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Efficacy of a Cardiovascular Behavioral Intervention Program and Full Body CT Scanning on Changes in Coronary Artery Calcium, Thoracic and Epicardial Fat

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Background

Limited data exist on the efficacy of multifactorial lifestyle programs on impacting the progression of atherosclerosis and body fat measures. We examined the efficacy of a lifestyle intervention program combined with a full body CT scan on progression of coronary artery calcium (CAC), thoracic and epicardial fat.

Methods

We studied 73 participants randomized to the RENEW [TM] lifestyle intervention program or standard of care. The RENEW [TM] Program included modules on responding to stress, enhancing the effects of relaxation, nourishing the immune system, physical activity, and social support. Participants received baseline and 2-year follow-up measures of risk factors and CAC (volume and Agatston score) from whole body computed tomography (CT); the intervention group also received a comprehensive physician consultation on the scan results. A subset also had epicardial and thoracic fat assessed by CT. We examined baseline-follow-up changes in CAC, epicardial and thoracic fat between treatment groups.

Results

Among 73 subjects (35 control and 38 intervention) who completed the program over 2 year follow-up, after adjustment for baseline CAC, age, gender, and risk factors, there were increases in (natural log units) both CAC vol-

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ume (mean=0.17, 95% confidence interval= [0.07–0.25] cm³) and CAC score (0.24 [0.11–0.36]) in the control group relative to the intervention group (–0.29 [-0.63–0.02] cm³ for volume (p=0.0071 relative to controls) and –0.25 [-0.58–0.09] for score (p=0.0031 relative to controls). In a subset of 42 subjects with measures of epicardial and thoracic fat, intervention pre-post changes in epicardial fat volume were 10.6 [-4.5–25.2] cm³ in controls and –6.9 [-19.2–5.3] cm³ in intervention group participants (p=0.081 for difference) and thoracic fat volume changes were 4.6 [-20.2–28.6] cm³ and –29.9 [-49.5 to –9.3] (p=0.044 for difference) in fully adjusted analyses.

Conclusions

Our findings suggest a potentially beneficial impact of a multifactorial behavioral intervention program combined with a full body CT scan consultation on retarding progression of CAC and on reducing epicardial and thoracic fat volume. Larger scale trials are needed to confirm findings and implications on cardiovascular outcomes.

Key words

Behavior, coronary calcium, cardiovascular disease, computed tomography, fat

Introduction

There is a wealth of data demonstrating that increased levels of coronary calcium (CAC) assessed by computed tomography (CT), a marker of atherosclerosis burden, predict future coronary heart disease (CHD), cardiovascular disease (CVD) events (1, 2), and mortality (3, 4) and improves risk prediction more than other biomarkers and measures of subclinical CVD (5). In addition, pericardial and visceral fat measured by CT has been shown to be related to prevalent CVD in the Framingham Heart Study (6) and both pericardial fat and thoracic fat are associated with a greater likelihood of major adverse cardiac events, with the former improving risk prediction (7). Epicardial fat has also been shown to relate to high risk plaque features and stenosis on CT angiography (8) and thoracic fat to the extent and severity of CAC (9).

We have previously shown progression of CAC to also relate to a greater risk of CHD events overall and independent of baseline CAC score (10). While several key CHD risk factors predict the progression of CAC (11), interventions shown to retard the progression of CAC are limited (12), and studies involving statin interventions have been negative (13, 14). A key question remains as to whether CAC progression more closely relates to progression of vulnerable plaque as opposed to plaque stabilization as others have suggested (15). CAC findings have also been noted to motivate individuals' adherence to lifestyle and medical therapy recommendations (16, 17) and a low-risk lifestyle to predict less progression of CAC (18). Also, among adolescents, epicardial fat was greater in those with unhealthy lifestyle habits (19), and in a small trial of adults with impaired glucose tolerance, a combined low-fat diet and endurance exercise program related to greater improvements in abdominal, thigh, and thoracic fat (20). While there are data documenting the association of behavioral and psychosocial factors with cardiovascular disease events (21), there are few investigations (22–24) that have examined whether a comprehensive lifestyle/behavioral intervention program may impact the progression of CAC or changes in epicardial or thoracic fat as measured by CT.

Our hypothesis was that the combination of a multifactorial behavioral intervention program with an intensive physician consultation of whole body CT results would beneficially impact on the progression of CAC and changes in epicardial and thoracic fat.

Materials and Methods

Eligible individuals included healthy volunteers, men or women aged 35 and over who provided informed consent to participate including the baseline, interim, and follow-up clinic visits, as well as willingness to participate in the on-line intervention (if selected to be in that group). Exclusions consisted of those with known cardiovascular disease, cancer, or any life-threatening or debilitating illness, including psychiatric illnesses, or significant difficulty with the English language that would preclude successful participation in the program. We initially enrolled 267 volunteer asymptomatic adults consisting of firefighters/police workers (n=173), active military personnel (n= 57) and community college staff (n= 37). The first two cohorts were among those included as target populations proposed based on the Department of Defense contract that funded the study, with the third cohort added to complete recruitment efforts. Participants were recruited by union leaders and/or direct advertisements to participants.

Subjects were randomized (using a blocked randomization list created by a computerized random assignment generator) either to an intervention group or to usual care. A whole body CT scan was performed using a multidetector CT scan on all participants at baseline with the results discussed by a physician only in the intervention group (since the physician feedback was part of the intervention), and after 2 years of follow-up a repeat scan was performed with a detailed evaluation of the results discussed by a physician with all participants (in part as a motivation to complete the study). The intervention group additionally received The RENEW™ Program (www.therenewprogram.net) of lifestyle intervention (as described below). Participants' physicians, regardless of study group were notified as to potentially significant findings needing further follow-up. The whole body CT was part of the approved protocol and was utilized to screen for possible pathology throughout the chest and abdomen and surrounding organs. This study was carried out in accordance with the recommendations of the Western Institutional Review Board with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Western Institutional Review Board and is registered in clinicaltrials.gov with Unique Protocol ID:20111268. The current analysis of CT findings reports on the primary outcome of changes in coronary calcium as well as on secondary outcomes of pericardial and thoracic fat.

The RENEWTM Program's comprehensive intervention was provided by a licensed behavioral therapist or trained lifestyle coach and included direct contact for all sessions via webcam. This consisted of 7 bi-monthly hour-long sessions over 16–18 weeks followed by an average of 15 monthly 30 minute check-in sessions (maintenance) over 80 weeks. This included modules on responding to stress, enhancing effects of relaxation, nourishing the immune system, physical activity, and social support. Specific interventions were included in all modules, for example: responding to stress more effectively (using solution focused, cognitive behavioral tools), enhancing the effects of relaxation (practicing mindfulness and understanding how this affects biochemistry), nourishing the immune system (nutrition, addressing previous eating habits and ways to improve, including medical needs and underlying emotional issues), energizing your body (physical activity addressing markers for wellness, healthy aging and sports performance), and welcoming others as support (social support and communication skills). A prescribed set of questions determined participants' level of coping skills associated with characteristics of resilience and health habits. Interventions in module one (stress) used these results to customize tools aimed at Type A Personality traits or dominance of Negative Appraisal, for example. Module one offered concrete solutions for participants to improve the way they address challenges based on these measurements. Interventions in module two (relaxation) were geared towards training participants to use the relaxation response in real life situations to gain mastery over their biochemistry, for improved sleep, and to become more aware of their personal stress signals. These improved life skills influenced the foods they habitually craved or ate regularly. Participants were guided in module three (nutrition) to make needed changes according to their medical needs and health habit surveys. Dietary suggestions were based on a Mediterranean style of eating combined with the Food Pyramid and participants medical needs, preferences and physical location. Additional topics included: organic foods, toxins in food and plastics, emotional vs. physical hunger, for example. Physical activity was addressed in module four and included issues of wellness, healthy aging or sports performance, depending on participants needs and according to American Heart Association guidelines. Care of the spine and how to strengthen core muscles was addressed by specific exercises, for example, in response to body scan report on those issues. Participants tracked their progress, reported obstacles and were guided to build a routine that included their medical needs and personal preferences. Module five (social support) included communication skills, how to build a social network and was customized to participants answers to prescribed questions regarding emotional and physical support. Module six (maintenance) addressed issues related to sustaining changes made over the course of the study. Topics explored included expectations, anticipating obstacles, staying inspired, how to get back on track and keeping your emphasis on feeling good, according to participants individual value system and medical needs based on their blood work, blood pressure, BMI and body scan report.

Coronary artery calcium (CAC) was assessed by a trained technologist with the Agatston score measured and volume score calculated, summed among the four major coronary arteries according to conventional methods (25). The QFAT™ software was uti-

lized to provide measures of epicardial and thoracic fat volume (in cm^3) as described previously (26) in a subset of participants who had the required DICOM-archived CT scan data both pre and post-intervention. Data for these analyses in earlier participants (who are included in the CAC analyses) were not available due to unavailability of the required DICOM-archived CT data.

We utilized the Student's t-test for continuous measures or Chi-square test of proportions for categorical measures to compare baseline demographic and clinical factors initially between subjects included versus not included in the current analysis as well as between included intervention and control group participants. Coronary calcium score was log-transformed with baseline and 2-year changes (mean and 95% confidence intervals) in CAC score and volume compared by the Student's t-test between groups, with analysis of covariance utilized for comparison of means (with 95% confidence intervals) adjusted for age, gender, baseline CAC score or volume, and standard risk factors between groups. Similar methodology was used to compare changes in epicardial and thoracic fat from baseline to follow-up between intervention groups, unadjusted and adjusted for covariates as well as baseline fat volume. These fully adjusted changes are also plotted for calcium score and volume changes and for thoracic and pericardial fat volume changes. An exploratory analysis was done to evaluate for changes in CAC density (Agatston score divided by area score) between groups among the subset of participants with CAC>0 at baseline. Finally, Pearson correlation analyses were done to examine within the overall sample the association between changes in key psychosocial indices of interest and changes in thoracic and pericardial fat volume as well as natural log of coronary calcium score and volume.

Results

Two hundred and sixty-seven subjects (mean age 45.8 years, 23.8% female) were enrolled, including 135 randomized to RENEW and 132 to standard care. 73 subjects had baseline and follow-up CT scan data available for analysis (35 control and 38 intervention) for the current analysis and report. Table 1 shows baseline demographic and clinical characteristics according to the 73 subjects included vs. 194 subjects not included in the current report. There were no significant differences in age, gender, or baseline cardiovascular risk factors between groups except for HDL–C cholesterol levels being significantly lower and baseline CAC scores, volumes, and the presence of CAC being significantly greater among those included subjects. Table 2, however, shows no differences in baseline risk factors or CAC scores or volume among those subjects who were randomized

Table 1. **Baseline Characteristics Between Included and Not Included Participants**

	Included (n=73)	Not Included (n=194)	p-value
Age (yr)	46.6±6.5	45.3±6.6	0.1654
Female Gender (%)	17 (23.3)	48 (24.9)	0.7558
Prior CHD[1] (%)	0 (0.0)	1 (0.5)	0.5245
Prior Diabetes[1] (%)	3 (4.1)	10 (5.2)	0.6427
Cholesterol Lowering Therapy (%)	13 (17.8)	19 (9.8)	0.1115
Total Cholesterol (mg/dL)	178.8±30.7	188.5±36.8	0.0524
HDL Cholesterol (mg/dL)	44.2±12.8	50.7±16.7	0.0015
Glucose (mg/dL)	88.5±16.6	90.9±21.1	0.3442
Waist (inches)	39.0±5.7	37.9±4.9	0.1090
Weight (lbs)	201.7±38.1	194.3±36.4	0.1530
Pulse (Beats/Sec)	61.3±11.5	63.9±10.3	0.0852
Diastolic Blood Pressure (mmHg)	78.2±9.0	80.0±12.5	0.2087
Systolic Blood Pressure (mmHg)	117.7±12.3	118.6±11.2	0.6031
CAC Present (score>0) (n,%)	31 (42.5)	52 (26.8)	0.0115
CAC Volume	41.6±91.5	27.1±104.1	0.2963
Natural Log Transformed CAC Volume[2]	1.7±2.1	1.0±1.8	0.0048
CAC Score	39.9±99.8	25.7±109.7	0.3362
Natural Log Transformed CAC Score[2]	1.5±2.0	0.8±1.7	0.0145

[1] Two Sided Fisher's Exact Test. 2Natural Log (Variable+1). Values indicate mean + standard deviation or n (%).
Sample sizes across variables vary slightly due to available data. CAC=coronary artery calcium; HDL=high density lipoprotein

Table 2. **Baseline Characteristics by Groups**

	Intervention n=38		Control n=35		P-value
	N	%	N	%	
Gender (Female %)	12	31.6	5	14.3	0.0807
Prior Diabetes[1]	1	2.6	2	5.7	0.6038
	Mean	**SD**	**Mean**	**SD**	
Age (yr)	47.4	6.7	45.8	6.2	0.2975
Total Cholesterol (mg/dL)	179.2	25.8	178.3	35.9	0.9101
HDL Cholesterol (mg/dL)	45.1	11.4	43.2	14.4	0.5573
Triglycerides (mg/dL)	140.9	79.7	131.4	108.2	0.6798
LDL Cholesterol (mg/dL)	108.5	28.9	111.0	32.4	0.7476
Non-HDL Cholesterol (mg/dL)	131.0	34.6	129.4	29.1	0.8362
Total Cholesterol/HDL	4.2	1.2	4.4	1.4	0.5896
Glucose (mg/dL)	88.5	17.5	88.5	15.8	0.9949
Waist (inches)	38.3	5.8	39.8	5.4	0.2841
Weight (lbs)	195.3	36.0	208.7	39.6	0.1400
Pulse (Beats/Sec)	62.3	10.7	60.3	12.4	0.4669
Diastolic Blood Pressure (mmHg)	77.3	7.8	79.2	10.2	0.3748
Systolic Blood Pressure (mmHg)	117.2	13.6	118.3	10.9	0.7123
CAC Volume	28.7	61.2	55.6	115.3	0.2249
Natural Log Transformed CAC Volume[2]	1.4	2.0	2.0	2.2	0.2393
Coronary Calcium Score	25.2	65.1	55.9	126.4	0.2035
Natural Log Transformed CAC Score[2]	1.2	1.9	1.8	2.2	0.2151

1. Two Sided Fisher's Exact Test.
2. Natural Log (Variable+1). CAC=coronary artery calcium; HDL=high density lipoprotein, LDL=low density lipoprotein

to the intervention vs. control groups among the 73 included subjects. Absolute baseline and log-transformed CAC scores and volumes are also presented.

The Figure 1 shows the distribution of the unadjusted changes in log-transformed CAC score for intervention and control groups noting increases in CAC score were more frequent among control compared to intervention group participants. Table 3 shows results of unadjusted and adjusted changes in CAC volume and score. From analyses fully adjusted for baseline volume or score, age, sex, LDL-cholesterol, systolic blood pressure, smoking status and diabetes, the control group showed progression of CAC volume (0.17) and score (0.24) relative to the intervention group (–0.29 for volume, p=0.007 relative to control and –0.25 for score, p=0.003 relative

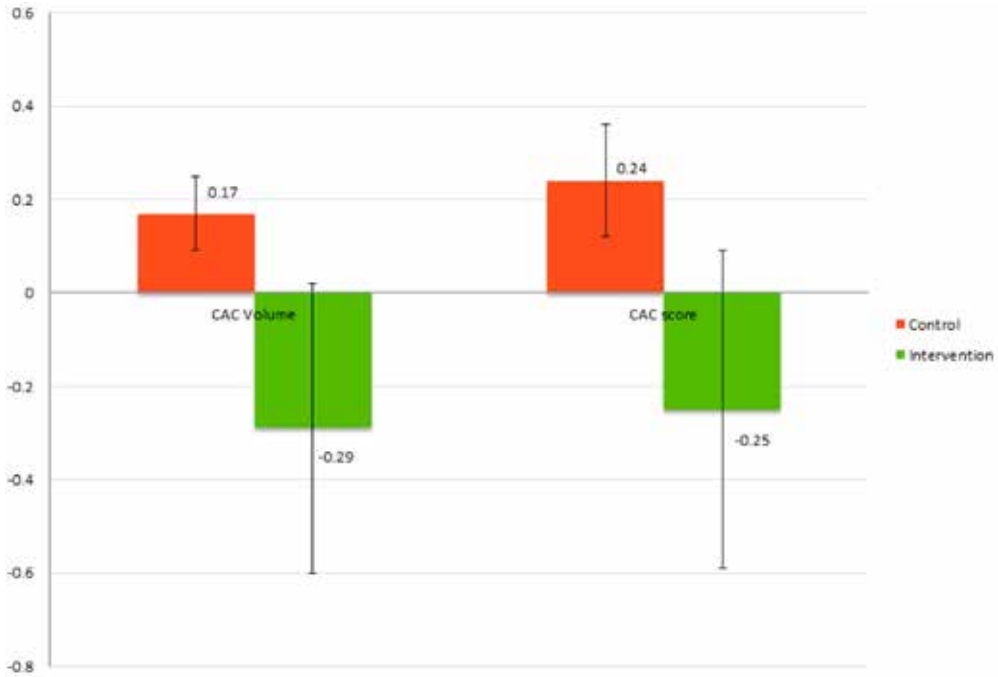

Figure 1. Adjusted Changes of CAC Volume and CAC Score between Control and Intervention Group. p<0.01 comparing the change between control and intervention group for both CAC volume and CAC score

Table 3. **Changes in Coronary Volume and Coronary Calcium Scores (log-transformed) Within and Between Intervention Groups**

	Control (n=35)	Intervention (n=38)	p-value
Unadjusted			
CAC Volume	0.45 (–1.10–2.00)	0.18 (–0.86–1.22)	0.0837
CAC Score	0.55 (–0.96–2.06)	0.20 (–0.88–1.28)	0.0264
Adjusted[1]			
CAC Volume	0.44 (0.21–0.66)	0.19 (–0.02–0.41)	0.1246
CAC Score	0.53 (0.31–0.76)	0.21 (–0.01–0.43)	0.0428
Adjusted[2]			
CAC Volume	0.17 (0.07–0.25)	–0.29 (–0.63–0.02)	0.0071
CAC Score	0.24 (0.11–0.36)	–0.25 (–0.58–0.09)	0.0031

1. Numbers were displayed as means with 95%Confidence Interval
2. Adjusted for Baseline Volume or Score Value;
3. Adjusted for baseline volume or score value, age, sex, LDL –Cholesterol, systolic blood pressure, smoking status and diabetes.
CTL = control group (n=35), INT = intervention group (n=38)

to control). In an exploratory analysis of changes in CAC density in the subset of participants with CAC volume >0 at baseline and follow-up (14 intervention and 17 control group participants), there were no significant differences in CAC density change either in unadjusted analyses (0.25 vs. 0.52 for intervention vs. control group, participants, respectively, p=0.34) or fully adjusted analyses (–0.47 vs.–0.07, p=0.42).

In a subset of 42 subjects with measures of epicardial and thoracic fat, adjusted baseline measures in epicardial fat volume and thoracic fat volume were not significantly different between intervention and control groups (107.8 cm^3 vs. 122.5 cm^3 for epicardial fat and 183.3 cm^3 vs. 214.9 cm^3 for thoracic fat); however, in fully adjusted analyses (including baseline fat volume and all other covariates), intervention group pre-post changes in epicardial fat volume were 17.5 cm^3 lower (p=0.0807) and thoracic fat volume 34.5 cm^3 lower (p=0.0437) when compared to the control group (Figure 2,Table 4).

We also examined components of the RENEW Program and whether increases in score components were associated with reductions in epicardial or thoracic fat, or reduced progression of CAC. From fully adjusted analyses, subjects with increases (improvements) in the following psychosocial measures had significant (p<0.05 to p<0.01) decreases in thoracic fat: social support network (p=0.037), cognitive

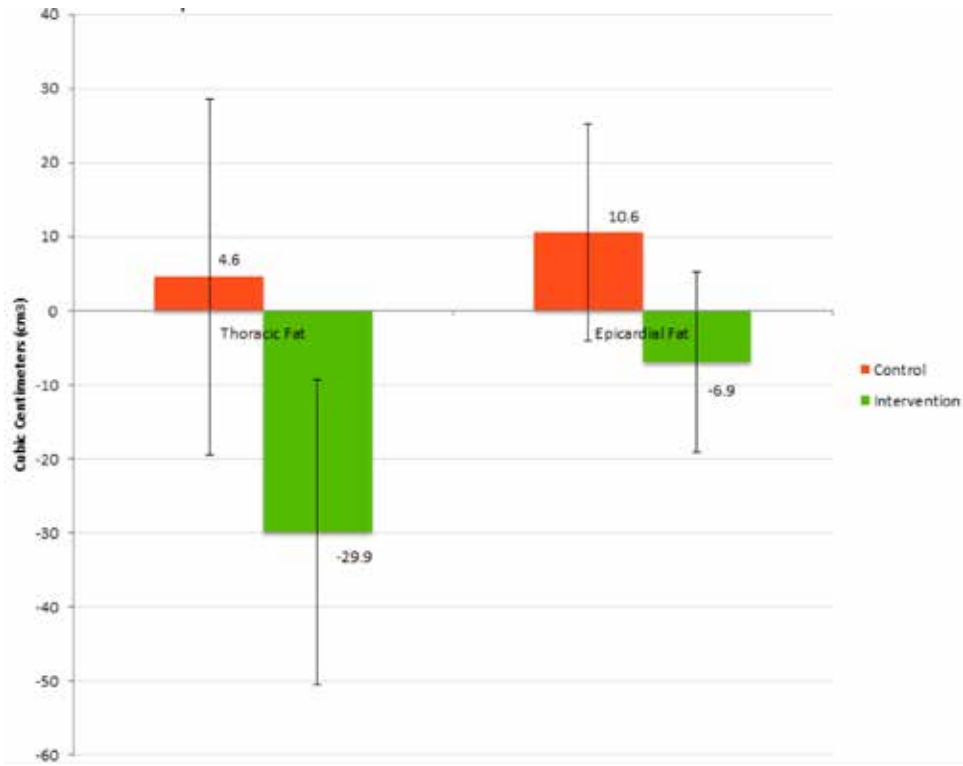

Figure 2. Adjusted Changes of Thoracic Fat and Epicardial Fat between Control and Intervention Group. p<0.05 comparing thoracic fat change and p=0.0807 comparing epicardial fat change between control and intervention group.

Table 4. **Difference of Epicardial and Thoracic Fat Change Between Control and Intervention Groups**

Dependent Variable		Control (n=19)	Intervention (n=23)	Parameter (Slope)	p-value
Baseline					
Epicardial Volume	Unadjusted	122.5 (53.1–191.9)	107.8 (–1.2–214.4)	–14.7	0.32
Epicardial Volume	Adjusted	111.7 (92.2–131.2)	111.4 (95.3–127.4)	–0.4	0.98
Thoracic Fat Volume	Unadjusted	214.9 (–74.2–355.6)	183.3 (–20.0–386.6)	–31.6	0.27
Thoracic Fat Volume	Adjusted	190.8 (151.2–230.4)	196.6 (164.0–229.3)	5.8	0.83
Changes from baseline to follow-up					
Epicardial Volume	Unadjusted	12.1 (–43.0–67.2)	–5.6 (–53.6–42.4)	–17.7	0.035
Epicardial Volume	Adjusted	10.6 (–4.5–25.2)	–6.9 (–19.2–5.3)	–17.5	0.081
Thoracic Fat Volume	Unadjusted	–4.5 (–109.6–100.6)	–23.0 (–123.0–77.0)	–18.5	0.26
Thoracic Fat Volume	Adjusted	4.6 (–20.2–28.6)	– 29.9 (–49.5- –9.3)	–34.5	0.044

Numbers were displayed as means with 95 %Confidence Interval

Method=0 (Control) (n=19); Method=1 (Intervention)(n=23)

Covariates: age, gender, race, BMI, hypertension, HDL –C, LDL –C, current smoker, diabetes, and additionally when comparing adjusted differences in changes between intervention and control groups, the baseline epicardial or thoracic fat volume.

hardiness (p=0.044), negative appraisal coping style (p=0.035), alcohol recreational drugs and cigarettes (ARC) score (p=0.012), and psychological well-being (p=0.026); epicardial fat: social support network (p=0.018), type A behavior (p=0.0094), cognitive hardiness (p=0.0025), negative appraisal coping style (p=0.025), coping style threat minimization (p=0.014), exercise (p=0.0079), and rest and sleep (p=0.0055); progression of CAC volume: stress (p=0.025).

Discussion

Our clinical trial suggests a web based (direct contact), comprehensive behavioral intervention program (The RENEW Program™) combined with a detailed physician review of whole body CT results may have a beneficial impact on atherosclerosis progression by reducing the progression of CAC (as a marker of atherosclerotic burden) as well as reducing both epicardial and thoracic fat measured by repeat CT scans over a two-year period. Previous studies have shown the extent of progression of CAC relates to increased risks of CHD events, even independent of baseline CAC score (10) and measures of both pericardial and thoracic fat to relate to cardiovascular events (6–7), epicardial fat to high risk plaque features (8) and thoracic fat to subclinical atherosclerosis (9).

There are limited data on the efficacy of behavioral interventions on reducing CHD event risk. The Recurrent Coronary Primary Prevention Study showed modification of Type A Behavior in CHD patients to reduce recurrent CHD events (27); however, the ENRICHD Clinical Trial also in CHD patients showed modification of depression not to reduce recurrent events or mortality (28). Moreover, observational data from the Multiethnic Study of Atherosclerosis (18) have shown subjects following a healthy lifestyle (based on a score consisting of diet, exercise, body mass index, and smoking status) to have both less progression of CAC over 3.1 years as well as lower all-cause mortality over 7.6 years.

Clinical trials involving statin therapy have not been shown to have an impact on changes in CAC (14, 15); however, a single dietary supplement trial involving aged garlic extract has shown positive effects in retarding progression of CAC (29) as well as increase in epicardial, pericardial, and periaortic adipose tissue (30). More recent data suggests statins may have an impact on stabilizing atherosclerotic plaque (31, 32). While we have previously shown progression of CAC to relate to greater risks of future CHD events (10), there is controversy as to whether CAC progression is a sign of atherosclerotic progression or stabilization, and some have argued further study should be done to understand this before investigations are proposed to utilize CAC progression as an efficacy endpoint (15).

The potential role of CAC screening in modifying preventive behaviors has been previously documented by our group and others. We previously showed in an observational study of 703 men and women aged 28–84 who received CAC scanning, that the CAC score was independently associated with participants' new

Table 5. **Adjusted Regression Coefficients (with 95% confidence limits) for the Change in Clinical Measures (Thoracic Fat, Epicardial Fat, CAC score and CAC volume) with the Change in Psychosocial Measures.**

	Thoracic Fat	Epicardial Fat	CAC Volume	CAC Score
Prevention Score	−110.93 (−259.94–38.08) (p=0.12)	−54.48 (−127.17–18.20) (p=0.12)	−0.69 (−1.96–0.58) (p=0.26)	−0.15 (−1.76–1.46) (p=0.84)
Stress	−1.32 (−11.42–8.79) (0.77)	−2.00 (−6.69–2.70) (p=0.35)	−0.08 (−0.14- −0.01) (p=0.025)	−0.08 (−0.17–0.01) (p=0.062)
Health Habits	−4.55 (−12.92–3.82) (p=0.25)	−2.92 (−6.71–0.86) (p=0.11)	0.01 (−0.04–0.06) (p=0.77)	0.03 (−0.03–0.09) (p=0.30)
Social Support Network	−3.31 (−6.37- -0.25) (p=0.037)	−1.77 (−3.15- -0.39) (p=0.018)	−0.01 (−0.05–0.03) (p=0.56)	0.01 (−0.04–0.06) (p=0.68)
Type A Behavior	−4.80 (−14.20–4.59) (p=0.27)	−4.69 (−7.87- -1.50) (0.0094)	−0.01 (−0.09–0.07) (0.87)	0.03 (−0.07–0.13) (p=0.51)
Cognitive Hardiness	−2.70 (−5.31- -0.09) (p=0.044)	−1.71 (−2.63- -0.80) (p=0.0025)	<0.01 (−0.03–0.03) (p=0.98)	0.01 (−0.02–0.04) (p=0.49)
Coping Style Positive Appraisal	−6.76 (−15.88–2.37) (p=0.13)	−2.16 (−7.06–2.75) (p=0.34)	−0.06 (−0.19–0.08) (p=0.39)	−0.03 (−0.20–0.14) (p=0.73)
Coping Style Negative Appraisal	−14.25 (−27.20- −1.30) (p=0.035)	−7.27 (−13.36- -1.17) (p=0.025)	−0.05 (−0.19–0.10) (p=0.51)	−0.01 (−0.19–0.16) (p=0.88)
Coping Style Threat minimization	−11.20 (−22.75–0.35) (0.056)	−6.57 (−11.37- -1.76) (p=0.014)	−0.05 (−0.23–0.13) (p=0.59)	0.06 (−0.16–0.28) (p=0.59)
Coping Style Problem Focus	−8.85 (−18.36–0.67) (0.064)	−3.93 (−8.81–0.95) (p=0.10)	−0.06 (−0.20–0.07) (p=0.33)	−0.03 (−0.19–0.14) (p=0.74)
ARC score	−17.97 (−30.68- -5.25) (p=0.012)	−7.06 (−14.59–0.47) (p=0.063)	−0.12 (−0.30–0.07) (p=0.21)	−0.07 (−0.31–0.17) (p=0.53)
Psychological Well Being	−3.35 (−6.18- -0.52) (p=0.026)	−1.40 (−2.95–0.14) (p=0.070)	−0.04 (−0.09–0.01) (p=0.083)	−0.03 (−0.09–0.04) (p=0.39)
Health Habits-Exercise	−14.02 (−28.13–0.09) (0.051)	−8.48 (−14.04- -2.91) (p=0.0079)	<-0.01 (−0.16–0.16) (p=0.99)	0.09 (−0.10–0.27) (p=0.34)
Health Habits-Rest Sleep	−9.54 (−20.89–1.80) (p=0.088)	−6.60 (−10.63- -2.56) (p=0.0055)	−0.09 (−0.20–0.02) (p=0.095)	−0.06 (−0.20–0.08) (0.36)
Health Habits- Eating	−14.59 (−38.28–9.11) (p=0.19)	−9.05 (−19.70–1.60) (p=0.086)	−0.08 (−0.24–0.08) (p=0.29)	−0.07 (−0.27–0.13) (0.47)
Beck Score	3.73 (−5.63–13.09) (p=0.12)	−1.67 (−29.99–26.64) (0.59)	<-0.01 (−0.05–0.05) (p=0.97)	002 (−0.04–0.08) (p=0.57)

ARC Score: alcohol recreational drugs and cigarettes.
Adjusted for age, gender, race, BMI, hypertension, diabetes, HDL–C, LDL–C, smoking status.
Sample size=42 for thoracic fat and epicardial fat; sample size=73 for CAC volume and CAC score.

aspirin usage, cholesterol medication, consulting with a physician, losing weight, decreasing dietary fat, but also increased worry, noting that potentially important risk-reducing behaviors may be reinforced by the knowledge of a positive coronary artery scan, independent of preexisting coronary risk factor status (16). More recently, Rozanski et al. showed in the EISNER clinical trial, which randomized over 2.000 intermediate risk persons to CAC scanning vs. no scanning, an increase in the Framingham Risk Score (FRS) in the no-scan group compared to change in Framingham risk in the scan group (0.7 ± 5.1 vs. 0.002 ± 4.9, p = 0.003). Within the scan group, the baseline CAC score was additionally associated with an improvement in risk factors and FRS (p<0.01) (17).

Some studies have also examined relationships of lifestyle modification efforts with CAC progression or changes in body or epicardial fat. In the SAFE-LIFE randomized trial of patients with established CHD, while lifestyle modification with stress reduction showed reductions in blood pressure, heart rate, and need for anti-ischemic medications, there was

no impact on change in CAC score (22). A study of 64 Japanese Americans showed the combination of an American Heart Association step 2 diet combined with endurance and stretching exercise to reduce subcutaneous, thoracic, and thigh fat measured by CT (20), A recently published systematic review and meta-analyses of the effects of lifestyle interventions on ectopic fat deposition described overall decreases on fat in the liver, heart, and pancreas (23), but not general thoracic fat, and others have described diet-induced weight loss to impact of diet and/or exercise only focused interventions on changes in epicardial fat only (24). Our study showed that certain components of our prescribed intervention program, including increased social support, cognitive hardiness, negative appraisal coping style, exercise, and good sleep habits appeared to be inversely related to changes in thoracic and/or epicardial fat, but not coronary calcium.

Our study has strengths and weaknesses. An important strength is the systematic collection of risk factors and standardized assessment of coronary calcium and measures of epicardial and thoracic fat by CT. An important limitation of the study is that follow-up CT scan data were not available in over 50 % of randomized subjects, due largely to logistical reasons preventing a repeat scan from being performed; in addition, availability of epicardial and thoracic fat measures was limited to subjects with DICOM-archived data available. However, when comparing baseline characteristics, intervention vs. control group participants who did complete were roughly comparable to those who did not complete the study, with the exception of having greater amounts of coronary calcium and lower HDL –C levels, suggesting our results in the participants who did complete the study are moderately generalizable to the larger group of randomized participants. Also, while the study was randomized, the nature of the intervention (lifestyle management and scan consultation) precluded blinding of participants and staff. While our findings regarding CAC score and volume as well as thoracic fat volume did reach statistical significance, even in fully adjusted analyses (adjusting for baseline CAC score and volume or baseline thoracic fat volume, as well as other risk factors), our sample sizes are small and the results need to be treated with caution and need validation in larger samples. In addition, the clinical significance of the degree of CAC progression differences and changes in epicardial or thoracic fat between the groups in terms of future event risk is uncertain although clearly these measures have been shown to relate to cardiovascular event risk and atherosclerosis in other studies (6–8). Further, this analysis does not identify the relative effect of specific behavioral factors (e.g., dietary, exercise, or stress management components) or the relative contribution of the physician consultation versus the lifestyle intervention program on changes in CAC progression, epicardial or thoracic fat. Larger-scale studies with multiple treatment arms would be needed to better document this.

Our data suggests a multifactorial, web based, direct contact behavioral intervention combined with a physician-provided consultation of whole body CT results may have had a beneficial effect on retarding progression of CAC as well as epicardial and thoracic fat measures by CT. Further study in a larger sample of subjects and identification of which specific measures (e.g., certain behavioral modification or face-to-face physician-provided consultation) is needed to confirm these findings. Moreover, the clinical significance of changes in these measures over baseline measures of CAC or epicardial or thoracic fat, as well as other clinical risk factors in the prediction of long-term clinical outcomes needs to be further established.

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Author Contributions

NW and WF contributed to the writing of the manuscript, WF, DD, and CP did the analysis and managed the data, and AE, JC, HE, and CP conducted the clinic visits. LW, HE, AE, and DD provided critical review and revision of the content of the manuscript.

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