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ORIGINAL COMMUNICATION

Lifestyles correlate with stroke recurrence in Chinese inpatients with first-ever acute ischemic stroke

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Abstract

Objectives The previous studies have shown that recurrent stroke (RS) adversely affects the life of survivors of ischemic stroke (IS). However, lifestyle associated with RS has received a little systematic study in Chinese Han patients. We aimed to perform a comprehensive assessment of lifestyle and the potential risk factors associated with RS in Chinese Han inpatients with first-ever acute ischemic stroke by conducting a long-term follow-up.

Methods Using a prospective and longitudinal design, we recruited 421 patients with first-ever acute ischemic stroke who were consecutively admitted to the Acute Stroke Unit between November 2012 and January 2014. Demographic data, vascular risk factors, previous Rankin scale score, and etiology were collected at study intake. Multivariable Cox regression model was used to investigate the influencing factors for RS.

Results Fifty-seven (13.5%) patients experienced RS during the 1-year follow-up period. Multivariable Cox regression analysis revealed that smoking [hazard ratio (HR), 2.153; 95% confidence interval (CI), 1.263–3.671], high-density lipoprotein cholesterol (HDL) (HR 0.438; 95% CI 0.211–0.911), housework (HR 0.488; 95% CI 0.256–0.933), ischemic heart disease (IHD) (HR 2.998; 95% CI 1.281–7.020), daily consumption of fresh fruits (HR 0.477; 95% CI 0.278–0.819), and good sleep quality (HR 0.375; 95% CI 0.216–0.650) were associated with RS among stroke patients.

Conclusions Our results suggest that healthy lifestyle (high fruit intake, smoking cessation, housework, and good sleep quality), higher HDL levels, and lack of IHD may be associated with a lower risk of RS in patients with first-onset IS.

Keywords Cerebral infarction · Lifestyle · Recurrent stroke · Risk factors · Stroke

Introduction

Ischemic stroke (IS) is a leading cause of death and long-term disability in many countries [1]. While stroke mortality rates have reduced due to advances in medical treatment, this has led to an increase in the number of individuals living with the residual effects of stroke [2]. Up to 25% of stroke survivors experience the recurrent ischemic events [1]. Morbidity and mortality rates associated with recurrent stroke (RS) are higher than those associated with primary stroke, with a near doubling of the 30-day fatality rate after a first RS as compared to that after first-ever stroke [3]. Identification of patients who are at an imminent risk of RS is important to improve post-stroke outcomes.

Risk factors for progression of IS are classified according to the potential for modification (non-modifiable, modifiable, or potentially modifiable factors). Non-modifiable risk factors, such as advanced age or ethnicity, serve as markers of high stroke risk, whereas modifiable risk factors, such as

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hypertension and asymptomatic cerebral stenosis, are amenable to interventions for lowering the risk of stroke [4]. The initial stroke severity, delayed admission, living situation, sleep disorders, stroke subtype, vascular risk factors, and other socioeconomic factors have been shown to increase the possibility of RS [5–8].

Stroke is one of the leading causes of death, and the major cause of long-term disability in China and has brought enormous social and economic burdens [9]. China has 2.5 million new stroke cases each year and 7.5 million stroke survivors [10]. The previous study found that the cumulative 5-year risk of RS was about 20%, even in patients already on aggressive medical treatment [11]. Patient suffering an RS has poorer outcomes and higher hospitalization costs than those with a first-ever stroke. To reduce the burden of RS, traditionally, the major focus for prevention has focused on management of risk factors, such as the treatment of hypertension, diabetes, high cholesterol, and so on. However, lifestyle adjustments (good sleep quality, healthier diets, housework, and smoking cessation) cannot be ignored; the study assessing the relationship between lifestyle modification and risk of RS is scarce in Chinese population. To the best of our knowledge, this paper is the first to perform a comprehensive assessment of lifestyle associated with RS in Chinese patients with first-ever IS by conducting a long-term follow-up.

Methods

Source of data

All consecutive patients with first-ever acute ischemic stroke (AIS) treated at the Guangdong Second Provincial General Hospital (located in the southeastern part of China) between November 2012 and January 2014 were recruited in the study. The hospital provides neurological care to more than 1 million population in Southern China. Our stroke team consists of neurologists and nurses who specialize in acute stroke therapy. The inclusion criteria were: patients admitted to the hospital with first-ever IS [clear ischemic infarct confirmed on Magnetic Resonance Imaging (MRI) diffusion sequences], defined according to the World Health Organization, in whom hemorrhagic stroke or other stroke mimicking lesions were excluded by brain imaging, and who presented within 7 days of symptom onset (Fig. 1). Patient exclusion criteria were: (1) within the time window for thrombolysis; (2) cerebral hemorrhage confirmed by head computed tomography; (3) severe heart, hepatic, or renal disease and/or malignant disease; (4) severe mental illness or dementia; (5) history of IS; (6) previous history of carotid endarterectomy or carotid artery stenting.

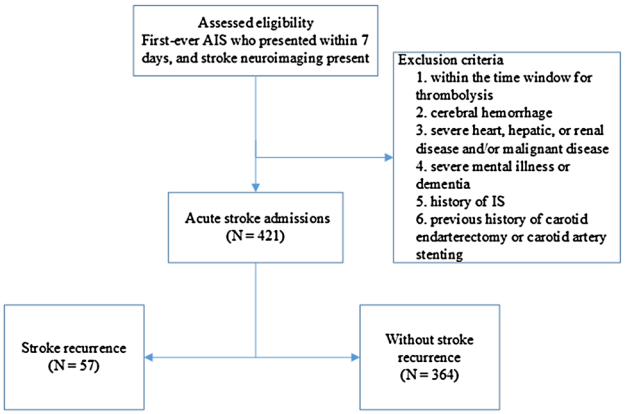

Fig. 1 Schematic illustration of the patient-selection criteria

Stroke severity was evaluated at admission as per the National Institute of Health Stroke Scale (NIHSS; higher scores indicate greater severity) by a stroke neurologist certified (XTL) in the use of this scale. Stroke etiology was determined according to the criteria of the Trial of Org 10,172 in Acute Stroke Treatment (TOAST) classification [12]. The endpoint was a composite of first recurrence of stroke (including transient ischemic attack, or death from cerebrovascular causes). A research nurse (XYL), who was blinded to the radiological findings, collected admission details, demographic data, past medical history, and complete physical examination findings within 7 days of admission. The criteria used to determine the prevalence of certain cardiovascular risk factors at baseline have been previously described [13]; blood pressure classification (0 indicated < 140 mm Hg systolic or < 90 mm Hg diastolic; 1 indicated 140–159 mm Hg systolic or 90–99 mm Hg diastolic; 2 indicated 160–179 mm Hg systolic or 100–109 mm Hg diastolic; 3 indicated ≥ 180 mm Hg systolic or ≥ 110 mm Hg diastolic), light diet (food which has a light taste, not salty, not spicy, and not oily), and daily consumption of fresh fruits (not processed fruit including frozen, dried, or canned fruit or fruit juice). The extent of atherosclerotic burden was graded according to previously reported criteria (0 indicated < 50% stenosis; 1 indicated 50–99% stenosis; 2 indicated occlusion) [14]. The blood vessels responsible for cerebral infarction were divided into anterior circulation, posterior circulation, and both anterior as well as posterior cerebral circulation. In addition, residence situation was categorized as living alone vs living with a spouse/partner or an adult family member (sibling or child over 18 years of age or parent) at the time of index stroke for cases. The self-reported education level was categorized as no education, education up to primary, secondary, and university or above level.

Definition of RS and main variables

RS was defined as new neurological deficit lasting for at least 24 h after the incident stroke (confirmed by computed tomography/magnetic resonance imaging) and which was not attributable to edema, mass effect, or hemorrhagic transformation of the incident infarct [15]. RS was sub-classified into ischemic or hemorrhagic type. Follow-up was performed by trained telephone interviewers (XLL and LJF) at 1, 3, 6, and 12 months and annually thereafter. All recurrences were entered in a stroke data bank independently by the study neurologist (HKL). During follow-up, information about RS was obtained from the patients and relatives. If the patient died during follow-up period, the relatives were contacted to clarify whether the patient had an RS since the last follow-up.

Sleep disorder was defined as occurrence of at least one symptom of the disorder (difficulty in falling asleep, frequent sleep disruption during the night, waking up too early and not being able to get back to sleep, waking up feeling unrefreshed, snoring, unpleasant tingling feelings in the legs, or pauses in breathing) for at least a few nights in a week.

Elders were shown to be less likely to participate in regular physical activity; non-leisure time physical activity, especially housework, which comprises of the majority of physical activity, may substitute for the other types of activities. However, the relation between household-related activities and RS is not well characterized. For this purpose, housework was also included as an independent variable in the analysis of RS. Housework was defined as performance of routine household activities [such as dusting, washing dishes, hand washing of clothes, ironing, hanging up wet clothes, cooking, buying groceries, vacuuming, mopping floors, washing windows, washing cars, painting, wall papering, lawn mowing, outdoor gardening, and caring for another person (e.g., children, dependent spouse or another adult)] for at least 3 h per day on most days of the week. In addition, physical exercise was defined as over 30 min of aerobic exercise at least twice per week.

Data analysis

Statistical analysis was performed using the SPSS software, version 18.0 (SPSS Inc., Chicago, IL, USA). Baseline characteristics of the patients were compared between the two study groups (RS and non-RS groups). Proportions were used for categorical variables, and continuous variables were presented as means and standard deviations or median and interquartile range. Between-group differences were assessed using the *t* test in case of normally distributed continuous variables, and the Chi-squared test or Fisher's exact test in case of categorical variables. In addition, survival function and corresponding 95% confidence intervals (CI) for the follow-up period were estimated according to the Kaplan–Meier method. Backward elimination Cox proportional hazard regression models were used to analyze the predictors of survival, and stroke recurrence at 1 year, in which we included the predefined confounding factors as well as variables associated with $p < 0.15$ in the univariate analyses. Participants who did not experience the outcome events were censored at the most recent follow-up examination or most recent visit. Two-sided probability values < 0.05 were considered indicative of statistical significance.

Results

Baseline characteristics of study population

The study included 421 consecutive patients with first-ever AIS. The median age of patients was 65 (interquartile range 56–73) years; 129 (30.6%) patients were female. 71.5% of the patients had a history of hypertension, 44.7% had hyperlipidemia, 39.9% had diabetes, and 28.0% were current or former smokers. All patients were followed up (median follow-up: 366 days). During 12 months of follow-up, 57 (13.5%) patients experienced RS events (ischemic stroke: 51 patients; hemorrhagic stroke: 6 patients) (Fig. 2). Table 1 presents baseline characteristics of all 421 patients with and without RS who were followed up in this study. In the entire sample, 4 patients lived alone, and none of them have a spouse, which was not related to recurrence. The proportion of patients living alone was 1.0%, proportion of patients who did not live with their spouses was 39.7% (of whom 97.6% lived with their adult family members), proportion of patients with ischemic heart disease (IHD) was 4.0%, proportion of smokers was 28.0%, proportion of patients who reported good-quality sleep was 81.5%, and the proportion of patients who consumed fruits every day was 59.6%. The results of univariate analysis are shown in Table 1. Smoking ($p = 0.011$), daily consumption of fruits ($p = 0.001$), blood pressure classification ($p = 0.030$), sleep disorders ($p < 0.001$), and cerebral atherosclerotic burden ($p = 0.001$) were significantly different between patients with and without RS.

Association between RS and lifestyle

Recurrence rate was 35.3% vs 12.6% among patients with or without IHD, 20.3% vs 10.9% among smokers or non-smokers, 10.5% vs 26.9% among patients who experienced good-quality sleep or sleep disorder, and 9.2% vs 20.0% among patients who consumed fruits every day or not. In multivariate Cox regression analysis, high-density lipoprotein cholesterol (HDL), glycosylated hemoglobin, blood pressure levels at admission, treatment with antihypertensive agents,

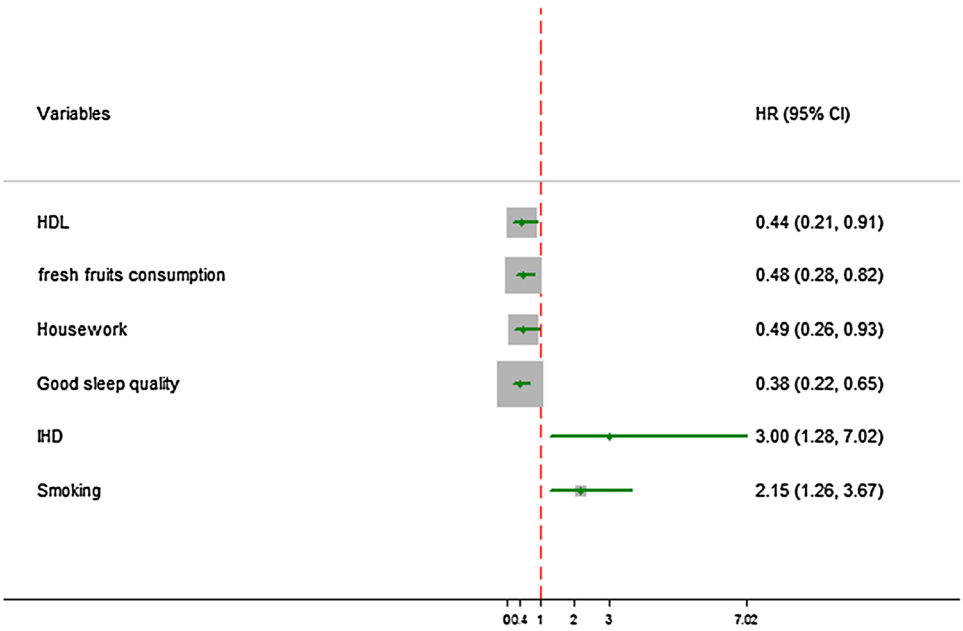

Fig. 2 Kaplan–Meier analysis of the risk of recurrent stroke within 1 year of the presenting event

physical exercise, living alone, and daily consumption of fruits were removed from the model because of a lack of significant association. The following variables were identified as independent predictors of 1-year RS: smoking [hazard ratio (HR), 2.153; 95% CI 1.263–3.671; $p=0.005$]; HDL (HR 0.438; 95% CI 0.211–0.911; $p=0.027$); housework (HR 0.488; 95% CI 0.256–0.933; $p=0.030$); IHD (HR 2.998; 95% CI 1.281–7.020; $p=0.011$); daily consumption of fruits (HR 0.477; 95% CI 0.278–0.819; $p=0.007$); and good sleep quality (HR 0.375; 95% CI 0.216–0.650; $p<0.001$) (Table 2; Fig. 3).

Discussion

To our best knowledge, this was the first study to assess lifestyle and cardiovascular risk factors with RS in a Chinese Han population. We found that lifestyle (housework, sleep quality, smoking, and consuming fruit every day), IHD, and HDL were significantly associated with RS.

An association between lifestyle and RS

Although physical exercise has generally been associated with reduced risk of cardiocerebrovascular events [16], there is limited evidence about the effects of housework on the incidence of RS. Interestingly, our data show that involvement in housework reduces the recurrence rate of IS and improves patient prognosis; however, additional studies are needed to confirm this relationship. Several reasons may explain this association. Housework, akin to physical exercise, was shown to improve vascular endothelial function [17], increase the HDL levels, and reduce inflammation and platelet aggregation [18]; all these factors are believed to play a key role in the development of cerebral atherosclerosis. In addition, housework can burn a certain amount of calories, which has been shown to be associated with reduced obesity. After acute medical and/or neurosurgical treatment for AIS, the early appropriate level of housework may promote recovery of the patient's neural function and may substitute for physical exercise, which can improve the daily life activities of the patients and, eventually, the quality of life.

The frequency of sleep disorders in patients with RS was 36.8%, which indicates that sleep disorder may be common in RS group. The underlying mechanism of this association is not clear. Other parasomnias, such as restless leg syndrome, have been associated with increased mortality in the general population [19]. Sleep is essential for the maintenance of health and normal functioning of the cortex. Adequate sleep is also essential to the energy metabolism of brain cells and has a neurorestorative effect [20]. Sleep disorders are closely related to stroke risk factors such as hypertension, diabetes, and obesity [21]. Obstructive sleep apnea is known to increase the risk of stroke. The underlying mechanism remains elusive; however, the primary reason is as follows: episodes of obstructive apnea can cause intermittent hypoxemia. This can lead to sympathetic activation, surge in blood pressure, and release of vasoconstrictive substances, which ultimately lead to sustained hypertension. Sleep is frequently disturbed after stroke, and some studies suggest that patients with stroke are prone to insomnia [22]. Post-stroke insomnia is often due to environmental factors or complications (respiratory infections, anxiety,

Table 1 Baseline characteristics of patients with and without recurrent stroke during follow-up

Characteristic	Recurrence ($n=57$)	No recurrence ($n=364$)	P value
Age, median (IQR), years	64 (58–71)	65 (56–73)	0.670
Admission NIHSS score, median (IQR)	3 (2–7)	3 (2–6)	0.295
Time between stroke onset and treatment, median (IQR), h	3 (1–5)	3 (1.25-6)	0.167
BMI, mean ± SD, kg/m^2	23.20 ± 2.40	23.59 ± 2.13	0.370
HCY, mean ± SD, mg/dL	16.93 ± 6.32	16.60 ± 6.28	0.723
HbA1c, mean ± SD, %	7.22 ± 2.19	6.65 ± 1.51	0.065
TG, mean ± SD, mmol/L	1.70 ± 0.85	1.64 ± 1.06	0.674
TC, mean ± SD, mmol/L	4.44 ± 1.14	4.70 ± 1.32	0.164
HDL, mean ± SD, mmol/L	1.02 ± 0.29	1.12 ± 0.39	0.067
LDL, mean ± SD, mmol/L	2.73 ± 0.91	2.89 ± 1.06	0.283
Female	15 (26.3)	114 (31.3)	0.440
Smoking[a]	24 (42.1)	94 (25.8)	0.011
Alcohol habit	7 (12.3)	31 (8.5)	0.357
Hypertension	43 (75.4)	258 (70.9)	0.479
Light diet (yes)	51 (89.5)	348 (95.6)	0.053
Consuming fruit every day (yes)[b]	23 (40.4)	228 (62.6)	0.001
Diabetes	24 (42.1)	144 (39.6)	0.716
Hyperlipidemia	26 (45.6)	162 (44.5)	0.876
IHD[a]	6 (10.5)	11 (3.0)	0.008
Statin use	42 (73.7)	279 (76.6)	0.625
Injured vessel			0.812
Anterior circulation	44 (77.2)	287 (78.8)	
Posterior circulation	12 (21.1)	67 (18.4)	
Both anterior and posterior cerebral circulation	1 (1.8)	10 (2.7)	
Hyperhomocysteinemia	23 (40.4)	136 (37.4)	0.666
Toast subtype			0.278
Large artery atherosclerosis	38 (66.7)	220 (60.4)	
Cardioaortic embolism	4 (7.0)	15 (4.1)	
Small artery occlusion	15 (26.3)	129 (35.4)	
Other causes and undetermined causes	0 (0)	0 (0)	
Antiaggregants	44 (77.2)	292 (80.2)	0.647
Antihypertensive agents	30 (52.6)	233 (64.0)	0.099
Antidiabetic agents	19 (33.3)	127 (34.9)	0.819
Blood pressure classification[b]			0.030
Normal	14 (24.6)	129 (35.4)	
Grade 1	7 (12.3)	39 (10.7)	
Grade 2	14 (24.6)	111 (30.5)	
Grade 3	22 (38.6)	85 (23.4)	
Education level			0.186
No education	2 (3.5)	7 (1.9)	
Primary	20 (35.1)	126 (34.6)	
Secondary	34 (59.6)	211 (58.0)	
University or above	1 (1.8)	20 (5.5)	
Sleep disorders (no)[b]	36 (63.2)	307 (84.3)	< 0.001
Living alone	1 (1.8)	3 (0.8)	0.083
Living with spouse/partner	40 (70.2)	214 (58.8)	0.103
CAB[b]			0.001
< 50% stenosis	25 (43.9)	247 (67.9)	
50–99% stenosis	22 (38.6)	78 (21.4)	
Occlusion	10 (17.9)	39 (10.7)	

Table 1 (continued)

Characteristic	Recurrence ($n=57$)	No recurrence ($n=364$)	P value
Housework[b]	12 (21.1)	146 (40.1)	0.006
Physical exercise	33 (57.9)	256 (70.3)	0.060

IQR interquartile range, *NIHSS* National Institutes of Health Stroke Scale, *IHD* ischemic heart disease, *HCY* homocysteine, *TG* triglyceride, *TC* total cholesterol, *HDL* High-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *CAB* cerebral atherosclerotic burden, *SD* standard deviation

[a]Data are presented as number (percentage) of study patients unless otherwise indicated

[b]Variables showing significant between-group difference

Table 2 Final Cox proportional hazards model showing predictors of 1 year stroke recurrence in patients with first-ever ischemic stroke ($n=421$)

	HR	95% CI	P
HDL	0.438	0.211–0.911	0.027
Smoking	2.153	1.263–3.671	0.005
Housework	0.488	0.256–0.933	0.030
Good sleep quality	0.375	0.216–0.650	< 0.001
IHD	2.998	1.281–7.020	0.011
Consuming fruit every day	0.477	0.278–0.819	0.007

HR hazard ratio, *CI* confidence interval

or depression). Less commonly, insomnia may be directly caused by brain damage (pontomesencephalic stroke, paramedian thalamic stroke, and left dorsomedial prefrontal cortex damage) [23, 24]. Therefore, prevention and treatment of complications and appropriate use of antidepressants and sedative-hypnotic drugs are recommended for these patients (except for patients with sleep apnea syndrome). The primary medications for insomnia are benzodiazepines, non-benzodiazepine sedatives, and melatonin agonists. In a cohort study, high annual benzodiazepine dose or long-term use of benzodiazepines was shown to increase the risk of stroke [25]. Therefore, it seems reasonable to use these drugs for a short time. Whether these treatments improve stroke outcome and recurrent risk needs to be further confirmed.

Tobacco smoking is a classical risk factor for cerebrovascular disease. This increased risk is especially

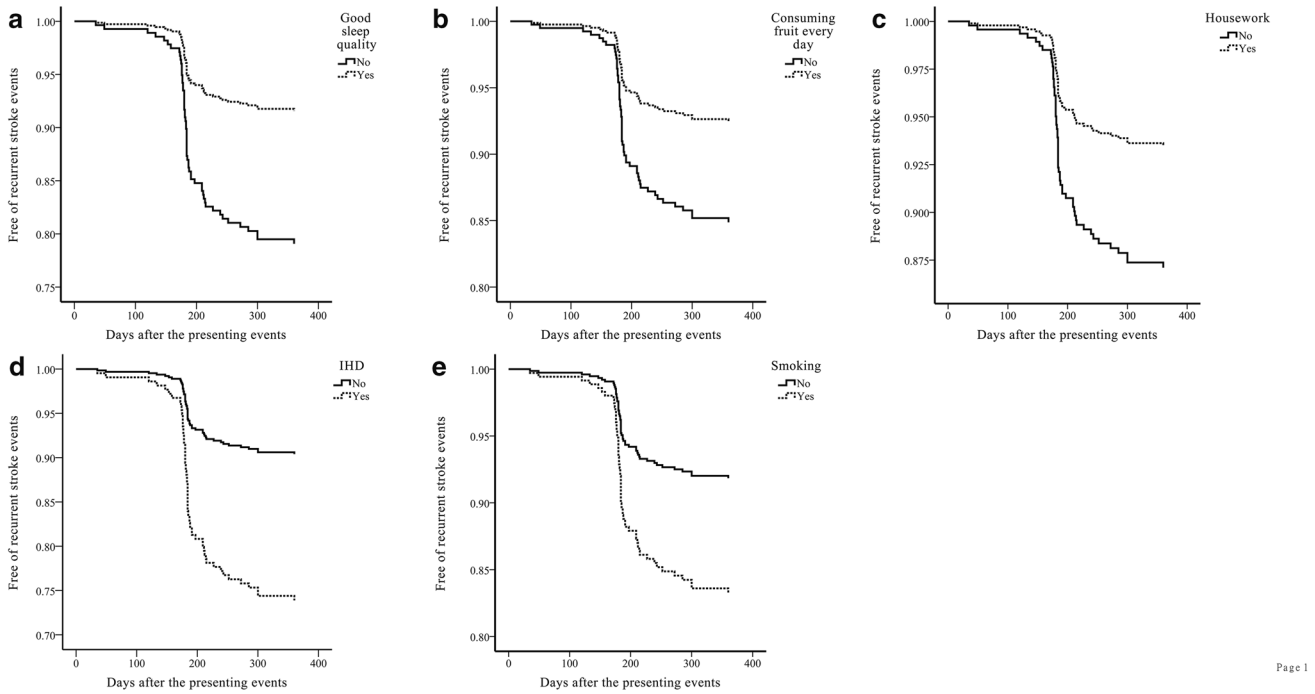

Fig. 3 Cox's proportional hazards regression model identifying predictors of recurrent stroke: **a** Patients with good sleep quality had a significantly lower recurrent risk than those without; **b** consuming fruit every day; **c** housework; **d** ischemic heart disease; **e** smoking

remarkable in patients with the associated hypertension and/or diabetes [26]. However, the effect of smoking on the increased risk of RS is not entirely clear in the literature. In our cohort, tobacco smoking was strongly associated with recurrence of IS at 1-year follow-up even after adjusting for traditional risk factors in Chinese patients with AIS. The evidence on smoking as one of the risk factors for first IS has been extensively discussed in the AHA/American Stroke Association's "Guidelines for the Primary Prevention of Stroke [27]." In contrast to the data on the relationship between tobacco smoking and risk of first cerebral stroke, data pertaining to the association with RS are relatively rare (HR 2.153; 95% CI 1.263–3.671). Other studies have also shown that long-term environmental exposure to tobacco increases post-stroke mortality [28]. Given the overwhelming evidence on harm of smoking and benefits of cessation, patients with RS should adopt the following behavioral and pharmacotherapeutic interventions [29]: quitting smoking (Class I; Level of Evidence C), avoiding environmental tobacco smoke (Class IIa; Level of Evidence B), and helping smokers to quit smoking by oral smoking cessation medications (Class I; Level of Evidence A).

Healthy lifestyle and higher intake of fruits and vegetables were shown to be associated with a reduced risk of ischemic and hemorrhagic stroke [30]. According to a previous prospective study, intake of citrus fruits and apples/pears, but not that of other fruits substantially reduces the risk of stroke [31]. In the present study, increased fruit intake showed an inverse association with the risk of RS (HR 0.477; 95% CI 0.278–0.819). Our findings reinforce the rationale for the current recommendations for the daily consumption of fresh fruits to reduce cardiovascular disease risk. However, which fruits are most beneficial and which major constituents are responsible for the health benefits remain to be determined. Specific flavonoids from citrus fruit and apples were shown to exert neuroprotective effects by improving blood flow, enhancing nitric oxide production, and by inhibiting platelet function [32, 33]. In addition, fresh fruits are rich in dietary fiber, potassium, vitamins, folate, antioxidants, and other active compounds which are known to have potential cardioprotective effects; in addition fresh fruits contain little fat or sodium and relatively few calories [34]. Light diet has been a prior concern for the prevention of cardiovascular diseases including IHD and IS; however, light diet was not associated with RS ($P=0.053$) in this study. The lower dietary fiber and vitamin C content of cooked vegetables may explain why light diet, in contrast to fresh fruits, was not related to RS. Furthermore, our results suggest that fresh fruit consumption but not light diet may reduce the risk of RS. Further prospective studies are needed to confirm these associations together with the further molecular mechanistic data on nutrients of fruits which potentially reduce the risk of IS.

The risk factor associated with RS

Ischemic heart disease (IHD) is a leading cause of morbidity and mortality among stroke patients after the acute phase and is strongly associated with stroke [35]. IS due to carotid atherosclerosis is an IHD risk equivalent; thus, IHD and cerebrovascular diseases are highly correlated [36]. However, increased risk of RS in patients with IHD is rarely reported. One of the most important findings of this study was the independent association between IHD and increased risk of RS after first-ever AIS, after adjusting for the other risk factors (HR 2.998; 95% CI 1.281–7.020). Hence, IHD may be regarded as an independent risk factor for RS. Noncardioembolic stroke and IHD may share several risk factors and pathogenetic pathways [11]. Therefore, patients with coexisting IHD and AIS should be more aggressively treated to reduce their risk of cardiovascular events. More studies should be conducted to investigate the feasibility of aggressive treatment. Although preventive therapies for RS and IHD share several similarities, some key differences do exist. For example, statins are an integral part of IHD preventive therapy but may be less effective for nonatherosclerotic stroke. Therefore, individualized treatment should be emphasized.

Association between HDL and RS

In this prospective cohort study among Chinese population, we did find an inverse relationship between baseline HDL level and RS (HR 0.438; 95% CI 0.211–0.911). This suggests that HDL may have a protective effect against RS in Chinese patients. In recent randomized clinical outcomes trials, increase in HDL-C levels reduced the risk of major coronary events [37]. In addition, a previous study suggested that low level of HDL is negatively associated with the risk of RS among mild-to-moderate stroke survivors [38]; however, whether HDL has a protective effect against different types of stroke is not clear. To the best of our knowledge, a few studies have addressed that HDL constitutes an independent risk factor for RS in Chinese patients with different subtypes of first-ever AIS. This result is explained by the fact that HDL plays an important role in reverse cholesterol transport, i.e., transferring cholesterol from peripheral tissues back to the liver. In addition, the main protective mechanisms of HDL are antioxidant, anti-inflammatory, anti-thrombotic, and endothelial protective effects [39, 40]. Given the potential role of HDL level as a predictor of recurrent IS, future studies should investigate whether residual risk of recurrent vascular events after stroke could be further decreased by raising HDL levels.

Strengths and limitations

Our study has certain strengths and limitations. Strengths include its prospective design and detailed information on RS risk factors, including smoking, living alone, physical exercise, housework, sleep disorders, and serum cholesterol, which enabled us to comprehensively control the potential confounding by these factors. The foremost limitation of the study is its single-center scope and the relatively small sample size of patients with a homogenous ethnic background; therefore, our findings may not be universally applicable. However, based on the rule of ten events per variable, the choice of sample size for this study is appropriate [41]. Since the follow-up was done telephonically, the incidence of silent RS may have been missed. However, our results suggest a protective effect of fresh fruit consumption against the risk of RS. Second, owing to the small sample size, the relationship between the risk factors and RS in the subgroups "other causes" and "undetermined causes" could not be determined. Third, because of the low coverage of social medical insurance in China, a patient's socioeconomic status also influences patients and their relatives' decisions on admission and receiving treatment [42]. As a result, hospital-based studies from developing countries are likely to be biased towards the more serious or complicated cases. In addition, follow-up was performed via the telephonic interview, which could result in inaccurate or incomplete medical information as compared to the personal interview.

Conclusions

In this prospective cohort study, IHD and low levels of HDL were independent predictors of RS. Our findings also suggest that RS may be reduced substantially by an active lifestyle (housework and good sleep quality), cessation of smoking, and fresh fruit intake. The main obstacle will be to educate and convince people on the benefits that can be expected from healthy lifestyle and nutrition.

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Compliance with ethical standards

Conflicts of interest The author declares that there is no competing interest.

Ethical standards The study protocol was approved by the Ethical Committee of the Guangdong Second Provincial General Hospital, and conformed to the ethical guidelines of the 1975 Declaration of Helsinki, with all participants in this study providing written informed consent.

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