Incidence and Risk Factors for Stroke in American Indians
The Strong Heart Study

Ying Zhang, MD, PhD; James M. Galloway, MD; Thomas K. Welty, MD; David O. Wiebers, MD;
Jack P. Whisnant, MD; Richard B. Devereux, MD; Jorge R. Kizer, MD, MSc;
Barbara V. Howard, PhD; Linda D. Cowan, PhD; Jeunliang Yeh, PhD; W. James Howard, MD;
Wenyu Wang, PhD; Lyle Best, MD; Elisa T. Lee, PhD

Background—There are few published data on the incidence of fatal and nonfatal stroke in American Indians. The aims of this observational study were to determine the incidence of stroke and to elucidate stroke risk factors among American Indians.

Methods and Results—This report is based on 4549 participants aged 45 to 74 years at enrollment in the Strong Heart Study, the largest longitudinal, population-based study of cardiovascular disease and its risk factors in a diverse group of American Indians. At baseline examination in 1989 to 1992, 42 participants (age- and sex-adjusted prevalence proportion 1132/100 000, adjusted to the age and sex distribution of the US adult population in 1990) had prevalent stroke. Through December 2004, 306 (6.8%) of 4507 participants without prior stroke suffered a first stroke at a mean age of 66.5 years. The age- and sex-adjusted incidence was 679/100 000 person-years. Nonhemorrhagic cerebral infarction occurred in 86% of participants with incident strokes; 14% had hemorrhagic stroke. The overall age-adjusted 30-day case-fatality rate from first stroke was 18%, with a 1-year case-fatality rate of 32%. Age, diastolic blood pressure, fasting glucose, hemoglobin $A_{1c,}$ smoking, albuminuria, hypertension, prehypertension, and diabetes mellitus were risk factors for incident stroke.

Conclusions—Compared with US white and black populations, American Indians have a higher incidence of stroke. The case-fatality rate for first stroke is also higher in American Indians than in the US white or black population in the same age range. Our findings suggest that blood pressure and glucose control and smoking avoidance may be important avenues for stroke prevention in this population. (***Circulation.* 2008;118:1577-1584.)**

Key Words: morbidity ■ mortality ■ stroke ■ risk factors

Although cardiovascular disease is the leading cause of death among American Indians,[1] no cohort study has examined the prevalence, incidence, and risk factors for stroke in this population. Available data on incidence of nonfatal or fatal stroke in American Indians come from a hospital case study[2] and from national survey data with a small number of American Indian participants.[3] Stroke mortality in American Indians has been described in several reports by use of regional or national death certificate data, which may misclassify race, as well as the causes of death.[4–7] To the best of our knowledge, there are no studies of stroke incidence, risk factors, and case mortality in a prospectively followed cohort of American Indians with accurate measurement of baseline biological parameters. Understanding the morbidity, mortality, and risk factors of stroke in American Indians is important so that appropriate prevention interventions can be implemented.

The present study was undertaken to determine stroke incidence among American Indians 45 to 74 years of age and to assess risk factors for incident stroke in this population.

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Methods

Study Population

The Strong Heart Study is a population-based cohort study of cardiovascular disease and its risk factors in 13 American Indian tribes/communities in southwestern Oklahoma, central Arizona, and North and South Dakota. Participants (n=4549; 2703 women) 45 to 74 years old underwent baseline examination from 1989 to 1992. The design, survey methods, and laboratory techniques have been described previously.[8–10] Participants in the present analysis (n=4507) had no history of stroke at the baseline examination. Among them, 306 participants had an incident stroke during a mean

follow-up of 13.4 years by the end of 2004. The first and third quartiles of follow-up time were 9.2 and 14.4 years, respectively. The Indian Health Service Institutional Review Board, institutional review boards of the participating institutions, and participating tribes approved the study. Informed consent was obtained from all participants.

Baseline Evaluation

Information on demographic factors, medical history, medication use, and personal health habits (physical activity, smoking, and alcohol consumption) was collected by personal interview. A physical examination was conducted, and fasting blood samples were collected for laboratory tests, including lipids, lipoproteins, and a 75-g oral glucose tolerance test. Anthropometric measurements were performed, and sitting blood pressure (first and fifth Korotkoff sounds) was measured 3 times consecutively with mercury sphygmomanometers (WA Baum Co, Copiague, NY) after 5 minutes of rest.[11] The averages of the second and third systolic and diastolic blood pressure measurements were used in the analysis.

Hypertension was defined by the criteria of the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Hypertension (JNC-7; systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medication).[12] Prehypertension was defined as systolic blood pressure 120 to 139 mm Hg or diastolic blood pressure 80 to 89 mm Hg. Normal blood pressure was defined as <120/80 mm Hg.

Diabetes was defined by the 1998 Provisional World Health Organization Report[13] (fasting glucose ≥7.0 mmol/L [126 mg/dL] or post–75-g oral glucose challenge blood glucose of ≥11.1 mmol/L [200 mg/dL], or use of an oral hypoglycemic agent or insulin). Impaired glucose tolerance was defined as fasting glucose <7.0 mmol/L with postchallenge glucose between 7.8 and 11.09 mmol/L (140 to 199.9 mg/dL). Impaired fasting glucose was defined as fasting glucose between 6.1 and 6.9 mmol/L (110 to 125.9 mg/dL) with postchallenge glucose <7.8 mmol/L. Impaired glucose tolerance and impaired fasting glucose were combined as 1 category designated as "impaired glucose metabolism." Normal glucose tolerance was defined as fasting glucose <6.1 mmol/L with postchallenge glucose <7.8 mmol/L. Fasting insulin in serum or plasma was measured by radioimmunoassay according to established methods.[14]

Microalbuminuria and macroalbuminuria were defined as urinary albumin/creatinine ratios of 30 to 299 mg/g and ≥300 mg/g, respectively. Past smoking was defined as having smoked at least 100 cigarettes in the subject's entire life, having smoked cigarettes regularly in the past, and not smoking currently. Current smoking was defined as having smoked at least 100 cigarettes in the subject's entire life, having smoked cigarettes regularly, and smoking currently. Past alcohol users were defined as those who had consumed at least 12 drinks of any kind of alcoholic beverage in their entire life and who drank their last drink at least 1 year ago. Current alcohol users were defined as those who consumed at least 12 drinks of any kind of alcoholic beverage in their entire life and who were drinking currently. Information on leisure-time and occupation-related physical activities was collected with a physical activity questionnaire. This questionnaire has been validated in Pima Indians and other populations. An estimate of the individual's self-reported physical activity level was averaged over the past year and expressed as hours per week.[15,16]

Outcome Variables

Incident strokes included fatal and nonfatal events that occurred between the baseline examination and December 31, 2004, in participants without a prior history of stroke.

Fatal Stroke

Fatal events included definite and possible fatal strokes. Deaths that occurred between the baseline examination and December 31, 2004, were confirmed through Indian Health Service or private hospital records and through direct contact by study personnel with participants' families or other informants.[1,8,9,17] The process of ascertaining stroke deaths has been reported previously.[1] Physician members of

the Strong Heart Study Mortality Committee reviewed all medical records, information obtained from informants and death certificates, and coroner's or medical examiner's reports when available. Two reviewers reviewed each chart, and if there was lack of agreement, the chart was then reviewed by the entire adjudication committee. If reviewers found the death was stroke related, the case was sent to neurologists (D.O.W., J.P.W.) for confirmation with previously described criteria[17] that differentiated cardioembolic, lacunar, and other thrombotic cerebral infarctions; intraparenchymal (intracerebral) hemorrhage; subarachnoid hemorrhage; and stroke of unknown type. Mortality follow-up data were available in 99.8% of the participants.

Nonfatal Stroke

The process to confirm nonfatal stroke was similar to that for fatal stroke. Neurologists (D.O.W., J.P.W.) made up the adjudication review committee and provided the final diagnosis for nonfatal events (definite and possible nonfatal strokes) that occurred from the baseline examination to the end of 2004 and for prevalent strokes that occurred before the baseline examination.[1,8,17,18] Stroke subtypes used were the same as described for fatal stroke. Transient ischemic attack was not included in the analysis. If more than 1 event occurred in the same individual, the date of the earliest event was considered the first stroke date.

Statistical Analysis

Person-time incidence rates of stroke were calculated in male, female, and both male and female participants for 3 study centers. Age-specific rates and age-adjusted rates, age- and sex-adjusted rates, and their 95% CIs were calculated. The US 1990 population was used as the standard population in all age-adjustments.

Overall and age-specific proportions of stroke subtypes among all strokes were provided. The proportion of persons with a history of stroke at baseline was calculated for males, females, and all participants for 3 centers. Age-specific, age-adjusted, and age- and sex-adjusted proportions and their 95% CIs were also calculated.

Age-adjusted 30-day and 1-year mortality rates and their 95% CIs for first stroke were calculated for both genders. Mean age at onset of first stroke was calculated for all incident stroke cases and cerebral infarction cases for 1989 to 2004 in both genders and 3 study centers.

Baseline characteristics including age, sex, body mass index, waist circumference, systolic and diastolic blood pressure, and LDL and HDL cholesterol are presented as means (SDs) for participants with or without incident stroke. The t test was used to compare means between 2 groups. Triglycerides, fasting glucose, 2-hour glucose, hemoglobin A_{1c} (HbA$_{1c}$), insulin, and physical activity are presented in quartiles (first quartile, median, third quartile). A nonparametric rank sum test[19] was used to compare the distribution of these variables between groups because of their skewed distributions. Proportions of women, prehypertension, hypertension, diabetes, macroalbuminuria, microalbuminuria, smoking, and alcohol use are presented in participants with and without incident stroke and were compared between groups by the χ^2 test. Two-tailed $P<0.05$ was considered to be statistically significant.

The incidence of stroke was also calculated according to different categories of risk factors, including blood pressure, HDL and LDL cholesterol levels, diabetes, fasting glucose, HbA$_{1c}$, smoking, and albuminuria. The log-rank test was used to compare the incidence of stroke among the categories. The calculation of incidence and the log-rank test were adjusted for age and sex.

Cox proportional hazard models were used to assess association of stroke with its potential risk factors, including age, gender, systolic and diastolic blood pressures, body mass index, waist circumference, LDL and HDL cholesterol, triglycerides, physical activity, smoking, alcohol use, microalbuminuria, and macroalbuminuria. Hypertension and prehypertension were entered in alternative models as categorical variables instead of systolic and diastolic blood pressure. All other covariates remained the same. Additional models considered HbA$_{1c}$ or diabetes instead of fasting glucose; all other covariates remained the same. The multivariable analyses were done separately

Table 1.   Age- and Sex-Specific Incidence Rates of Stroke per 100 000 Person-Years (1989–2004)

Sex and Age, y	Arizona		Oklahoma		South/North Dakota		Rates at All Centers	Whites*		Blacks†	FHS Cohort‡
	Rate	No.	Rate	No.	Rate	No.		Rate	No.		
Male											
45–54	472	16	280	11	284	11	340	61	9	N/A	N/A
55–64	960	14	872	19	938	23	920	363	39	N/A	433
65–74	687	5	1138	13	1113	10	1011	885	62	N/A	1112
Total	627	35	594	43	609	44	609			N/A	
AAR (95% CI)	689 (55–1324)		701 (0–1806)		717 (0–1829)		707 (0–1641)				
Female											
45–54	452	27	321	16	463	24	415	64	10	N/A	N/A
55–64	653	23	594	23	604	20	617	195	24	N/A	218
65–74	777	12	1035	21	1166	18	997	524	55	N/A	697
Total	561	62	551	60	618	62	576				
AAR (95% CI)	614 (202–1025)		622 (0–1509)		718 (0–1621)		653 (0–1378)				
Males and females											
45–54	459	43	303	27	387	35	384	63	19	320	135
55–64	743	37	694	42	746	43	727	273	63	637	323
65–74	748	17	1072	34	1146	28	1002	669	117	972	879
Total	584	97	568	103	614	106	588				
ASAR	649 (445–854)		659 (280–1038)		718 (337–1098)		679 (364–994)				

AAR indicates age-adjusted rate; ASAR, age- and sex-adjusted rate.

*In Rochester, Minn, 1985–1989.

†The Greater Cincinnati/Northern Kentucky Stroke Study, 1993.

‡Framingham Heart Study 1980-2003.

for all strokes and cerebral infarctions but not for hemorrhagic stroke because of the limited number of incident cases (n=37).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Prior Stroke

Among the 4549 participants at baseline, 42 had a history of stroke. The age- and sex-adjusted prevalence proportion was 1132/100 000. The prevalences for age groups of 45 to 54 years, 55 to 64 years, and 65 to 74 years were 450, 1130, and 1870 per 100 000, respectively. Age-adjusted prevalences for men and women were 1625 and 695 per 100 000, respectively. Age- and sex-adjusted prevalence for Arizona, Oklahoma, and South and North Dakota did not differ significantly and was 741/100 000 (10 cases, 95% CI 0 to 1511.9), 1352 (18 cases, 95% CI 0 to 2754.6), and 1193 (14 cases, 95% CI 0 to 3091.9), respectively.

Incidence Rate of Stroke

From 1989 to 2004, 306 incident strokes occurred among Strong Heart Study participants without a prior stroke, an age- and sex-adjusted incidence of 679/100 000 person-years (Table 1). The incidence increased with older age in both men and women in all 3 centers. The age-adjusted incidences for men and women were 707/100 000 and 653/100 000 person-years, respectively.

Stroke Subtypes

Cerebral infarctions were by far the predominant subtype of stroke, constituting 86% of incident stroke cases; 14% of subjects had hemorrhagic stroke, mostly intraparenchymal (Table 2). Intraparenchymal hemorrhages were more common in the youngest age group (45-to-54-year-olds).

Age of Occurrence of First Stroke

The mean age of occurrence of first stroke for all strokes and for cerebral infarction was 66.5 years. Arizona participants with

Table 2.   Proportion of Stroke Subtypes by Age (1989–2004)

Age, y	Cerebral Infarction		Intraparenchymal Hemorrhage		Subarachnoid Hemorrhage		Total
	Proportion, %	No.	Proportion, %	No.	Proportion, %	No.	
45–54	82	73	15.7	14	2.2	2	89
55–64	87.3	89	10.8	11	2	2	102
65–74	88.1	59	7.5	5	4.5	3	67
Total	85.7	221	11.6	30	2.7	7	258

Table 3.   Age-Adjusted 30-Day and 1-Year Mortality From First Stroke (1989–2004)

	Arizona		Oklahoma		South/North Dakota		
Time Point and Category	Mortality, %	No.	Mortality, %	No.	Mortality, %	No.	Total, %
30 Days							
Male	23.3 (15–30)*	8	16.1 (10–23)	7	16.2 (10–23)	7	18 (11–25)
Female	32 (25–38)	19	9.8 (5–14)	7	13.2 (8–18)	8	18.5 (13–24)
Male+female	29.1 (24–34)	27	12.4 (9–16)	14	14.7 (10–18)	15	18.3 (14-23)
1 Year							
Male	39.3 (30–47)	13	31.6 (23–40)	14	23.4 (16–31)	10	31 (23–39)
Female	44.7 (37–52)	26	21.5 (16–28)	14	30.9 (24–38)	18	33.1 (26–40)
Male+female	42.7 (37–48)	39	25.7 (21–31)	28	28 (23–33)	28	32.2 (27–38)

*95% confidence interval.

strokes were younger than Oklahoma participants with strokes (mean 65 versus 68 years old, respectively; $P=0.048$). The mean age of Dakota participants with strokes (66.4 years) did not differ from Oklahoma or Arizona. The average age of stroke onset was similar in men (66.2 years) and women (66.7 years; $P=0.60$).

Survival
Overall 30-day case fatality from first stroke was 18%, with a 1-year case-fatality rate of 32% (Table 3). Although the 30-day and 1-year case-fatality rates for men and women did not differ, fatality rates were higher in Arizona than in the other 2 centers.

Characteristics of Participants With or Without Incident Stroke
Participants with incident stroke were older; had higher systolic and diastolic blood pressures, triglycerides, fasting glucose, HbA$_{1c}$, insulin, and 2-hour glucose levels; had lower HDL cholesterol levels; and were less physically active at baseline than participants who remained stroke-free (Table 4). Hypertension, diabetes, microalbuminuria, and macroalbuminuria were

Table 4.   Comparison of Baseline Characteristics of the Strong Heart Study Participants With and Without Incident Stroke

Variables	Without Stroke (n=4201)	With Incident Stroke (n=306)	P
Age, y	56.1 (8.0)	59.3 (8.1)	<0.001
Female, %	59.5	60	0.8
Body mass index, kg/m^2	30.9 (6.4)	30.6 (5.3)	0.4
Waist circumference, cm	105.1 (14.7)	105.8 (13.3)	0.4
Systolic blood pressure, mm Hg	127.2 (19.6)	134.9 (20.2)	<0.001
Diastolic blood pressure, mm Hg	76.6 (10.1)	78.5 (10.8)	<0.002
LDL cholesterol, mmol/L	3.0 (0.9)	3.0 (0.9)	0.6
HDL cholesterol, mmol/L	1.2 (0.3)	1.1 (0.3)	0.005
Triglycerides, mmol/L	1.3 (0.9, 1.9)	1.5 (1.1, 2.2)	<0.001
Fasting glucose, mmol/L	6.3 (5.5, 9.4)	8.2 (5.9, 13.3)	<0.001
Two-hour glucose, mmol/L	7.8 (6.0, 11.5)	8.9 (6.2, 15.2)	0.02
Hemoglobin A$_{1c}$, %	5.6 (5.0, 7.9)	6.7 (5.5, 10.2)	<0.001
Insulin, pmol/L	96.2 (56.9, 155.4)	106.8 (67.8, 157.8)	0.03
Prehypertension, %	32.4	30.2	0.4
Hypertension, %	38	55.7	<0.001
Diabetes, %	47.3	69	<0.001
Microalbuminuria, %	18.4	27.1	<0.001
Macroalbuminuria, %	9.7	22.7	<0.001
Physical activity, h/wk	10 (1.8, 27.7)	6.9 (0.7, 24.6)	0.04
Current smoking, %	33.7	36.6	0.3
Past smoking, %	33.6	35.6	0.5
Current alcohol use, %	42.4	31.7	<0.001
Past alcohol use, %	41.5	50	0.003

Values in parentheses are SDs (when mean values are presented) or first and third quartiles (when median values are presented).

Table 5. Stroke Incidence (per 100 000 Person-Years) According to Different Risk Factors (Age and Gender Adjusted)

	N	No. of Strokes	Person-Years	Stroke Incidence
Blood pressure				
Normal	1283	43	19 041	301
Prehypertension	1449	92	15 563	539
Hypertension	1760	170	17 252	837
P*				<0.001
Systolic blood pressure, mm Hg				
<120	1641	66	19 825	361
120–139	1808	127	21 097	610
140–159	744	77	8136	756
≥160	294	34	2766	952
P*				<0.001
Diastolic blood pressure, mm Hg				
<80	2765	169	31 939	513
80–89	1281	97	14 955	711
90–99	354	28	4020	769
≥100	85	10	882	1540
P*				<0.001
HDL cholesterol, mmol/L				
<1.0 (40 mg/dL)	1544	126	17 693	750
1.0–1.54 (40–59 mg/dL)	2262	143	26 690	537
≥1.55 (60 mg/dL)	606	28	6918	429
P*				<0.001
LDL cholesterol, mmol/L				
<2.59 (100 mg/dL)	1346	92	14 993	617
2.59–3.35 (100–129 mg/dL)	1528	100	18 079	555
3.36–4.13 (130–159 mg/dL)	965	59	11 545	518
4.14–4.8 (160–189 mg/dL)	315	26	3794	705
≥4.9 (190 mg/dL)	115	8	1323	700
P*				0.94
Diabetes (WHO 1998 criteria)				
Normal	1332	50	16 334	312
Impaired glucose metabolism	891	43	11 112	393
Diabetes	2196	211	23 536	887
P*				<0.001
Fasting glucose, mmol/L				
<6.1 (110 mg/dL)	1873	81	22 691	367
6.1–6.9 (110–125 mg/dL)	679	40	8377	445
≥7.0 (126 mg/dL)	1783	172	19 387	889
P*				<0.001
HbA_{1c}, %				
<5	984	34	11 461	330
5–7	1899	115	23 282	471
>7	1290	130	13 709	971
P*				<0.001
				(Continued)

Table 5. Continued

	N	No. of Strokes	Person-Years	Stroke Incidence
Smoking				
Current	1527	112	17 168	709
Past	1516	109	17 468	514
Never	1457	85	17 318	491
P*				0.004
Albuminuria				
Normal	3084	148	38 014	395
Microalbuminuria	831	80	9074	885
Macroalbuminuria	464	67	3907	1708
P*				<0.001

*P value from log-rank test for comparison of survival curves among categories of the variables.

significantly more prevalent at baseline among participants with subsequent stroke, and those with incident stroke were more likely at baseline to be past alcohol users but less likely to be current alcohol users than those who remained stroke-free.

Risk Factors for Stroke

Participants with elevated baseline levels of blood pressure, fasting glucose, HbA_{1c}, and albuminuria had significantly higher incidence of stroke than those with normal levels (Table 5). Participants with lower levels of HDL cholesterol had significantly higher stroke incidence than those with higher levels. Baseline LDL cholesterol levels were not significantly related to stroke incidence, nor were those of non-HDL cholesterol (data not shown). Current smokers had significantly higher stroke incidence than past smokers and nonsmokers, as did participants with hypertension, prehypertension, diabetes, and impaired glucose compared with those who did not have those conditions.

In a Cox proportional hazard model for all strokes (Table 6), age, diastolic blood pressure, fasting glucose, smoking, and albuminuria were risk factors for stroke incidence. Current and past smokers had 2.4- and 1.6-fold higher risks of incident stroke, respectively, than never-smokers. Macroalbuminuria, and microalbuminuria increased the risk 3.3 and 1.7 times, respectively. When hypertension and prehypertension were put in the model instead of systolic and diastolic blood pressures, the risks of incident stroke were 2.2 and 1.8 times higher than in normotensive participants. When HbA_{1c} was put in the model instead of fasting glucose, each percent increase of HbA_{1c} was associated with a 1.15-fold higher risk of incident stroke. When diabetes and impaired glucose metabolism were put in the model instead of fasting glucose, they increased the risk of incident stroke by 2.1- and 1.2-fold, although the effect of impaired glucose metabolism was not statistically significant. The results of the multivariable model for cerebral infarction only (data not shown) are similar to the results for all strokes. Although insulin levels were associated with incident stroke in univariable analyses, the association was not significant after adjustment for other covariates.

Discussion

The present report provides the first detailed information on stroke incidence rates and risk factors in American Indians

Table 6.   Cox Proportional Hazards Model for All Strokes

Variables	P	Hazard Ratio (95% CI)*
Age, y	<0.001	1.07 (1.05–1.09)
Gender (male vs female)	0.77	0.95 (0.71–1.28)
Systolic blood pressure (per 20 mm Hg)	0.2	1.10 (1.0–1.22)
Diastolic blood pressure (per 10 mm Hg)	0.02	1.21 (1.1–1.48)
Body mass index (kg/m^2)	0.43	0.98 (0.94–1.03)
Waist circumference (cm)	0.95	1.00 (0.98–1.02)
LDL cholesterol, mmol/L	0.8	0.98 (0.85–1.14)
HDL-cholesterol, mmol/L	0.08	0.67 (0.43–1.05)
Triglyceride, mmol/L	0.9	0.99 (0.84–1.17)
Physical activity (h/wk)	0.68	1.00 (0.99–1.01)
Fasting glucose, mmol/L	<0.001	1.07 (1.04–1.1)
Current smoking (vs never smoking)	<0.001	2.38 (1.69–3.36)
Past smoking (vs never smoking)	0.006	1.6 (1.14–2.25)
Current alcohol users (vs never-users)	0.23	0.78 (0.51–1.17)
Past alcohol users (vs never-users)	0.87	1.03 (0.7–1.48)
Microalbuminuria (vs normal)	<0.001	1.73 (1.25–2.38)
Macroalbuminuria (vs normal)	<0.001	3.3 (2.29–4.77)
Alternative models		
Hypertension and prehypertension (instead of systolic and diastolic blood pressure)*		
Hypertension (vs normotensive)	<0.001	2.2 (1.5–3.2)
Prehypertension (vs normotensive)	0.005	1.75 (1.18–2.59)
HbA1$_c$ (instead of fasting glucose)*		
HbA$_{1c}$, %	<0.001	1.15 (1.08–1.21)
Diabetes and impaired glucose (instead of fasting glucose)*		
Diabetes (vs normal glucose tolerance)	<0.001	2.05 (1.41–3.0)
Impaired glucose metabolism (vs normal glucose tolerance)	0.49	1.17 (0.75–1.8)

*All other covariates remained the same.

derived from a large, prospectively followed population-based sample with a broad collection of risk factors and thorough morbidity and mortality surveillance.

Incidence

Compared with other populations of similar age followed up over a similar time period with similar diagnostic methods, the present report documents higher overall stroke incidence in American Indians than in either US whites[20,21] or blacks.[22] Incidence rates for stroke were higher in both sexes compared with whites,[20,21] but sex-specific data comparable to the present study were not available for blacks. We also could not find comparable data for a broad sample of the US Hispanic population, although 1 study reports a stroke incidence for Hispanics that is lower than for blacks but higher than for whites.[23]

Stroke Subtypes

Data pooled from the Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, and the Framingham Heart Study indicated that ischemic and hemorrhagic strokes account for 87% and 13% of all strokes, respectively,[24] almost identical to the proportions of subtypes of first stroke in the Strong Heart Study population. In younger age groups, however, there was a higher proportion of hemorrhagic stroke (mainly intraparenchymal hemorrhage) among American Indians.

Case Fatality of First Stroke

Among American Indians, both the 30-day and 1-year case-fatality rates after first stroke were higher in women than in men, similar to national data.[24] The pooled data from the Framingham Heart Study, Atherosclerosis Risk in Communities Study, and Cardiovascular Health Study showed that 1-year case fatality after a first stroke was 21% for men and 24% for women whose age was >40 years.[24] The 1-year mortality in participants in the Strong Heart Study was almost 1.5 times these rates.[24] We could not find comparable data in other populations for 30-day case fatality.

Risk Factors for Stroke

From the Cox proportional hazard model, age, diastolic blood pressure, fasting glucose, current and past smoking, microalbuminuria and macroalbuminuria, hypertension, prehypertension, HbA$_{1c}$, and diabetes were all risk factors for first stroke in American Indians. Age has been reported as the strongest nonmodifiable risk factor for stroke in several studies.[25–27] In American Indians, age was also a strong risk factor. Although men have a higher risk of stroke than women in other populations, sex was not a significant risk factor for stroke in the present study population.[28] The association between diastolic blood pressure and stroke has been demonstrated in both observational studies and clinical trials.[29,30] Although a clinical trial showed that active treatment of isolated systolic hypertension lowered the incidence of stroke by 42%,[31] systolic blood pressure was not a risk factor for incident stroke, whereas diastolic blood pressure was a risk factor in the Strong Heart Study population, which possibly was related to the fact that 83% of participants in the Strong Heart Study were <65 years old at enrollment. Hypertension and prehypertension were related to incident stroke when treated as categorical variables. Both current smoking and past history of smoking were related to increased stroke risk in the present study population, similar to several other studies.[32–34] Diabetes predicted incident stroke in several studies, with similar hazard ratios, possibly related to diabetic angiopathy in cerebral blood vessels.[25,35] Fasting glucose and HbA$_{1c}$ were significant risk factors for stroke. Fasting glucose has been shown to be a risk factor for stroke in people with or without diabetes in several studies.[36–38] The associations between microalbuminuria and macroalbuminuria and stroke were very strong, which probably reflects the widespread vascular damage of endothelial dysfunction. Further studies of the association between kidney function and stroke incidence are needed.[35,39,40]

Because of the small number of prevalent cases, it was not possible to compare stroke prevalence between the Strong Heart Study cohort and other populations.[20] We also could not compare the age of onset for first stroke with other populations[20] because of the different baseline age range in the Strong Heart Study population.

In summary, incidence and case-fatality rates of stroke in American Indians were high compared with other segments of the US population. Our findings confirm the strong associations between hypertension, diabetes, and cigarette smoking and risk of stroke. Each of these risk factors provides important avenues for intervention to reduce risk. The basis of the higher case fatality from stroke in this population deserves further study.

Acknowledgments

Disclosures
None.

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CLINICAL PERSPECTIVE

The incidence of stroke and its determinants have not been examined in a prospective and systematic fashion in the American Indian population. In this population-based study of American Indians who underwent standardized clinical and laboratory evaluation during the period 1989 to 1992 and regular follow-up through 2004, the rate of first stroke was unusually high. After we accounted for differences in age and sex, stroke incidence exceeded that recorded in community-based studies of white and, notably, black US populations, who have an especially high stroke rate. Moreover, the 1-year case-fatality rate after stroke in American Indians surpassed those of other populations. As in previous epidemiological studies, age, hypertension, diabetes mellitus, and smoking were independent predictors of stroke, as were microalbuminuria, macroalbuminuria, and hyperglycemia. Diastolic but not systolic blood pressure independently predicted stroke, which likely reflects a preponderance of participants <65 years of age. The independent relations of hypertension, diabetes, smoking, and albuminuria (a marker of vascular damage and inflammation) with stroke indicate that these factors heighten cerebrovascular risk in populations where they are prevalent. Clinicians may use this information to advise patients how to reduce the risk of stroke by modifying their health behaviors or lifestyles and consequently improve their risk factors. Amid the current worldwide epidemics of obesity and diabetes, the findings may also aid clinicians in determining prevention strategies that target such risk factors.