Neuroendocrinology Letters Volume 39 No. 8 2018
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

ORIGINAL ARTICLE

The association of serum lipid level with ischemic stroke in the elderly of Xinjiang

Yun-hua Yue [1], Xu-dong Bai [2], You-mei Li [1], Liang Hu [1], Ling-yun Liu [1], Jie-ping Mao [3], Xiao-ying Yang [3], Na-mu Dila [3]

1 Department of Neurology, Yangpu Hospital Tongji University School of Medicine, Shanghai, 200090, China
2 Department of Cardiology, Yangpu Hospital Tongji University School of Medicine, Shanghai, 200090, China
3 Department of Neurology, Friendship Hospital to Urumqi, 830049, China

Correspondence to: Yun-Hua Yue
Department of Neurology, Yangpu Hospital Tongji University School of Medicine, No. 450 Tengyue Road, Shanghai, 200090, China.
TEL: +8613916034986; E-MAIL: 447879206@qq.com

Submitted: 2018-01-19 Accepted: 2018-10-02 Published online: 2019-02-18

Key words: **ischemic stroke; serum lipids; hypertension; diabetes; plaque stability**

Neuroendocrinol Lett 2018; **39**(8):572–578 **PMID:** 30927763 NEL390818A09 © 2018 Neuroendocrinology Letters • **www.nel.edu**

Abstract

BACKGROUND: The aim of the present study is to determine the association of serum lipid level in the above 55-year-old age elderly with ischemic stroke (IS) in Xinjiang regions, China.

METHODS: 408 patients with IS and 347 healthy individuals as control in the ≥55-year-old elderly were selected for the present study in Xinjiang province of China from July 2010 to July 2012. Patients were divided into different groups according to the IS subtypes (large-artery atherosclerosis, LAA; cardio-aortic embolism CE; small-artery occlusion, SAO), plague stability, hypertension and diabetes. The serum lipid level including total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), Lipoprotein(a) (Lp(a)) and their ratios(TC/HDL, LDL/HDL, ApoA1/ApoB) were measured.

RESULTS: Patients in LAA group had higher ratio of TC/HDL, ApoA1/ApoB and lower level of ApoA1 than SAO group($p<0.05$); higher level of TC, HDL, LDL, TC/HDL, LDL/HDL, ApoA1/ApoB and lower level of ApoB compared with CE group. Patients in SAO group had higher level of LDL, ApoA1, ApoB, TC/HDL, LDL/HDL and ApoA1/ApoB than CE group. Patients with stable plaque had higher level of HDL and low level of LDL, ApoB, Lp(a), TC/HDL, LDL/HDL and ApoA1/ApoB than unstable plaque group. Patients with hypertension had higher level of TG, ApoB, Lp(a), LDL/HDL and ApoA1/ApoB than non-hypertensive group. Patients with diabetes had higher level of TC, TG, ApoB, TC/HDL, LDL/HDL, ApoA1/ApoB and low level of ApoA1 than non-diabetic group. Multiple logistic regression analysis revealed that high LDL, ApoB, LDL/HDL and ApoA1/ApoB might be the risk factors for ischemic stroke.

CONCLUSION: An abnormal serum lipid level of the patients with IS in older Xinjiang population is significantly associated with the stroke subtypes, plaque stability, hypertension and diabetes.

INTRODUCTION

Stroke was globally the second cause of death after heart disease (Donnan *et al.* 2008) .It incidence increased about 10% in the developing nations in the past decade although its incidence decreased around 10% in the developed world (Feigin *et al.* 2014) .Risk factors for stroke were extensively studied, which includes advanced age, dyslipidemia, heavy smoking, alcoholic intake, hypertension, diabetes genetic factor and lifestyle (Redgrave *et al.* 2010; Deng *et al.* 2011; Cardoso *et al.* 2012; Pierdomenico *et al.* 2013; Grufman *et al.* 2014). Among these risk factors, age is one of the most important risk factors for stroke. The study showed that the most patients with stroke frequently occur at over 45 year-old (Badhiwala *et al.* 2015). The other major risk factors include atherosclerosis and hyperlipidemia (Viola and Soehnlein, 2015).

Stroke is the first leading cause of death in China with high prevalence, mortality and morbidity (Liu *et al.* 2007; Bejot *et al.* 2016).The prevalence and incidence of ischemic stroke are much higher in Xinjiang than other regions of China (Liu *et al.* 2007; Hu and Sun, 2008). Furthermore, the Uighur population has higher risk of ischemic stroke than Han population within Xinjiang region because of genetic background, ethnic and lifestyle in Uighur population. Our and the other study indicated that the difference of IS incidence between Han and Uighur population may be relative to single nucleotide polymorphism (SNP) as well as their lifestyle (Wang *et al.* 2010; Yao *et al.* 2010; Liang *et al.* 2011; Quan *et al.* 2015; Yue *et al.* 2016) The difference of their genetic background not only is associated with the occurrence of IS, but also relative to response of treatment (Yue *et al.* 2016). It was well known that atherosclerosis is an important risk factor for IS occurrence, while atherosclerosis often is result of genetic and environment factors working together (Jander *et al.* 2001). The weather is cold, dry and a high altitude with relative low oxygen level in Xinjiang regions. Uighur population has special genetic background. It was reported that Uighur population with carotid artery atherosclerosis (CAAD) frequently occur CC/CS genotype mutation of Paraoxonase (PON) 2 311C allele (Han *et al.* 2013) .Our study showed that Uighur population with SNP rs2266788 of APOA5 gene significantly affected the therapy of atorvastatin (Yue *et al.* 2016) . Therefore, all these factors contribute to occurrence of IS in Uighur population. It was well known that the dysfunction of lipid metabolism, especially reducing the LDL level, attenuates the atherosclerosis process and reduces the incidence and mortality of ischemic stroke (Badimon *et al.* 2010; Kernan *et al.* 2014). However, whether the serum lipid level alone could be used as independent prognostic risk factor for ischemic stroke are controversial (Domingues-Montanari *et al.* 2008). It was found that the changes in the ratio of lipid level, such as TC (total cholesterol) to HDL (high-density lipoprotein-cholesterol) and LDL (low-density lipoprotein- cholesterol) to HDL predicted atherosclerosis progression better than LDL or HDL alone (Enomoto *et al.* 2011).

Here we explored the associations of serum lipid level and their ratios with ischemic stroke, plaque stability, hypertension and diabetes above 55-year-old people in Xinjiang region. This study may provide an excellent link between dyslipidemia in the elder and the risk factors of IS because of Xinjiang's special location.

MATERIALS AND METHODS

Study subjects

Ischemic stroke patients with older 55-year-old were enrolled from Department of Neurology of the Youyi Hospital of Wulumuqi from July 2010 to July 2012. The inclusion criteria were chosen according to clinical manifestation, brain MRI (magnetic resonance imaging), head CT (computed tomography), carotid duplex ultrasonography and transcranial Doppler record. These enrolled patients also haven't history of intracranial hemorrhage/stroke, subarachnoid hemorrhage, arteriovenous malformation, neoplasm, aneurysm, post operation or post trauma, infection diseases, autoimmune diseases, severe cardiac, renal and hepatic diseases. Age-, sex- and race-matched healthy volunteers who were undergoing routine physical examination were recruited as control group. The controls had no clinical evidence of any cerebrovascular diseases. All subjects agreed by the hospital ethics committee and signed informed consent.

Study protocol

The study population was selected in the people aged ≥55 years. The subjects' history of medical, alcohol intake and smoking habits was recorded by a questionnaire. Smoking and alcohol intake was classified as smoking every day (more than one cigarette per day) for more than one year and drinking at least once a week with more than 50 mL, respectively. Patients body mass index (BMI) were calculated as weight (kg) divided by the square of height (m^2) according to their body height > and weight. BMI ≥28 was classified as obesity. Blood pressure (BP) was measured in the right arm twice with a mercury sphygmomanometer after subjects had rested in a supine position for more than 5 minutes. The second BP with the fifth-phase diastolic pressure was used for analysis. Hypertension was classified as systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg. Diabetes was classified as FPG (fasting plasma glucose) ≥7.0 mmol/L and/or 2 hours PG (plasma glucose) ≥11.1 mmol/L or already diagnosed as diabetes patients. The stroke subtypes (LAA, large-artery atherosclerosis; CE, cardio-aortic embolism; SAO, small-artery occlusion) were classified as demonstrated before (Han *et al.* 2007).

Blood samples for the evaluation of lipid levels were obtained from subjects between (7 AM and 11 AM),

after at least 12 h of fasting. Plasma levels of TC, TG, HDL, LDL, ApoA1, ApoB and Lp (a) were measured by commercially available enzymatic assay kits supplied by Biosino Bio-Technology and Science Incorporation (China) and an OLYMPUS auto-analyzer (Japan).

Carotid atherosclerotic plaque measurement

Carotid IMT (intima-media thickness) was measured by duplex ultrasonography (PHILIPS iE33, USA) with a 7.5-MHz transducer in the sitting position. Longitudinal B-mode images at the diastolic phase of the cardiac cycle were recorded. IMT was measured using fine slide calipers at three levels of the lateral and medial walls one to three centimeters proximal to the carotid bifurcation. These six combined near- and far-wall measurements were averaged. The plaque type was classified asdescribed (Martin *et al.* 2002).

Statistical analysis

Clinical data about continuous variables were expressed as mean±SD (standard deviation). Homogeneity of variances was assessed with Levene's test. Comparison between two groups was assessed by *t*-test. And differences among groups were assessed by one-way ANOVA test. Enumerated data comparison among groups was assessed by Pearson's chi-squared test. The association between risk factors and ischemic stroke was assessed by logistic regression analysis. All statistical analyses were performed with SPSS 20.0 (IBM). A *p*-value under 0.05 was considered as statistically significant.

RESULTS

A total of 408 ischemic stroke patients as well as 347 healthy individuals with the elderly ≥55 year-old were recruited. Among them, 242 were men and 166 were women; 250 were Han population (average age, 67.6±11.4 years old) and 158 were Uighur population (average age, 68.3±12.0 years old). 347 healthy volunteers were enrolled as control group matching with age, sex and racial. The clinical characteristics of the stroke patients were presented in Table 1. We found that there was no significant difference among these three subgroups (LAA, SAO and CE group) of stroke patients from the perspective of age, sex, BMI, hypertension, diabetes, smoking and alcohol intake (Table 1). However, there are significant low 24h SBPV (24 hour systolic blood pressure variability) and 24hDBPV (24 hour diastolic blood pressure variability) in SAO group than other two groups.

By contrast**,** patients in LAA group had higher ratio of TC/HDL, ApoA1/ApoB and lower level of ApoA1 than SAO group; higher level of TC, HDL, LDL, TC/HDL, LDL/HDL, ApoA1/ApoB and lower level of ApoB compared with CE group. Patients in SAO group had higher level of LDL, ApoA1, ApoB, TC/HDL, LDL/HDL and ApoA1/ApoB than CE group (Table 2).

Patients with stable plaque had higher level of HDL and low level of LDL, ApoB, Lp(a), TC/HDL, LDL/HDL and ApoA1/ApoB than unstable plaque group (Table 3).

Table 1. Clinical characteristics of the stroke patients.

	LAA (n=172)	SAO (n=189)	CE (n=47)	χ^2	*p*-value
Age (Year)	68.52±13.28	69.17±15.41	67.26±11.73	1.686	0.093
Male (%)	58.7	59.8	59.5	0.042	0.137
Han (%)	61.1	61.6	61.7	1.725	0.094
BMI (kg/m2)	24.20±3.34	23.80±3.45	23.90±4.17	1.267[a]	0.542
Hypertension (%)	70.9	72.0	69.2	0.001[b]	0.978
Diabetes (%)	33.1	31.2	29.8	0.689[a]	0.407
Smoking (%)	32.8	34.3	34.6	1.590[a]	0.207
Alcohol intake (%)	19.8	17.5	17.0	0.104[a]	0.747
SBP (mmHg)	149.60±21.40	144.30±14.17	135.50±13.62	1.947	0.067
DBP (mmHg)	83.52±15.12	80.34±21.25	76.22±17.69	1.143	0.141
24hSBPV	0.15±0.02	0.11±0.03	0.14±0.05	3.479[a]	0.024
24hDBPV	0.18±0.04	0.14±0.02	0.17±0.05	4.172[a]	0.011
Hcy (μmol/L)	5.81±1.62	5.26±1.77	5.61±1.82	1.267[a]	0.887

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; 24hSBPV: 24 hour systolic blood pressure variability; 24hDBPV: 24 hour diastolic blood pressure variability; Hcy: homocysteine. a: $p<0.01$; b: $p<0.05$.

Table 2. Serum lipids level comparison among LAA, SAO and CE Group.

	LAA (n=172)	SAO (n=189)	CE (n=47)	χ2	*p*-value (LAA vs SAO)	*p*-value (LAA vs CE)	*p*-value (SAO vs CE)
TC (mmol/L)	5.23±1.17	4.85±1.16	4.72±1.18	1.98	0.067	0.041	1.172
TG(mmol/L)	1.71±0.93	1.67±1.03	1.59±0.94	1.24	0.137	0.084	0.214
HDL(mmol/L)	0.90±1.07	0.90±0.97	0.90±1.01	0.97	0.081	0.001	0.064
LDL(mmol/L)	3.07±2.24	3.44±2.37	2.84±2.11	5.16[a]	0.070	0.004	0.007
ApoA1 (g/L)	0.80±0.18	1.00±0.25	0.90±0.15	2.44	0.026	0.311	0.017
ApoB (g/L)	0.80±0.22	0.90±0.34	0.90±0.21	6.83 [a]	0.133	0.001	0.002
Lp(a) (mg/L)	234.80±72.56	214.20±68.29	199.70±56.63	2.35	0.781	0.116	0.925
TC/HDL	5.57±1.67	5.05±1.48	4.77±1.33	6.57 [a]	0.028	0.001	0.031
LDL/HDL	3.31±1.11	3.58±1.07	2.87±1.04	7.42 [a]	0.068	0.039	0.011
ApoA1/ApoB	1.16±0.28	1.09±0.33	0.86±0.31	5.99 [a]	0.002	0.001	0.012

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; Apo a1: apolipoprotein A1; ApoB: apolipoprotein B; a: $p<0.05$

Patients with hypertension had higher level of TG, ApoB, Lp (a), LDL/HDL and ApoA1/ApoB than non-hypertensive group (Table 4).

Patients with diabetes had higher level of TC, TG, ApoB, TC/HDL, LDL/HDL, ApoA1/ApoB and low level of ApoA1 than non-diabetic group (Table 5).

Multiple logistic regression analysis revealed that hypertension, diabetes, LDL, ApoB, LDL/HDL, ApoA1/ApoB might be the risk factors for ischemic stroke (Table 6).

DISCUSSION

Our results here demonstrated that the serum lipid level of the patients with ischemic stroke in Xinjiang was significantly associated with the stroke subtypes, plaque stability, hypertension and diabetes.

Stroke is the leading cause of death in China with high prevalence, mortality and morbidity of which ischemic stroke (IS) accounts for at least 70% of the stroke cases. (Liu *et al.* 2007; Bejot *et al.* 2016) Atherosclerosis

Table 3. Lipids level comparison between stable and unstable plaque group.

	Stable plaque n=126	Unstable plaque n=282	t	*p*-value
TC (mmol/L)	4.99±1.13	5.28±1.82	1.42	0.073
TG (mmol/L)	1.69±0.83	1.77±1.03	1.58	0.160
HDL (mmol/L)	1.02±1.07	0.88±0.97	–4.77	0.001
LDL (mmol/L)	3.08±2.24	3.44±2.37	2.83	0.011
ApoA1 (g/L)	1.01±0.18	0.97±0.25	0.96	0.453
ApoB (g/L)	0.88±0.20	0.94±0.24	3.25	0.002
Lp(a) (mg/L)	125.12±76.24	176.39±87.43	2.94	0.001
TC/HDL	4.37±0.94	5.12±1.16	3.87	0.001
LDL/HDL	3.11±1.02	3.69±1.06	2.12	0.036
ApoA1/ApoB	1.12±0.34	1.23±0.36	5.32	0.000

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; Apo a1: apolipoprotein A1; ApoB: apolipoprotein B

Table 4. Lipids level comparison between hypertension and non-hypertension group.

	Hypertension (n=281)	Non-Hypertension (n=127)	t	*p*-value
TC (mmol/L)	5.11±1.15	4.78±1.82	–1.82	0.055
TG (mmol/L)	1.78±0.93	1.58±1.01	–2.58	0.014
HDL(mmol/L)	0.98±0.36	1.01±0.27	0.77	0.560
LDL(mmol/L)	3.37±1.62	3.31±1.91	0.83	0.440
ApoA1 (g/L)	1.01±0.18	1.03±0.25	0.08	1.380
ApoB (g/L)	0.96±0.30	0.88±0.29	2.61	0.001
Lp(a) (mg/L)	217.31±64.71	152.26±72.66	4.62	0.001
TC/HDL	5.27±1.15	4.79±1.32	0.92	0.390
LDL/HDL	3.54±0.99	3.21±1.02	2.27	0.048
ApoA1/ApoB	1.18±0.28	1.08±0.36	3.12	0.016

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; Apo a1: apolipoprotein A1; ApoB: apolipoprotein B

is a common risk factor for ischemic stroke and it is tightly related to abnormal lipid metabolism (Viola and Soehnlein, 2015). Data have shown that high serum level of TC, especially LDL, promotes the atherosclerosis development and lowering the LDL level would attenuate the atherosclerosis process (Dusitanond *et al.* 2005; Baigent *et al.* 2011; Cui *et al.* 2012; Boronat *et al.* 2014). Therefore, lipid-lowering therapy is the most common strategy to treat ischemic stroke (Goldstein *et al.* 2011). Furthermore, diabetes and hypertension patients have higher risk of IS development (Corriere *et al.* 2013; Mann *et al.* 2013). And antihypertensive therapy significantly reduces the risk of IS (Sipahi *et al.* 2012; O'Connor *et al.* 2013).

In the present study, ischemic stroke patients were divided into different groups according to the IS subtypes (LAA, CE and SAO), plague stability, hypertension and diabetes. Then the associations of serum lipid level with different stroke subtypes were analyzed. Because the ratio of lipid level is better than lipid level alone to predict IS development (Enomoto *et al.* 2011) and ApoA1/ ApoB ratio is better than alone LDL in detecting cardiovascular risk (Carnevale Schianca *et al.* 2011). These methods were introduced into current study. Our data showed that TC/HDL or LDL/HDL and ApoA1/ApoB are important risk factors of IS development in the elderly of Xinjiang. For example, patients in LAA group had higher ratio of TC/HDL, ApoA1/ApoB than SAO and CE group; Patients in SAO group had higher level of TC/HDL, LDL/HDL and ApoA1/ApoB than CE group; patients with stable plaque had low level of TC/HDL, LDL/HDL and ApoA1/ApoB than unstable plaque group; patients with hypertension had higher level of LDL/HDL and ApoA1/ApoB than non-hypertensive group; patients with diabetes had higher level of TC/HDL, LDL/HDL, ApoA1/ApoB than non-diabetic group. Furthermore, multiple logistic regression analysis revealed that LDL/HDLand ApoA1/ApoB might be the risk factors for ischemic stroke, which is in accordance with previous reports (Shahar *et al.* 2003; Tirschwell *et al.* 2004; Amarenco *et al.* 2009).Quan et al reported that impaired fasting glucose (IFG) in Uighur population is higher than that in Han (Quan *et al.* 2015).This high IFG contributes to dyslipidemia in Uighur. In addition to our report about SNP difference of lipid metabolism relative genes in Han and Uighur (Yue *et al.* 2016). Abudokelimu *et al.* showed that there are also difference in cholesterol absorption gene Numb SNP genotype of Han and Uighur population (Abudoukelimu *et al.* 2015). Therefore, dyslipidemia in different population can caused by their unique genetic background as well as environment factors.

Table 5. Lipids level comparison between diabetes and non-diabetes group.

	Diabetes (n=129)	Non-Diabetes (n=279)	t	*p*-value
TC (mmol/L)	5.61±1.15	4.68±1.82	–6.21	0.000
TG (mmol/L)	1.92±0.83	1.58±0.95	–3.79	0.002
HDL (mmol/L)	0.95±0.41	1.00±0.46	1.12	0.360
LDL (mmol/L)	3.21±2.57	3.17±2.01	1.04	0.620
ApoA1 (g/L)	0.96±0.18	1.09±0.25	2.01	0.045
ApoB (g/L)	0.96±0.30	0.88±0.29	2.61	0.001
Lp(a) (mg/L)	228.71±70.22	216.23±65.14	1.49	0.170
TC/HDL	5.81±1.15	4.72±1.32	4.32	0.001
LDL/HDL	3.38±1.01	3.16±1.02	1.79	0.041
ApoA1/ApoB	1.17±0.33	1.09±0.21	2.75	0.020

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; Apo a1: apolipoprotein A1; ApoB: apolipoprotein B.

CONCLUSION

Our study showed that the serum lipid level of the patients with ischemic stroke was significantly associated with the stroke subtypes, plaque stability, hypertension and diabetes. Furthermore, hypertension, diabetes, LDL, ApoB, LDL/HDL and ApoA1/ApoB might be the risk factors of ischemic stroke.

Table 6. Multiple logistic regression analysis.

Risk factor	β	SE	Wald	*p*-value	OR	95%CI
Hypertension	1.798	0.173	108.540	<0.001	6.037	4.305–8.467
Diabetes	0.544	0.203	7.163	0.007	1.723	1.157–2.567
LDL	1.323	0.584	5.634	0.007	0.387	0.233–0.935
ApoB	6.467	1.828	12.523	0.001	1.142	1.075–1.311
LDL/HDL	1.388	0.769	6.781	0.017	0.369	0.217–0.871
ApoA1/ApoB	1.903	0.399	22.707	0.001	1.612	1.016–2.767

LAA: large-artery atherosclerosis; SAO: small-artery occlusion; CE: cardio-aortic embolism; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; Apo a1: apolipoprotein A1; ApoB: apolipoprotein B.OR: odds ratio; CI: confidence interval

ACKNOWLEDGEMENT

This study is supported by the project of science committee and health and birth control committee of Yangpu District of Shanghai in 2015 (No. 20150015).

REFERENCES

1 Abudoukelimu M, Fu ZY, Maimaiti A, Ma YT, Abudu M, Zhu Q, Adi D, Yang YN, Li XM, Xie X, Liu F, Chen BD (2015). The association of cholesterol absorption gene Numb polymorphism with Coronary Artery Disease among Han Chinese and Uighur Chinese in Xinjiang, China. Lipids Health Dis. **14**: 120.
2 Amarenco P, Goldstein LB, Callahan A, 3rd, Sillesen H, Hennerici MG, O'Neill BJ, Rudolph AE, Simunovic L, Zivin JA, Welch KM, Investigators S (2009). Baseline blood pressure, low- and high-density lipoproteins, and triglycerides and the risk of vascular events in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial. Atherosclerosis. **204**: 515–520.
3 Badhiwala JH, Nassiri F, Alhazzani W, Selim MH, Farrokhyar F, Spears J, Kulkarni AV, Singh S, Alqahtani A, Rochwerg B, Alshahrani M, Murty NK, Alhazzani A, Yarascavitch B, Reddy K, Zaidat OO, Almenawer SA (2015). Endovascular Thrombectomy for Acute Ischemic Stroke: A Meta-analysis. JAMA. **314**: 1832–1843.
4 Badimon L, Vilahur G, Padro T (2010). Nutraceuticals and atherosclerosis: human trials. Cardiovasc Ther. **28**: 202–215.
5 Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson *et al.* (2011). The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. **377**: 2181–2192.
6 Bejot Y, Daubail B, Giroud M (2016). Epidemiology of stroke and transient ischemic attacks: Current knowledge and perspectives. Rev Neurol (Paris). **172**: 59–68.
7 Boronat M, Garcia-Canton C, Lopez-Rios L, Quevedo V, Lorenzo DL, Batista F, Riano M, Novoa FJ (2014). Potential implications of the choice among three alternative treatment targets for apolipoprotein B100 in the management of patients with type 2 diabetes and chronic kidney disease. Diab Vasc Dis Res. **11**: 53–59.
8 Cardoso CR, Marques CE, Leite NC, Salles GF (2012). Factors associated with carotid intima-media thickness and carotid plaques in type 2 diabetic patients. J Hypertens. **30**: 940–947.
9 Carnevale Schianca GP, Pedrazzoli R, Onolfo S, Colli E, Cornetti E, Bergamasco L, Fra GP, Bartoli E (2011). ApoB/apoA-I ratio is better than LDL-C in detecting cardiovascular risk. Nutr Metab Cardiovasc Dis. **21**: 406–411.
10 Corriere M, Rooparinesingh N, Kalyani RR (2013). Epidemiology of diabetes and diabetes complications in the elderly: an emerging public health burden. Curr Diab Rep. **13**: 805–813.
11 Cui R, Iso H, Yamagishi K, Saito I, Kokubo Y, Inoue M, Tsugane S, Group JS (2012). High serum total cholesterol levels is a risk factor of ischemic stroke for general Japanese population: the JPHC study. Atherosclerosis. **221**: 565–569.
12 Deng HB, Jiang CQ, Tomlinson B, Liu B, Lin JM, Wong KS, Cheung BM, Lam TH, Thomas GN (2011). A polymorphism in transforming growth factor-beta1 is associated with carotid plaques and increased carotid intima-media thickness in older Chinese men: the Guangzhou Biobank Cohort Study-Cardiovascular Disease Subcohort. Atherosclerosis. **214**: 391–396.
13 Domingues-Montanari S, Mendioroz M, del Rio-Espinola A, Fernandez-Cadenas I, Montaner J (2008). Genetics of stroke: a review of recent advances. Expert Rev Mol Diagn. **8**: 495–513.
14 Donnan GA, Fisher M, Macleod M, Davis SM (2008). Stroke. Lancet. **371**: 1612–1623.
15 Dusitanond P, Eikelboom JW, Hankey GJ, Thom J, Gilmore G, Loh K, Yi Q, Klijn CJ, Langton P, van Bockxmeer FM, Baker R, Jamrozik K (2005). Homocysteine-lowering treatment with folic acid, cobalamin, and pyridoxine does not reduce blood markers of inflammation, endothelial dysfunction, or hypercoagulability in patients with previous transient ischemic attack or stroke: a randomized substudy of the VITATOPS trial. Stroke. **36**: 144–146.
16 Enomoto M, Adachi H, Hirai Y, Fukami A, Satoh A, Otsuka M, Kumagae S, Nanjo Y, Yoshikawa K, Esaki E, Kumagai E, Ogata K, Kasahara A, Tsukagawa E, Yokoi K, Ohbu-Murayama K, Imaizumi T (2011). LDL-C/HDL-C Ratio Predicts Carotid Intima-Media Thickness Progression Better Than HDL-C or LDL-C Alone. J Lipids. **2011**: 549137.
17 Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson L, Truelsen T, O'Donnell M, Venketasubramanian N, Barker-Collo S, Lawes CM, Wang W, Shinohara Y, Witt E, Ezzati M, Naghavi M, Murray C, Global Burden of Diseases I, Risk Factors S, the GBDSEG (2014). Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet. **383**: 245–254.
18 Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, Creager MA, Culebras A, Eckel RH, Hart RG, Hinchey JA, Howard VJ, Jauch EC, Levine SR, Meschia JF, Moore WS, Nixon JV, Pearson TA, American Heart Association Stroke C, Council on Cardiovascular N, Council on E, Prevention, Council for High Blood Pressure R, Council on Peripheral Vascular D, Interdisciplinary Council on Quality of C, Outcomes R (2011). Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. **42**: 517–584.
19 Grufman H, Schiopu A, Edsfeldt A, Bjorkbacka H, Nitulescu M, Nilsson M, Persson A, Nilsson J, Goncalves I (2014). Evidence for altered inflammatory and repair responses in symptomatic carotid plaques from elderly patients. Atherosclerosis **237**: 177–182.
20 Han L, Xu XJ, Liang XH, Ma J (2013). Association of paraoxonase polymorphisms with carotid artery atherosclerosis in essential hypertension patients. Genet Mol Res **12**: 5174–5185.
21 Han SW, Kim SH, Lee JY, Chu CK, Yang JH, Shin HY, Nam HS, Lee BI, Heo JH (2007). A new subtype classification of ischemic stroke based on treatment and etiologic mechanism. Eur Neurol **57**: 96–102.
22 Hu D, Sun Y (2008). Epidemiology, risk factors for stroke, and management of atrial fibrillation in China. J Am Coll Cardiol **52**: 865–868.
23 Jander S, Sitzer M, Wendt A, Schroeter M, Buchkremer M, Siebler M, Muller W, Sandmann W, Stoll G (2001). Expression of tissue factor in high-grade carotid artery stenosis: association with plaque destabilization. Stroke. **32**: 850–854.
24 Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, *et al.* (2014). Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. **45**: 2160–2236.
25 Liang DP, Yao XG, Li NF, Zhang DL, Guo YY, Lin L, Zhou L, Li WC, Yan ZT, Wang HM, Luo WL, Chang JH (2011). [Epidemiological survey of lipid levels and factors in Kazakan people over 30-year old in Fukang of Xinjiang]. Zhonghua Yu Fang Yi Xue Za Zhi. **45**: 440–443.
26 Liu M, Wu B, Wang WZ, Lee LM, Zhang SH, Kong LZ (2007). Stroke in China: epidemiology, prevention, and management strategies. Lancet Neurol. **6**: 456–464.
27 Mann JF, Anderson C, Gao P, Gerstein HC, Boehm M, Ryden L, Sleight P, Teo KK, Yusuf S, investigators O (2013). Dual inhibition of the renin-angiotensin system in high-risk diabetes and risk for stroke and other outcomes: results of the ONTARGET trial. J Hypertens. **31**: 414–421.
28 Martin S, Pedro-Botet J, Joven J, Simo JM, Ladona MG, Pavesi M, Rubies-Prat J (2002). Heterozygous apolipoprotein (a) status and protein expression as a risk factor for premature coronary heart disease. J Lab Clin Med. **139**: 181–187.
29 O'Connor PJ, Vazquez-Benitez G, Schmittdiel JA, Parker ED, Trower NK, Desai JR, Margolis KL, Magid DJ (2013). Benefits of early hypertension control on cardiovascular outcomes in patients with diabetes. Diabetes Care. **36**: 322–327.
30 Pierdomenico SD, Mancini M, Cuccurullo C, Guglielmi MD, Pierdomenico AM, Di Nicola M, Di Carlo S, Lapenna D, Cuccurullo F (2013). Prediction of carotid plaques in hypertensive patients by risk factors, left ventricular hypertrophy, and epicardial adipose tissue thickness. Heart Vessels. **28**: 277–283.

31 Quan L, Hu L, Zhang L, Jiang S (2015). Differences of prevalence of dyslipidemia and risk factors related to LDL-c in the patients with abnormal fasting glucose between Uygur and Han in Xinjiang. Int J Clin Exp Med. **8**: 22403–22410.
32 Redgrave JN, Lovett JK, Rothwell PM (2010). Histological features of symptomatic carotid plaques in relation to age and smoking: the oxford plaque study. Stroke. **41**: 2288–2294.
33 Shahar E, Chambless LE, Rosamond WD, Boland LL, Ballantyne CM, McGovern PG, Sharrett AR, Atherosclerosis Risk in Communities S (2003). Plasma lipid profile and incident ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Stroke. **34**: 623–631.
34 Sipahi I, Swaminathan A, Natesan V, Debanne SM, Simon DI, Fang JC (2012). Effect of antihypertensive therapy on incident stroke in cohorts with prehypertensive blood pressure levels: a meta-analysis of randomized controlled trials. Stroke. **43**: 432–440.
35 Tirschwell DL, Smith NL, Heckbert SR, Lemaitre RN, Longstreth WT, Jr., Psaty BM (2004). Association of cholesterol with stroke risk varies in stroke subtypes and patient subgroups. Neurology. **63**: 1868–1875.
36 Viola J, Soehnlein O (2015). Atherosclerosis – A matter of unresolved inflammation. Semin Immunol. **27**: 184–193.
37 Wang L, Tao Y, Xie Z, Ran X, Zhang M, Wang Y, Luo X, Hu M, Gen W, Wufuer H, Li L, Ren J, Mao X (2010). Prevalence of metabolic syndrome, insulin resistance, impaired fasting blood glucose, and dyslipidemia in Uygur and Kazak populations. J Clin Hypertens (Greenwich). **12**: 741–745.
38 Yao XG, Frommlet F, Zhou L, Zu F, Wang HM, Yan ZT, Luo WL, Hong J, Wang XL, Li NF (2010). The prevalence of hypertension, obesity and dyslipidemia in individuals of over 30 years of age belonging to minorities from the pasture area of Xinjiang. BMC Public Health. **10**: 91.
39 Yue YH, Bai XD, Zhang HJ, Li YM, Hu L, Liu LY, Mao JP, Yang XY, Dila NM (2016). Gene Polymorphisms Affect the Effectiveness of Atorvastatin in Treating Ischemic Stroke Patients. Cell Physiol Biochem. **39**: 630–638.