Risk factors associated with VAP and atherosclerotic cardiovascular disease

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Abstract: Objective To investigate whether the risk factors related to VAP (vertical gradient centrifugal method for blood lipid detection) have significant influence on the risk of atherosclerotic cardiovascular disease (ASCVD).Methods Fisher test was used to determine whether each factor had an impact on the risk of ASCVD, and Baseline Logistic regression was used to calculate the specific impact of all factors on the risk of ASCVD. Results All the variables had significant influence on the risk of ASCVD (Fisher's accurate test for all factors, P<.0001).The older the age, the higher the risk of disease (healthy population: OR=1 Medium risk: OR=1.19 high risk: OR=1.16 high risk: OR=1.24);The risk of disease in female is usually lower than that in male (healthy population: OR=1 Medium risk: OR=0.26 Extremely high risk: OR=0.29);The higher the concentration of lipoprotein residues (RLP), the higher the risk of disease (healthy population: OR=1 Medium risk: OR=25.18 high risk: OR=31.41 High risk: OR=3.81);The higher the concentration of intermediate density lipoprotein (IDL), the higher the probability of moderate risk and high risk (healthy population: OR=1 Moderate risk: OR=667.42 high risk: OR=699.13);The higher the concentration of low density lipoprotein cholesterol (LDL-C), the higher the probability of moderate risk and high risk, and the lower the probability of extremely high risk (healthy population: OR=1 Moderate risk: OR=2.30 high risk: OR=1.87 Extremely high risk: OR=0.53);The higher the concentration of high-density lipoprotein cholesterol (HDL-C), the lower the probability of extremely high risk (healthy population: OR=1 Extremely high risk: OR=0.17);The higher the total cholesterol (TC) concentration, the higher the probability of moderate OR high risk, and the lower the probability of extremely high risk (healthy population: OR=1 Moderate risk: OR=2.27 high risk: OR=2.43 extremely high risk: OR=0.52);When LDL density mode was A/B, patients had A higher probability of moderate risk and extremely high risk than those with density mode A (healthy population: OR=1 Moderate risk: OR=4.08 Extremely high risk: OR=3.04).When THE LDL density pattern was B, the

probability of patients with moderate risk was higher than that when the density pattern was A (healthy population: OR=1, moderate risk: OR=4.76).The higher the concentration of low-density lipoprotein particles (LDL-P), the higher the probability of moderate risk and high risk (healthy group: OR=1 Moderate risk: OR=1.002 High risk: OR=1.002);The higher the lipoprotein A [Lp (a)] concentration, the higher the probability of extremely high risk (healthy population: OR=1 Extremely high risk: OR=1.002).**Conclusion VAP related factors can significantly affect the risk of ASCVD, so in-depth study of these factors can effectively predict and treat cardiovascular and cerebrovascular diseases.**

Key words: VAP; Atherosclerotic cardiovascular disease; Cardiovascular and cerebrovascular diseases; Lipoprotein a

Analysis of VAP-related factors corresponding to the risk of atherosclerotic cardiovascular disease

The Abstract: Objective to analyze the significance of factors related to VAP(vertical auto profile) technology corresponding to the risk of occurrence of ASCVD(Atherosclerotic cardiovascular disease).Methods Using Fisher Exact Test to extrapolate whether each factor has significant effect on the risk of ASCVD, then to estimate the specific effect each has on the risk through Baseline Logistic Regression. Results All factors using have significant effects to the risk of ASCVD (each with Fisher Exact Test P<.0001). Among all factors, Increasing in age will promote the risk(Health people: OR=1 Medium risk: OR=1.19 High risk: OR=1.16 Extremely High risk: OR=1.24); Women have commonly lower risk than men(Health people: OR=1, High risk: OR=0.26, Extremely High risk: OR=0.29); The higher the concentration of lipoprotein residue (RLP) is, the higher the risk is(Health people: OR=1, Medium risk: OR=25.18, High risk: OR=31.41, Extremely High risk: OR=3.81); the higher the concentration of Intermediate-density lipoprotein (IDL) or Low-density lipoprotein particles (LDL-P) is, The greater the probability that the patient is at medium and high risk(Heath people: OR=1, medium risk: OR=667.42/1.002, High risk: OR=699.13/1.002); the higher the concentration of Low-density lipoprotein cholesterol (LDL-C) or total cholesterol (TC) is, the greater the probability that the patient is at medium risk and high risk, The lower the probability the patient is at extremely

high risk(Health people: OR=1, Medium risk: OR=2.30/2.27, high risk: OR=1.87/2.43, Extremely high risk: OR=0.53/0.52); the probability the patient is at extremely high risk is inversely related to the concentration of High-density Lipoprotein cholesterol (HDL-C)(Health people: OR=1, Extremely high risk: OR=0.17); the patients have higher probability in medium or extremely high risk when the LDL-mode is A/B rather than A(Health People: OR=1, Medium risk: OR=4.08, Extremely high risk: OR=3.04); the patients have higher probability in medium risk when the LDL-mode when the LDL-mode is B rather than A(Health People: OR=1, Medium risk: OR=4.76); The probability the patients at extremely high risk is positively related to the concentration of lipoprotein-a[Lp (a)] Health people: OR=1, Extremely high risk: OR=1.002). Conclusions The factors related to VAP will significantly affect The risk of ASVD. Thus, further study of these factors will effectively help to predict and cure cardiovascular disease.

Key words: VAP; Atherosclerotic cardiovascular disease; Cardiovascular disease; Lp(a)

Cardiovascular disease or Cardiovascular disease (CVD) is a general term for Cardiovascular and cerebrovascular diseases, including coronary heart disease, cerebrovascular disease, rheumatic heart disease, etc., which can lead to multi-system lesions of nerves, vision, language, urinary tract and movement, and may be life-threatening in severe cases. Cardiovascular and cerebrovascular diseases are the leading killer of all mankind, killing about 17.9 million people every year, 80% of whom die from heart attack or stroke [].[1]

The Report on Cardiovascular Diseases in China 2018 [] points out that the prevalence of hypertension in Chinese population is still on the rise, and blood pressure level is in continuous, independent and direct positive correlation with cardiovascular risk, and the prevalence of hypertension varies among different ethnic groups.[2]According to a study, both low density lipoprotein and total cholesterol in Chinese population are at a high level and increasing year by year [].[3]Therefore, it is of great significance to carry out blood lipid examination and standardization of measurement results for comprehensive prediction, diagnosis and treatment of CVD.

Most of the lipids in the blood bind to proteins to form lipoproteins. In the traditional sense, Serum lipoprotein is divided into low-density lipoprotein (LDL) and high-density lipoprotein (HDL). HDL, Intermediate density lipoprotein (IDL), Very low density lipoprotein (VLDL) and Chylomicron (CM).In the American Cholesterol Education Program's CVD measures, Serum low-density lipoprotein cholesterol (LDL-C) and High density lipoprotein cholesterol (HDL-C) were studied. Hdl-c) concentration was measured as one of the indicators. Epidemiological and clinical studies have shown that HDL-C is negatively associated with the incidence of many cardiovascular diseases. Subjects at high risk of cardiovascular disease, such as peripheral artery disease or abdominal aortic aneurysm patients, may also have higher levels of LDL [].[4]LDL multi-molecule complex is heterogeneous in physical characteristics and can be divided into a series of subcomponents with different density, volume and dynamic behavior, which are closely related to the risk of CVD [].[5]HDL can also be divided into HDL-C subcomponents according to density, and each subcomponent has its own function [].[6]In addition, lipoprotein (A) [Lp (a)] is also closely related to the occurrence of CVD, and there are genetic differences. Levels of lipoprotein (A) [Lp (a)] vary by race; for example, black people have higher Lp(A) levels than whites, Asians, and Hispanics [].[7]By analyzing each lipoprotein subcomponent and Lp (A) and combining with traditional blood lipid examination, the risk of CVD can be more accurately evaluated and the probability of CVD occurrence can be predicted, so as to facilitate early intervention and reduce the morbidity and mortality of CVD.

Statistical method

SAS and R statistical analysis software were used for statistical analysis. During the analysis, Fisher's accurate test was first used to test the independence of all types of variables and the risk of ASCVD to determine whether the risk factors used would significantly affect the risk of ASCVD. Risk factors were analyzed using baseline logistic regression and Odds Ratio(OR) with an extremely 95% confidence interval to describe its impact on the risk of disease. $P<0.05$ indicated statistically significant difference.

2 the results

2.1 Independence Verification

In order to determine whether each factor has an impact on the risk of ASCVD for independent verification, the factors are classified. The age of patients was divided into young and middle-aged (less than 40 years old), middle-aged (40-49 years old) and middle-aged and elderly (over 50 years old) according to Chinese age classification standards and data characteristics. Lipoprotein residues (RLP), intermediate density lipoprotein (IDL), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), total cholesterol (TC), low density lipoprotein particles (LDL-P), and lipoprotein A [Lp (A)] are classified as "normal" and "abnormal" according to their respective criteria.

Since each factor has a cell number less than 10 (5%), Fisher's accurate test is used for independence test.×191The results showed that all the risk factors had statistical significance on the risk of ASCVD (all P<.0001).Therefore, the specific impact of each risk factor on the risk of disease was analyzed next.

Table 1 Independent test of risk factors and ASCVD incidence

	Risk of ASCVD (Risk)					
		Healthy people N = 70 (36.6%)	In a crisis N = 23 (12.0%)	At high risk of N = 22 (11.5%)	Very high risk N = 76 (39.8%)	Fisher accurately tested P value *
Gender, n (%)						The <. 0001
	Male, n = 124	34 (27.42)	18 (14.52)	14 (11.29)	58 (46.77)	
	Female, n = 67	36 (53.73)	5 (7.46)	8 (11.94)	18 (26.87)	
Age group, n(%)						The <. 0001
	Young and middle-aged, n=55	44 (80.00)	2 (3.64)	5 (9.09)	4 (7.27)	

	Middle-aged, n = 51	21 (41.18)	7 (13.73)	6 (11.76)	17 (33.33)	
	Middle and old age, n=85	5 (5.88)	14 (16.47)	11 (12.94)	55 (64.71)	
Lipoprotein residue (RLP), N (%)						The <. 0001
	Normally, n = 108	50 (46.30)	3 (2.78)	3 (2.78)	52 (48.15)	
	Abnormal, n=83	20 (24.10)	20 (24.10)	19 (22.89)	24 (28.92)	
Intermediate density lipoprotein, n(%)						The <. 0001
	Normally, n = 147	59 (40.14)	11 (7.48)	10 (6.80)	67 (45.58)	
	Abnormal, n=44	11 (25.00)	12 (27.27)	12 (27.27)	9 (20.45)	
LDL cholesterol (LDL-C),n(%)						The <. 0001
	Normally, n = 129	49 (37.98)	9 (6.98)	10 (7.75)	61 (47.29)	
	Is not normal, n = 62	21 (33.87)	14 (22.58)	12 (19.35)	15 (24.19)	
High-density lipoprotein						The <. 0001

cholesterol (HDL-C), N (%)						
	Normally, n = 134	57 (42.54)	19 (14.18)	14 (10.45)	44 (32.84)	
	Abnormal, n=57	13 (22.81)	4 (7.02)	8 (14.04)	32 (56.14)	
Total cholesterol, N (%)						The <. 0001
	Normally, n = 109	41 (37.61)	4 (3.67)	7 (6.42)	57 (52.29)	
	Abnormal, n=82	29 (35.37)	19 (23.17)	15 (18.29)	19 (23.17)	
LDL density pattern, n(%)						The <. 0001
	A, n=108	49 (45.37)	8 (7.41)	12 (11.11)	39 (36.11)	
	A/B, n=55	12 (21.82)	8 (14.55)	6 (10.91)	29 (52.73)	
	B, n=28	9 (32.14)	7 (25.00)	4 (14.29)	8 (28.57)	
Low density lipoprotein particles (LDL-P)), N (%)						The <. 0001
	Low, n = 34)	11 (32.35)	0	0	23 (67.65)	

	, n = 79	37 (46.84)	7 (8.86)	7 (8.86)	28 (35.44)	
	High, n = 74	20 (27.03)	16 (21.62)	14 (18.92)	24 (32.43)	
	High, n = 4	2 (50.00)	0	1 (25.00)	1 (25.00)	
Lipoprotein a [Lp (a)],n(%)						The <. 0001
	Normally, n = 146	58 (39.73)	19 (13.01)	20 (13.70)	49 (33.56)	
	Abnormal, n=45	12 (26.67)	4 (8.89)	2 (4.44)	27 (60.00)	

2.2 Baseline Logistic regression

All the Odds ratios in the table are estimated Odds ratios (OR) calculated by baseline logistic regression. Except for THE LDL density pattern and gender, the OR of all other variables in the table is the OR of the control group (healthy population) after and before each 1 unit increase of the variable. The LDL density model adopts "A" as the control group of this variable. Male was used as the control group for this variable.

The RISK of moderate risk increased by 0.19 times (P<.0001, 95%CI:1.11-1.27), and the risk of high risk increased by 0.16 times (P<.0001) 95%CI:1.09-1.23), and the risk of very high risk OR increased 0.24-fold (P<.0001, 95%CI:1.17-1.32).When gender was female, the OR of patients with moderate risk decreased 0.74 times (P=0.0167, 95%CI: 0.09-0.79), and there was no statistical difference in THE OR of patients with high risk (P=0.2207, 95%CI: 0.20-1.45), and the OR of extremely high risk was reduced by 0.71 times (P=0.0007, 95%CI:0.15-0.59).For each 1(mmol/L) increase in the concentration of lipoprotein residues (RLP), the risk of intermediate OR increased 24.18 times (P<.0001, 95%CI:5.16-122.77). The OR of high-

risk patients increased 30.41-fold (P<.0001, 95%CI:6.34-155.53), and the OR of high-risk patients increased 3.81-fold (P=0.0390, 95%CI:1.07-13.58).For each 1 (mmol/L) increase in intermediate density lipoprotein (IDL) concentration, the risk of intermediate density lipoprotein (IDL) increased 667 fold [P<.0001, 95%CI: 35.98-(>999)], and the risk of high risk increased 699 fold [P<.0001, 95%CI: 35.98-(>999)]. 36.45-(>999)], and there was no statistical difference in OR of extremely high risk (P=0.2466, 95%CI:0.41-31.84).For each 1 (mmol/L) increase in low-density lipoprotein cholesterol (LDL-C), there was a 1.3-fold increase in MEDIUM-risk OR (P=0.0027, 95%CI:1.34-3.97), and a 0.87fold increase in high-risk OR (P=0.0228, 95%CI: 1.09-3.20), and 0.47-fold reduction in the risk of very high risk OR (P=0.0015, 95%CI: 0.36-0.79).For each 1 mmol/L increase in hdL-C, there was no significant difference in OR between moderate and high risk patients (P=0.0938, 95%CI:0.12-1.18;P=0.1370, 95%CI:0.14-1.31), and the risk of very high risk OR decreased by 0.83 times (P<.0001, 95%CI:0.07-0.40).For each 1 (mmol/L) increase in total cholesterol (TC) concentration, the OR of patients with moderate risk increased 1.27 times (P=0.0002, 95%CI:1.35-3.81), and the OR of patients with high risk increased 1.43 times (P=0.0001, 95%CI: 1.43-4.15), and the OR of extremely high risk was reduced by 0.48 times (P=0.0003, 95%CI:0.36-0.74).When THE LDL density pattern was A/B, the OR of patients with moderate risk increased 3.08 times (P=0.2592, 95%CI:1.23-13.10), while there was no statistical difference in THE OR of patients with high risk (P=0.4921, 95%CI:0.64-6.55). The risk of disease was 2.04 times higher for highly high-risk OR (P=0.0150, 95%CI:1.37-6.71).When THE LDL density pattern was B, the OR of patients with moderate risk increased 3.76 times (P=0.1427, 95%CI:1.38-16.44), and there was no statistical difference in THE OR of patients with high risk and extremely high risk (P=0.7214, 95%CI: 0.48-6.91; P=0.3981, 95%CI: 0.39-3.16).Each 1 (nmol/L) increase of low-density lipoprotein particles (LDL-P) was associated with a 0.002-fold increase in medium-risk OR (P=0.0030, 95%CI:1.001-1.004). The OR of high-risk patients increased by 0.002 times (P=0.0032, 95%CI:1.001-1.004), while there was no statistical difference in THE OR of high-risk patients (P=0.0664, 95%CI:0.998-1.000).For every 1 (mg/L) increase of lipoprotein A [Lp (A)], there was no significant difference in OR

between moderate and high risk patients (P=0.9534, 95%CI:0.998-1.002). The risk of disease was increased by 0.002-fold for highly high-risk OR (P=0.0018, 95%CI:1.001-1.003).

Table 2 OR of related risk factors and risk of ASCVD

		Risk of ASCVD (Risk)									
		Healthy people	In a crisis			At high risk of			Very high risk		
		OR	OR	P values	95% confidence interval	OR	P values	95% confidence interval	OR	P values	95% confidence interval
age		1	1.19	The <.0001	1.11-1.27	1.16	The <.0001	1.09-1.23	1.24	The <.0001	1.17-1.32
gender	Female - male	1	0.26	0.0167	0.09-0.79	0.54	0.2207	0.20-1.45	0.29	0.0007	0.15-0.59
Lipoprotein residue (RLP)		1	25.18	The <.0001	5.16-122.77	31.41	The <.0001	6.34-155.53	3.81	0.0390	1.07-13.58
Intermediate density lipoprotein (IDL)		1	667.42	The <.0001	35.98 - (> 999)	699.13	The <.0001	36.45 - (> 999)	3.62	0.2466	0.41-31.84
Low density lipoprotein cholesterol, LDL-C		1	2.30	0.0027	1.34-3.97	1.87	0.0228	1.09-3.20	0.53	0.0015	0.36-0.79

High-density lipoprotein Cholesterol (HDL-C)		1	0.38	0.093 8	0.12-1.18	0.43	0.137 0	0.14-1.31	0.17	The <. 0001	0.07-0.40
Total cholesterol (TC)		1	2.27	0.000 2	1.35-3.81	2.43	0.000 1	1.43-4.15	0.52	0.000 3	0.36-0.74
LDL densit y patter n	A/B-A	1	4.08	0.259 2	1.23-13.10	2.04	0.492 1	0.64-6.55	3.04	0.015 0	1.37-6.71
	B-A	1	4.76	0.142 7	1.38-16.44	1.82	0.721 4	0.48-6.91	1.12	0.398 1	0.39-3.16
Low density lipoprotein particles (LDL-P)		1	1.002	0.003 0	1.001-1.004	1.002	0.003 2	1.001-1.004	0.99 9	0.066 4	0.998-1.000
Lipoprotein, A [Lp (a)]		1	1.000	0.953 4	0.998-1.002	0.999	0.477 9	0.996-1.002	1.00 2	0.001 8	1.001-1.003

Note:

*OR: IF OR is greater than 1, the probability of occurrence of the event is greater than that of the control group, and if OR is less than 1, the probability of occurrence of the event is smaller than that of the control group. This value can be used to measure the correlation between risk factors and disease risk.

*95% confidence interval (95%CI) : OR has a 95% probability of falling within this interval, which can be used as an auxiliary p-value to judge whether OR is significant: when P value >(=0.05), if the 95% confidence interval of OR does not contain 1, it can also be said that OR is significant.α

3 discuss

According to a report on Chinese adult cardiovascular and cerebrovascular research, the proportion of men at high risk of cardiovascular and cerebrovascular disease is higher than that of women, and the higher the age, the higher the

proportion of high-risk patients [], which is consistent with the conclusion of this study.[8]It is recommended that patients with suspected cardiovascular and cerebrovascular diseases be examined and treated as soon as possible. Male patients should pay more attention to their physical condition. Studies have shown [] that small diameter lipoprotein residue (RLP-C) is an independent risk factor for cardiovascular and cerebrovascular diseases.[9]In this study, we found that increased concentrations of lipoprotein residues (RLP) and intermediate density lipoprotein (INTERMEDIATE density lipoprotein) significantly increased the risk of disease. According to a study [], HDL-C has no significant influence on the risk of cardiovascular and cerebrovascular diseases.[10]According to Chinese Guidelines for the Prevention and treatment of dyslipidemia in adults [], HDL-C is negatively correlated with ASCVD.[11]In this study, the increase of HDL-C did not significantly affect the probability of intermediate and high risk, but significantly reduced the probability of extremely high risk. Ldl-c and total cholesterol are important risk factors for ASCVD in Chinese guidelines for the prevention and treatment of dyslipidemia in adults. In this study, increased LDL-C and total cholesterol significantly increased the probability of high risk ASCVD, but significantly reduced the risk of very high risk ASCVD. Therefore, lipoprotein residue (RLP) is a better predictor of risk. This conclusion is consistent with the 1971 Framingham study [] that RLP-C is an independent risk factor for ASCVD rather than total cholesterol, HDL-C, and LDL-C.[12]For THE LDL density pattern, when the density pattern was A/B, the probability of intermediate risk and extremely high risk was significantly increased. When the density mode was B, the probability of moderate risk increased significantly. New progress and application analysis of VAP detection of plasma lipoprotein subcomponents [] indicates that LDL-P is closely related to the residual risk of cardiovascular and cerebrovascular diseases (some patients still have the risk of cardiovascular and cerebrovascular diseases after reaching the standard of LDL-C).[13]This study did not investigate the residual risk, but it could be concluded that the increase of LDL-P would significantly increase the probability of medium-high risk. Lipoprotein A [Lp (a)] is positively correlated with the risk of cardiovascular and cerebrovascular diseases [].[14]This

study found that the increase in lipoprotein A significantly increased the probability of having a very high risk of developing the disease. Therefore, VAP-related risk factors can affect the risk of ASCVD. Therefore, in-depth study on the separation and detection methods of such factors can effectively prevent and treat cardiovascular diseases.

reference

[1]World Health Organization (WHO). Cardiovascular diseases . Available at https://who.int/cardiovascular_diseases/en/ (2019) , Accessed 18th Jan 2019

[2] Hu SZ, Gao RL, Liu LS, et al. Chinese Report on Cardiovascular Diseases 2018[G]. Chinese Journal of Circulation, 2019, 34 (3):209-220

[3]Zhao Shuiping, Wang Yongjun, Mu Yiming, et al. Prevalence of dyslipidaemia in patients treated with lipid-lowering agents in China: Integrative integrative medicine: an integrative integrative approach [J]. Journal of integrative medicine,2014,235(2).

[4] Mi Chunfang, LIU Qingping. Clinical significance and detection progress of plasma low density lipoprotein and high density lipoprotein subcomponents [J]. Chinese journal of arteriosclerosis,2017,25(10):1054-1060.

[5] Sun Haoxing, WANG Hua, WANG Changcheng, et al. Low density lipoprotein subcomponents and their detection methods [J]. Journal of laboratory medicine & clinical medicine,2018,15(16):2505-2508.

[6] Zheng Huifei, Cong Hui, Wang Huimin, Jin Qinghui, Zhao Jianlong. High density lipoprotein subclass detection method [J]. Journal of clinical laboratory,2009,27(06):477-479.

[7]Khera AV, Everett BM, Caulfield MP, et al. Lipoprotein(a) concentrations, rosuvastatin therapy, and residual vascular risk: (Justification for the use of statins in prevention: An experimental study on the feasibility of a novel rosuvastatin model [J]. Circulation, 2014,129 (6) : 635-642.

[8] Zhang M. Study on the risk of cardiovascular and cerebrovascular diseases among Adults in China [D]. Chinese Center for Disease Control and Prevention,2017. (in Chinese)

[9] Li L. Study on anti-atherosclerosis mechanism and dyslipidemia syndrome type of Tiaozhi Tongmai Granule based on NF-κB pathway [D]. Beijing University of Chinese Medicine,2018.

[10] Dai Huamin. Association analysis of low density lipoprotein with acute cerebral infarction [D]. Nanjing University,2019.

[11] Zhu Junren, Gao Runlin, ZHAO Shuiping, Lu Guoping, Zhao Dong, Li Jianjun. Chinese Journal of Circulation,2016,31(10):937-953. (in Chinese)
[12]Kannel WB, Castelli WP, Gordon T, et al. Serum cholesterol, lipoproteins, and risk of coronary heart disease: The Framingham Study [J]. Ann Intern Med,1971,74:1-12.
[13] Liang Chunzi, Zhu Man, Tu Jiancheng. New progress and application analysis of plasma lipoprotein subcomponents by VAP [J]. Lab med,2019,34(01):76-81. (in Chinese)
[14] Qin Qunting, Deng Xiuting, Lu Wensheng. Research progress of lipoprotein (a) [J]. Chinese journal of arteriosclerosis,2018,26(02):194-200.