Published in final edited form as:

J Psychosom Res. 2010 February ; 68(2): 131–137. doi:10.1016/j.jpsychores.2009.08.009.

Vital exhaustion increases the risk of ischemic stroke in women but not in men: Results from the Copenhagen City Heart Study

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Abstract

Background—Several studies have indicated an association between depression and the development of stroke, but few studies have focused on gender differences, although both depression and stroke are more common in women than in men. The aim of the present study was to describe whether vital exhaustion, a measure of fatigue and depression, prospectively predicts ischemic and hemorrhagic strokes in a large cohort, with particular focus on gender differences.

Methods—The cohort was composed of 5219 women and 3967 men without cardiovascular disease who were examined in the Copenhagen City Heart Study in 1991–1994. Subjects were followed for 6–9 years. Fatal and nonfatal strokes were ascertained from the Danish National Register of Patients. Cox proportional hazards model was used to describe vital exhaustion as a potential risk factor for stroke.

Results—Four hundred nine validated strokes occurred. A dose–response relationship between vital exhaustion score and the risk of stroke was found in women reaching a hazard ratio (HR) of 2.27 (95% confidence interval: 1.42–3.62) for the group with the highest score. HR was only slightly attenuated by multivariate adjustment. There was no association between vital exhaustion score and stroke in men. HR was strongest for ischemic stroke, whereas no association was seen for hemorrhagic stroke.

Conclusion—Vital exhaustion, a measure of fatigue, conveyed an increased risk of ischemic stroke in women, but not in men, in this study sample.

Keywords

Depression; Fatigue; Ischemic stroke; Validated strokes; Risk factors

Introduction

In the last 10–15 years, growing attention has been given to depression as an independent risk factor that may contribute to the development of cardiovascular disease. Several studies have found an association between depression and ischemic heart disease [1–3], although the association has also been questioned [4]. The possible association between depression

and stroke has also been investigated, and most studies found depression to be a predictor of stroke [5–17]. However, only a few of these studies differentiate between ischemic stroke and hemorrhagic stroke, even though the risk factors associated with these types of stroke are different [6,12,14]. Furthermore, both stroke and depression are more common in women than in men, but most studies have not addressed possible gender difference in the association between depression and stroke.

Vital exhaustion is a construct of items reflecting fatigue, hopelessness, and lack of concentration. Kopp et al. [18] showed that vital exhaustion differs from depression, although there is undoubtedly an overlap between the two constructs.

The aim of the present study was to describe whether vital exhaustion, a measure of fatigue and depression, prospectively predicts stroke in a large study based on the general population. Another objective was to determine whether these symptoms could predict ischemic stroke rather than intracerebral hemorrhage and whether effects differ by gender.

Methods

Population

This study uses data collected during the third examination (1991–1994) of the Copenhagen City Heart Study (CCHS). CCHS was initiated in 1976 as a longitudinal study of an age-stratified random sample of individuals aged 20 years and above. New subjects aged 20–49 years were introduced into the study during the second and third examinations in 1981 and 1991, respectively. The present study is based on data from the third examination comprising 10,135 individuals (response rate, 61%). Five hundred ninety-three subjects were excluded due to prior hospital discharge with a diagnosis of stroke or myocardial infarction obtained from the Danish National Register of Patients for the period 1977 onwards. Subjects with data missing from one or more items in the vital exhaustion score were also excluded ($n=356$). Thus, the study sample consisted of 9186 individuals: 5219 women and 3967 men with an age range of 22–99 years.

Variables

Cardiovascular risk factors were assessed using a self-administered questionnaire, physical examination, and paraclinical tests. Vital exhaustion was measured using a previously described 17-item questionnaire [1] modified from Appels [19]. There were three possible answers to each item: “yes,” “no,” and “I do not know” (the latter was classified as “no”). To explore associations between vital exhaustion and the outcome of interest, we summed the positive responses (“yes”) for each person and divided them into four categories: 0, 1–4, 5–9, and 10–17, with 0 as the reference group. This categorization has been used previously [1]. Risk factor covariates were measured as follows: *Tobacco* consumption was categorized into never smokers, ex-smokers, current smokers of 1–15 g/day tobacco, and current smokers of >15 g/day tobacco. Current tobacco consumption was calculated by equating a cigarette to 1 g of tobacco, a cheroot to 3 g of tobacco, and a cigar to 5 g of tobacco. *Alcohol* consumption was categorized into five groups according to weekly intake: no alcohol consumption, 1–7 U/week, 7–14 U/week, 15–21 U/week, and >21 U/week. One unit was defined as 9–13 g of alcohol. *Diabetes* was self-reported as a “yes” or a “no.” *Physical activity* in leisure time was classified into three groups as follows: passive or light activity <2 h/week (sedentary lifestyle), light activity 2–4 h/week, and light activity >4 h/week or high activity >2 h/week. *Socioeconomic status* was categorized according to educational level, employment, and household income. Educational level was classified as follows: <8 years of schooling (completed primary school), 8–11 years of schooling, and >11 years of schooling. Employment was categorized into “self-employed or superior skilled employee,”

“subordinate skilled employee,” “unskilled employee/unemployed,” and “retired/working at home.” Household income was classified into four quartiles. *Medicine* use was self-reported as use of antihypertensive medications, anticholesterol medications, hormone replacement therapy, and tranquilizers. *Cohabitation* was categorized as “living alone” or “not living alone.” *Systolic blood pressure* was measured in sitting position after 5 min of rest and divided into four categories: “<120 mmHg,” “120–140 mmHg,” “140–160 mmHg,” and “>160 mmHg.” *Body mass index* (BMI) was calculated as weight (kg) divided by height squared (m²) and categorized into four groups: BMI<18.5, 18.5 BMI<25, 25 BMI<30, and BMI 30, according to the standard definition of underweight, normal weight, overweight, and obesity, respectively. *Atrial fibrillation* was registered using an electrocardiogram on physical examination and classified by trained nurses based on the Minnesota Code [20]. *Blood lipids* and *blood glucose* were measured in nonfasting state.

End point

End points were first ever strokes (both fatal and nonfatal) ascertained from the Danish National Register of Patients (*International Classification of Diseases, Tenth Revision*, I60–I69). Two neurologists independently validated all strokes based on discharge letters, medical records, computed tomography/magnetic resonance imaging descriptions, autopsy reports, and/or angiography reports [21]. All strokes were classified into three categories: ischemic stroke ($n=233$), intracerebral hemorrhage ($n=55$), and unspecified stroke ($n=121$). For statistical analysis, ischemic stroke and unspecified stroke were pooled based on the fact that 85% of all strokes are ischemic. Transient ischemic attacks were not considered as strokes and were excluded.

Statistical analysis

Cox proportional hazards model was used to describe vital exhaustion as a potential risk factor for stroke. Age was used as an underlying timescale, and age at baseline was used as entry time. Age at stroke (fatal or nonfatal), death, loss to follow-up (<1%), or end of follow-up was defined as censoring age, whichever came first. After model control of each variable, covariates were treated as categorical variables, as described above (i.e., dummy variables compared to a reference group). Statistical analyses were performed according to type of stroke and gender.

The assumption of proportional hazards was tested formally as described by Grambsch and Thernau [22]. Then models were fitted with three different levels of adjustments: the first model adjusted for age (in the time axis), the second model adjusted for traditional biological and behavioral risk factors, and the third model adjusted for socioeconomic risk factors. The models were examined for men and women combined and separately. For the combined model, interaction between the genders was tested. To avoid the possibility of reverse causation, we repeated analyses after exclusion of the first 2 years of follow-up. All statistical analyses were performed with STATA, version 10.

Results

Table 1 presents the baseline characteristics of the study sample by gender. Approximately half of the study population were smokers, and about 12–13% had a sedentary lifestyle. Women were older and had higher vital exhaustion scores. A larger proportion of women were living alone and had lower household income. Men had a more adverse risk profile: higher alcohol consumption, more diabetes cases, higher systolic blood pressure, and more atrial fibrillation cases. Seventy-two percent of the women were menopausal.

Tables 2 and 3 present the relationship between vital exhaustion and potential confounders, by gender. Increasing vital exhaustion score was significantly associated with smoking, sedentary lifestyle, diabetes, low education, and low income in both genders, and with alcohol consumption, use of antihypertensive drugs, and living alone in men only. Notably, systolic blood pressure was lower in patients with higher vital exhaustion scores even after excluding participants taking antihypertensive drugs.

There were 409 validated strokes: 55 hemorrhagic, 233 verified ischemic, and 121 unspecified. After exclusion of hemorrhagic strokes, the risk of stroke increased with increasing vital exhaustion sum score in women, but not in men (Table 4). Hazard ratio (HR) in women attenuated from 2.58 [95% confidence interval (95% CI): 1.59–4.20] to 2.19 (95% CI: 1.31–3.66) for sum scores of 10–17 by adjustment for traditional and socioeconomic risk factors (test for trend, $P=.005$). For ischemic stroke examined separately (data not shown), the HR for vital exhaustion sum scores of 10–17 in women attenuated from 2.64 (95% CI: 1.38–5.04) to 2.04 (95% CI: 1.04–4.00) (test for trend, $P=.03$). Vital exhaustion sum scores of 1–4 did not increase the risk of stroke. When analyzing hemorrhagic strokes ($n=55$), we found no relationship with vital exhaustion, but the statistical power was limited.

Results were unchanged after exclusion of the first 2 years of follow-up. The number of end points was reduced from 354 to 258 (verified ischemic and unspecified strokes pooled), but HR increased to 2.32 ($P=.005$) for vital exhaustion sum scores of 10–17 in women adjusted for traditional and socioeconomic factors.

Discussion

In this study, which is the largest prospective study to date, a relationship between increasing vital exhaustion score and the risk of stroke was found in women, but not in men. Extensive control for potential confounders attenuated the results, but a significant association was retained.

Only two previous studies have looked at vital exhaustion and the risk of stroke. Schuitemaker et al. [23] found that vital exhaustion increased the risk of stroke by 13% per vital exhaustion point (95% CI: 1.04–1.23). However, the study was limited by the small number of incident cases ($n=14$) and could neither be analyzed by gender nor adjusted for multiple confounders. Schwartz et al. [24] reported the puzzling finding that although both current smoking and high vital exhaustion score were fairly strong risk factors, neither significantly increased the risk of ischemic stroke in the absence of the other. Together, the risk of stroke was increased by almost threefold (HR=2.71; 95% CI: 1.52–4.80). Gender differences were not studied.

Vital exhaustion and depression overlap in their construct, as mentioned. Several studies have investigated the relationship between depression and stroke [5–17,25,26], and most studies found depression to be a predictor of stroke in healthy people [5–17] even after adjusting for traditional and socioeconomic risk factors. Only three studies have discriminated between ischemic stroke and hemorrhagic stroke. In a study of 879 persons, Ohira et al. [6] reported that among people with high depression scores, the relative risk (RR) of ischemic stroke was 2.7 (95% CI: 1.2–6.0). They found no association between depression and cerebral hemorrhage in a research based on a relatively small number of stroke cases ($n=20$). May et al. [12] and Simons et al. [14] also discriminated between ischemic stroke and hemorrhagic stroke, but excluded the latter from further research. Simons et al. found that the elderly ($n=2805$) with depressive symptoms in the highest tertile had a 41% (95% CI: 1.01–1.96) higher risk of ischemic stroke than those in the lowest

tertile. May et al. found in a study of 2201 men an RR of 2.56 (95% CI: 0.97–6.75) for fatal stroke ($n=17$), but no significant relationship for nonfatal and transient ischemic attack.

Few studies discriminate between men and women. Jonas and Mussolino [9] found a statistically significant association between depression and stroke for men (RR=1.68; 95% CI: 1.02–2.75), while the association was nearly significant for women (RR=1.52; 95% CI: 0.97–2.38). Gump et al. [11] reported an HR of 2.03 (95% CI: 1.20–3.44) for stroke mortality in depressed men. Simonsick et al. [16] found divergent results in different geographical regions. As an explanation for this, a lower overall rate of stroke and a low blood pressure level in those cohorts with no association were suggested.

This study found an association between vital exhaustion and ischemic stroke in women, but not in men. The gender difference puzzled us. Women and men may have described symptoms of depression differently, which might have caused the vital exhaustion construct to have more overlap with depression in women. McGowan et al. [27] investigated the association between vital exhaustion and depression. They found that women had higher vital exhaustion scores than men, but they found no significant gender difference in depression score. However, studying vital exhaustion as a risk factor for ischemic heart disease in CCHS, Prescott et al. [1] did not find any gender difference. Thus, the possibility of different associations between vital exhaustion and stroke and myocardial infarction, respectively, being due to different pathways should also be considered.

Several pathways have been suggested to explain the link between depression and cardiovascular disease [28,29]. First, there seems to be a general clustering of behavioral risk factors such as smoking, unhealthy diet, alcohol consumption, and physical inactivity among depressed people. We found that approximately 20% of the risk associated with vital exhaustion was explained by adverse health behavior, and we cannot rule out that some of the remaining risk is caused by unmeasured confounding (e.g., by diet). Second, depression and cardiovascular diseases may be symptoms of the same pathophysiological process. For example, Steffens et al. [30] demonstrated an association between small basal ganglia lesions and depressive symptoms in a population of older people. This could indicate that the presence of depressive symptoms may be a sign of “silent cerebral infarction” and, therefore, an early sign of arteriosclerosis. Another interesting hypothesis is that cytokines released in response to vessel tissue injury relay information to other parts of the body, including the brain, where they provoke the feeling of lack of well-being and tiredness [31]. However, associations were not affected by exclusion of the first 2 years, making “reverse causation” less likely. Third, depression may be the direct cause of the pathophysiological changes that lead to cardiovascular disease. Several theories, including increased levels of fibrinogen, catecholamine, and platelet activation, have been suggested [28,29].

The study has several strengths. The prospective design makes it possible to detect signs of vital exhaustion before the onset of stroke. We excluded participants with cardiovascular disease from baseline and 2 years forward, with the intention of excluding participants with subclinical cardiovascular disease from the beginning of the examination. This resulted in increased estimates.

The use of validated strokes also strengthens this study. Krarup et al. [21] investigated the validation of strokes within the CCHS cohort. One in six strokes diagnosed in the Danish National Register of Patients did not meet the criteria of the World Health Organization stroke definition, and a number of strokes classified as “unspecified” were found to be ischemic. The discharge-diagnosis-based register therefore tends to overestimate the number of cerebrovascular events and to underestimate the number of ischemic strokes. The large sample size of 9542 participants, the participants' wide age range, and the 409 validated

strokes during the 6- to 9-year follow-up period, as well as the wide range of confounders included in the analysis, are to be considered strengths. Copenhagen has a mortality rate higher than that of the rest of the country. However, because of nonresponders with higher mortality rates, this population has a mortality rate lower than that of Copenhagen in total. This does not change the internal validity [32].

The study also has limitations. First, the signs of vital exhaustion are self-reported. The response rate on the third examination was 61%, which may cause a study sample of “selected survivors” with reduced generalizability. The variables, including depression score, were only measured on the third examination; thereby, variables changing over time were not considered. Diet information was not collected during the examination, and this and other unmeasured confounders may be of importance. We did not find a relationship between intracerebral hemorrhage and vital exhaustion. This could be the result of the relatively few cases of intracerebral hemorrhage.

In conclusion, vital exhaustion, a measure of fatigue and depression, conveyed an increased risk of ischemic stroke in women, but not in men, in a dose–response-dependent way (unadjusted). However, approximately 20% of excess risk was explained by traditional and socioeconomic risk factors. There was no significant association between vital exhaustion and intracerebral hemorrhage. To our knowledge, this work is the first to study vital exhaustion as a risk factor for stroke in relation to possible gender differences. Further studies are needed to confirm these findings.

Acknowledgments

This work was supported by The Danish Heart Foundation, The Health Insurance Foundation, The Lundbeck Foundation, and the Heart, Lung, and Blood Institute of the US National Institutes of Health (grant R01 HL54780).

Appendix A. The vital exhaustion construct

	Women (<i>n</i> =5454; 57.2%) [<i>n</i> (%)]	Men (<i>n</i> =4088; 42.8%) [<i>n</i> (%)]	<i>p</i> ^a
Do you think you have come to a dead end?	332 (6.3)	263 (6.6)	.543
Do you feel that you want to give up?	396 (7.5)	222 (5.6)	<.001
Do you sometimes wish you were dead?	419 (7.9)	237 (5.9)	<.001
Do you feel altogether weak?	444 (8.4)	231 (5.8)	<.001
Do you feel dejected?	679 (12.8)	295 (7.4)	<.001
Do you feel fine (no)?	747 (14.1)	501 (12.6)	.028
Do you, at the moment, feel that you do not have what it takes?	962 (18.2)	410 (10.3)	<.001
Do you have feelings of hopelessness recently?	1147 (21.7)	565 (14.1)	<.001
Do you sometimes feel that your body is like a battery running out?	1119 (20.6)	669 (16.8)	<.001
Do you ever wake up with a feeling of exhaustion?	1235 (23.3)	568 (14.2)	<.001
Do you lately have difficulty concentrating?	1081 (20.4)	718 (18.0)	.003
Do you lately feel listless?	1311 (24.7)	798 (20.0)	<.001
Do little things irritate you more than they used to?	1207 (22.8)	888 (22.2)	.534
Do you sometimes just feel like crying?	1760 (33.2)	516 (12.9)	<.001
Do you feel you have not accomplished much recently?	1383 (26.1)	794 (19.9)	<.001
Do you sometimes have difficulty coping?	1952 (36.8)	988 (24.7)	<.001
Do you often feel tired?	2483 (46.6)	1472 (36.7)	<.001

^aP-value from, chi-square test.

Appendix B. Vital exhaustion and confounders, by gender

Variables	HR (95% CI)	Variables	HR (95% CI)
Vital exhaustion, score 0; women	1 (reference)	Diabetes, no	1 (reference)
Vital exhaustion, score 1–4; women	1.04 (0.68–1.58)	Diabetes, yes	1.78 (1.16–2.72)
Vital exhaustion, score 5–9; women	1.38 (0.86–2.22)	Systolic blood pressure, <120 mmHg	1 (reference)
Vital exhaustion, score 10–17; women	2.19 (1.31–3.66)	Systolic blood pressure, 120–140 mmHg	2.43 (1.28–4.62)
Vital exhaustion, score 0; men	1 (reference)	Systolic blood pressure, 140–160 mmHg	3.01 (1.58–5.72)
Vital exhaustion, score 1–4; men	1.30 (0.89–1.91)	Systolic blood pressure, >160 mmHg	4.74 (2.48–9.04)
Vital exhaustion, score 5–9; men	0.95 (0.52–1.71)	Atrial fibrillation, no	1 (reference)
Vital exhaustion, score 10–17; men	0.83 (0.35–1.96)	Atrial fibrillation, yes	2.43 (1.45–4.09)
Smoking, never smokers	1 (reference)	Antihypertensive medication, no	1 (reference)
Smoking, ex-smokers	1.21 (0.85–1.73)	Antihypertensive medication, yes	1.66 (1.24–2.22)
Smoking, 1–15 g/day	1.31 (0.88–1.95)	Income, Quartile 1	1.78 (1.03–3.10)
Smoking, >15 g/day	2.05 (1.42–2.96)	Income, Quartile 2	1.30 (0.76–2.23)
BMI<18.5 (kg/m ²)	3.04 (1.62)	Income, Quartile 3	1.12 (0.65–1.94)
18.5 BMI<25 (kg/m ²)	1 (reference)	Income, Quartile 4	1 (reference)
25 BMI<30 (kg/m ²)	0.78 (0.59–1.02)		
BMI 30 (kg/m ²)	0.87 (0.62–1.22)		

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Table 1

Baseline characteristics of the total cohort, by gender

	Women (<i>n</i> =5454; 57%)	Men (<i>n</i> =4088; 43%)	<i>p</i> ^a
Age (years) [mean (S.D.)]	59.1 (15.4)	56.6 (15.5)	<.001
Stroke [<i>n</i> (%)]	225 (4.1)	184 (4.5)	.26
Age at stroke (years) [mean (S.D.)]	75.4 (9.7)	72.2 (9.8)	<.001
Vital exhaustion score [mean (S.D.)]	3.5 (3.8)	2.5 (3.4)	<.001
Current smokers ^b [<i>n</i> (%)]	2451 (45.4)	2135 (52.9)	<.001
Alcohol consumption per week [mean (S.D.)]	5.6 (7.5)	14.0 (15.5)	<.001
Sedentary lifestyle [<i>n</i> (%)]	685 (12.8)	520 (12.9)	.86
Self-reported diabetes [<i>n</i> (%)]	131 (2.4)	170 (4.2)	<.001
BMI (kg/m ²) [mean (S.D.)]	25.2 (4.7)	26.0 (3.9)	<.001
Systolic blood pressure (mmHg) [mean (S.D.)]	137.4 (23.8)	140.0 (21.1)	<.001
Antihypertensive medication [<i>n</i> (%)]	643 (11.9)	364 (9.0)	<.001
Permanent atrial fibrillation [<i>n</i> (%)]	48 (0.9)	84 (2.1)	<.001
School education <8 years [<i>n</i> (%)]	1864 (34.6)	1326 (32.8)	.07
Low household income [<i>n</i> (%)]	1350 (25.7)	658 (16.4)	<.001
Living alone [<i>n</i> (%)]	2391 (44.2)	1235 (30.4)	<.001

^a*P*-value from chi-square test or *t* test.^bCompared to noncurrent smokers.

Table 2

Association between vital exhaustion and baseline variables in women

	Vital exhaustion score				<i>p</i> ^a
	0 (<i>n</i> =1358; 26.0%)	1–4 (<i>n</i> =2311; 44.3%)	5–9 (<i>n</i> =1067; 20.4%)	10–17 (<i>n</i> =483; 9.3%)	
Stroke ^b [<i>n</i> (%)]	39 (2.9)	64 (2.8)	38 (3.6)	28 (5.8)	.004
Current smokers ^c [<i>n</i> (%)]	545 (40.2)	1040 (45.0)	524 (49.1)	277 (57.4)	<.001
Alcohol consumption per week [mean (S.D.)]	5.6 (7.3)	5.7 (7.0)	5.7 (7.5)	6.1 (10.3)	.210
Sedentary lifestyle [<i>n</i> (%)]	97 (7.2)	240 (10.4)	164 (15.5)	137 (28.5)	<.001
Self-reported diabetes [<i>n</i> (%)]	23 (1.7)	48 (2.1)	28 (2.6)	23 (4.8)	<.001
BMI (kg/m ²) [mean (S.D.)]	25.2 (4.4)	25.0 (4.4)	25.4 (4.9)	25.8 (5.2)	.009
Systolic blood pressure (mmHg) [mean (S.D.)]	140.1 (23.6)	136.7 (24.4)	135.5 (22.9)	137.4 (23.4)	<.001
Antihypertensive medication [<i>n</i> (%)]	166 (12.3)	258 (11.2)	131 (12.3)	65 (13.5)	.481
Atrial fibrillation [<i>n</i> (%)]	9 (0.7)	20 (0.9)	8 (0.8)	7 (1.6)	.190
School education <8 years [<i>n</i> (%)]	467 (34.4)	711 (30.8)	377 (35.3)	219 (45.5)	<.001
Low household income [<i>n</i> (%)]	309 (23.5)	494 (22.0)	281 (27.0)	182 (38.8)	<.001
Living alone [<i>n</i> (%)]	614 (45.3)	955 (41.3)	457 (42.8)	247 (51.1)	.190

^a *P*-value, test for trend.^b Ischemic and unspecified strokes.^c Compared to noncurrent smokers.

Table 3

Association between vital exhaustion and baseline variables in men

	Vital exhaustion score					<i>P</i> ^a
	0 (<i>n</i> =1417; 35.7%)	1–4 (<i>n</i> =1790; 45.1%)	5–9 (<i>n</i> =535; 13.5%)	10–17 (<i>n</i> =225; 5.7%)		
Stroke ^b [<i>n</i> (%)]	50 (3.6)	78 (4.4)	16 (3.0)	11 (4.9)		.625
Current smokers ^c [<i>n</i> (%)]	690 (48.7)	962 (53.7)	301 (56.3)	152 (67.6)		<.001
Alcohol consumption per week [mean (S.D.)]	12.5 (12.5)	14.4 (14.8)	15.1 (17.0)	17.3 (26.1)		<.001
Sedentary lifestyle [<i>n</i> (%)]	122 (8.6)	196 (11.0)	102 (19.1)	75 (33.6)		<.001
Self-reported diabetes [<i>n</i> (%)]	42 (3.0)	65 (3.6)	35 (6.5)	23 (10.2)		<.001
BMI (kg/m ²) [mean (S.D.)]	25.9 (3.6)	26.0 (3.9)	26.1 (4.2)	26.6 (4.9)		.036
Systolic blood pressure (mmHg) [mean (S.D.)]	142.5 (21.7)	139.1 (20.5)	137.2 (19.8)	136.7 (19.5)		<.001
Antihypertensive medication [<i>n</i> (%)]	103 (7.3)	166 (9.4)	55 (10.3)	28 (12.6)		.002
Atrial fibrillation [<i>n</i> (%)]	21 (1.5)	37 (2.1)	9 (1.8)	7 (3.3)		.135
School education <8 years [<i>n</i> (%)]	441 (31.2)	556 (31.1)	181 (33.8)	110 (48.9)		<.001
Low household income [<i>n</i> (%)]	167 (12.0)	266 (15.0)	122 (23.1)	66 (29.3)		<.001
Living alone [<i>n</i> (%)]	352 (24.9)	512 (28.6)	215 (40.2)	111 (49.3)		<.001

^a *P*-value, test for trend.^b Ischemic and unspecified strokes.^c Compared to noncurrent smokers.

Table 4

Vital exhaustion and risk of “ischemic stroke”

Vital exhaustion score	Adjusted for age				Adjusted for age, tobacco, diabetes, BMI, systolic blood pressure, atrial fibrillation, and antihypertensive drugs				Adjusted for age, tobacco, diabetes, BMI, systolic blood pressure, atrial fibrillation, antihypertensive drugs, and income			
	Women		Men		Women		Men		Women		Men	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
0	1.00		1.00		1.00		1.00		1.00		1.00	
1–4	1.16	0.78–1.73	1.42	0.99–2.03	1.10	0.72–1.66	1.33	0.91–1.94	1.04	0.68–1.58	1.30	0.89–1.91
5–9	1.57	1.00–2.46	0.98	0.56–1.72	1.50	0.94–2.41	0.99	0.55–1.79	1.38	0.86–2.22	0.95	0.52–1.71
10–17	2.58	1.59–4.20	1.72	0.90–3.32	2.44	1.47–4.04	0.90	0.38–2.11	2.19	1.31–3.66	0.83	0.35–1.96
<i>P^a</i>	<0.001		0.20		0.001		0.87		0.005		0.83	
<i>P^b</i>	0.15				0.040				0.039			

Stroke was defined as ischemic stroke and stroke unspecified.

The variables alcohol consumption, physical inactivity, anticholesterol drugs, hormone replacement therapy, tranquilizers, blood lipids, blood glucose, education, employment, and living alone were insignificant in the Cox proportional hazards model and excluded from the final model.

^a *P*-value, test for trend.^b *P*-value for interaction between the genders for men and women combined.