

Lifestyle Interventions and Carotid Plaque Burden: A Comparative Analysis of Two Lifestyle Intervention Programs in Patients with Coronary Artery Disease

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ABSTRACT

Background: The cardioprotective effects of intensive lifestyle regimens in primary prevention have been elucidated; however, there is a paucity of data comparing the effects of different lifestyle regimens in patients with established coronary artery disease (CAD) or CAD equivalent, specifically vis-à-vis carotid plaque regression.

Methods: We performed a randomized, single-center, single-blind study in 120 patients with established CAD. Patients were randomly assigned to either 9 months of the Complete Health Improvement Program (CHIP), an outpatient lifestyle enrichment program that focuses on improving dietary choices, enhancing daily exercise, increasing support systems, and decreasing stress; or to 9 months of an ad hoc, nonsequential combination of various healthy living classes offered separately through a health maintenance organization and referred to as the Healthy Heart program. Baseline and 9-month change in carotid intima-media thickness (CIMT) were measured.

Results: Among 120 participants, data were analyzed for 79, of which 68 (86%) completed the study. Both average CIMT and average maximum CIMT increased over 9 months, but the changes between groups were insignificant. There were marked differences in the mean body mass index favoring the CHIP group (-1.9 [standard deviation = 1.9]; $p < 0.001$) and statistically significant within-group improvements in blood pressure, triglyceride level, 6-minute walk test result, self-assessment well-being score, and Patient Health Questionnaire-9 score that were not observed between groups.

Conclusion: Neither the CHIP nor Healthy Heart was effective in inducing plaque regression in patients with established CAD after a 9-month period. However, both were effective in improving several CAD risk factors, which shows that the nonsequential offering of healthy lifestyle programs can lead to similar outcomes as a formal, sequential, established program (CHIP) in many aspects. These results have important implications as to how lifestyle changes will be implemented as tertiary prevention measures in the future.

plant-based diet has on various cardiac risk factors such as body mass index (BMI), non-high-density lipoprotein (HDL) cholesterol, blood pressure, type 2 diabetes, and metabolic syndrome.¹⁵⁻¹⁹ Among the limitations of the aforementioned studies are a lack of a head-to-head comparison of lifestyle improvement programs using plant-based diets, a lack of testing such a program in a heterogeneous group of people, and the lack of a validated test to serve as measure for the CAD burden. Because a substantial percentage of patients are surviving their initial cardiac event with improved short- and long-term outcomes, it would be valuable to determine if there is an optimal lifestyle improvement program for tertiary prevention of established CAD.²⁵⁻³⁵ We aimed to answer these questions by testing 2 types of lifestyle improvement programs head-to-head in a heterogeneous population and by using carotid intima-media thickness (CIMT) as an indirect measure of the effect of these programs on CAD.

INTRODUCTION

Coronary artery disease (CAD) continues to be a major cause of morbidity and mortality in developed countries and is the cause of one-fifth of deaths in the US.¹ Although CAD death rates have declined worldwide since the turn of the century, it remains our leading cause of death.¹⁻³ Modification of cardiovascular risk factors is responsible for nearly half of the decrease in deaths secondary to CAD, but much more effort is needed.⁴ Changes in lifestyle such as smoking cessation, regular physical activity, and combined dietary changes have been shown to reduce mortality by 20% to 35%.^{5,6} Among the dietary changes, a plant-based diet has been proposed as an effective way to reduce

the massive CAD burden, mainly because cardiovascular disease rarely develops in populations that consume a plant-based diet.⁷⁻¹⁴ Additionally, meta-analyses have shown a reduced risk of CAD development and occurrence of CAD events or cerebrovascular disease events with a plant-based diet.¹⁵⁻¹⁹ It is for these reasons that a plant-based diet is one of the healthy eating patterns recommended by the 2015 to 2020 Dietary Guidelines for Americans.²⁰

Clinical trials have examined the use of lifestyle improvement with whole-foods, plant-based diets in the treatment of established CAD.²¹⁻²⁴ Multiple prospective studies, reviews, and meta-analyses have demonstrated the positive effects that a

Lifestyle Improvement Programs

The Complete Health Improvement Program (CHIP) is an intensive outpatient lifestyle program that emphasizes a whole foods, low-fat, plant-based diet with moderate exercise and stress relief. It was

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selected to represent the best of the commercial programs available to the public because it is intensive (18 sessions covering the major topics of lifestyle improvement in detail), convenient (outpatient format with no more than 2 classes per week), relatively affordable (average cost of \$400 per person for the entire program as of 2015), and well documented in the extant literature as consistent and effective in improving the various risk factors for CAD.³⁶⁻³⁹

The Healthy Heart (HH) program is a nonsequential combination of various outpatient healthy lifestyle classes, which we organized for this study. It represents the best of the existing lifestyle resources available at our integrated care health maintenance organization and is also intensive (> 12 sessions) and affordable (all classes offered at no copayment), and covers the same topics as those covered in CHIP and in the aforementioned literature.²¹⁻²⁴ Classes included stress relief; healthy eating that focused on low-fat, Mediterranean, and plant-based diets; and lowering blood pressure and cholesterol.

Test and Study Objective

CIMT was chosen as the test to measure the outcome because it is a noninvasive, well-validated surrogate cardiovascular endpoint.⁴⁰⁻⁴⁷

The primary objective of this study was to evaluate whether either of the programs (CHIP or HH) leads to improvements in arterial plaque in patients with established CAD by measuring the CIMT. The secondary aims were to determine if either of the programs improves any of the following: Patient quality of life (QoL score using the Ferrans and Powers' Quality of life index and Patient Health Questionnaire-9 [PHQ-9] depression screen), BMI, waist-hip ratio, hemoglobin A_{1c} (HbA_{1c}), lipid levels, blood pressure, and performance in the 6-minute walk test.

METHODS

The study included adult patients with established or known CAD, which was defined as having a diagnosis of at least one of the following on their medical problem list: Coronary artery disease, chronic angina, or atherosclerosis of the aorta. Exclusion criteria were unstable angina or acute

coronary syndrome, both ST and non-ST segment elevation myocardial infarctions within 60 days before the start of the program; current pregnancy; life expectancy less than 1 year such as in patients with terminal cancer or those under hospice care; current chemotherapy; advanced or end-stage organ disease; active alcohol or drug abuse problems; inability to tolerate a high-fiber diet secondary to active inflammatory bowel disease; inability to understand spoken English because the program includes videos that are available only in English; and previous participation in CHIP or the health education classes.

All patients were randomly assigned to either the CHIP group or HH group. In both groups, sessions lasted approximately 90 to 120 minutes and were taught by a certified health educator experienced in teaching these programs. Those in the HH group participated in health education classes that encompassed 12 weekly sessions, which included 1 HH class, 1 Living Well with High Blood Pressure class, 1 Becoming Vegetarian: Facts & Myths class, 1 whole-foods, low-fat, plant-based cooking demonstration, 2 Cholesterol Lowering classes, and 6 Mind-Body Health classes. Afterward, participants could attend an in-person weight management and health maintenance support group or use telephone health coach appointments with health educators (wellness coaching by phone) every other week for 6 months. The class teachers and phone coaches were not among the study investigators and were not informed about the study.

The patients randomly assigned to CHIP participated in an introductory session followed by 2 classes per week for the first 6 weeks, 1 class per week for weeks 7 to 12, and then 1 class every 2 weeks for 6 months. Food demonstrations were included as part of the 9-month program every other week in the first 3 months and once per month for the last 6 months.

Participants from both the CHIP and HH groups turned in exercise records weekly and a lifestyle evaluation form monthly. Patients recorded the number of steps walked, and quarterly totals were announced in class for those with the most steps. Study participants received recommendations that were based on the results

from the lifestyle evaluation. Participants from both groups also had access to an in-person appointment with a registered dietitian and/or personal trainer if they desired it. This was not part of the core of either program. A physician and study investigator were available on-site for assistance if subjects had any questions during all sessions for both groups. Support phone calls by staff were done to follow-up on those in either group who missed sessions, appeared to be struggling, or who requested more frequent follow-up. Calls were logged.

The primary effectiveness endpoint was change in the arterial plaque, as determined by the measurement of the CIMT at 9 months. Secondary endpoints included self-assessment well-being (QoL) and PHQ-9 scores, BMI, waist-hip ratio, blood pressure, short-term QoL as assessed by the 6-minute walk test, HbA_{1c}, and lipid profile.

Before treatment, participants underwent baseline assessment of their CIMT, QoL score, the depression questionnaire (PHQ-9) score, body weight, height, BMI, systolic and diastolic blood pressures, heart rate, 6-minute walk test performance, HbA_{1c}, total cholesterol levels, triglyceride concentrations, low-density lipoprotein (LDL) and HDL values, and high-sensitivity C-reactive protein.

Body weight, BMI, waist circumference, and blood pressure were repeated at monthly intervals. Blood tests were repeated at 6 weeks and 3, 6, and 9 months. The CIMT, the QoL questionnaire, the PHQ-9, and 6-minute walk test were repeated after 9 months.

A standard B-mode ultrasound examination was used to evaluate CIMT and the presence of carotid plaque. The ultrasound scan was performed in the anterior, lateral, and posterior projections of the right and left carotid arteries. A total of 3 measurements were performed on the far and near walls of the common carotid artery, bifurcation, and internal carotid arteries. The mean maximum CIMT was calculated by averaging the values of the maximum intima-media thickness from 10 preselected segments of the carotid arteries. *Carotid plaque* was defined as endoluminal protrusion of the arterial lumen of at least 0.5 mm

or 50% of the surrounding CIMT and/or demonstration of a CIMT greater than 1.5 mm. Software designed for this purpose was used to allow automated CIMT measurements, statistical analysis for scoring, storage of measurements for future reference, and evaluation of progression. An experienced sonographer, who was blinded to the study group that patients were assigned to, performed all ultrasonography.

Categorical variables are represented as frequencies and percentages, and continuous variables are shown as mean and standard deviation (SD). The χ^2 test was used to compare categorical variables between groups. As for the continuous variables, differences between groups were assessed with the Wilcoxon rank sum test (Mann-Whitney test) at baseline and at the conclusion of the study. The Wilcoxon signed-rank test was used to look at

differences within patients from the start to the end of the study, which were then compared between groups with another Wilcoxon rank sum test.

RESULTS

Of 1000 patients with CAD who met the study criteria, 120 initially agreed to participate and were randomly assigned to either the CHIP or HH group (Figure 1). However, when called for scheduling for the study, 11 and 12 patients declined from the CHIP and HH groups, respectively. Early in the study, an additional 9 patients from the CHIP group and 8 from the HH group quit the study for various reasons, including personal health, family, disagreement with concepts taught in CHIP, difficulty with traveling, and inconsistent attendance in the classes. Additionally, 1 patient in the CHIP group died shortly after the start of the study secondary to a stroke and was thus not included in the baseline data. Baseline data were available for 39 participants in the CHIP group and 40 in the HH group, with similar baseline characteristics in both groups (Table 1). During the course of the study, 3 participants did not complete follow-up and 1 died in the CHIP group, and 7 did not complete follow-up in the HH group. This left 35 and 33 participants in the CHIP and HH groups, respectively.

The effects that the studied lifestyle interventions had on QoL, various cardiac risk factors, blood markers, and CIMT are shown in Table 2. The QoL score improved significantly within the CHIP group (mean = 2, SD = 5; $p = 0.004$) but not within the HH group ($p = 0.3$) or between groups ($p = 0.8$). Although no significant difference was observed in the PHQ-9 scores between groups ($p = 0.3$), there was an improvement within the CHIP group (mean = -1.4, SD = 3.3; $p = 0.01$) and HH group (mean = -1.3, SD = 2.5; $p = 0.01$).

The BMI decreased significantly in the CHIP group (mean = -1.9, SD = 1.9; $p < 0.001$) but not in the HH group ($p = 0.09$). The difference between groups in the final BMI at 9 months was also significant ($p = 0.01$), as was the change within patients over the 9 months ($p < 0.001$). Waist-hip ratio also decreased significantly in the CHIP group (mean = -0.03,

Table 1. Baseline characteristics

Characteristic	HH group (n = 40)	CHIP group (n = 39)	p value
Age, y, mean (SD)	66.1 (7.7)	65.6 (10.5)	> 0.99
Female, no. (%)	13 (33)	21 (54)	0.06
Ethnicity			
White	25 (63)	27 (69)	0.64
Black	6 (15)	7 (18)	0.64
Hispanic	6 (15)	4 (10)	0.64
Asian	2 (5)	0 (0)	0.64
Declined to state	1 (3)	1 (3)	0.64
QoL score, mean (SD)	23 (4)	22 (4)	0.19
PHQ-9 score, mean (SD)	2.9 (3.1)	4.3 (4.6)	0.37
6-min walk test, mean (SD), min	463 (92)	455 (96)	0.36
Anthropometric measures, mean (SD)			
Weight, kg	93.8 (19.9)	84.8 (16.7)	0.04
BMI, kg/m ²	31.2 (6.1)	29.3 (5.7)	0.12
Waist-hip ratio	0.96 (0.08)	0.94 (0.08)	0.30
Vital signs, mean (SD)			
SBP, mmHg	136 (20)	139 (19)	0.46
DBP, mmHg	75 (12)	77 (12)	0.78
Pulse, min	66 (10)	68 (14)	0.76
Medication use, mean (SD)			
Beta-blocker	0.68 (0.47)	0.82 (0.39)	0.14
Antiplatelet	0.93 (0.27)	0.92 (0.27)	0.97
Statin	0.93 (0.27)	0.87 (0.34)	0.44
ACEI or ARB	0.75 (0.44)	0.64 (0.49)	0.30
Serology and lipid profile			
CRP, mg/L	3.4 (4.9)	2.6 (3.2)	0.79
HbA _{1c}	6.6 (1.2)	6.4 (1.6)	0.26
Lpa, mg/L	104 (113)	81 (98)	0.31
LDL-C, mg/L	80 (36)	80 (27)	0.56
HDL-C, mg/L	46 (11)	48 (15)	0.88
Triglycerides, mg/L	131 (79)	118 (56)	0.44
Total cholesterol, mg/L	151 (41)	151 (30)	0.65
Carotid intima-media thickness, mm			
Average	0.89 (0.13)	0.89 (0.18)	0.49
Average maximum	1.77 (0.72)	1.61 (0.45)	0.29

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CHIP = Complete Health Improvement Project; CRP = C-reactive protein; DBP = diastolic blood pressure; HbA_{1c} = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HH = Healthy Heart; LDL-C = low-density lipoprotein cholesterol; Lpa = lipoprotein a; PHQ-9 = Patient Health Questionnaire-9; QoL = quality of life questionnaire; SBP = systolic blood pressure; SD = standard deviation.

SD = 0.07; $p < 0.001$) and the HH group (mean = -0.02, SD = 0.05; $p = 0.01$). The difference between groups was also statistically significant ($p = 0.02$). Blood pressure at baseline and throughout the study was well controlled. Although there was no significant difference between systolic and diastolic blood pressures between groups ($p = 0.5$ for both), there was within both the CHIP group (systolic = -11.7 [SD = 18.1]; $p = 0.001$; diastolic = -6.4 [SD = 11.7]; $p = 0.007$) and the HH heart group (systolic = -14.1 [SD = 18.5]; $p < 0.001$; diastolic = -3.3 [SD = 12.8]; $p = 0.04$). Similarly, no significant difference was observed in the 6-minute walk test between groups ($p = 0.9$), but there was a difference within the CHIP group (mean = 51.5 min, SD = 50.1; $p < 0.001$) and HH group (mean = 43.1 min, SD = 72.7; $p < 0.001$).

An improvement in triglyceride levels was observed within the HH group (mean = -14.07, SD = 28.23; $p = 0.01$). However, there was no significant change in the CHIP group ($p = 0.7$) or between groups ($p \geq 0.99$). Regarding the HbA_{1c}, the CHIP group showed improvement (mean = -0.14, SD = 1.27; $p = 0.01$), but there was no significant change in the HH group ($p = 0.09$) or between groups ($p = 0.08$). As for the rest of the blood markers, there were no significant differences within or between groups for levels of total cholesterol, HDL cholesterol, LDL cholesterol, lipoprotein a, or C-reactive proteins as shown in Table 2.

The CIMT was measured using the right and left sides, the near and far walls, and the anterior, lateral, and posterior positions. The average of these 12 measurements, called average CIMT, and the average of the maximum of the 12 measures, called average maximum CIMT, were then calculated. Both the average CIMT and average maximum CIMT increased over 9 months, but the changes between groups were insignificant ($p = 0.45$ and $p = 0.15$, respectively). For the average CIMT, the changes within the CHIP group (0.02, SD = 0.12; $p = 0.2$) and HH group (0.03, SD = 0.12; $p = 0.07$) were insignificant. However, with respect to the average maximum CIMT, the changes within the CHIP group (0.30, SD = 0.50; $p < 0.001$) and within the HH

group (0.32, SD = 0.90; $p = 0.003$) were significant (Figure 2). These differences seen within patients were not statistically significant compared between groups ($p = 0.85$).

DISCUSSION

Some clinical trials have demonstrated coronary plaque regression after an intensive lifestyle program in patients with established CAD. However, these studies are limited in that they did not definitely prove the superiority of one lifestyle program vs another because they either used a usual care control group or had no control group. They also used a more invasive or expensive method to evaluate their outcomes, such as coronary angiography.^{48,49} We aimed to do a comparative analysis of 2 lifestyle programs and use CIMT as a more feasible evaluation method. Other studies that have used CIMT in the past have fallen into 2 categories: Those that

used mean CIMT and those that used maximal CIMT.⁴⁴ This study used 12 measurements to look at both mean and maximal CIMT in the same population. Furthermore, various interesting secondary outcomes such as inflammatory markers and other serologic findings were examined, and all patients were part of an integrated health system where they received robust, optimal health care. They were well matched and represented the “real world” as a result of their socioeconomic and demographic characteristics.

This study demonstrated that neither CHIP nor HH effectively reversed plaque burden in the short term when used as a tertiary preventive measure in CAD. There was an increase in the average maximum CIMT within groups without a significant difference between the CHIP and HH groups. However, it is still possible that these programs could have slowed the progression of atherosclerotic disease,

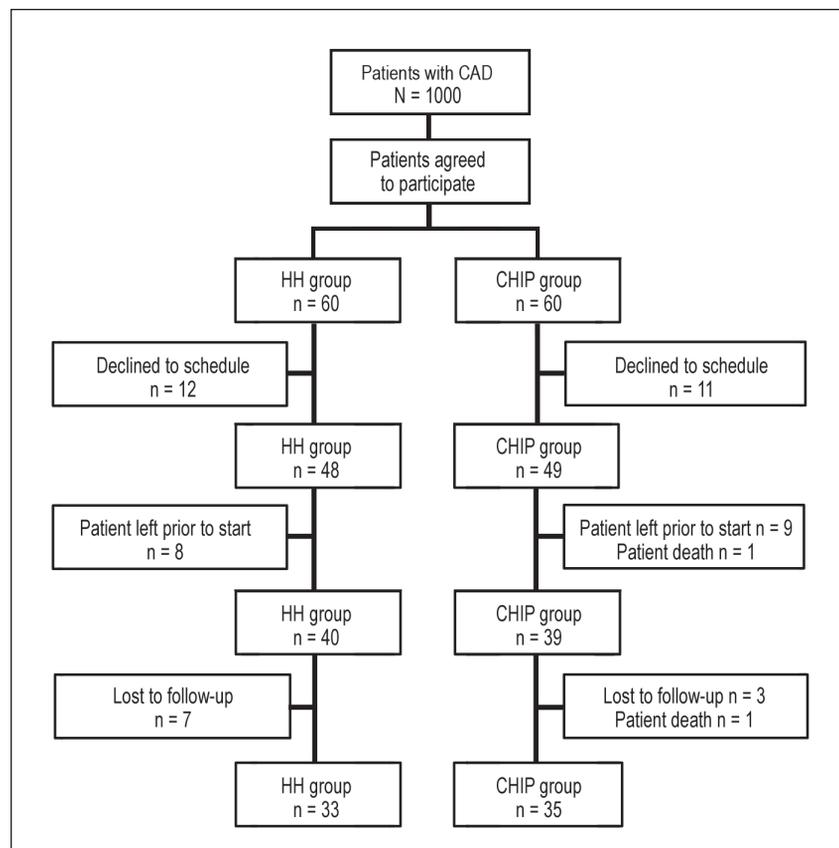


Figure 1. Flow diagram demonstrating patient recruitment and attrition.

CAD = coronary artery disease; CHIP = Complete Health Improvement Program; HH = Healthy Heart.

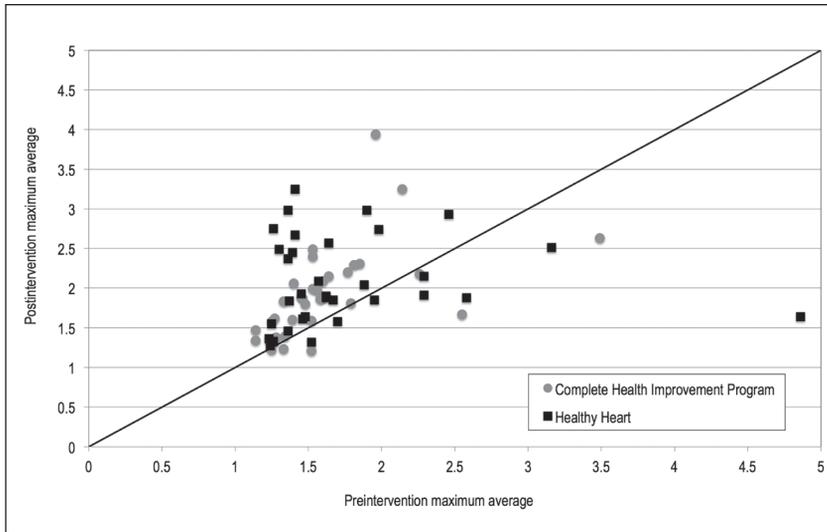


Figure 2. Progression of average maximum carotid intima-media thickness (in mm) in both Complete Health Improvement Program and Healthy Heart groups.

especially given that these patients were followed up only over 9 months. Most studies that showed the beneficial effects of lipid-lowering therapy, antihypertensive agents, and other medications on CIMT usually had a follow-up of 18 months or greater, sometimes as long as 4 years.⁵⁰⁻⁵⁹ It is thus possible that there may have been a significant reduction in CIMT that would have been appreciated if there was a longer follow-up period. Although more intensive lifestyle regimens have demonstrated plaque regression,^{48,49} this is likely owing to a combination of both longer follow-up times and the use of a control group as a comparator arm.

The current study showed significant differences in some of the secondary endpoints within groups. The CHIP group showed improvement in the QoL score, BMI, waist-hip ratio, and HbA_{1c}. The BMI and waist-hip ratio were the

Characteristic	HH group			CHIP group			p value ^c	p value ^d
	Baseline	Follow-up	p value ^b	Baseline	Follow-up	p value ^b		
QoL score	23 (4), 39	24 (3), 28	0.28	22 (4), 39	24 (4), 36	0.004	0.78	0.08
PHQ-9 score	2.9 (3.1), 39	1.5 (2.1), 28	0.01	4.3 (4.6), 38	2.7 (3.7), 36	0.01	0.28	> 0.99
Anthropometric measures								
BMI, kg/m ²	31.2 (6.1), 40	29.5 (6.4), 32	0.09	29.3 (5.7), 39	26.5 (4.7), 31	< 0.001	0.01	< 0.001
Waist-hip ratio	0.96 (0.08), 39	0.95 (0.07), 33	0.01	0.94 (0.08), 39	0.91 (0.10), 36	< 0.001	0.02	0.24
Vital signs								
SBP, mmHg	136 (20), 40	125 (13), 32	< 0.001	139 (19), 39	127 (12), 29	0.001	0.45	0.82
DBP, mmHg	75 (12), 40	71 (11), 32	0.04	77 (12), 39	70 (10), 29	0.007	0.53	0.36
Pulse/min	66 (10), 40	66 (10), 32	0.55	68 (14), 38	67 (11), 29	0.46	0.89	0.91
6-min walk test	463 (92), 39	506 (89), 33	< 0.001	455 (96), 39	504 (120), 36	< 0.001	0.89	0.15
Serology and lipid profile								
HbA _{1c}	6.6 (1.2), 40	6.5 (1.2), 28	0.09	6.4 (1.6), 39	6.2 (1.1), 35	0.01	0.08	0.56
Lpa, mg/L	104 (113), 39	114 (127), 26	0.23	81 (98), 39	106 (108), 27	0.46	0.49	0.82
LDL-C, mg/L	80 (36), 40	70 (25), 27	0.09	80 (27), 39	77 (25), 35	0.51	0.25	0.78
HDL-C, mg/L	46 (11), 40	49 (14), 28	0.14	48 (15), 39	47 (12), 35	0.42	0.41	0.11
Triglycerides, mg/L	131 (79), 40	119 (90), 28	0.01	118 (56), 39	113 (68), 35	0.72	0.96	0.17
Total cholesterol, mg/L	151 (41), 40	141 (37), 28	0.16	151 (30), 39	146 (32), 35	0.47	0.58	0.99
CRP, mg/L	3.4 (4.9), 38	2.6 (5.1), 27	0.53	2.6 (3.2), 39	9.3 (31.3), 34	0.43	0.97	0.74
Carotid intima-media thickness, mm								
Average	0.89 (0.13), 39	0.92 (0.13), 33	0.07	0.89 (0.18), 39	0.91 (0.17), 35	0.24	0.45	0.98
Average maximum	1.77 (0.72), 39	2.08 (0.56), 33	0.003	1.61 (0.45), 39	1.91 (0.58), 35	< 0.001	0.15	0.85

^a Values are mean (standard deviation), no. of patients. Impact of lifestyle interventions on quality of life cardiac risk factors, serologic findings, lipid profile, and carotid intima-media thickness.

^b p value refers to within-group difference (baseline to follow-up).

^c p value refers to between-group differences at the end of the study.

^d p value compares between groups the differences within patients from the start to the end of the study.

ACE = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CHIP = Complete Health Improvement Project; CRP = C-reactive protein; DBP = diastolic blood pressure; HbA_{1c} = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HH = Healthy Heart; LDL-C = low-density lipoprotein cholesterol; Lpa = lipoprotein a; PHQ-9 = Patient Health Questionnaire-9; QoL = quality of life questionnaire; SBP = systolic blood pressure.

only secondary endpoints that were significantly different even between groups. The HH group showed an improvement in triglyceride levels. Additionally, both groups had lower systolic and diastolic blood pressures as well as improvements in the PHQ-9 score and 6-minute walk test. This confirms that intensive lifestyle programs can positively affect multiple cardiac risk factors. Although this is clear and established, it also shows that the nonsequential offering of healthy lifestyle programs (HH) can lead to similar outcomes as a formal, sequential, established program (CHIP) in many aspects. This has important implications as to how lifestyle changes will be implemented as tertiary prevention measures in the future.

This study has some limitations. Although both CHIP and HH advocated for particular dietary patterns and although dietary questionnaires were used before and after, they are not the best forms of evidence for the effects of a particular dietary pattern. The first reason is that both programs encouraged broad lifestyle changes (exercise, stress relief, and diet), making it inappropriate to pinpoint diet alone as the cause of the outcome. The second reason is that complete dietary adherence is difficult to ascertain in the community setting and dietary questionnaires are subject to several biases. Thus, this study is better defined as one testing the outcomes of participation in a program rather than the outcomes of following a particular diet. The short duration of the study was cited earlier as a limitation as well. Furthermore, CIMT remains a controversial marker for cardiovascular disease and thus limits interpretation of these results.

CONCLUSION

Neither the CHIP nor HH was effective in inducing plaque regression in patients with established CAD after a 9-month period. However, both were effective in improving several CAD risk factors and could thus potentially reduce CAD, especially in conjunction with an exercise program. Further studies with longer follow-up and larger sample sizes can examine whether the risk factor improvement may lead to plaque regression. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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