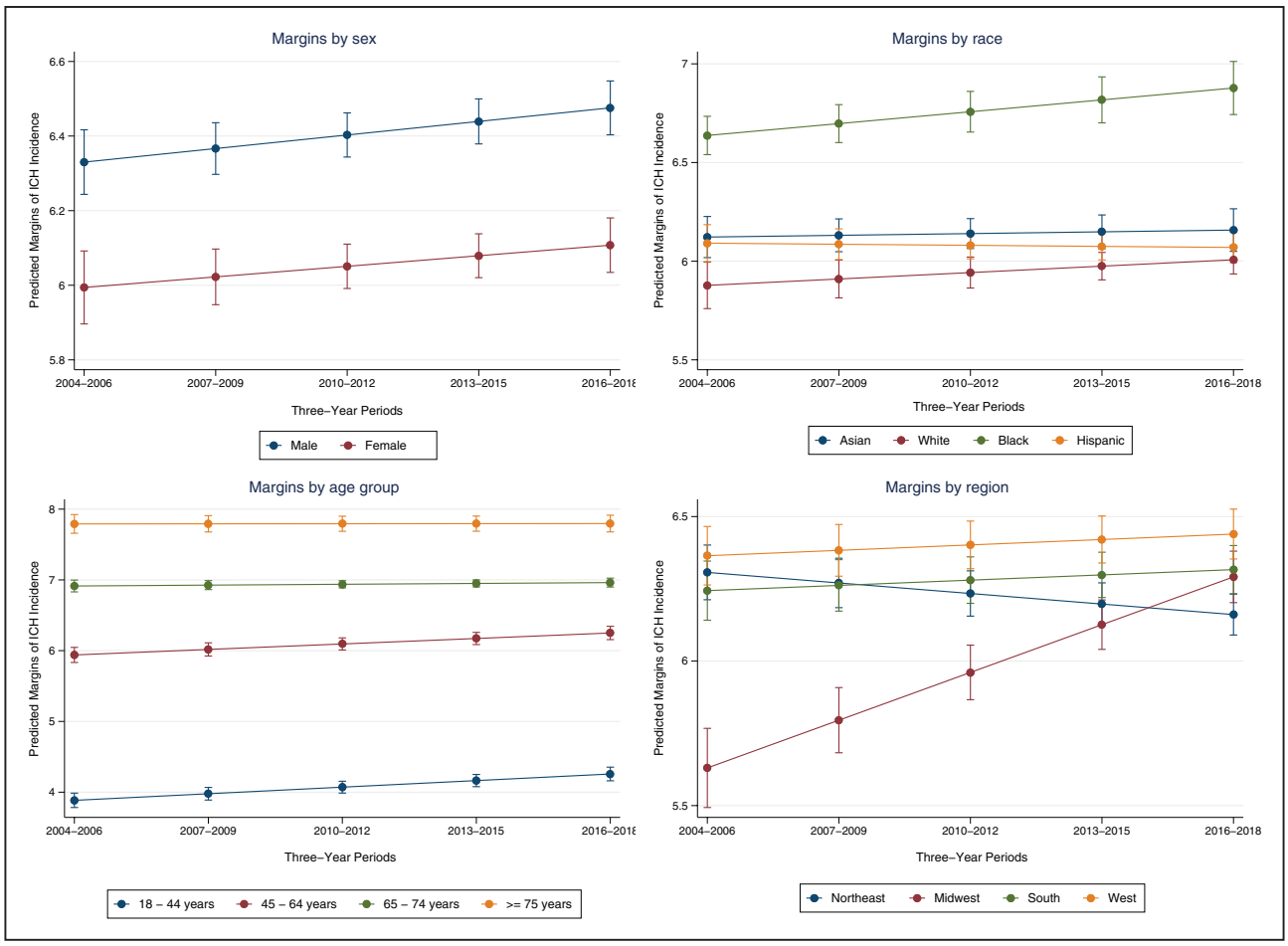

Figure 2. Predicted margins (linear prediction) of intracerebral hemorrhage (ICH) incidence over time stratified by sex, race, age, and hospital region.

with rising prevalence of hypertension and anticoagulant use among ICH hospitalized patients.

We demonstrate that ICH incidence trends are largely driven by rising incidence among the young and the middle-aged. Although previous small studies have reported similar findings,[3] our study provides this evidence at the national level. This finding is of enormous public health importance as the burden of ICH among young adults will result in longer-lasting disability, higher health care costs, and potential loss of economic productivity. We may also infer that control of ICH risk factors among this demographic is suboptimal; consequently, future ICH prevention efforts should aggressively target young and middle-aged Americans.

We found ICH incidence among NHB to be significantly higher than all other race/ethnicity subgroups. Higher prevalence of uncontrolled cardiovascular risk factors, particularly hypertension, among Blacks may potentially explain this observation.[8] Future studies should, therefore, comprehensively evaluate the prevalence and management of race-specific ICH risk factors. As has been previously reported across various demographic sub-groups,[9] our analyses demonstrated higher ICH incidence among males (versus females) up till an older age (≥75 years), following which there was no difference in ICH incidence between males and females. Further studies are needed to evaluate biological and behavioral risk factors contributing to sex differences in ICH incidence.

We also report regional differences in ICH incidence trends, whereby ICH incidence rate is rising significantly faster in Midwest, South and West subregions, relative to Northeast. However, the reasons for these differences are not fully explained by our data.

Other potential limitations include probable inclusion of recurrent ICH events, which may overestimate ICH incidence, and identification of ICH by ICD codes rather than neuroimaging information. Also, although NIS covers over 90% of US hospitalizations, we may have missed a small proportion of ICH hospitalizations, which may underestimate ICH incidence. However, given the acute nature of ICH, which is followed by immediate hospitalization in 95% of cases,[10] our methods conform with recommendations for incidence rate estimation using NIS.[5] Moreover, annual recurrent ICH is reported to be <5%,[11] and the accuracy of ICD codes for identifying ICH cases is reported to be up to 100%.[6]

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CONCLUSIONS

Despite improvements in control and prevention of risk factors, nationwide ICH incidence has increased in the past 15 years. Minority populations continue to experience disparate ICH burden. Higher rates of increase in ICH incidence among young and middle-aged Americans are particularly concerning and warrant targeted primary prevention programs.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

RECORD checklist
Appendix S1
Tables S1–S4

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