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Research article

Associations of cognitive impairment and longitudinal change in cognitive function with the risk of fatal stroke in middle-aged to older Chinese

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ABSTRACT

It is unclear whether cognitive impairment and the longitudinal change in cognition are associated with the risk of fatal stroke in aging populations. Based on the Guangzhou Biobank Cohort Study data a sum of 26,064 participants at baseline and all deaths caused by stroke in a mean follow-up of 14.3 years (standard deviation = 3.2) were included, and the Cox proportional hazard regression was used in this prospective cohort study. Cognitive impairment was respectively associated with an increased risk of fatal strokes (the adjusted hazard ratio (aHR) = 1.38, 95% CI1.16–1.64, $P < 0.001$) and fatal ischaemic stroke (aHR = 1.39, 95% CI1.10–1.77, $P = 0.007$), compared to median cognition; the Delayed Word Recall Test (DWRT) score was associated with a decreasing trend for the risk of fatal strokes in a restricted cubic spline analysis; the longitudinal DWRT score decline was associated with the increased risks of fatal strokes (aHR = 1.42, 95% CI 1.11–1.82, $P = 0.006$) and fatal haemorrhagic stroke (aHR = 1.75, 95% CI 1.10–2.78, $P = 0.02$), compared to the longitudinal DWRT score rise. In summary, cognitive impairment and the longitudinal decline in DWRT scores were associated with the increased risk of fatal strokes; early screening of cognitive function should be conducive to predictive intervention in fatal stroke among relatively healthy middle-aged to older populations.

1. Introduction

Stroke in the World Health Organization clinical criteria was defined as rapidly developing clinical signs of (usually focal) disturbance of local or global brain dysfunction, lasting ≥24 h or leading to death [1]. The Global Burden of Disease reported that approximately 101 million people worldwide suffered from stroke in 2019, making it the second cause of death and the third cause of disability [2], and meantime up to 28.76 million Chinese suffered from stroke [3]. It follows that global stroke has become a public health issue. The main cardiovascular risk factors for stroke include hypertension, high total cholesterol, high-density lipoprotein

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cholesterol, obesity, diabetes mellitus, smoking, short ischaemic attacks, and atrial fibrillation, and the proportion of deaths after the stroke due to pre-existent cardiovascular risk factors before stroke was 27%, this suggests that we must continue to study the factors that cause another 73% of stroke deaths [4]. Cognitive impairment is prevalent and may impact on mortality of the aging population; it is a broad diagnosis of cognitive function, including the full spectrum of mild cognitive impairment (MCI), moderate cognitive impairment, and dementia. MCI is a reversible, daily activity-independent, all-cause mortality-promoting transition state [5,6] between normal cognition and early manifestations of dementia and is a risk factor for dementia [7], wherein pre-stroke dementia linked to the mortality risk of stroke [8]. Additionally, moderate cognitive impairment was related to all-cause mortality [9]; Cognitive impairment is also associated with an increased mortality risk of cardiovascular diseases [10,11]. Previous studies have focused mainly on the relationships between cognitive impairment and those in patients with stroke in a model of retrospective analysis. Among stroke cases with good clinical recovery at three months, the prevalence of any cognitive impairment was 71%, with memory, visual construction and executive functioning most frequently impaired [12]. Multivariate analyses released that the post-stroke prevalence ratio of cognitive impairment increased with older age (2% for each year of age), ethnicity (2.2 fold higher in the black group), and socioeconomic status (42% increased in manual workers) [13]. However, it is not well documented whether cognitive impairment and the longitudinal change in cognitive function are associated with the risk of fatal stroke. Here, we employed a model of prospective analysis to assess the associations of cognitive impairment and the longitudinal change in cognitive function with the risks of fatal stroke (strokes, ischaemic stroke, and haemorrhagic stroke) in relatively healthy middle-aged to older Chinese populations.

2. Methods

2.1. Participants

A prospective cohort study was conducted among all study participants in the Guangzhou Biobank Cohort Study (GBCS) from September 2003 to April 2021. As a tripartite collaborative project between the Guangzhou Twelfth People's Hospital, the University of Hong Kong, China, and the University of Birmingham, UK, GBCS participants at baseline (from September 2003 to January 2008) were recruited from the Guangzhou Health and Happiness Association for Respectable Elders (GHHARE), a large non-social organization with 10 branches in all districts of Guangzhou. The GHHARE membership is open to Guangzhou residents aged $\geq$50 and a monthly fee of RMB 4 (approximately 50 cents) is required. All surviving participants at baseline were invited to return for the 1st follow-up (from March 2008 to December 2012), and the next follow-ups since then continued every 5 years. The trained nurses at the Guangzhou Twelfth People's Hospital conducted face-to-face interviews to collect information on participants through a computerized questionnaire, including demographic information, socio-economic status, lifestyle, self-reported personal history of illness, and physical examination items; all laboratory tests (fasting blood glucose, lipids, etc.) were completed by the trained staff in the clinical laboratory. This study was reviewed and approved by the Guangzhou Medical Ethics Society, and each subject must read the informed voluntary consent form before receiving the questionnaire and physical examination, and then sign or fingerprint to participate. The reliability of the questionnaires was tested by recalling 200 randomly selected subjects for re-interviewing the satisfied results [14]. Details of GBCS, GHHARE, and prospective studies have been reported previously [15,16].

2.2. Exposure indicators

The Delayed Word Recall Test (DWRT), specifically used in population-based epidemiological studies and screening examinations, was employed in this study, it has been known as a sensitive tool for cognitive function measurement [17,18]. All participants at baseline (2003–2008) and the 1st follow-up (2008–2012) conducted the DWRT examination (a learning task of a 10-word list), wherein the modified 10 words include soy sauce, arm, letter, chairman, ticket, grass, corner, stone, and book; these words adhere to suit Chinese culture and dialectal conventions [19,20]. Every investigator read the words face-to-face, and each word was repeated at 1-s intervals; this process was repeated 3 times; the participants were asked to recall those words as far as possible 5 min later, and a score of 1 was given for each correct word. The maximum DWRT score is 10; a score $<$4 was defined as cognitive impairment; the mean DWRT score was 5.5 (standard deviation (SD) = 1.85). Subjects of this study were divided into 3 groups: cognitive impairment (the DWRT score $<$4), median cognitive function (the DWRT score 4–6), and better cognitive function (the DWRT score $\geq$7) [21].

3. Outcomes

Information on the underlying causes of death was obtained primarily through a record linkage of the Guangzhou Centre for Disease Control and Prevention. The outcome was a fatal stroke (up to April 2021) due to available information on the severity, infarct volume, lesion site, and infectious complications; causes of stroke were coded according to the 10th version of the International Classification of Diseases (ICD) as follows: I60–I69 for strokes, I60.0-I62.9 and I69.0-I69.2 for haemorrhagic, I63.0-I63.9 and I69.3 for ischaemic, and the other codes for unclassified. When the certificates were not issued by a health care provider, causes were verified by the GZCDC (being as a part of the quality assurance program through a cross-checking of past medical history) and verbal autopsies (conducted by 5 senior clinicians from the Guangzhou Twelfth People's Hospital, the Universities of Hong Kong, China, and Birmingham, UK).

3.1. Potential confounders

The risk factors for stroke were chosen as confounders including age, gender, education, smoking, alcohol consumption, physical activity (PA), body mass index (BMI), hypertension, diabetes mellitus, sleep duration, and dyslipidaemia. Model 1 was crude without an adjustment for any confounders. Model 2 was adjusted for 11 confounders (including sex, age, sleep duration, education, smoking (never, ever, and current), alcohol consumption (never, ever, and current), PA, BMI, hypertension, diabetes, and dyslipidaemia). Diabetes was defined as a self-reported diagnosis or taking hypoglycemic medications or fasting blood glucose ≥7.0 mmol/L [22]. Hypertension was defined as a self-reported diagnosis or taking antihypertensive medications or a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg [23]. Dyslipidaemia was defined as total cholesterol ≥6.2 mmol/L or low-density lipoprotein ≥4.1 mmol/L or high-density lipoprotein <1.0 mmol/L or triglycerides ≥2.3 mmol/L or taking lipid-lowering medications. PA was determined using the International Physical Activity Questionnaire (IPAQ) [24], wherein inactive (not reaching the moderate and active PA levels), moderate (not reaching active but ≥3 days of high-intensity PA and a total of ≥480 MET-min, or ≥5 days of all intensities of PA combined and a total of ≥600 MET-min per week), and active (high-intensity PA ≥3 days and a total of ≥1,500 MET-min, or a total of ≥7 days of all intensities PA and a total of ≥3,000 MET-min of PA per week) were given by corresponding activity intensities and metabolic energy (MET) values.

3.2. Statistical analysis

The Pearson χ^2 test and one-way analysis of variance (ANOVA) were used to compare categorical and continuous variables between different DWRT groups. Continuous variables were expressed as mean ± SD; Categorical variables were expressed as frequencies and percentages, respectively. The Restricted Cubic Spline (RCS) analysis was used to depict the trend in the relationship between cognitive

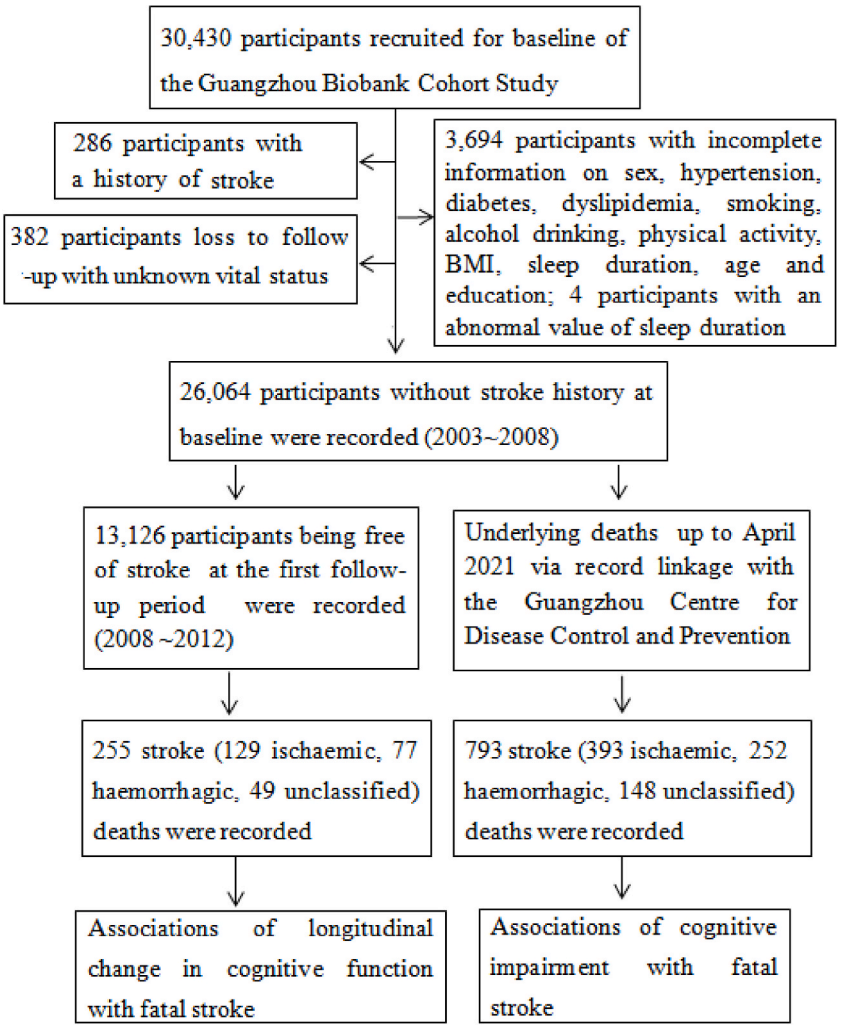

Fig. 1. Flow diagram of the participants selected for analyses in this study.

score and fatal stroke. Associations of cognitive function and the DWRT Score Change (DWRTc) with stroke were analyzed in the Cox proportional regression model with an unadjusted hazard ratio (HR), adjusted HR (aHR), and 95% confidence intervals (CI), wherein the DWRTc was calculated as the formula: DWRTc = $DWRT_{the\ 1st\ follow\text{-}up}$—$DWRT_{baseline,}$ and DWRTc rise (the DWRTc level >0), DWRTc stable (the DWRTc level = 0), and DWRTc decline (the DWRTc level <0) were given. All analyses of this study were performed using the IBM SPSS Windows Statistical System (version 26.0, Armonk, NY, USA) and R Studio (version 4.1.3); all *P* values were two-sided and a statistical significance was defined as $P < 0.05$.

4. Results

4.1. Basic characteristics at baseline

Among the screened total of 30,430 participants in this study, the numbers of excluded participants were 286 due to a stroke history, 382 due to loss of vital status, 4 due to abnormal sleep duration, and 3,694 due to missing values in variables (sex, hypertension, diabetes, dyslipidaemia, smoking, alcohol consumption, physical activity, BMI, sleep duration, age, and education); eventually, a total of 26,064 subjects without a stroke history at baseline were included, and 793 strokes (393 ischaemic, 252 haemorrhagic, and 148 unclassified) deaths were recorded after a mean follow-up time of 14.3 (SD = 3.2) years or a total person-years of 374,017 years; additionally, a total of 13,126 subjects without a stroke history at the 1st follow-up were included for a longitudinal assessment, wherein 255 strokes (129 ischaemic, 77 haemorrhagic, 49 unclassified) deaths were recorded (Fig. 1).

Table 1 shows the basic characteristics of the GBCS participants at baseline. Compared to those with DWRT <4, the participants

Table 1
Baseline characteristics by the DWRT scores in the GBCS participants (n = 26,064).

Characteristic	the DWRT scores			
	cognitive impairment	median cognition	better cognition	*P* value
	<4	4–6	≥7	
Number, n	3,359	15,436	7,269	
Age (mean (SD))	65.15 (7.07)	62.23 (6.90)	59.94 (6.51)	<0.001
Sleep duration (mean (SD))	6.81 (1.47)	6.92 (1.36)	6.99 (1.28)	<0.001
Sex, n (%)				<0.001
female	2,354 (70.1)	10,837 (70.2)	5,518 (75.9)	
male	1,005 (29.9)	4,599 (29.8)	1,751 (24.1)	
Body mass index, kg/㎡				0.046
<18.5	168 (5.0)	705 (4.6)	276 (3.8)	
18.5–23.9	1,665 (49.6)	7,688 (49.8)	3,688 (50.7)	
24–27.9	1,180 (35.1)	5,498 (35.6)	2,611 (35.9)	
≥28	346 (10.3)	1,545 (10.0)	694 (9.5)	
Education, n (%)				<0.001
primary	2,194 (65.3)	6,837 (44.3)	2,031 (27.9)	
middle school	1,018 (30.3)	7,294 (47.3)	4,339 (59.7)	
college	147 (4.4)	1,305 (8.5)	899 (12.4)	
Smoking, n (%)				<0.001
never	2,610 (77.7)	12,231 (79.2)	6,128 (84.3)	
Former	352 (10.5)	1,583 (10.3)	493 (6.8)	
current	397 (11.8)	1,622 (10.5)	648 (8.9)	
Alcohol consumption, n (%)				<0.001
never	2,492 (74.2)	10,856 (70.3)	4,168 (57.3)	
former	117 (3.5)	388 (2.5)	149 (2.0)	
current	750 (22.3)	4,192 (27.2)	2,952 (40.6)	
Physical activity, n (%)				<0.001
inactive	269 (8.0)	1,355 (8.8)	532 (7.3)	
moderate	1,491 (44.4)	6,448 (41.8)	2,638 (36.3)	
active	1,599 (47.6)	7,633 (49.4)	4,099 (56.4)	
Hypertension, n (%)				<0.001
no	1,729 (51.5)	8,663 (56.1)	4,423 (60.8)	
yes	1,630 (48.5)	6,773 (43.9)	2,846 (39.2)	
Dyslipidaemia, n (%)				<0.001
no	1,707 (50.8)	7,635 (49.5)	3,422 (47.1)	
yes	1,652 (49.2)	7,801 (50.5)	3,847 (52.9)	
Diabetes, n (%)				<0.001
no	2,815 (83.8)	13,407 (86.9)	6,429 (88.4)	
yes	544 (16.2)	2,029 (13.1)	840 (11.6)	
Fatal strokes, n (%)	191 (5.7)	482 (3.1)	120 (1.7)	<0.001
Fatal ischaemic stroke, n (%)	96 (2.9)	245 (1.6)	52 (0.7)	<0.001
Fatal haemorrhagic stroke, n (%)	53 (1.6)	154 (1.0)	45 (0.6)	<0.001
Fatal unclassified stroke, n (%)	42 (1.3)	83 (0.5)	23 (0.3)	<0.001

DWRT: Delayed Word Recall Test; hypertension: systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, and a medication or diagnosis; Diabetes: fasting blood glucose ≥7 and a medication or diagnosis; dyslipidaemia: total cholesterol ≥6.2 mmol/L, triglyceride ≥2.3 mmol/L, low density lipoprotein ≥4.1 mmol/L, high density lipoprotein <1.0 mmol/L, and a medication or diagnosis.

with DWRT ≥7 were younger and more females, had higher education but less sleep duration, shared more current alcohol consumption, active physical activity, and dyslipidaemia but less hypertension, diabetes, BMI ≥28 kg/㎡, former and current smoking, and fatal strokes.

4.2. Cognitive impairment and the risk of fatal stroke occurrence

RCS showed a decreasing trend in relationship between the DWRT score and the risk of fatal strokes, with a cutoff value of the DWRT = 5 (Fig. 2A); participants with cognitive impairment shared increased risks of fatal strokes (aHR = 1.38, 95% CI1.16–1.64, $P < 0.001$), fatal ischaemic stroke (aHR = 1.39, 95% CI1.10–1.77, $P = 0.007$), and fatal unclassified stroke (aHR = 1.69, 95% CI1.16–2.46, $P = 0.007$), respectively, compared to those without cognitive impairment and after adjusting for a series of confounders (Fig. 3).

4.3. The longitudinal change in cognitive function and the risk of fatal stroke occurrence

RCS revealed an increased risk of fatal strokes among those with a DWRT decline but a gradually decreasing trend among those with a DWRT rise (Fig. 2B). According to the basic characteristics at the 1st follow-up (Fig. 1), participants with a DWRT decline were older, had more sleep duration, and fatal strokes, but had less hypertension, diabetes, dyslipidaemia, BMI≥28 kg/㎡, alcohol consumption (former and current), smoking (former and current), and active PA, compared to those with a DWRT rise (Table 2). Participants with a DWRT decline had an increased risk of fatal strokes (aHR = 1.45, 95% CI 1.10–1.91, P = 0.009) and fatal haemorrhagic stroke (aHR = 1.92, 95% CI 1.15–3.22, P = 0.01), compared to those with a DWRT rise and after adjusting for a range of confounders (Fig. 4). Participants with a DWRT rise had faintly decreased risks of fatal strokes (aHR = 0.74, 95% CI 0.52–1.04, $P = 0.08$) and fatal haemorrhagic stroke (aHR = 0.59, 95% CI 0.32–1.11, $P = 0.10$), compared to those with a DWRT stable and after adjusting for a range of confounders (Fig. 5).

5. Discussion

In this study, we found that cognitive impairment was associated with increased risks of fatal strokes and fatal ischaemic stroke; a DWRT decline was also associated with increased risks of fatal strokes and haemorrhagic stroke; these results were independent of age, sex, diabetes, hypertension, dyslipidaemia, smoking, alcohol consumption, body mass index, physical activity, sleep duration, and educational attainment. This is the first presentation of the association of longitudinal change in cognitive function with the risk of fatal strokes in aging populations.

The associations of cognitive function with stroke events have been released in recent decades. Patients with ischaemic or haemorrhagic stroke suffer commonly from cognitive impairment [25]; pre- and post-stroke MMSE (Simple Mental State Examination) scores decline in relation to ischaemic stroke [26]; post-stroke cognitive impairment linked to a poor outcome [27]. Such studies focused mainly on cognitive function and post-stroke events.

For pre-stroke cognitive impairment (PCI) on stroke events, patients with MCI shared a higher risk of ischaemic stroke [28], and 13.8% of patients with stroke in France suffered from MCI, wherein pre-existing MCI was associated with 90-day mortality [29]. A number of 30% of patients with ischaemic or haemorrhagic stroke in Norway suffered from PCI [30], wherein PCI was related to cerebrovascular lesions [31]. Severe cognitive impairment was related to a higher risk of stroke in the UK [32]. However, the patients with cognitive impairment and in stroke rehabilitation in the UK had fewer treatments than those without cognitive impairment [33]. PCI has been prevalent worldwide and should be taken its linkage with stroke events into account. Among a series of our findings, we paradoxically showed that cognitive impairment was associated with the increased risks of fatal strokes and fatal ischaemic stroke, and

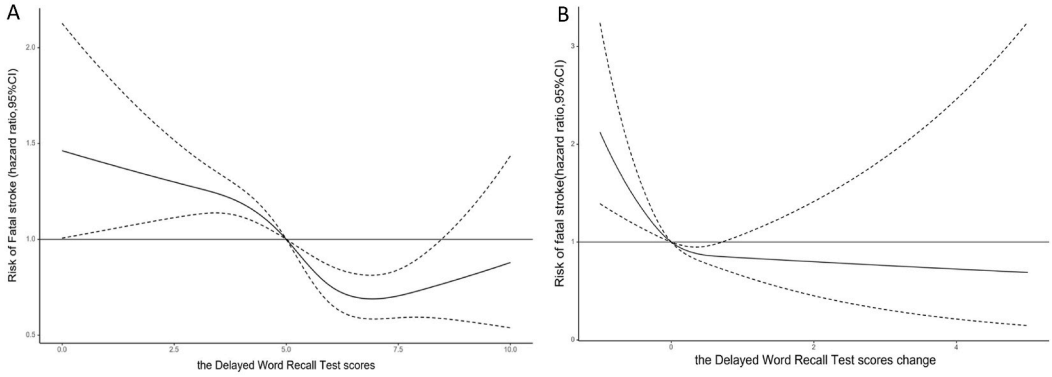

Fig. 2. Associations of the DWRT score (A, n = 26,064) and the DWRT score change (B, n = 13,126) with the risk of fatal strokes in the Restricted Cubic Spline analysis with four knots. The solid line represents the adjusted hazard ratios, with dashed lines showing 95% confidence intervals. A multivariate adjustment was used, including sex, age, diabetes, hypertension, dyslipidaemia, smoking, alcohol consumption, physical activity, body mass index, sleep duration, and education.

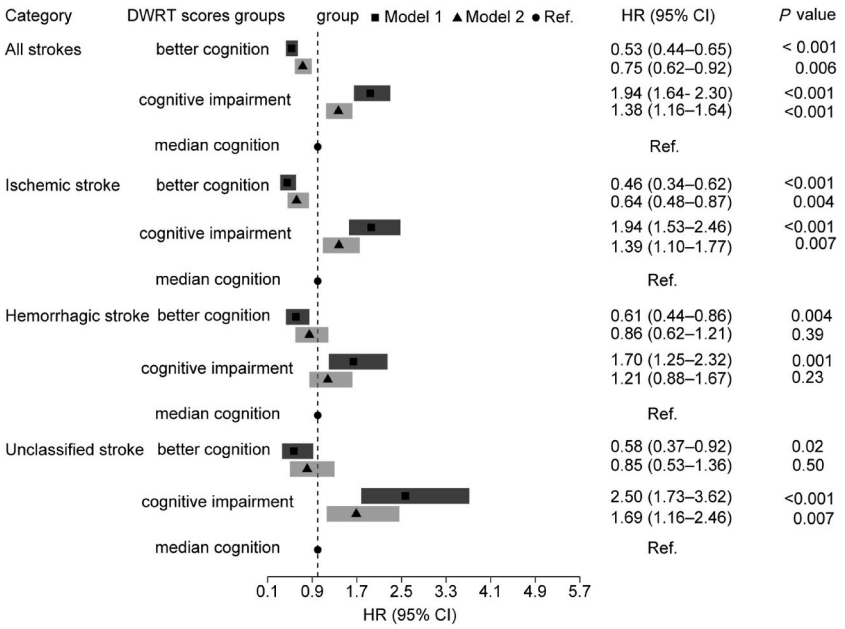

Fig. 3. Associations of DWRT score with the risk of fatal strokes in the GBCS participants (n = 26,064). The graph plots the unadjusted (Model 1) and the adjusted (Model 2) hazard ratios, 95% confidence intervals, and *P* values for DWRT scores. The adjusted confounders include sex, age, diabetes, hypertension, dyslipidaemia, smoking, alcohol consumption, physical activity, body mass index, sleep duration, and education.

the longitudinal change in cognitive function was associated with the risk of not only fatal strokes but fatal haemorrhagic stroke. Such results suggest that cognitive impairment is a complex indicator to assess the risk of stroke in aging populations, this is possibly due to cognitive impairment being related to a decreased ability to care for oneself in daily activities and memory loss affecting the medications in stroke events [34], and then leads to an increased mortality risk in older populations [35,36].

The main strength of our work is that all analytic data especially the completed assessments of cognitive function were from GBCS. Robust inference of a random linkage of the risk of fatal stroke to pre-stroke cognitive impairment was observed in different outcomes by cognitive impairment and longitudinal changes in cognitive function. However, an unexpected result stated that more subjects (n = 6239, 47%) exhibited better performance in DWRT score changes (Table 2). As cognitive function normally decreases with aging, it's reasonable to assume those participants with slightly smaller year ages and more levels of PA, current alcohol consumption, and never smoking, apart from that the performance of cognitive tests might fluctuate.

There are several limitations to our study. First, the DWRT measurements may not be accurate and comprehensive enough for diagnosis; the Mini-Mental State Examination should be employed for further verification. Second, cognitive impairment includes a broad spectrum of mild- and moderate-cognitive impairment, and dementia although stratified analyses were not conducted because of a lack of data from other neuropsychological tests. Third, the subjects are from South China only and the number of strokes is not sufficient to be further tested and verified, therefore, more cases from GBCS or other national cohorts should be included in the future. Fourth, the longitudinal data from a starting point to follow-ups is lengthy due to the same performance as the baseline; more longitudinal changes in cognitive function should be assessed by linear mixed and group-based trajectory models in subsequent cohort studies. Fifth, the unclassified strokes limited the ability to address fatal strokes, especially ischaemic and haemorrhagic strokes.

6. Conclusion

Cognitive impairment was associated with increased risks of fatal strokes and fatal ischaemic stroke; the longitudinal change in DWRT decline was associated with increased risks of fatal strokes and fatal haemorrhagic stroke. Therefore, early screening of cognitive function should be conducive to predictive intervention in fatal stroke among relatively healthy middle-aged to older populations.

Funding

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Table 2
Characteristics according to the DWRT changes of the GBCS participants at the 1st follow-up (n = 13,126).

Characteristics	the DWRT changes			*P* value
	rise	stable	decline	
	>0	= 0	<0	
Number, n	6239	2478	4409	
Age (mean (SD))	64.7 (6.76)	64.6 (7.00)	65.1 (7.19)	0.003
Sleep duration (mean (SD))	6.97 (1.19)	7.09 (1.25)	7.02 (1.25)	<0.001
Sex, n (%)				<0.001
female	4540 (72.8%)	1807 (72.9%)	3041 (69.0%)	
male	1699 (27.2%)	671 (27.1%)	1368 (31.0%)	
Body mass index, kg/㎡				0.537
<18.5	322 (5.16%)	119 (4.80%)	196 (4.45%)	
18.5–23.9	3084 (49.4%)	1197 (48.3%)	2165 (49.1%)	
24–27.9	2204 (35.3%)	891 (36.0%)	1577 (35.8%)	
≥ 28	629 (10.1%)	271 (10.9%)	471 (10.7%)	
Education, n (%)				0.506
primary	2275 (36.5%)	884 (35.7%)	1634 (37.1%)	
middle school	3355 (53.8%)	1371 (55.3%)	2347 (53.2%)	
college	609 (9.76%)	223 (9.00%)	428 (9.71%)	
Smoking, n (%)				0.03
never	5222 (83.7%)	2033 (82.0%)	3592 (81.5%)	
former	506 (8.11%)	209 (8.43%)	396 (8.98%)	
current	511 (8.19%)	236 (9.52%)	421 (9.55%)	
Alcohol consumption, n (%)				<0.001
never	2129 (34.1%)	945 (38.1%)	1732 (39.3%)	
former	145 (2.32%)	76 (3.07%)	175 (3.97%)	
current	3965 (63.6%)	1457 (58.8%)	2502 (56.7%)	
Physical activity, n (%)				0.017
inactive	79 (1.27%)	24 (0.97%)	43 (0.98%)	
moderate	1207 (19.3%)	429 (17.3%)	764 (17.3%)	
active	4953 (79.4%)	2025 (81.7%)	3602 (81.7%)	
Hypertension, n (%)				0.303
no	3337 (53.5%)	1290 (52.1%)	2301 (52.2%)	
yes	2902 (46.5%)	1188 (47.9%)	2108 (47.8%)	
Dyslipidaemia, n (%)				0.892
no	2682 (43.0%)	1054 (42.5%)	1901 (43.1%)	
yes	3557 (57.0%)	1424 (57.5%)	2508 (56.9%)	
Diabetes, n (%)				0.094
no	5426 (87.0%)	2151 (86.8%)	3772 (85.6%)	
yes	813 (13.0%)	327 (13.2%)	637 (14.4%)	
Fatal strokes, n (%)	97 (1.55%)	50 (2.02%)	108 (2.45%)	0.004
Fatal ischemic stroke, n (%)	56 (0.90%)	23 (0.93%)	50 (1.13%)	0.45
Fatal hemorrhagic stroke, n (%)	25 (0.40%)	16 (0.65%)	36 (0.82%)	0.02
Fatal unclassified stroke, n (%)	16 (0.26%)	11 (0.44%)	22 (0.50%)	0.10

Hypertension: systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, medication or diagnosis; diabetes: fasting blood glucose ≥7, medication or diagnosis; dyslipidaemia: total cholesterol ≥6.2 mmol/L, triglyceride ≥2.3 mmol/L, low density lipoprotein ≥4.1 mmol/L, high density lipoprotein <1.0 mmol/L, and medication or diagnosis.

Data availability statement

Data presented in this study are included in the article/supp. Material/referenced in the article; further inquiries can be directed to the corresponding authors.

Ethics statement

The study was approved by the Guangzhou Medical Ethics Committee of the Chinese Medical Association (No. 2002Z2-E2051). Informed consent was obtained from all the participants and the guardians of dead participants before participation. All methods in this study were performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

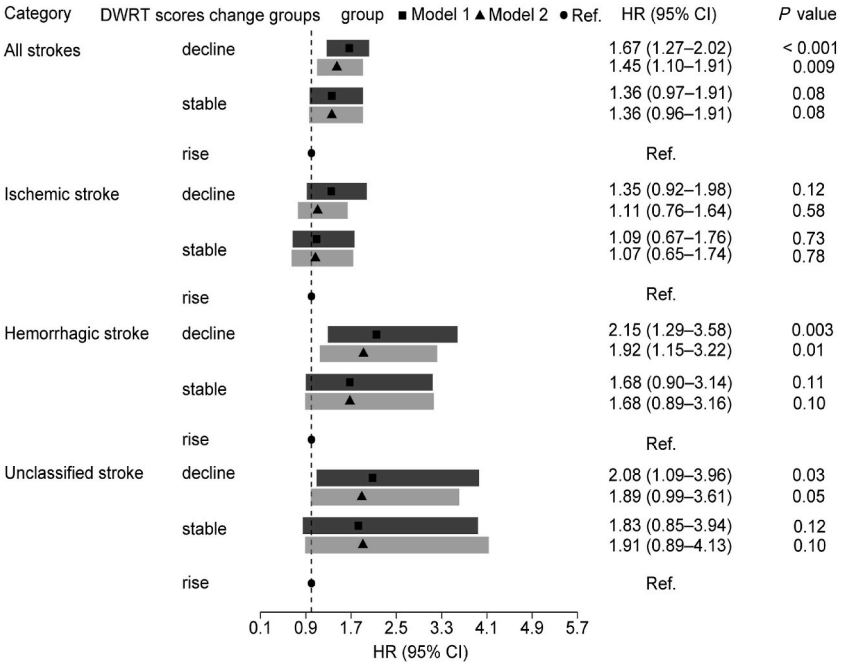

Fig. 4. Associations of the DWRT score change with the risk of fatal strokes in the GBCS participants (n = 13,126). The graph plots the unadjusted (Model 1) and the adjusted (Model 2) hazard ratios, 95% confidence intervals, and *P* values for the DWRT score changes. The adjusted confounders include sex, age, diabetes, hypertension, dyslipidaemia, smoking, alcohol consumption, physical activity, body mass index, sleep duration, and education.

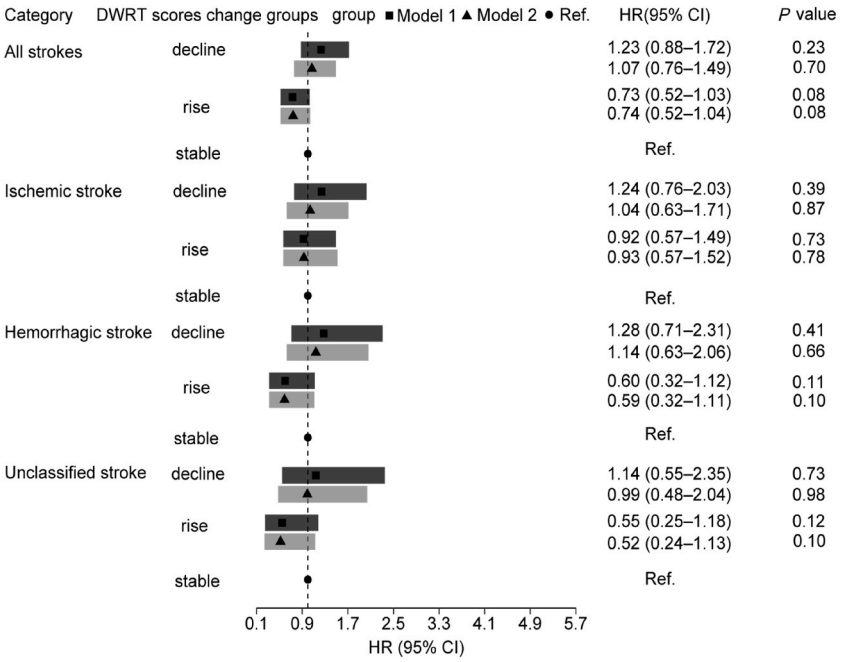

Fig. 5. Associations of the DWRT score change with the risk of fatal strokes in the GBCS participants (n = 13,126). The graph plots the adjusted and unadjusted hazard ratios, 95% confidence intervals, and *P* values for the DWRT score changes. The adjusted confounders include sex, age, diabetes, hypertension, dyslipidaemia, smoking, alcohol consumption, physical activity, body mass index, sleep duration, and education.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

aHR	adjusted hazard ratio
DWRT	Delayed Word Recall Test
MCI	mild cognitive impairment
ICD	International Classification of Diseases
SD	standard deviation
BMI	body mass index
CI	Confidence interval
MET	metabolic energy
GBCS	Guangzhou Biobank Cohort Study
GZCDC	Guangzhou Centers for Disease Control and Prevention
RCS	Restricted Cubic Spline.

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