Anger Expression and Incident Stroke

Prospective Evidence From the Kuopio Ischemic Heart Disease Study

Susan A. Everson, PhD, MPH; George A. Kaplan, PhD; Debbie E. Goldberg, MS;
Timo A. Lakka, MD, PhD; Juhani Sivenius, MD, PhD; Jukka T. Salonen, MD, PhD, MScPH

Background and Purpose—High levels of anger are associated with an increased risk of coronary heart disease and hypertension, but little is known about the role of anger in stroke risk.

Methods—Anger expression style and risk of incident stroke were examined in 2074 men (mean age, 53.0±5.2 years) from a population-based, longitudinal study of risk factors for ischemic heart disease and related outcomes in eastern Finland. Self-reported style of anger expression was assessed by questionnaire at baseline. Linkage to the FINMONICA stroke and national hospital discharge registers identified 64 first strokes (50 ischemic) through 1996. Average follow-up time was 8.3±0.9 (mean±SD) years.

Results—Men who reported the highest level of expressed anger were at twice the risk of stroke (relative hazard, 2.03; 95% CI, 1.05 to 3.94) of men who reported the lowest level of anger, after adjustments for age, resting blood pressure, smoking, alcohol consumption, body mass index, low-density and high-density lipoprotein cholesterol, fibrinogen, socioeconomic status, history of diabetes, and use of antihypertensive medications. Additional analysis showed that these associations were evident only in men with a history of ischemic heart disease (n=481), among whom high levels of outwardly expressed anger (high anger-out) predicted >6-fold increased risk of stroke after risk factor adjustment (relative hazard, 6.87; 95% CI, 1.50 to 31.4). Suppressed anger (anger-in) and controlled anger (anger-control) were not consistently related to stroke risk.

Conclusions—This is the first population-based study to show a significant relationship between high levels of expressed anger and incident stroke. Additional research is necessary to explore the mechanisms that underlie this association. (***Stroke***. **1999;30:523-528.**)

Key Words: anger ■ epidemiology ■ ischemia ■ risk factors ■ stroke

Previous research has shown that high levels of anger and hostility are significantly associated with increased cardiovascular disease morbidity and mortality,[1–3] although results are not unequivocal.[4,5] Less is known about the role of anger and hostility in cerebrovascular disease or stroke; however, this association is plausible and available evidence is suggestive.

For example, anger expression style has been related to higher resting blood pressure and prevalent as well as incident hypertension,[6–11] although the literature is mixed with regard to whether suppressed anger (anger-in) or outwardly expressed anger (anger-out) increases risk for hypertension. We recently reported that both styles of anger expression in the extreme were associated with excess hypertension risk in middle-aged men.[11] Research also has shown that high levels of anger and hostility are associated with the prevalence, severity, and progression of atherosclerosis or coronary artery disease.[12–15] Moreover, anger and hostility have been associated with several behavioral and biological risk factors for stroke, including greater alcohol and tobacco use, less leisure-time physical activity, higher body mass index (BMI), and higher cholesterol and lipoprotein levels.[16–19]

Finally, 2 early case reports[20–21] and a case-control study[22] concluded that stroke victims had problems managing angry, hostile, and aggressive feelings, and an abstract that reported prospective data from the Framingham Heart Study[23] indicated that stroke incidence over 10 years of follow-up was increased in subjects with tension, anxiety, and anger. However, full details of the latter finding were never published.

Given these observations, the objective in this study was to examine the influence of anger expression style on risk of

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From the Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor (S.A.E, G.A.K); Human Population Laboratory, Public Health Institute, Berkeley, Calif (D.E.G.); Research Institute of Public Health, University of Kuopio, Kuopio, Finland (T.A.L., J.T.S.); and Department of Neurology, University Hospital of Kuopio, Kuopio, Finland (J.S.).

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Correspondence to Susan A. Everson, PhD, MPH, Department of Epidemiology, University of Michigan School of Public Health, 109 S Observatory St, Ann Arbor, MI 48109-2029. E-mail severson@umich.edu

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stroke. This report is from the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD), a longitudinal study designed to examine the relationships between various behavioral and psychosocial risk factors and mortality and morbidity due to cardiovascular diseases and related outcomes. Available data on health habits, illness history, and physiological and anthropometric measures enabled us to examine potential confounding by known risk factors for stroke.

Subjects and Methods

Study Population

The KIHD study is a population-based study of psychological, social, behavioral, and biological risk factors for atherosclerotic vascular disease, ischemic heart disease, mortality, and other outcomes[24] among middle-aged men from the Kuopio region in Eastern Finland, an area of high coronary morbidity and mortality.[25] A total of 2682 participants (82.9% of those eligible), aged 42, 48, 54, or 60 years, were enrolled in the study between March 1984 and December 1989. The protocol for the KIHD study was approved by and conducted in accordance with research guidelines set forth by the Research Ethics Committee of the University of Kuopio. All participants gave informed consent and none received remuneration.

For the present study, subjects were excluded if they had a history of stroke (n=60), incomplete information on the measure of anger expression (n=496) or missing data on covariates (n=52). (The anger expression scales were administered as part of a psychosocial questionnaire that was added to the KIHD study in 1988. Participants who had completed their baseline examination before May 1, 1988, were mailed the questionnaire and asked to complete and return it. Failure to return the questionnaire through nonparticipation, illness, death, or loss to follow-up accounts for the large number of participants with missing data on the anger scales.) Thus, 2074 men without a history of stroke and with complete information on the measure of anger expression and all covariates were eligible for the current study. A comparison of the 548 KIHD subjects with missing data on the anger expression scales or covariates to the 2074 participants with complete data revealed that participants and nonparticipants did not differ in age, high-density and low-density lipoprotein cholesterol (HDL and LDL, respectively), fibrinogen, alcohol consumption, or use of medication for hypertension. However, nonparticipants were more likely to have diabetes and to smoke and had higher blood pressure, greater BMI, and lower incomes than participants ($P<0.04$). Table 1 presents baseline subject characteristics.

Baseline Examinations

Examinations were performed over 2 days, 1 week apart, and consisted of a variety of biochemical, physiological, anthropometric, and psychosocial measures. Medical history and medication use were checked during a medical examination at the baseline examination.

Measurement of Anger Expression

The Spielberger Anger Expression scales[26] were used to measure self-reported levels of anger expression style: outward expression ('anger-out'), inward expression ('anger-in'), and control ('anger-control') of anger. Previous research indicates that these measures are valid and reliable in Finnish samples.[27] Each scale consists of 8 items with statements such as "I say nasty things," "I tend to harbor grudges that I don't tell anyone about," and "I keep my cool." Participants indicated the extent to which each statement describes their general feelings or actions when angry or mad with responses coded from 1 ("hardly ever") to 4 ("almost always"). Previous confirmatory factor analyses[28] of these scales with the KIHD cohort revealed that 7 of the original 24 items on these 3 scales had inadequate goodness-of-fit indices (eg, Tucker-Lewis coefficient); thus, the anger scales were recalculated, and 2 items from the anger-out scale, 4 items from the anger-in scale, and 1 item from the anger-control scale were excluded. Separate scores for each scale were obtained by summing across the items in each scale. Cronbach's α coefficients were $\alpha=0.78$, $\alpha=0.73$, and $\alpha=0.89$ for anger-out, anger-in, and anger-control, respectively.

TABLE 1. Baseline Subject Characteristics

Anger expression scales	
Anger-out	10.6 (2.7)
Anger-in	7.6 (2.2)
Anger-control	21.1 (4.1)
Age, y	53.0 (5.2)
BMI, kg/m^2	26.7 (3.5)
SBP, mm Hg	133.7 (16.9)
DBP, mm Hg	88.4 (10.4)
LDL, mmol/L	4.0 (1.0)
HDL, mmol/L	1.3 (0.3)
Fibrinogen, g/L	3.0 (0.6)
Alcohol consumption, g/wk*	85.6 (131.0)†
Smoking status	
Never, %	27.5
Former, %	40.2
Current, pack-years	25.7 (18.9)
Diabetes, %	4.8
Hypertension, %	20.8
Income, FIM	79 790 (51 535)

FIM indicates Finnish marks. Values are mean (SD) or prevalence (in percentage).

*One drink has ≈13 g of alcohol.

†Average weekly alcohol consumption excludes 13.6% of participants, who reported that they did not consume alcohol.

Ascertainment of Strokes

Incident strokes between 1984 and 1992 were ascertained through the FINMONICA stroke register.[29] Information on stroke incidence between 1993 and December 31, 1996, was obtained by computerized linkage to the national hospital discharge registry. Diagnostic information was collected from hospitals and classified by one neurologist (J.S.) with diagnostic criteria identical to the FINMONICA criteria. A total of 64 first strokes were identified, 50 of which were ischemic (Ninth International Classification of Disease codes ICD 430 to 438). Average time until follow-up was 8.3±0.9 years(mean±SD).

Assessment of Baseline Covariates

Age. Age at baseline was modeled by dummy-coded variables for ages 48, 54, and 60, with age 42 as the referent.

BMI. BMI was calculated as weight (kg) divided by height (m^2) and modeled continuously.

Smoking. Cigarette smoking was assessed by self-report and modeled continuously as pack-years of smoking.

Alcohol consumption. Alcohol consumption, modeled continuously, was assessed by a questionnaire on drinking behavior over the previous 12 months and a 4-day dietary record and calculated as grams of alcohol per week.

Systolic blood pressure (SBP). Blood pressure was measured with a random zero sphygmomanometer (Hawksley) by a trained observer and calculated as the average of 2 supine and 2 seated measurements obtained during a 25-minute rest period. Resting SBP was modeled continuously.

Socioeconomic status (SES). SES was based on yearly income and modeled as a categorical variable in quintiles.

Medications and prevalent chronic diseases. Information on medication for hypertension, diabetes, and other disorders was obtained from a self-administered questionnaire and confirmed during the medical interview. Medications were grouped and coded by a nurse with the Nordic Pharmacopoeia coding system. Prevalence of diabetes was assessed by medication review and fasting blood glucose level, obtained from whole blood samples after at least 12 hours of overnight fasting and measured with the glucose dehydrogenase method after precipitation of the proteins with trichloroacetic acid (Granutest 100, Merck). A person was considered diabetic if he currently used diet or took medication to control diabetes or if he had a fasting blood glucose level of ≥6.7 mmol/L (120 mg/dL). Prevalence of diabetes and use of antihypertensive medications were each modeled as dummy-coded variables. Participants were considered to have prevalent ischemic heart disease (IHD) at baseline if they had a history of angina pectoris or previous myocardial infarction, currently used antiangina medication, or had positive findings of angina according to the London School of Hygiene Cardiovascular Questionnaire.[30]

Lipids. Venous samples were obtained after fasting and abstinence from smoking for 12 hours, abstinence from alcohol for 3 days, and abstinence from analgesics for 7 days. After a 30-minute supine rest, blood was drawn without tourniquet, with Terumo Venoject VT-100 PZ vacuum tubes (Terumo). Samples were cooled immediately on ice (4°C). HDL and LDL were separated from fresh plasma with the use of precipitation and ultracentrifugation and measured enzymatically (Boehringer Mannheim).

Data Analyses

The association between scores on the anger expression scales and incident stroke was assessed with the use of a series of age-adjusted Cox proportional hazards models[31] with scores modeled both continuously and categorically. Subsequent age-adjusted models examined potential confounding by resting SBP, BMI, smoking, alcohol consumption, LDL, HDL, SES, fibrinogen, prevalence of diabetes, and use of medication for hypertension. Statistical analyses were performed with the PHREG procedure from SAS version 6.12 (SAS Institute).

Results

Age-adjusted Cox proportional hazards models that examined the association between anger expression style measured continuously and stroke incidence, including both hemorrhagic and ischemic stroke, showed modest, nonsignificant associations between each 1-point increase in anger-out and stroke risk (RH 1.05; 95% CI, 0.97 to 1.14) and each 1-point increase in anger-in and stroke risk (RH 0.93; 95% CI, 0.83 to 1.05). Anger-control was not related to risk of stroke (RH 1.00; 95% CI, 0.94 to 1.06). However, with anger-out modeled categorically, men with scores in the top one third of the scale were at 85% increased risk of stroke over the 8 years of follow-up, relative to men with low anger-out scores ($P<0.06$). This risk increased to 2-fold after adjustment for age, BMI, resting SBP, smoking, weekly alcohol consumption, SES, HDL, LDL, fibrinogen, prevalent diabetes, and use of antihypertensive medication ($P<0.035$). Men with scores in the middle tertile of the anger-out scale were at 75% increased risk of stroke after risk factor adjustment, but this increase was only marginally significant ($P<0.09$) (Table 2). In contrast, anger-in and anger-control were not consistently related to risk of stroke when modeled categorically, although men in the middle tertile of anger-control scores had a somewhat lowered risk of stroke that was nonsignificant, relative to low scorers on this scale.

TABLE 2. Anger Expression Style and Incidence of Stroke: KIHD Risk Factor Study, 1984–1996

	Model 1		Model 2	
	RH	95% CI	RH	95% CI
Anger-out				
Upper tertile	1.85	0.97, 3.52	2.03	1.05, 3.94
Middle tertile	1.62	0.86, 3.08	1.75	0.92, 3.34
Lower tertile	1.00	Referent	1.00	Referent
Anger-in				
Upper tertile	0.91	0.52, 1.58	0.98	0.56, 1.72
Middle tertile	0.90	0.44, 1.82	0.94	0.47, 1.92
Lower tertile	1.00	Referent	1.00	Referent
Anger-control				
Upper tertile	1.01	0.57, 1.77	1.04	0.59, 1.85
Middle tertile	0.59	0.31, 1.14	0.67	0.34, 1.30
Lower tertile	1.00	Referent	1.00	Referent

No. of strokes studied is 64. Model 1 adjusted for age; Model 2 adjusted for age, resting SBP, BMI, LDL and HDL, fibrinogen, smoking, weekly alcohol consumption, SES, prevalent diabetes, and use of antihypertensive medication.

Ischemic Stroke

The majority (78%) of strokes in our sample were attributed to ischemic causes. Thus, we examined the association between anger expression style and risk of ischemic stroke in separate Cox models. A threshold effect was observed for anger-out, with both the middle and upper tertiles of scorers at more than twice the risk of ischemic stroke, relative to low scorers (upper tertile: RH 2.44; 95% CI, 1.10 to 5.39; middle tertile: RH 2.40; 95% CI, 1.11 to 5.22). Risk-factor adjustment potentiated these associations slightly (upper tertile: RH 2.73; 95% CI, 1.21 to 6.14; middle tertile: RH 2.58; 95% CI, 1.18 to 5.63). Neither anger-control nor anger-in was consistently related to risk of ischemic stroke (data not shown).

Effect of Prevalent IHD

Because coronary heart disease (CHD) is a known risk factor for stroke[32] and because previous research has identified anger and mental stress as triggers for myocardial ischemia and coronary syndromes,[33–35] we then looked at the association between anger-out and incident stroke, stratified by prevalent IHD. Forty-three strokes (30 due to ischemia) occurred in 1593 men without IHD, whereas 21 strokes (20 due to ischemia) occurred in 481 men with IHD at baseline. Anger-out was not consistently related to incident stroke in men without prevalent IHD (data not shown). However, among the 481 men with IHD at baseline (but no previous stroke), men who scored in the top tertile on the anger-out scale had a nearly 6 times greater risk of having a stroke during the follow-up period, relative to the reference group of low scorers (RH 5.75; 95% CI, 1.30 to 25.5). This relationship was strengthened by risk factor adjustment (RH 6.87; 95% CI, 1.50 to 31.4). Men in the middle tertile were at increased risk also; however, this association was not statistically significant (RH 2.6; 95% CI, 0.53 to 12.9).

Discussion

To our knowledge, this is the first epidemiological study to demonstrate a significant prospective association between

anger expression and incident stroke. Men who frequently expressed their anger outwardly when provoked were twice as likely to experience a stroke in the subsequent 8 years than men who were more even-tempered, after taking into account known stroke risk factors in a multivariate analysis. Other styles of anger expression, namely anger-in and anger-control, were not associated with increased stroke risk with or without risk factor adjustment.

The lack of association between anger-in and stroke risk is somewhat surprising for 2 reasons. First, much of the extant literature on the role of anger and hostility in cardiovascular mortality and morbidity, and particularly hypertension, has focused on the association between inhibition or suppression of anger and cardiovascular end points (see References 6, 7, 36, and 37). This is driven partly by Alexander's classic hypothesis[38] that postulated that chronic inhibition of anger would lead to sustained blood pressure elevations. However, several studies have identified a significant relationship between expressed anger and higher resting blood pressure levels or cardiovascular disease (see References 2, 8, and 34). Second, we previously reported that both anger-out and anger-in, in the extreme, are associated with excess risk of hypertension after 4 years in a subset of 537 initially normotensive KIHD participants.[11] In that article, we noted that the observed pattern of findings was consistent with work by Linden and colleagues[39,40] that suggested that expressions of hostility or anger that are deviations from normal in either direction may be related to adverse cardiovascular consequences. It is unclear why anger-in would be related to hypertension risk but not stroke risk in our sample, although the number of participants in the present study is nearly 4 times greater than in our previous study. Additional exploration of the mechanisms that underlie the association between anger-out and risk of stroke may provide clues to this apparent discrepancy.

We found that recognized stroke risk factors did not confound and indeed appeared to slightly potentiate the association between anger-out and risk of stroke in our multivariate models with either all strokes or ischemic strokes as the outcome. Therefore, we calculated the correlations between anger-out and the covariates in the models, with adjustments for age. Limited associations were revealed. The largest positive correlation was with weekly alcohol consumption ($r = 0.10$), and the largest negative correlation was with HDL ($r = -0.06$) ($Ps < 0.01$). Certain covariates were modestly correlated with one another ($r = -0.10$ to $r = 0.29$). The slight potentiation of stroke risk associated with high levels of anger-out in the multivariate models appears to result from the combination of covariates in the models but cannot be explained by the minimal correlations between anger-out and those risk factors.

This relative lack of confounding by known stroke risk factors raises the question of how anger expression increases stroke risk. Our data strongly suggest an ischemic mechanism. Results were stronger for ischemic strokes than for all strokes combined, and the effect of anger on stroke risk was pronounced among men with a history of IHD and essentially nonexistent among those without. Men with IHD who were in the top tertile of scores on the anger-out scale were at nearly 6 times the risk of stroke relative to men with low anger-out scores. This finding is based on a limited number of strokes (n=21) that occurred in a relatively small group (n=481); however, it is consistent with research that has found a positive association between anger and hostility and atherosclerotic disease severity and progression[13–15] and with studies that indicate that the effects of hostility may be stronger in persons with a history of CHD.[41–43] It is plausible that anger could increase the likelihood of a stroke triggered by vasoconstriction or blockage of a blood vessel to the brain, which would be more likely to occur in persons with prevalent IHD than without or in persons with more severe disease.[32]

Related autonomic and neuroendocrine mechanisms also may underlie the relation between anger expression and stroke risk. Prior research has shown that anger and hostility are associated with excessive autonomic and neuroendocrine activation, especially under conditions of stress, and in individuals who experience frequent episodes of anger.[9,44–47] Cross-sectional data from the baseline KIHD examination show that the men in the present study who reported high levels of outwardly expressed anger also showed greater SBP responses in anticipation of an exercise stress test, which is reflective of exaggerated sympathetic arousal. These men also experienced a greater frequency of anger, as indicated by higher hostility scores, and reported more stressful working conditions, as indicated by higher scores on a measure of job demands (data not shown). In addition, recent studies indicate that anger and hostility are associated with increased platelet activation and reactivity,[42,43,48] which are likely to be mediated by serotonergic and adrenergic dysfunction.[43,49] The association between hostility and platelet activation appears to be strongest under conditions of stress and, as noted, in patients with CHD.[42,43] We did not examine platelet functioning in the KIHD participants. However, taken together, available evidence suggests that excessive sympathetic arousal and associated neuroendocrine activation in response to stress and frequently experienced angry outbursts also could underlie the observed association between anger expression and incident stroke. These and related hypotheses await additional research.

It is unclear how a tendency to express anger outwardly may be temporally related to stroke over 8 years of follow-up. The present study was not designed to address this issue. Data from the Framingham Study indicate that strokes are more likely to occur on Monday morning and during the winter.[50] Whether episodes of anger occurring at these times are more likely to trigger cerebrovascular events is unknown, although evidence suggests that they are. Uncontrolled case studies suggest that strong emotions and especially anger may precede or trigger acute myocardial infarction or sudden cardiac death,[51–53] and recent clinical studies confirm this.[34,54] The mechanisms by which anger increases stroke risk may be further understood by identifying the temporal association between episodes of anger and initiation of stroke.

The present study was conducted in a relatively homogeneous population of middle-aged white males; thus, results may not be generalizable to nonwhite samples or women. Stroke rates are known to vary by age, race, and sex[55,56] as do levels of reported hostility and anger.[57,58] Therefore, addi-

tional research is needed to examine the associations between anger and stroke in female and minority populations and to better understand the person and environmental characteristics as well as the underlying mechanisms that link anger expression style to increased risk of stroke.

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