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The association between atherogenic index of plasma and stroke in Chinese middle-aged and elderly population: a national cross-sectional study

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Abstract

Objective: To investigate the association between atherogenic index of plasma (AIP) and stroke. *Methods:* The 2015 China Health and Retirement Longitudinal Study (CHARLS) survey was used in this study. Logistic regression was adopted to examine the relationship between AIP, calculated as log (TG/HDL), and stroke. Subgroup analysis was used to further explore the associated factors. Restricted cubic spline (RCS) regression was adopted to estimate the non-linear association. Receiver operator characteristic (ROC) analysis was utilized to calculate the cutoff value of AIP. *Results:* In this study, 13,027 participants aged 45 years above were enrolled. The odds ratios in the fully adjusted logistic model across the quartiles of AIP were 1.00 (reference), 1.09 (95% CI 0.69–1.72), 1.62 (95% CI 1.06–2.49), 1.07 (1.08–2.58), respectively. Non-linear association between AIP and stroke was not found using RCS regression (p for non-linearity > 0.05). The subgroup analyses showed that the association between AIP and stroke varied in different gender, alcohol and cigarette consumption, but the interaction effects were insignificant (all $p > 0.05$). The cutoff value of AIP was 0.82, and the area under the curve (AUC) was 0.57.
Conclusion: Elevated AIP is significantly associated with the increased risk of stroke in the middle-aged and elderly Chinese, indicating that AIP may be a predictive factor for stroke among the Chinese middle-aged and elderly.

Keywords: AIP, stroke, CHARLS, aging population, Chinese

INTRODUCTION

Stroke is a severe disease which can cause high incidence of disability and death.[1] With over 2 million incident cases annually, stroke is associated with heavy social burden in China. The incidence of stroke is expected to increase further as a result of population ageing, high prevalence of risk factors (e.g., hypertension), and inadequate management.[2]

Although the mortality due to stroke has reduced, the diagnose and prediction for stroke remains unsatisfactory.[3,4] Many factors have been identified as potential markers for stroke. For example, osteoprotegerin[5], asymmetric dimethylarginine[6], tumor necrosis factor-alpha[7], galectin-3[8] and neuron-specific enolase[9], have been shown to predict stroke, but the predictive values of these indicators are still limited. Among the numerous markers, traditional laboratory indexes related to dyslipidemia, such as triglyceride(TG)[10], total cholesterol (TC)[11] and lipoprotein[12] are of great importance. However, existing methods for measuring the above indicators is associated with a range of limitations, including high cost and technical difficulty. Therefore, the effective prognostic markers remain to be explored. AIP is one of the lipid metabolism indicators, which is cheap and easy to acquire compared with the other indicators. It was proposed for the first time as an atherogenic index, which has closely correlation with lipo-protein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)).[13] Previous studies have demonstrated it is a biomarker of coronary syndrome.[14] Besides, it is also considered as a predictor for rapid plaque progression beyond traditional risk factors.[15] However, few studies have examined the relationship between AIP

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and stroke in Chinese middle-aged and elderly population.

Therefore, this study aimed to evaluated whether AIP could be a predictor of stroke in Chinese middle aged and elderly. We used a dataset from the CHARLS and performed this large population-based study.

METHODS

Data source and sample

In this study, CHARLS 2015 survey dataset was adopted to explore the association between AIP and stroke. CHARLS is a nationally representative longitudinal survey of persons in China 45 years of age or older, including assessments of social, economic, and health circumstances of community-residents. It examines health and economic adjustments to rapid ageing of the population in China.[16] Till now, 4 cycles of investigations were performed and released in 2011, 2013, 2015 and 2018, respectively. Since blood samples were only contained in the survey in 2011 and 2015, we choose the CHARLS survey dataset in 2015 to perform further analysis.

CHARLS 2015 survey samples 21,095 participants from 28 provinces in China. The flowchart of data cleansing was listed in Supplemental Figure 1, and after data cleansing, a total of 13,027 subjects remained for further analysis in this study.

Measures of variables

The AIP is calculated as log (TG/HDL), and it is proposed for the first time by Dobiásová as an atherogenic index, which has closely correlation with lipo-protein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)).[13] In this study, venous blood of participants was collected and centrifuged into plasma, then the plasma was stored at -20°C and transported to Chinese Center for Disease Control and Prevention in Beijing within 2 weeks. Blood biomarkers, including TG, HDL, blood glucose, low-density lipoprotein (LDL), were determined using enzymatic colorimetric tests.

All the participants were interviewed face to face by well-trained researchers. The evaluation of stroke was mainly based on a questionnaire. The participants were asked, “Have you been diagnosed with stroke by a doctor?” Answers from respondents were recorded by the researchers.[17,18] This self-reported diagnostic method has been shown to be reliable to ascertain nonfatal events.[19] In this study, stroke was treated as a kind of cerebrovascular disease, and it include ischemic stroke and intracerebral hemorrhage.

Covariates

Basic characteristics such as demographic features, health status, blood biomarkers, and medical histories was recorded in the CHARLS 2015 survey. In this study, age, gender, marital status, settlements, cigarette consumption, alcohol consumption, body mass index, nap duration were extracted; blood urea nitrogen (BUN) was divided as 0–20 mg/dl and >20 mg/dl.[20] LDL is classified into two groups >120 mg/dl and <120 mg/dl. Total cholesterol is classified into >200 mg/dl and <200 mg/dl. Hyperuricemia is defined as a blood uric acid concentration higher than 420 µmol/l. Center for Epidemiologic Studies Depression scale (CESD)-10 questionnaire was adopted, and scores >10 were defined as depression. Arthritis, digestive diseases, renal diseases and hepatic diseases were investigated by interviewers or determined in the labs.

Statistical analyses

In this study, variables were described as mean ± standard deviation (SD), proportions (%) and median (25–75% quartile) according to the data types. Chi-square test, ANOVA, and Kruskal–Wallis tests were used in categorical and continuous variables, respectively, to test the differences of covariates among different AIP quartiles. To avoid the collinearity between variables, correlation coefficients were calculated using Pearson or Spearman tests before performing regressions.

The association between AIP and the risk of stroke was explored using logistic regression analyses. The regression results were expressed as odds ratio (OR) with 95% confidence intervals (95% CI). A set of regression models were built to test the robustness of conclusions: Model 1 –univariate logistic regression between AIP and prevalent stroke; Model 2 – adjusting for demographic features including age, gender, martial, settlements, sleep and nap duration; Model 3 – further adjusting for smoke, alcohol consumption, BMI, depression on Model 2; Model 4 –further adjusting for smoke, alcohol consumption, BMI, depression on Model 3; Model 5 – further adjusting for hepatic disease. Additionally, the multiplicative interaction between AIP and covariates was tested by subgroup analyses. Further, RCS regression (three knots, at 10, 50, 90 quartiles) was used to visualize the association between AIP and stroke. ROC analysis was adopted to calculate the cutoff value of AIP. All analyses and figures were made using STATA (16.0) and R3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). $p < 0.05$ (two-sided) was seen as significant in statistics.

RESULTS

Baseline characteristics of participants attending CHARLS in 2015

In this survey, a total of 13,027 respondents were enrolled in the final analyses, and the characteristics of participants were summarized in Table 1. The mean age of participants was 60.03 ± 10.09 years and 6,053 (46.5%) of them were men. All participants were categorized into four groups according to the quartiles of AIP, and the ranges of the AIP quartiles were -1.23 to 0.43, 0.43 to 0.84, 0.84 to 1.31, and 1.31 to 3.61, respectively.

The association between AIP and stroke

To assess the association between AIP and stroke, five models were built. The prevalence of stroke was 1.47%, 1.84%, 2.67% and 2%. Across the AIP quartiles, and the ORs were listed in Table 2. In model 1, univariate logistic regression was adopted. Compared with the first quartile of AIP, the ORs were 1.26 (95% CI 0.86-1.84) in the second quartile, 1.84 (95% CI 1.29-2.62) in the third quartile, and 1.79 (95% CI 1.25-2.56) in the fourth quartile (p for trend <0.001). In model 2, the positive association between AIP and stroke became stronger when adjusting for demographic features including age, gender, martial, settlements, sleep and nap duration, and the ORs were 1.21 (95% CI 0.80-1.84), 1.97 (95% CI 1.34-2.88), 2.14 (95% CI 1.46-3.15) across Q2 to Q4 (p for trend <0.001). The same situation was also found in the other models. Table 2 displayed the positive association between AIP and stroke exists across the quartiles of AIP in model 3, model 4 and model 5, besides, all the p for trend values showed statistical significance ($p < 0.01$).

The analyses of interaction effect

In this part, subgroup analysis was adopted to identify the interaction effect. In all the stratified groups, $p > 0.05$, which means no significant interaction effect between AIP and sleep duration, alcohol consumption, - cigarette consumption and depression was found. Compared with Q1 in the female subgroup, the ORs were 1.29 (95% CI 0.63-2.64), 2.05 (95% CI 1.05-4.01), 2.37 (95% CI 1.21-4.62) across Q2 to Q4. In the Non-drinker subgroup, the ORs of Q2 to Q4 were 1.08 (95% CI 0.63-1.84), 1.73 (95% CI 1.05-2.84) and 1.75 (95% CI 1.06-2.90), respectively. In the non-smoker subgroup, the ORs were 1.75 (95% CI 0.89-3.44), 2.36 (95% CI 1.22-4.57) and 2.31 (95% CI 1.18-4.52) across Q2 to Q4. In all the 3 subgroups above, $p < 0.05$ in Q3 and Q4 (Table 3).

Restricted cubic spline regression

To examine whether the AIP index has non-linear relationship with prevalence of stroke, RCS regression was utilized to confirm the non-linear trend. The results of RCS regression did not detect a non-linear association between AIP and stroke in males, females and the overall population (Figure 1). All p for trend were > 0.05.

Sensitivity analyses after interpolation of missing values

Missing values of covariates were interpolated using multivariate imputation by chained equations based on random forest methods. After imputing missing values, the significant association between AIP and stroke remains unchanged in all the five models adjusting for different covariates. ORs in the third and fourth quartiles increased significantly in Table 4 (all $p < 0.05$), which remained consistent the results in Table 2. Besides, the RCS regression also did not identify non-linear trend between AIP and stroke in males, females and the overall population (all $p > 0.05$ in Figure 2).

ROC analysis for stroke

ROC analysis was adopted to further evaluate the predictive power of AIP index to stroke. The outcome showed that the AUC were 0.57 (0.54–0.60) for the prevalent stroke. And the cutoff value of AIP was 0.82. It indicated that AIP has predictive power for stroke (Figure 3).

DISCUSSION

Stroke is a prevalent and mortal disease worldwide. It has over 2 million new cases annually in China, and the incidence is expected to increase due to the aging of the population.[2] Though previous studies pay more attention to the risk factors and markers from different perspectives, the association between AIP and stroke is rarely addressed. In this study, the CHARLS survey dataset in 2015

Table 1: Baseline clinical profiles of participants attending the 2015 CHARLS survey

Clinical characteristics	Total participants N = 13027	Q1 N = 3259	Q2 N = 3255	Q3 N = 3257	Q4 N = 3256	P
Age, mean (SD)	60.03 (10.09)	60.57 (10.42)	60.24 (10.21)	60.15 (10.10)	59.17 (9.55)	< 0.001
Gender						< 0.001
Male	6053 (46.5%)	1629 (50.0%)	1470 (45.2%)	1461 (44.9%)	1493 (45.9%)	
Female	6974 (53.5%)	1630 (50.0%)	1785 (54.8%)	1796 (55.1%)	1763 (54.1%)	
Marital status						< 0.001
With spouse present	10812 (83.0%)	2665 (81.8%)	2671 (82.1%)	2702 (83.0%)	2774 (85.2%)	
Others	2215 (17.0%)	594 (18.2%)	584 (17.9%)	555 (17.0%)	482 (14.8%)	
Settlements						< 0.001
Rural area	3238 (25.3%)	594 (18.6%)	744 (23.2%)	901 (28.1%)	999 (31.3%)	
Suburb area	9558 (74.7%)	2605 (81.4%)	2457 (76.8%)	2303 (71.9%)	2193 (68.7%)	
Cigarette consumption						0.002
Current-smoker	3591 (27.6%)	978 (30.1%)	859 (26.4%)	874 (26.9%)	880 (27.0%)	
Non-smoker	7743 (59.5%)	1849 (56.9%)	2008 (61.7%)	1951 (60.0%)	1935 (59.4%)	
Ever-smoker	1679 (12.9%)	425 (13.1%)	385 (11.8%)	429 (13.2%)	440 (13.5%)	
Alcohol consumption						< 0.001
Drink more than once a month	3417 (26.3%)	1048 (32.2%)	825 (25.4%)	779 (24.0%)	765 (23.5%)	
Drink less than once a month	1157 (8.9%)	278 (8.5%)	281 (8.6%)	308 (9.5%)	290 (8.9%)	
None of These	8439 (64.9%)	1927 (59.2%)	2148 (66.0%)	2164 (66.6%)	2200 (67.6%)	
Body mass index						< 0.001
< 18.5 Kg/m2	725 (5.7%)	380 (11.8%)	194 (6.1%)	106 (3.3%)	45 (1.4%)	
≥ 18.5 & < 24 Kg/m2	6087 (47.5%)	2055 (63.9%)	1706 (53.3%)	1316 (41.2%)	1010 (31.6%)	
≥ 24 & < 28 Kg/m2	4263 (33.3%)	611 (19.0%)	1001 (31.3%)	1275 (39.9%)	1376 (43.1%)	
≥ 28 Kg/m2	1734 (13.5%)	172 (5.3%)	300 (9.4%)	501 (15.7%)	761 (23.8%)	
Nap						< 0.001
No	5248 (41.3%)	1447 (45.8%)	1380 (43.5%)	1232 (38.7%)	1189 (37.5%)	
Yes	7447 (58.7%)	1715 (54.2%)	1794 (56.5%)	1953 (61.3%)	1985 (62.5%)	
Sleep duration						0.036
< 6 hours	6334 (50.2%)	1651 (52.7%)	1564 (49.7%)	1593 (50.4%)	1526 (48.3%)	
6-8 hours	5049 (40.0%)	1183 (37.7%)	1283 (40.7%)	1265 (40.0%)	1318 (41.7%)	
> 8 hours	1224 (9.7%)	301 (9.6%)	303 (9.6%)	303 (9.6%)	317 (10.0%)	
Blood urea nitrogen						< 0.001
< 20 mg/dL	11153 (85.6%)	2658 (81.6%)	2783 (85.5%)	2856 (87.7%)	2856 (87.7%)	
≥ 20 mg/dL	1874 (14.4%)	601 (18.4%)	472 (14.5%)	401 (12.3%)	400 (12.3%)	
Low density lipoprotein						< 0.001
< 120 mg/dL	9877 (75.8%)	2629 (80.7%)	2405 (73.9%)	2237 (68.7%)	2606 (80.0%)	
≥ 120 mg/dL	3149 (24.2%)	630 (19.3%)	849 (26.1%)	1020 (31.3%)	650 (20.0%)	
Total cholesterol						< 0.001
< 200 mg/dL	9218 (70.8%)	2494 (76.5%)	2447 (75.2%)	2243 (68.9%)	2034 (62.5%)	
≥ 200 mg/dL	3809 (29.2%)	765 (23.5%)	808 (24.8%)	1014 (31.1%)	1222 (37.5%)	
Hyperuricemia	1562 (12.0%)	194 (6.0%)	296 (9.1%)	423 (13.0%)	649 (19.9%)	< 0.001
Depression	3895 (33.0%)	1016 (34.4%)	1001 (33.9%)	921 (31.2%)	957 (32.4%)	0.037
Arthritis	4288 (32.9%)	1121 (34.4%)	1037 (31.9%)	1039 (31.9%)	1091 (33.5%)	0.074
Digestive diseases	2917 (22.4%)	767 (23.5%)	746 (22.9%)	712 (21.9%)	692 (21.3%)	0.12
Kidney diseases	807 (6.2%)	226 (6.9%)	192 (5.9%)	198 (6.1%)	191 (5.9%)	0.24
Liver diseases	527 (4.0%)	144 (4.4%)	119 (3.7%)	134 (4.1%)	130 (4.0%)	0.47

N: number; Q: quartile; CHARLS: China Health and Retirement Longitudinal Study

Table 2: Odds ratio (95% CI) for prevalent stroke by quartiles of AIP

Quartiles of AIP	Q1	Q2	Q3	Q4	P for trend
Cases	48	60	87	85	-
Prevalence (%)	1.47	1.84	2.67	2.61	-
Model 1	1.00 (reference)	1.26 (0.86-1.84)	1.84 (1.29-2.62)***	1.79 (1.25-2.56)***	< 0.001
Model 2	1.00 (reference)	1.21 (0.80-1.84)	1.97 (1.34-2.88)***	2.14 (1.46-3.15)***	< 0.001
Model 3	1.00 (reference)	1.10 (0.70-1.72)	1.60 (1.05-2.46)*	1.76 (1.14-2.71)**	< 0.01
Model 4	1.00 (reference)	1.06 (0.67-1.67)	1.57 (1.03-2.42)*	1.66 (1.07-2.57)*	< 0.01
Model 5	1.00 (reference)	1.09 (0.69-1.72)	1.62 (1.06-2.49)*	1.67 (1.08-2.58)*	< 0.01

Multivariate logistic regression was adopted to examine the association between AIP and stroke. The Q1 was set as the reference group. Model 1: univariate logistic regression; Model 2: adjusting for age, gender, martial, region, sleep and nap; Model 3: further adjusting for smoke, drink, BMI and CESD based on Model 2; Model 4: further adjusting for uric, BUN and LDL based on Model 3; Model 5: further adjusting for liver disease, kidney disease, digestive disease and arthritis based on Model 4. Q: quartile. AIP: atherogenic index of plasma
*p < 0.05; **p < 0.01; ***p < 0.001.

Table 3: Association between quartiles of AIP and stroke stratified by sleep duration, alcohol and cigarette consumption, and depression

Factors	Q1	Q2	Q3	Q4	*P* for interaction
Gender					0.213
Male	1.00	0.95 (0.52-1.73)	1.36 (0.77-2.40)	1.20 (0.65-2.20)	
Female	1.00	1.29 (0.63-2.64)	2.05 (1.05-4.01)*	2.37 (1.21-4.62)*	
Alcohol consumption					0.688
More than once a month	1.00	1.19 (0.40-3.57)	0.98 (0.31-3.06)	1.67 (0.55-5.06)	
Less than once a month	1.00	1.13 (0.20-6.28)	1.65 (0.34-8.02)	0.84 (0.14-5.15)	
Non-drinker	1.00	1.08 (0.63-1.84)	1.73 (1.05-2.84)*	1.75 (1.06-2.90)*	
Cigarette consumption					0.901
Current-smoker	1.00	0.65 (0.25-1.66)	1.31 (0.60-2.85)	1.41 (0.62-3.21)	
Non-smoker	1.00	1.75 (0.89-3.44)	2.36 (1.22-4.57)*	2.31 (1.18-4.52)*	
Ever-smoker	1.00	0.73 (0.28-1.95)	1.03 (0.41-2.56)	1.10 (0.44-2.80)	
Depression					0.555
Yes	1.00	0.84 (0.41-1.71)	1.76 (0.94-3.29)	1.77 (0.91-3.27)	
No	1.00	1.31 (0.72-2.40)	1.49 (0.82-2.71)	1.61 (0.88-2.96)	
Sleep duration					0.461
< 6 hours	1.00	1.19 (0.66-2.18)	1.59 (0.89-2.83)	1.72 (0.95-3.10)	
6-8 hours	1.00	1.38 (0.59-3.22)	2.09 (0.93-4.71)	2.39 (1.07-5.34)	
> 8 hours	1.00	0.35 (0.07-1.85)	1.08 (0.32-3.66)	0.34 (0.07-1.60)	

Models were adjusted for the same covariates as model 5 in Table 2. Stratification variables were not adjusted in the corresponding models. Q: quartile.
*p < 0.05; **p < 0.01

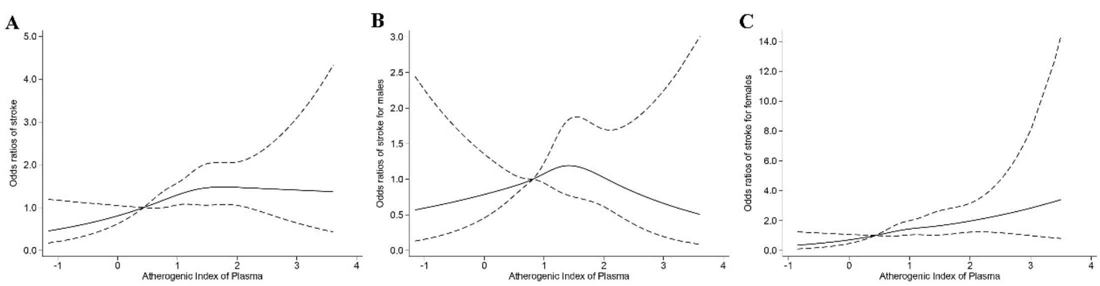

Figure 1. Results of RCS regression
(A): RCS results for the prevalent stroke. (B): RCS results for the prevalent stroke in male. (C): RCS results for the prevalent stroke in female. In Figure 1A, the RCS regression model was adjusted as model 5. RCS: restricted cubic spline.

Table 4: Sensitivity analyses after interpolation of missing values.

Quartiles of AIP	Q1	Q2	Q3	Q4
Cases	48	60	87	85
Prevalence (%)	1.47	1.84	2.67	2.61
Model 1	1.00	1.26 (0.86-1.84)	1.84 (1.29-2.62)***	1.79 (1.25-2.56)***
Model 2	1.00	1.31 (0.89-1.93)	1.93 (1.34-2.76)***	2.02 (1.41-2.91)***
Model 3	1.00	1.19 (0.81-1.75)	1.69 (1.16-2.44)**	1.66 (1.13-2.43)***
Model 4	1.00	1.17 (0.79-1.73)	1.64 (1.13-2.38)**	1.56 (1.06-2.29)*
Model 5	1.00	1.20 (0.81-1.77)	1.67 (1.15-2.43)**	1.56 (1.06-2.30)*

Models were adjusted as we did in Table 2. Q: quartile. *p < 0.05; **p < 0.01; ***p < 0.001.

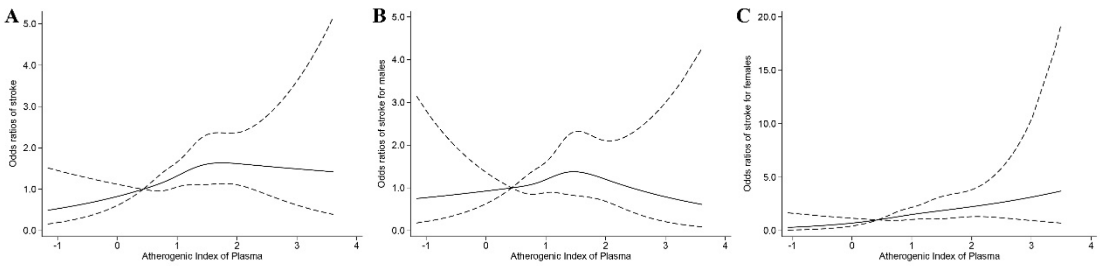

Figure 2. RCS regression after interpolation
(A): RCS results for the prevalent stroke after interpolation. (B): RCS results after interpolation in male. (C): RCS results after interpolation in female. The RCS regression model was adjusted as model 5 in Figure 1A.

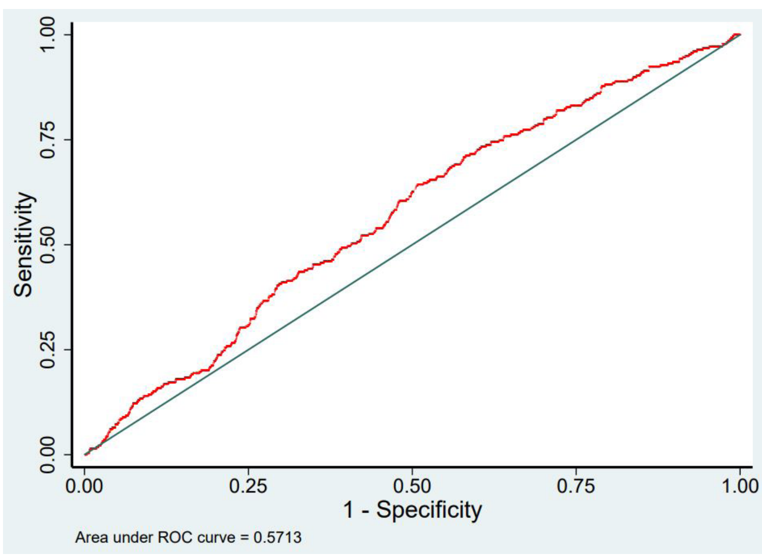

Figure 3. The receiver operating characteristic curve (ROC) for prevalent and incident stoke. ROC: The receiver operating characteristic curve

was used in this national cross-sectional study. We found that respondents with increased AIP have higher association with stroke.

Previous studies reported the factors like dyslipidemia, hypertension, diabetes, smoking, alcohol consumption and high sodium intake are the most common and modifiable risk factors for stroke[21,22], among which dyslipidemia was demonstrated to play an important role. Other findings also provide evidence that indexes related to dyslipidemia could be potential markers for stroke.[23-25] AIP is one of the lipid metabolism indicators. It was proposed for the first time as an atherogenic index, which has closely correlation with lipo-protein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)).[13] Based on this, a series of studies about AIP have been reported, and the research areas involved cardiovascular disease, urinary diseases, metabolic syndrome, and obstructive sleep apnoea.[26-29] Overall, as an index calculated from the TG and HDL, it is mainly studied in the disease caused by or related with dyslipidaemia, especially in cardiovascular disease (CVD). Some studies have shown AIP as a reliable predictive index for CVD risk in morbid-obese people who had no history of CVD, and can accurately distinguishes whether morbid obesity complicated with diabetes or not.[30] It has also been reported that AIP may be a strong marker for predicting the risk of CAD in postmenopausal women.[31] Besides, AIP is found to be closely associated to the coronary atherosclerosis in specific clinical conditions.[14,31] Moreover, Sujatha *et al.* have reported the elevation of AIP in the stroke patients in a retrospective study involving 620 subjects[32], but the sample size seems not adequate, and a positive association between AIP and stroke was not demonstrated. Although, a previous study has showed that AIP was associated with the prevalence of ischemic stroke[33], its participants was confined to residents from the rural region of Liaoning province in China, the results may not be applicable throughout the nation. In this study, we found a positive association between the AIP and stoke, and there was general trend of increased risk of stroke with higher AIP Based on this study, early interventions for this high-risk population with high AIP may be carried out across the nation, to reduce the incidence of stroke.

Some previous studies have suggested that the effect of AIP may differ according to gender. For example, the association between AIP and the uric acid seems more evident in the female than in male.[34,35] To explore whether gender affect the results, subgroup analyses was performed. We found the ORs in the Q3 and Q4 quartiles were apparently higher than that in Q1 and Q2, and the results has statistical significance, while this was not seen in the male groups. Similarly, when stratified by alcohol consumption and cigarette consumption, the association only existed across the Q3 and Q4 quartiles in the non-smoker and non-drinker. This phenomenon could be contributed by many potential factors. Cigarette smoke exposure can cause the disturbance of lipid metabolism[36], resulting in the aberration from AIP. Some authors have also confirmed that participants exposed to alcohol have higher odds to develop liver dysfunction[37], which can lead to dyslipidemia. In addition, cigarette consumption can aggravate alcohol consumption.[38] Alcohol and cigarette consumption are more common, compared with female group. Besides, AIP can be influenced by estrogen.[39] All of these factors combined may partially explain the results we described in the subgroup analysis. Many markers related to stroke have been reported, for example, Chen reported that asymmetric dimethyarginine as marker and mediator in ischemic stroke, but the predictability still needed to be further confirmed.[6] Galectin-3 is also reported to be a marker for the prediction of stroke incidence and clinical prognosis[8], although galectin-3 is relatively expensive and laboratory test difficult to access. Traditional stroke markers such as TG and TC seem to be less sensitive, and its roles needs to be enhanced by other factors.[10,11] Compared with other currently used markers, AIP is easier to be accessed both in laboratory tests and calculation, and is less costly. Therefore, it is a potentially useful marker to predict stroke. When combined with the other markers, it may improve the precision of predicting stroke, which may reduce the social burden of stroke. To our knowledge, this is the first study confirming the positive association between AIP and stroke on a national scale with a large study population inclusive of multiple ethnic groups.

There are limitations in this study. First, this study was based on the CHARLS survey in 2015, which means it should be further verified in other countries or regions. Second, this research was designed as a cross-sectional study, which limits the confirmation of its causal effects. Further longitudinal studies should thus be carried out.

DISCLOSURE

Ethics: The CHARLS study was approved by research ethics committees of Peking University (IRB00001052-13074). All participants provided written informed consent. No experimental interventions were performed.

Conflicts of interest: None

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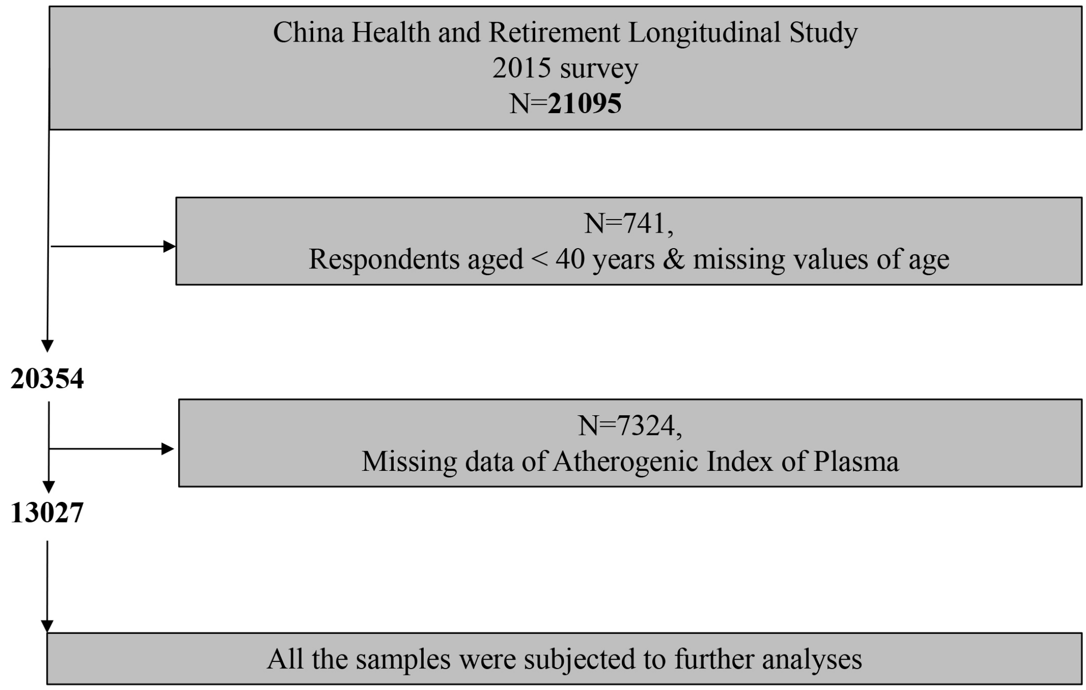
Supplemental Figure 1: Sample flow chart.



N: number.