ORIGINAL RESEARCH

Influence of Management of Intensive Weight, Blood Pressure, and Lipids on Disease Severity in Patients with Carotid Atherosclerosis

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ABSTRACT

Context • Cardiovascular diseases (CVDs caused by atherosclerosis, such as coronary heart disease and stroke, have become major causes of death and disability worldwide. Atherosclerosis is the primary pathological factor causing CVDs. Managing weight, blood pressure, and lipids is one of the tenets of chronic-disease management, including atherosclerosis.

Objective • The study intended to investigate the effects of managing weight, blood pressure, and lipids on disease severity in patients with carotid atherosclerosis.

Design • The research team designed a randomized, controlled trial.

Setting • The study took place in the pediatric department at the First Hospital of Hebei Medical University in Shijiazhuang, Hebei Province, China.

Participants • Participants were 380 patients with carotid atherosclerosis who entered the hospital between March 2018 and June 2020.

Intervention • Participants were randomly assigned, using the random-number-table method, to an intervention or a control group, with 190 participants in each group. Both groups received anti-atherosclerotic treatments, and the intervention group also took part in a program for combined management of weight, blood pressure, and blood lipids.

Outcome Measures • All measurements occurred at baseline and postintervention. Using a questionnaire, the study measured the changes in the two groups related to alcohol consumption, smoking, high-fat diet, high-salt diet, and lack of exercise. A physical examination provided participants' weights, blood pressures, and lipid levels, and the Self-Care Ability Assessment Scale (ESCA) provided the changes in their self-management ability. A carotid-artery examination measured parameters related to carotid atherosclerosis, including intima-media thickness (IMT), Crouse scores, plaque-class scores, and plaque-grade scores.

Results • At baseline, no statistically significant differences existed between the groups. Postintervention, the intervention group had significantly greater decreases than the control group for alcohol consumption, smoking, high-fat diet, high-salt diet, lack of exercise, weight, blood pressure, lipid levels, intima-media thickness (IMT) scores, Crouse scores, and plaque-grade scores. Postintervention, the intervention group had significantly greater increases than the control group for self-responsibility, health knowledge, self-concept, and self-care-skills scores.

Conclusions • A program for management of body weight, blood pressure, and blood lipids can effectively control the severity of carotid atherosclerosis, can prevent the disease's progression, and can be promoted as a clinical application. (*Altern Ther Health Med.* [E-pub ahead of print.])

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In recent years, with changes in people's lifestyles and dietary habits, the disease spectrum of people in China has also changed, with cardiovascular diseases (CVDs),[1,2] malignant tumors,[3] and other chronic degenerative diseases becoming the most important causes of death. CVDs caused by atherosclerosis, such as coronary heart disease and stroke, have become major causes of death and disability worldwide.[4,5]

Information released by China's Cardiovascular Disease Center in 2018 showed that the number of people suffering from cardiovascular and cerebrovascular diseases in China was as high as 290 million.[1] Cardiovascular-induced death

has been ranked first in China, accounting for more than 40% of mortality, and CVDs can have a serious impact on people's health.[1,6]

Atherosclerosis is the primary pathological factor causing CVDs, and controlling the process of atherosclerosis can effectively prevent CVDs.[7,8] Atherosclerosis is a systemic disease that occurs in the large and medium-sized arteries, with the carotid artery being one of the most common sites of involvement.[9] Carotid atherosclerotic plaque can lead to carotid artery stenosis, resulting in inadequate intracranial blood supply, and ruptured plaque is an important cause of stroke.[10]

The degree of carotid atherosclerosis can indirectly reflect systemic vascular lesions and is an important clinical predictor of cardiovascular and cerebrovascular events.[11,12] Polak et al found that the vessel wall is altered in the early stages of atherosclerosis.[13] Those researchers also found that the intima-media thickness (IMT) score can act as an independent predictor for the diagnosis of atherosclerosis, and a higher IMT indicates a greater risk of atherosclerosis. The Crouse score is widely accepted as a quantitative index to evaluate the severity of atherosclerosis, which can be obtained by adding up the thickness of all the individual plaques measured in the carotid arteries bilaterally.[14]

A combination of risk factors can cause the formation of carotid atherosclerosis, including not only alcohol consumption, smoking, and obesity[15,16] but also other controllable risk factors, such as hypertension and high levels of blood lipids.[17,18] Therefore, a comprehensive approach in clinical practice is needed to prevent the onset and development of atherosclerosis.

In recent years, chronic-disease management has gained the attention of the majority of clinicians and patients, and managing weight, blood pressure, and lipids is one of the tenets of chronic-disease management.[19,20] The ratio in serum of low-density lipoprotein cholesterol (LDL-C) to high-density lipoprotein cholesterol (HDL-C) could be a useful marker for predicting the presence of carotid plaque in the general population.[21] As early as 2001, Lakka et al's study found that abdominal obesity can accelerate carotid atherosclerosis.[22] In addition, hypertension has been shown to have a major role in the pathogenesis of atherosclerosis.[23]

Choo et al have confirmed that effective management measures for patients with atherosclerosis can effectively delay the disease.[24] Managing patients' lipid profiles, obesity, and hypertension, in parallel with treatment of carotid atherosclerosis, may help with their recovery.

However, few studies have occurred on the effects of managing weight, blood pressure, and lipids on disease severity in patients with carotid atherosclerosis. Therefore, the current study intended to investigate the effects of managing weight, blood pressure, and lipids on disease severity in patients with carotid atherosclerosis.

METHODS

Participants

The research team designed a randomized, controlled trial. The study took place in the Health Management Center at the First Hospital of Hebei Medical University in Shijiazhuang, Hebei Province, China. Potential participants were patients with carotid atherosclerosis who had entered the hospital between March 2018 and June 2020.

Potential participants were included in the study if they: (1) met the diagnostic criteria for carotid atherosclerosis using ultrasound, and (2) had a normal spirit. Potential participants were excluded from the study if they: Severe cognitive impairment; Severe organ failure; Unstable periods of chronic diseases such as hypertension; Patients with malignant tumors.

All participants signed informed consent. The study's protocol was developed based on the relevant requirements of the Declaration of Helsinki of the World Medical Association.[12]

Procedures

Intervention. Participants were randomly assigned, using the random-number-table method, to an intervention or a control group, with 190 participants in each group. The intervention included regular appointments at the hospital for participants.

Outcome measures. All measurements occurred at baseline and postintervention. Participants' changes in alcohol consumption, smoking, high-fat diet, high-salt diet, exercise, weights, blood pressures, and lipid levels were compared. A questionnaire developed by the research team was self-rated by participants and included questions about demographics, alcohol consumption, smoking, high-fat diet, high-salt diet, and exercise level. A physical examination measured such indicators as weight and height, blood pressure, blood lipids, and fasting blood sugar.

The Self-Care Ability Assessment Scale (ESCA)[26] was used for comparison of self-management ability. Carotid atherosclerosis was also measured with a carotid-artery examination using the SSD3500 Aloka color Doppler ultrasound (manufacturer, city, state, country), at a probe frequency of 12MHz to measure the vessel's IMT. That examination also measured participants' Crouse scores, plaque-class scores, and plaque-grade scores.

Intervention

Control group. The control group received lipid-lowering statin drugs and anti-platelet-aggregation drugs according to the Chinese Expert Recommendations for the Diagnosis and Treatment of Carotid Atherosclerotic Diseases in the Elderly.[27]

Intervention group. The intervention group received the same statin lipid-lowering drugs and anti-platelet-aggregation drugs as the control group did and also participated in a program for management of weight, blood pressure, and lipids for one year.

Specifically, the research team established a group of medical practitioners who would collaborate with participants to manage their weights, blood pressures, and lipids. The group consisted of a neurologist, a cardiologist, an

endocrinologist, a psychologist, two general practitioners, a weight manager (dietitian), and three nursing staff. This group conducted a comprehensive analysis of each participant's health records and developed a personalized management program.

The research team set up a management room in which the medical group could meet participants in person, and the team could contacted participants through WeChat or by telephone every week to guide and supervise the program's implementation.

A graded approach was used to manage participant's weights, blood pressures, and lipids. The main contents of the visits included lifestyle interventions, discussion of possible complications related to the disease, instruction on medication use, and education on possible organ impairment. Lifestyle management mainly included guidance on a eating a healthy diet, discontinuing smoking and use of alcohol, participating in proper exercise, reducing salt intake, maintaining psychological balance, and controlling weight.

For participants with normal weights, blood pressures, and blood lipids, a primary management method was used, with the participant making one visit to the management office every two months and receiving assistance in lifestyle management.

For participants with simple abnormal weights, blood pressures, or blood lipids, secondary management was used. This level included one visit to the management office every month and one visit through WeChat or by telephone every week. Their medication guidance was strengthened, and they received lifestyle management.

For participants who also had abnormal weights, blood pressures, and dyslipidemia, tertiary management was used. They were required to visit the management office twice a month for visits and were contacted twice a week through WeChat or by telephone, to strengthen their medication guidance while helping them manage their lifestyles.

For participants who had abnormal weights, blood pressures, and lipids, the fourth level of management was used. They were required to visit the management room twice a month for visits and were contacted four times a week through WeChat or by telephone to strengthen medication guidance while helping them manage their lifestyles.

Outcome Measures

Lack of exercise. This variable was defined as outdoor exercise of fewer than three times a week and less than 30 min each time.[28]

High-fat diet. A high-fat diet was defined as a ratio of the daily intake of total fat to total calories of >30%.[29]

High-salt diet. A high-salt diet was defined as an intake of daily salt of >6g.[30]

Self-management ability.[26] This test measures self-responsibility, health knowledge, self-concept, and self-care skills. Higher scores on ESCA indicate better self-management ability.

Carotid-artery examination. The scoring for carotid-atherosclerotic plaque was based on the site of the carotid atherosclerotic plaque, its size, its morphology and the echogenic characteristics of the IMT score,[31] the Crouse score,[32] the plaque-class scores, and the plaque-grade score.[33]

Table 1. Demographics of the Intervention and Control Groups at Baseline

Characteristics	Intervention Group n = 190 Mean ± SD	Control Group n = 190 Mean ± SD	t/χ^2	*P* value
Age, y	57.32 ± 6.17	57.28 ± 6.09	0.064	.949
Gender, n (%)			0.103	.748
Males	167 (87.90)	169 (88.95)		
Females	23 (12.10)	21 (11.05)		
Weight, kg	66.46 ± 10.87	65.95 ± 10.43	0.471	.638
Height, cm	172.02 ± 18.28	171.01 ± 18.19	0.540	.590
BMI, kg/cm2	25.82 ± 3.29	25.79 ± 3.26	0.089	.929
FBS, mmol/L	5.21 ± 0.23	5.19 ± 0.19	0.924	.356
Education, n (%)			0.017	.896
College or higher	153 (80.53)	154 (81.05)		
Senior middle school and below	37 (19.47)	36 (18.95)		

Abbreviations: BMI, body mass index; FBS, fasting blood glucose.

Statistical Analysis

SPSS 21.0 software was used to analyze the data. The data were expressed as means ± standard deviations (SDs), and the *t* test was used. The counted data were expressed as number (%), and the chi-square χ^2 test was used. Differences were considered statistically significant at $P < .05$.

RESULTS

Participants

The study included and analyzed the data of 380 participants. Participants in the intervention group, 167 men and 23 women, ranged in age from 53 to 63 years old, with a mean age of 57.32 ± 6.17 years. Participants in the control group, 169 males and 21 females, ranged in age from 52 to 63 years old, with a mean age of 57.28 ± 6.09 years. No statistically significant differences existed between in the groups at baseline (Table 1).

Lifestyle Variables

At baseline, no statistically significant differences were found between the groups in alcohol consumption, smoking, high-fat diet, high-salt diet, or lack of exercise. Postintervention, alcohol consumption, smoking, high-fat diet, high-salt diet, and lack of exercise were significantly lower in the intervention group than in the control group, with $P < .05$ (Table 2)

Physical Examination

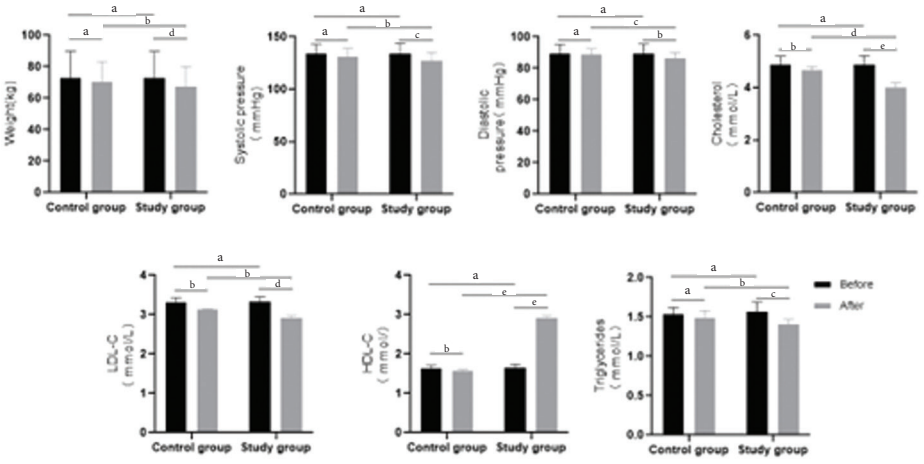
At baseline, no statistically significant differences existed in weight, blood pressure, or lipid levels between the groups.

Table 2. Comparison of the Alcohol Consumption, Smoking, High-fat Diet, High-salt Diet and Lack of Exercise Between the Intervention and Control Groups

Groups	Timepoint	Smoking n (%)	Drinking n (%)	High-fat Diet n (%)	High-salt Diet n (%)	Lack of Exercise n (%)
Intervention Group, n = 190	Baseline	54 (28.42)	59 (31.05)	39 (20.53)	38 (20.00)	39 (20.53)
	Postintervention	9 (4.74)[a,b]	8 (4.21)[a,b]	3 (1.58)[a,b]	4 (2.11)[a,b]	3 (1.58)[a,b]
Control Group, n = 190	Baseline	52 (27.37)	58 (30.53)	38 (20.00)	29 (15.26)	30 (15.79)
	Postintervention	41 (21.58)	45 (23.68)	33 (17.37)	31 (16.32)	33 (17.37)

*$P < .05$, indicating a significant difference between the intervention group and the control group at baseline
#$P < .05$, indicating a significant difference between the intervention group and the control group postintervention

Figure 1. Comparison of Weight, Blood Pressure, and Lipid Levels Between the Intervention and Control Groups



[a]$P > .05$, indicating no significant differences between the groups at baseline
[b]$P < .05$, indicating a statistically significant difference between the groups postintervention
[c]$P < .01$, indicating a statistically significant difference between the groups postintervention
[d]$P < .001$, indicating a statistically significant difference between the groups postintervention
[e]$P < .0001$, indicating a statistically significant difference between the groups postintervention

Abbreviations: Before, baseline; After, postintervention; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

Postintervention, the intervention group had significantly greater decreases than the control group for weight, with $P < .05$; systolic blood pressure, with $P < .05$; diastolic systolic blood pressure, with $P < .01$; cholesterol, with $P < .001$; low density lipoprotein cholesterol (LDL-C), with $P < .05$; high density lipoprotein cholesterol (HDL-C), with $P < .0001$; and triglycerides, with $P < .05$ (Figure 1).

Self-management Ability

No statistically significant differences were found between the groups in the scores for self-responsibility, health-knowledge, self-concept, and self-care skills at baseline. Postintervention, the intervention group had significantly greater increases than the control group for self-responsibility, with $P < .01$; health-knowledge, with $P < .05$; self-concept, with $P < .01$; and self-care scores with $P < .01$ (Figure 2).

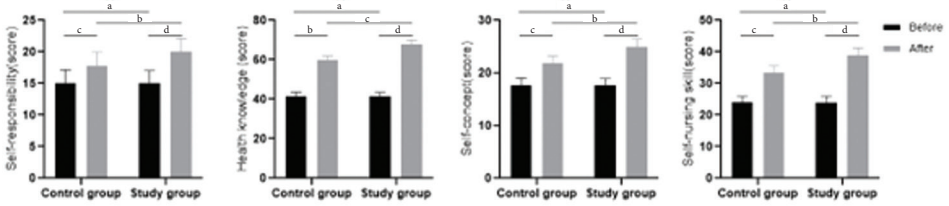
Carotid Atherosclerosis Index

At baseline, no statistically differences existed between the groups in the IMT score, Crouse score, plaque-grade score, or plaque numbers. Postintervention, no significant difference was found between the groups in the number of plaques, but the intervention group had significantly greater decreases than the control group for the IMT score, with $P < .01$; Crouse, with $P < .001$; and plaque grade, with $P < .01$ (Figure 3).

DISCUSSION

In the current study, the intervention group's weights, blood pressures, and lipid levels were significantly lower than those in the control group postintervention, suggesting that program managing weight, blood pressure, and lipids can effectively reduce the weights of patients with carotid atherosclerosis and promote the return to normal blood pressures and lipid levels.

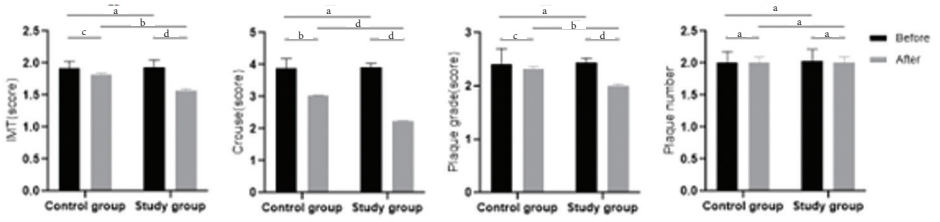
Figure 2. Comparison of Self-management Ability Between the Intervention and Control Groups



[a]$P > .05$, indicating no significant differences between the groups at baseline
[c]$P < .05$, indicating a statistically significant difference between the groups postintervention
[b]$P < .01$, indicating a statistically significant difference between the groups postintervention
[d]$P < .001$, indicating a statistically significant difference between the groups postintervention

Abbreviations: Before, at baseline; After, postintervention.

Figure 3. Comparison of Carotid Atherosclerosis-related Parameters Between the Intervention and Control Groups



[a]$P > .05$, indicating no significant differences between the groups postintervention
[b]$P < .01$, indicating a statistically significant difference between the groups postintervention
[c]$P > .05$, indicating no significant differences between the groups at baseline
[d]$P < .001$, indicating a statistically significant difference between the groups postintervention

Abbreviations: Before, at baseline; After, postintervention.

In the current study, the progression of carotid atherosclerosis was determined using the IMT, Crouse, and plaque-grade scores and the plaque numbers from multiple perspectives, and postintervention, the IMT, Crouse and plaque-grade scores of the intervention group were significantly lower than those of the control group, indicating an improvement in symptoms in patients with carotid atherosclerosis after a program for management of weights, blood pressures, and lipids.

However, the majority of the participants included in the current study were highly educated, and Kubota et al suggested that a population with better healthcare conditions and higher health awareness had better outcomes.[34] Thus the results of this study may not be fully representative of the entire population.

Therefore, the current research team would like to expand the scope of a study in the future, with additional observation indicators, longer follow-up, and continuous optimization of the management protocol to improve the current study, using a larger sample size.

CONCLUSIONS

Managing patients' weights, blood pressures, and lipids by developing an individualized management program for patients can effectively reduce and delay the progression of carotid atherosclerosis, with the program creating a potential model for managing atherosclerosis. In addition, the management program might be used clinically as an adjunctive treatment for carotid atherosclerosis.

AUTHORS' DISCLOSURE STATEMENT

The authors declare there is no conflict of interest.

REFERENCES

1. Ma L-Y, Chen W-W, Gao R-L, et al. China cardiovascular diseases report 2018: an updated summary. *J Geriatr Cardiol*. 2020;17(1):1-8.
2. Deng J, Guo M, Li G, Xiao J. Gene therapy for cardiovascular diseases in China: basic research. *Gene Ther*. 2020;27(7-8):360-369. doi:10.1038/s41434-020-0148-6
3. Zhai C, Cai Y, Lou F, et al. Multiple Primary Malignant Tumors - A Clinical Analysis of 15,321 Patients with Malignancies at a Single Center in China. J Cancer. 2018;9(16):2795-2801. Published 2018 Jul 16. doi:10.7150/jca.25482.
4. Getz GS, Reardon CA. Atherosclerosis: cell biology and lipoproteins. *Curr Opin Lipidol*. 2020;31(5):286-290. doi:10.1097/MOL.0000000000000704
5. Kinoshita M, Yokote K, Arai H, et al; Committee for Epidemiology and Clinical Management of Atherosclerosis. Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017. *J Atheroscler Thromb*. 2018;25(9):846-984. doi:10.5551/jat.GL2017
6. Shen C, Ge J. Epidemic of Cardiovascular Disease in China: Current Perspective and Prospects for the Future. *Circulation*. 2018;138(4):342-344. doi:10.1161/CIRCULATIONAHA.118.033484

7. Pedro-Botet J, Climent E, Benaiges D. Atherosclerosis and inflammation. New therapeutic approaches. *Med Clín (Barc)*. 2020;155(6):256-262. doi:10.1016/j.medcli.2020.04.024
8. Glanz VY, Sobenin IA, Grechko AV, Yet SF, Orekhov AN. The role of mitochondria in cardiovascular diseases related to atherosclerosis. Front Biosci (Elite Ed). 2020;12(1):102-112. Published 2020 Jan 1. . doi:10.2741/e860
9. Kattoor AJ, Pothineni NVK, Palagiri D, Mehta JL. Oxidative Stress in Atherosclerosis. Curr Atheroscler Rep. 2017;19(11):42. Published 2017 Sep 18. doi:10.1007/s11883-017-0678-6.
10. Zhang C, Ye L, Zhang Q, Wu F, Wang L. The role of TRPV1 channels in atherosclerosis. *Channels (Austin)*. 2020;14(1):141-150. doi:10.1080/19336950.2020.1747803
11. Simion V, Zhou H, Haemmig S, et al. A macrophage-specific lncRNA regulates apoptosis and atherosclerosis by tethering HuR in the nucleus. Nat Commun. 2020;11(1):6135. Published 2020 Dec 1. doi:10.1038/s41467-020-19664-2.
12. Bilanges B, Alliouachene S, Pearce W, et al. Vps34 PI 3-kinase inactivation enhances insulin sensitivity through reprogramming of mitochondrial metabolism. Nat Commun. 2017;8(1). *Published*. 1804;2017(Nov):27. doi:10.1038/s41467-017-01969-4
13. Polak JF, Szklo M, O'Leary DH. Carotid Intima-Media Thickness Score, Positive Coronary Artery Calcium Score, and Incident Coronary Heart Disease: The Multi-Ethnic Study of Atherosclerosis. J Am Heart Assoc. 2017;6(1):e004612. Published 2017 Jan 21. doi:10.1161/JAHA.116.004612.
14. Jiang D, Wang Y, Chang G, et al. DNA hydroxymethylation combined with carotid plaques as a novel biomarker for coronary atherosclerosis. *Aging (Albany NY)*. 2019;11(10):3170-3181. doi:10.18632/aging.101972
15. Hannuksela ML, Liisanantti MK, Savolainen MJ. Effect of alcohol on lipids and lipoproteins in relation to atherosclerosis. *Crit Rev Clin Lab Sci*. 2002;39(3):225-283. doi:10.1080/10408360290795529
16. Wang Z, Wang D, Wang Y. Cigarette Smoking and Adipose Tissue: The Emerging Role in Progression of Atherosclerosis. *Mediators Inflamm*. 2017;2017:3102737. doi:10.1155/2017/3102737
17. Yao BC, Meng LB, Hao ML, Zhang YM, Gong T, Guo ZG. Chronic stress: a critical risk factor for atherosclerosis. *J Int Med Res*. 2019;47(4):1429-1440. doi:10.1177/0300060519826820
18. Chistiakov DA, Melnichenko AA, Myasoedova VA, Grechko AV, Orekhov AN. Mechanisms of foam cell formation in atherosclerosis. *J Mol Med (Berl)*. 2017;95(11):1153-1165. doi:10.1007/s00109-017-1575-8
19. Otieno HA, Miezah C, Yonga G, et al. Improved blood pressure control via a novel chronic disease management model of care in sub-Saharan Africa: real-world program implementation results. *J Clin Hypertens (Greenwich)*. 2021;23(4):785-792. doi:10.1111/jch.14174
20. Lee JA, Choi M, Lee SA, Jiang N. Effective behavioral intervention strategies using mobile health applications for chronic disease management: a systematic review. BMC Med Inform Decis Mak. 2018;18(1):12. Published 2018 Feb 20. doi:10.1186/s12911-018-0591-0.
21. Yang C, Sun Z, Li Y, Ai J, Sun Q, Tian Y. The correlation between serum lipid profile with carotid intima-media thickness and plaque. BMC Cardiovasc Disord. 2014;14:181. Published 2014 Dec 9. doi:10.1186/1471-2261-14-181.
22. Lakka TA, Lakka HM, Salonen R, Kaplan GA, Salonen JT. Abdominal obesity is associated with accelerated progression of carotid atherosclerosis in men. *Atherosclerosis*. 2001;154(2):497-504. doi:10.1016/S0021-9150(00)00514-1
23. Su TC, Jeng JS, Chien KL, Sung FC, Hsu HC, Lee YT. Hypertension status is the major determinant of carotid atherosclerosis: a community-based study in Taiwan. *Stroke*. 2001;32(10):2265-2271. doi:10.1161/str.32.10.2265
24. Choo J, Lee J, Cho JH, Burke LE, Sekikawa A, Jae SY. Effects of weight management by exercise modes on markers of subclinical atherosclerosis and cardiometabolic profile among women with abdominal obesity: a randomized controlled trial. BMC Cardiovasc Disord. 2014;14:82. Published 2014 Jul 10. doi:10.1186/1471-2261-14-82.
25. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. 2013. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.
26. Xu W, Lian G, Huang W. Effect of dual track continuous health education on patients with endometrial cancer after operation. *Diabetes New World*. 2021;14:82.
27. Liu M; Committee of cardio-cerebro-vascular Disease of China Association of Gerontology and Geriatrics, Chinese College of Cardiovascular Physician of Chinese Medical Doctor Association. Chinese expert consensus on the diagnosis and treatment of hypertension in the elderly. Aging Med (Milton). 2018;1(2):106-116. *Published*. 2017;2018(Jun):11. doi:10.1002/agm2.12020
28. Dimeo F, Bauer M, Varahram I, Proest G, Halter U. Benefits from aerobic exercise in patients with major depression: a pilot study. *Br J Sports Med*. 2001;35(2):114-117. doi:10.1136/bjsm.35.2.114
29. Lucas CP, Boldrin MN, Reaven GM. Effect of orlistat added to diet (30% of calories from fat) on plasma lipids, glucose, and insulin in obese patients with hypercholesterolemia. *Am J Cardiol*. 2003;91(8):961-964. doi:10.1016/S0002-9149(03)00112-7
30. Giltinan M, Walton J, Mcnulty B, et al. Sodium (Na) intakes in Irish adults[J]. Proceedings of The Nutrition Society, 2011, 70(OCE3)..
31. Touboul PJ, Labreuche J, Vicaut E, Amarenco P; GENIC Investigators. Carotid intima-media thickness, plaques, and Framingham risk score as independent determinants of stroke risk. *Stroke*. 2005;36(8):1741-1745. doi:10.1161/01.STR.0000174490.23495.57
32. Karádi I, Mészáros Z, Csányi A, et al. Serum semicarbazide-sensitive amine oxidase (SSAO) activity is an independent marker of carotid atherosclerosis. *Clin Chim Acta*. 2002;323(1-2):139-146. doi:10.1016/S0009-8981(02)00189-4
33. Aono J, Ikeda S, Katsumata Y, et al. Correlation between plaque vulnerability of aorta and coronary artery: an evaluation of plaque activity by direct visualization with angioscopy. *Int J Cardiovasc Imaging*. 2015;31(6):1107-1114. doi:10.1007/s10554-015-0669-z
34. Kubota Y, Heiss G, MacLehose RF, Roetker NS, Folsom AR. Association of Educational Attainment With Lifetime Risk of Cardiovascular Disease: The Atherosclerosis Risk in Communities Study. *JAMA Intern Med*. 2017;177(8):1165-1172. doi:10.1001/jamainternmed.2017.1877