Published in final edited form as:
Stroke. 2011 November ; 42(11): 3075–3079. doi:10.1161/STROKEAHA.111.623157.

Carotid Intima-Media Thickness, Electrocardiographic Left Ventricular Hypertrophy and Incidence of Intracerebral Hemorrhage

Aaron R. Folsom, MD, MPH[1], **Hiroshi Yatsuya, MD, PhD**[2], **Bruce M. Psaty, MD, PhD**[3], **Eyal Shahar, MD, MPH**[4], and **W. T. Longstreth Jr., MD, MPH**[5]

[1]Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN

[2]Department of Public Health & Health Systems, Graduate School of Medicine, Nagoya University, Nagoya, Japan

[3]Cardiovascular Health Research Unit, Departments of Medicine, Epidemiology and Health Service; University of Washington, and Group Health Research Institute, Group Health Cooperative, Seattle, WA

[4]Division of Epidemiology and Biostatistics, Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, AZ

[5]Departments of Neurology and Epidemiology, University of Washington, Seattle, WA

Abstract

Background and Purpose—Carotid intima-media thickness (IMT) and electrocardiographic left ventricular hypertrophy (ECG-LVH) are two subclinical cardiovascular disease measures associated with increased risk of total and ischemic strokes. Increased IMT and ECG-LVH also may reflect end-organ hypertensive effects. Information is scant on the associations of these subclinical measures with intracerebral hemorrhage (ICH). We hypothesized that greater carotid IMT and the presence of ECG-LVH would be independently associated with increased ICH incidence.

Methods—Among 18,155 participants initially free of stroke in the Atherosclerosis Risk in Communities Study (ARIC) and the Cardiovascular Health Study (CHS), we assessed carotid IMT, carotid plaque, and ECG-LVH. Over a median of 18 years of follow-up, 162 incident ICH events occurred.

Results—After adjustment for other ICH risk factors, carotid IMT was associated positively with incidence of ICH in both ARIC and CHS. The risk was lowest in study-specific quartile 1, elevated 1.6 to 2.6-fold in quartiles 2–3, and elevated 2.5 to 3.7-fold in quartile 4 ($p<0.05$ for both studies). In CHS, having a carotid plaque was associated with a 2-fold (95% CI = 1.1–3.4) greater ICH risk than having no plaque, but only 1.2-fold (95% CI = 0.76–2.0) greater ICH risk in ARIC.

Address for correspondence: Aaron R. Folsom, MD, Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, 1300 South 2nd Street, Suite 300, Minneapolis, MN 55454. Phone: + 1 612-626-8862; Fax: +1 612-624-0315; folso001@umn.edu.

Disclosures
None.

ECG-LVH carried a hazard ratio of ICH of 1.7 (95% CI = 0.77–3.7) in CHS and 2.8 (95% CI = 1.2–6.4) in ARIC.

Conclusions—Our data suggest that people with carotid atherosclerosis and possibly LVH are at increased risk not only of ischemic stroke but also of ICH.

Keywords

atherosclerosis; left ventricular hypertrophy; intracerebral hemorrhage; prospective study; risk factors

Despite a sizeable decline over the last half century, stroke remains the third leading cause of death in the United States.[1] Intracerebral hemorrhage (ICH) is less common in the U.S. than ischemic stroke, but ICH has a high case-fatality. Persons of African American or Asian ancestry have higher ICH rates than do whites. Other established risk factors for ICH include age, hypertension, and low blood total cholesterol.[2,3]

Whether other vascular risk factors are involved in ICH etiology is less clear. In one meta-analysis, additional ICH risk factors included male sex and high alcohol intake, but smoking, diabetes, and physical inactivity did not elevate risk.[2] Another meta analysis of studies from the Asian-Pacific region found smoking and possibly diabetes associated with greater ICH risk, whereas body mass index and blood triglycerides were unrelated to ICH.[3] In a previous report on ICH occurrence through 2002 in the Atherosclerosis Risk in Communities Study (ARIC) and the Cardiovascular Health Study (CHS), ICH risk factors included age, African American ethnicity, higher systolic blood pressure, lower LDL-cholesterol and triglycerides, and high fibrinogen.[4,5]

Follow-up of the ARIC and CHS cohorts has been extended for five more years, which allows us to examine additional potential risk markers for ICH. Carotid intima-media thickness (IMT) and electrocardiographic left ventricular hypertrophy (ECG-LVH) are two subclinical cardiovascular disease measures associated with increased risk of total and ischemic strokes. Increased IMT and ECG-LVH also may reflect end-organ hypertensive effects. Information is scant on the associations of these subclinical measures with ICH. We hypothesized that greater carotid IMT and the presence of ECG-LVH would be independently associated with increased ICH incidence.

Methods

Study Populations

The ARIC study cohort comprised a sample of 15,792 individuals aged 45–64 years old at baseline when recruited between 1987–1989, from four communities: Forsyth County, North Carolina; Jackson, Mississippi (African Americans only); Washington County, Maryland; and the northwestern suburbs of Minneapolis, Minnesota.[6] The CHS cohort comprised adults randomly sampled from Medicare eligibility files from four communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania.[7] CHS initially recruited 5,201 participants in 1989–1990, and added 687 African-Americans in 1992–1993. These studies received approval from relevant human subjects review boards, and all participants gave consent.

Baseline Assessments

As previously described,[4,5] the use of similar methods in ARIC and CHS to assess most risk factors allowed for the pooling of the studies for many analyses. ARIC and CHS obtained standard resting 12-lead ECGs. ECG-LVH was defined two ways: (1) by Minnesota Codes

(3-1 or 3-3) and (any of 4-1 to 4-3 or 5-1 to 5-3), which represent high amplitude left chest R waves and ST-T changes,[8] and (2) by Cornell voltage criteria.[9]

High resolution B-mode ultrasound (Biosound 2000 II SA; Biosound, Indianapolis, IN, USA) was used in ARIC to measure IMT bilaterally in the extracranial carotid arteries, in the areas of the common carotid artery (1 cm proximal to the dilatation of the carotid bulb), the carotid bifurcation (1 cm proximal to the flow divider), and the internal carotid artery (1 cm distal to the flow divider). The mean IMT values at the six carotid sites were combined to produce an overall mean IMT. Correlations between scans at different visits 7–10 days apart, performed by different sonographers and read by different readers were 0.77, 0.73, and 0.70 for the bifurcation, internal and common carotid, respectively. The presence of atherosclerotic plaque at any of the six segments was recorded by ARIC ultrasound readers as wall thickness in excess of 1.5 mm or the presence of lumen encroachment or irregular intimal surface and/or image characteristics indicative of structural heterogeneity of the arterial wall.[10]

In CHS, trained technicians used high-resolution B-mode ultrasonography (Toshiba SSA-270A, Toshiba American Systems, Tustin, CA) to obtain one longitudinal image of the common carotid artery and three images of the internal carotid artery, bilaterally.[11,12] Arterial segments imaged in CHS were similar to those in ARIC, but CHS sonographers focused on imaging the largest lesion or thickness. Ultrasounds were centrally read for mean and maximum IMT as previously described.[12] IMT repeatability data in CHS have been published.[12] Carotid plaque, defined by the appearance of the largest focal lesion, was classified by surface characteristics, echogenicity, and texture. Absence of plaque was defined as a smooth intimal surface with no regional discrete plaque. Intermediate risk plaques were hyperdense, calcified or homogeneous plaques, or those with a mildly irregular surface. High-risk plaques had an irregular or ulcerated surface, or were hypodense or heterogeneous plaques occupying more than 50% of the total plaque volume. For this analyses, intermediate risk and high risk plaques were grouped and compared with no plaque.

Stroke Ascertainment and Criteria

ARIC identified nonfatal and fatal hospitalized strokes through yearly phone interviews, reported deaths, and surveillance, abstraction, and review of hospital records.[13] CHS identified fatal and nonfatal hospitalized and nonhospitalized strokes via semiannual phone interviews, reported deaths, and abstraction and review of relevant hospital records identified from Medicare utilization files.[14,15]

ARIC adapted National Survey of Stroke criteria for its stroke definition.[16] These criteria require stroke to have evidence of sudden or rapid onset of neurological symptoms that persist for >24 hours or lead to death, and have no other apparent cause such as trauma, tumor, infection, or anticoagulation therapy. A definite ICH met one of the following criteria: (1) CT or MRI showing intraparenchymal hematoma; (2) Demonstration at autopsy or surgery of ICH; or (3) at least one major or two minor neurological deficits; and a bloody spinal fluid on lumbar puncture; and cerebral angiography demonstrates an avascular mass effect and no evidence of aneurysm or arteriovenous malformation; and no CT or MRI. A probable ICH met criteria (3), other than cerebral angiography, but had a decreased level of consciousness or coma lasting 24 hours or until the participant died. In ARIC, 99% of hospitalized strokes received a CT or MRI.

CHS adopted stroke criteria similar to the Systolic Hypertension in the Elderly Program (SHEP).[14,17] A suspected event was classified as a stroke if there was a rapid onset neurological deficit lasting >24 hours or until death. The event could not be caused by

trauma, tumor, or infection, but in contrast to ARIC, an ICH while on anti-coagulation therapy did not preclude an ICH classification in CHS. Only 13 participants with an ICH in CHS were potentially taking anticoagulation medication. Their exclusion had little impact on results, as would be expected from the small numbers and because anti-coagulation was only weakly correlated with exposures of interest. A suspected hemorrhagic stroke was classified as an ICH if (1) there was CT or MRI evidence of ICH, or (2) bloody cerebrospinal fluid on lumbar puncture with a focal deficit, or (3) autopsy or surgical evidence indicated ICH. In CHS, 83% of stroke events (88% of ICHs) had brain imaging.

Data Analysis

The combined cohort had 21,680 participants at baseline with follow-up through December 31, 2007. For analysis, we excluded any participants who reported a history of stroke at baseline (*n*=582) or were not African-American or White (*n*=87), or who were missing carotid IMT, carotid plaque, or ECG-LVH data (*n*=1,773), or who were missing covariates (*n*=1,083), leaving 18,155 (13,079 in ARIC, 5,076 in CHS). The outcome of interest was the first definite or probable incident ICH.

The associations of baseline carotid IMT (study-specific quartiles or continuous), carotid plaque (yes, no), or ECG-LVH (yes, no) with incident ICH were of primary interest. Study-specific analyses of IMT were used because of the difference in protocols for ARIC (mean IMT) and CHS (maximum IMT). Hazard ratios were calculated using Cox proportional hazard models as implemented in SAS 9.2 (SAS Institute, North Carolina). We adjusted for baseline variables associated with ICH in our previous reports.[4,5] Model 1 included age (continuous), race (African American, white), cigarette smoking (yes, no), LDL-cholesterol (continuous), natural log triglycerides (continuous), and fibrinogen (continuous). Model 2 added systolic blood pressure (continuous). A quadratic term for systolic blood pressure was also tested but was found to be unimportant. Two-way multiplicative interactions between IMT or LVH and age, study (ARIC, CHS), sex, and race were examined, and none was significant at $p<0.01$.

In a sensitivity analysis, we reran results after imputing missing values for the main exposure variables (IMT, plaque, and LVH) and covariates. We did this to include the maximum sample size possible. We used multiple imputation, a strategy that replaces each missing value with a random sample of plausible values that represent the uncertainty about the right value to impute.[18] Imputation was carried out using PROC MI in SAS, separately for ARIC and CHS. Hazard ratio and 95% CI estimates were derived using PROC MIANALYZE by combining the results of analyses carried out on five imputed datasets.

Results

As depicted in Table 1, the combined ARIC and CHS cohort initially free of stroke and used in this analysis, included 18,155 participants, of whom 44% were men, 21% African-American, and 28% were older than 65 at baseline (i.e., in CHS). Over a median of 18 years of follow-up, 162 ICH events were identified in this analytic subset (69 ARIC and 93 CHS). The crude incidence rate of ICH was approximately 5 times higher in CHS (15 per 10,000 person-years) than in ARIC (3 per 10,000 person-years), reflecting the difference in age of the two cohorts.

Similar to previously reported results,[4,5] now with further follow-up, the simultaneously-adjusted hazard ratios of ICH for major risk factors were: 1.61 (95% CI 1.21–2.15) per 10 years of age; 1.57 (1.10–2.25) for African Americans versus whites; 1.44 (1.25–1.66) per 20.5 mmHg (one SD) increment of systolic blood pressure; 0.76 (0.64–0.90) per 38.2 mg/dL (one SD) LDL-cholesterol increment; 0.58 (0.40–0.85) per natural-log triglyceride

increment; 1.24 (1.08–1.43) per 65.6 mg/dL (one SD) increment of fibrinogen; and 1.57 (1.07–2.30) for current smokers versus current nonsmokers. After accounting for those risk factors, sex, alcohol intake and diabetes were unassociated with ICH incidence.

Carotid IMT was associated positively with incidence of ICH in both ARIC and CHS (Table 2). In Model 1, which excluded blood pressure, the risk was lowest in study-specific quartile 1, elevated 1.67 to 2.73-fold in quartiles 2–3, and elevated 2.77-fold (CHS) to 4.26-fold (ARIC) in quartile 4. Quadratic IMT terms were not significant in the ICH regression models. In continuous IMT Model 1, ICH incidence rose 25–39% per standard deviation increment of IMT (Table 2). Adjustment for systolic blood pressure in Model 2 moderately attenuated the associations between carotid IMT and ICH incidence. For example, in Model 2, ICH incidence was estimated to rise 19–34% per standard deviation increment of IMT (Table 2).

Having a carotid plaque was associated with a 2.05-fold greater ICH risk than having no plaque in CHS, but only 1.35-fold greater ICH risk in ARIC (Table 2, Model 1). Adjustment for systolic blood pressure (Model 2) attenuated these hazard ratios to 1.95 and 1.24, respectively.

As Table 3 shows, ECG-LVH was relatively rare, but carried a hazard ratio of ICH in Model 1 of 1.98 (CHS) to 3.67 (ARIC). Overall, using the Cornell voltage criterion for ECG-LVH, the hazard ratio for ICH was 2.53 (95% CI 1.45–4.43) in Model 1 and 2.07 (1.18–3.65) with further adjustment for blood pressure in Model 2.

In the sensitivity analysis (not shown) to impute missing data and increase sample size (yielding 84 ICH events in ARIC and 104 in CHS), results were slightly weaker but qualitatively similar. For example, ICH incidence rose 16–29% per standard deviation of IMT in the imputed analysis, compared with 19–34% in Model 2 of Table 2. With imputation, the Model 2 hazard ratios for ICH in relation to carotid plaque were: 1.58 (95% CI 0.96–2.62) for CHS and 1.42 (0.89–2.27) for ARIC, which were similar to the unimputed values in Table 2. Likewise, the sensitivity analysis involving imputed data yielded an overall Model 2 hazard ratio for ICH of 1.88 (1.15–3.20) for the Cornell LVH criterion, only somewhat smaller than the hazard ratio of 2.07 in Table 3.

Discussion

In these prospective population-based studies, the incidence rate of ICH was increased approximately 3-fold in participants in the highest versus lowest quartile of carotid IMT (ARIC and CHS, separately). ICH incidence also was increased approximately 2-fold in CHS participants with carotid plaque and 2- to 3-fold in participants with ECG-LVH (ARIC and CHS, combined). The observed associations were independent of other measured ICH risk factors, namely age, race, cigarette smoking, fibrinogen, and lower cholesterol and triglyceride levels. Systolic blood pressure seemed to account for part of the observed associations, as evidenced by a comparison of Model 1 and Model 2 hazard ratios.

A major limitation of our study is the small number of ICH events, which limited statistical power. Some measures (e.g., ECG-LVH) could be pooled between ARIC and CHS, but others could not (carotid IMT and ECHO-LVH), which further limited power. To maximize sample size, we ran a sensitivity analysis using imputed data for missing values; results were similar to the main analysis. We did not have information on location of ICH (for example, lobar versus nonlobar); evidence suggests that ICH risk factors differ by location.[19,20]

The interpretation of the associations observed is somewhat complicated. It does not seem likely that increased carotid IMT/plaque or LVH would be direct causes of ICH. At least

part of these associations seemed explained by high blood pressure being associated with carotid IMT plaque, LVH, and ICH. Yet, adjustment for blood pressure level did not fully eliminate the associations, but measurement error may provide for incomplete adjustment. Instead, these associations may merely reflect the fact that carotid atherosclerosis and LVH represent integrated measures of hypertensive end-organ damage, not accounted for by simply adjusting for blood pressure. These end-organ pathologies may include weakening of intracerebral arteries, or perhaps increased risk of amyloid angiopathy.

Regardless of any etiologic implications, our data do suggest people with carotid atherosclerosis and possibly LVH are not only at increased risk of ischemic stroke but also of ICH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the staff and participants of the ARIC and CHS studies for their important contributions.

Sources of Funding

The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C). The Cardiovascular Health Study is funded by National Heart, Lung, and Blood Institute Grant/Contract numbers N01-HC-85239, N01-HC-85079 through N01-HC-85086; N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133; HL080295, HL-075366; National Institute on Aging grant/contract numbers AG-023269, AG-15928, AG-20098, and AG-027058; University of Pittsburgh Claude. D. Pepper Older Americans Independence Center grant number P30-AG-024827; with additional contribution from the National Institute of Neurological Disorders and Stroke. See also http://www.chs-nhlbi.org/pi.htm

References

1. Heron, M. National Vital Statistics Reports. Vol. 58. Hyattsville, MD: National Center for Health Statistics; 2010 March 31. Deaths: Leading causes for 2006. 2010
2. Ariesen MJ, Claus SP, Rinkel GJ, Algra A. Risk factors for intracerebral hemorrhage in the general population: A systematic review. Stroke. 2003; 34:2060–2065. [PubMed: 12843354]
3. Woodward M, Huxley H, Lam TH, Barzi F, Lawes CM, Ueshima H. A comparison of the associations between risk factors and cardiovascular disease in Asia and Australasia. Eur J Cardiovasc Prev Rehabil. 2005; 12:484–491. [PubMed: 16210936]
4. Sturgeon JD, Folsom AR, Longstreth WT Jr, Shahar E, Rosamond WD, Cushman M. Hemostatic and inflammatory risk factors for intracerebral hemorrhage in a pooled cohort. Stroke. 2008; 39:2268–2273. [PubMed: 18535282]
5. Sturgeon JD, Folsom AR, Longstreth WT Jr, Shahar E, Rosamond WD, Cushman M. Risk factors for intracerebral hemorrhage in a pooled prospective study. Stroke. 2007; 38:2718–2725. [PubMed: 17761915]
6. The Atherosclerosis Risk in Communities (ARIC) Study: Design and objectives. The ARIC Investigators. Am J Epidemiol. 1989; 129:687–702. [PubMed: 2646917]
7. Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, et al. The Cardiovascular Health Study: Design and rationale. Ann Epidemiol. 1991; 1:263–276. [PubMed: 1669507]
8. Prineas, RJ.; Crow, RS.; Blackburn, H. The Minnesota Code Manual of Electrocardiographic Findings. Standards and Procedures for Measurement and Classification. Littleton, MA: John Wright; 1982.

9. Crow RS, Prineas RJ, Rautaharju P, Hannan P, Liebson PR. Relation between electrocardiography and echocardiography for left ventricular mass in mild systemic hypertension: results from Treatment of Mild Hypertension Study. Am J Cardiol. 1995; 75:1233–1238. [PubMed: 7778546]
10. Li R, Duncan BB, Metcalf PA, Crouse JR III, Sharrett AR, Tyroler HA, et al. B-mode-detected carotid artery plaque in a general population. Stroke. 1994; 25:2377–2383. [PubMed: 7974576]
11. Mukamal KJ, Kronmal RA, Mittleman MA, O'Leary DH, Polak JF, Cushman M, et al. Alcohol consumption and carotid atherosclerosis in older adults: the Cardiovascular Health Study. Arterioscler Thromb Vasc Biol. 2003; 23:2252–2259. [PubMed: 14563651]
12. O'Leary DH, Polak JF, Wolfson SK Jr, Bond MG, Bommer W, Sheth S, et al. Use of sonography to evaluate carotid atherosclerosis in the elderly. The Cardiovascular Health Study. CHS Collaborative Research Group. Stroke. 1991; 22:1155–1163. [PubMed: 1926258]
13. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, 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. [PubMed: 10187871]
14. Longstreth WT Jr, Bernick C, Fitzpatrick A, Cushman M, Knepper L, Lima J, et al. Frequency and predictors of stroke death in 5,888 participants in the Cardiovascular Health Study. Neurology. 2001; 56:368–375. [PubMed: 11171903]
15. Ives DG, Fitzpatrick AL, Bild DE, Psaty BM, Kuller LH, Crowley PM, et al. Surveillance and ascertainment of cardiovascular events. The Cardiovascular Health Study. Ann Epidemiol. 1995; 5:278–285. [PubMed: 8520709]
16. Robins M, Weinfeld FD. The national survey of stroke. Study design and methodology. Stroke. 1981; 12:I7–I11. [PubMed: 7222169]
17. Rationale and design of a randomized clinical trial on prevention of stroke in isolated systolic hypertension. The Systolic Hypertension in the Elderly Program (SHEP) Cooperative Research Group. J Clin Epidemiol. 1988; 41:1197–1208. [PubMed: 2905387]
18. Rubin, DB. Multiple Imputation for Nonresponse in Surveys. New York, NY: John Wiley & Sons, Inc.; 1987.
19. Woo D, Sauerbeck LR, Kissela BM, Khoury JC, Szaflarski JP, Gebel J, et al. Genetic and environmental risk factors for intracerebral hemorrhage: preliminary results of a population-based study. Stroke. 2002; 33:1190–1195. [PubMed: 11988589]
20. Baker ML, Hand PJ, Wong TY, Liew G, Rochtchina E, Mitchell P, et al. for the Multi-Centre Retinal Stroke Study Group. Retinopathy and lobar intracerebral hemorrhage: insights into pathogenesis. Arch Neurol. 2010; 67:1224–1230. [PubMed: 20937950]

Table 1

Mean Values (Standard Deviations) or Prevalences (%) of Participant Characteristics at Baseline, ARIC and CHS

Characteristic	ARIC (n=13,079)	CHS (n=5,076)
Age (years)	54.2 (5.8)	72.7 (5.5)
Systolic blood pressure (mm Hg)	120.7 (18.5)	135.9 (21.5)
Low density lipoprotein cholesterol (mg/dl)	137.4 (39.1)	129.8 (35.4)
Log-triglycerides	4.70 (0.48)	4.82 (0.41)
Fibrinogen (mg/dl)	301.3 (64.2)	323.0 (66.7)
Intima-media thickness (mm)	0.74 (0.18)	1.24 (0.34)
Usual ethanol intake (g/week)	42.7 (94.3)	39.9 (170.9)
Race (% white)	75.8%	85.7%
Sex (% women)	44.4%	41.7%
Current smoking (% yes)	25.5%	11.9%
Diabetes (% yes)	9.5%	15.1%
Carotid plaque (% yes)	33.6%	77.9%
Left ventricular hypertrophy (Minnesota code) (% yes)	1.8%	4.6%
Left ventricular hypertrophy (Cornell voltage) (% yes)	2.0%	5.2%

Table 2

Incidence Rates and Multivariate-Adjusted Hazard Ratios and 95% Confidence Intervals (95% CI) of Intracerebral Hemorrhage (ICH) According to Carotid Intima-Media Thickness (IMT) and Carotid Plaque, ARIC and CHS

		Quartile of IMT†				Per 1 SD increment of IMT‡	Carotid Plaque	
		1	2	3	4		No	Yes
ARIC	IMT quartile range (mm)	<0.62	0.62–0.70	0.70–0.81	>0.81			
	n ICH/N at risk	6/3,269	18/3,270	16/3,270	29/3,270	--	40/8,690	29/4,389
	Incidence Rate§	1.0	3.1	2.8	5.5	--	2.6	4.0
	Model 1 Hazard Ratio*	1.0	2.73	2.37	4.26	1.39	1.0	1.35
	95% CI	--	1.08–6.91	0.92–6.14	1.71–10.6	1.15–1.68	--	0.83–2.22
	Model 2 Hazard Ratio**	1.0	2.64	2.21	3.70	1.34	1.0	1.24
	95% CI	--	1.04–6.67	0.85–5.72	1.48–9.28	1.10–1.63	--	0.76–2.04
CHS	IMT quartile range (mm)	<0.98	0.98–1.17	1.17–1.44	>1.44			
	n ICH/N at risk	18/1,269	27/1,269	21/1,269	27/1,269	--	15/1,124	78/3,952
	Incidence Rate§	10.0	16.2	13.9	21.6	--	9.5	16.8
	Model 1 Hazard Ratio*	1.0	1.82	1.67	2.77	1.25	1.0	2.05
	95% CI	--	0.99–3.33	0.88–3.18	1.48–5.18	1.01–1.55	--	1.17–3.58
	Model 2 Hazard Ratio**	1.0	1.76	1.56	2.49	1.19	1.0	1.95
	95% CI	--	0.96–3.22	0.82–2.98	1.33–4.69	0.96–1.48	--	1.11–3.42

†IMT quartiles were study-specific.

‡One SD of IMT was ARIC: 0.19 mm and CHS: 0.34 mm

§Crude incidence rate per 10,000 person-years

*Adjusted for age (continuous), race (African American, white), current smoking (yes, no), LDL cholesterol (continuous), natural log triglycerides (continuous), and fibrinogen (continuous).

**Adjusted for Model 1 variables plus systolic blood pressure (continuous)

Table 3

Incidence Rates and Multivariate-Adjusted Hazard Ratios and 95% Confidence Intervals (95% CI) of Intracerebral Hemorrhage (ICH) According to Left Ventricular Hypertrophy (ECG-LVH), ARIC and CHS

		ECG-LVH (MN Codes)		ECG-LVH (Cornell Criteria)	
		No	**Yes**	**No**	**Yes**
ARIC	*n* ICH/N at risk	64/12,843	5/236	62/12,817	7/262
	Incidence Rate*	2.9	15.3	2.8	18.2
	Model 1 Hazard Ratio†	1.0	2.77	1.0	3.67
	95% CI	--	1.09–7.06	--	1.64–8.20
	Model 2 Hazard Ratio‡	1.0	2.00	1.0	2.79
	95% CI	--	0.76–5.25	--	1.22–6.41
CHS	*n* ICH/N at risk	87/4,842	6/234	86/4,814	7/262
	Incidence Rate*	14.5	27.2	14.4	26.5
	Model 1 Hazard Ratio†	1.0	2.02	1.0	1.98
	95% CI	--	0.87–4.68	--	0.91–4.31
	Model 2 Hazard Ratio‡	1.0	1.63	1.0	1.69
	95% CI	--	0.69–3.83	--	0.77–3.71
ARIC + CHS	*n* ICH/N at risk	151/17,685	11/470	148/17,631	14/524
	Incidence Rate*	5.3	20.1	5.2	21.6
	Model 1 Hazard Ratio†	1.0	2.25	1.0	2.53
	95% CI	--	1.20–4.22	--	1.45–4.43
	Model 2 Hazard Ratio‡	1.0	1.73	1.0	2.07
	95% CI	--	0.91–3.28	--	1.18–3.65

*Crude incidence rate per 10,000 person-years

†Adjusted for age (continuous), race (African American, white), current smoking (yes, no), LDL cholesterol (continuous), natural log triglycerides (continuous), and fibrinogen (continuous).

‡Adjusted for Model 1 variables plus systolic blood pressure (continuous)