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Motivational effects of coronary artery calcium scores on statin adherence and weight loss

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Aim The aim of this study was to assess the effect on adherence to statin therapy and assess the effect of beneficial changes in behavior that resulted in weight loss in patients who underwent coronary artery calcium (CAC) scoring with cardiac computed tomography.

Background Despite convincing data demonstrating the benefits of HmGCoA inhibitors for both primary and secondary prevention of coronary heart disease, they remain underused. Also, despite convincing data demonstrating the benefits of weight loss for both primary and secondary prevention of coronary heart disease, it remains difficult to motivate behavioral changes resulting in weight loss. In this study, we assess whether higher CAC scores are associated with increased compliance with statin medication and whether higher CAC scores are associated with beneficial lifestyle behaviors resulting in weight loss.

Methods We retrospectively analyzed patients that had undergone baseline CAC testing and returned for a follow-up scan. All patients had weight documented and were administered a questionnaire regarding compliance to medications. The primary endpoint was measurable weight loss between visit one and visit two and the self-reported compliance to statin use.

Results The study population with data regarding statin compliance consisted of 2608 individuals (72% men, mean age 58 ± 8 years) who were followed for a mean of

4.1 ± 3.2 years after an initial CAC scan. Overall, statin compliance was lowest (27.4%) among those with CAC = 0, and gradually increased with higher CAC scores (1–99, 39.2%; 100–399, 53.6%; ≥ 400 , 58.8%; $P < 0.001$ for trend). In the group analyzed for weight loss the study population consisted of 1078 individuals (68% men, mean age 60 ± 8 years) who were followed for a mean of 4.1 ± 3.2 years after an initial CAC scan.

Conclusion Overall, behavioral modification resulting in weight loss was lowest (19.8%) among those with CAC = 0, and gradually increased with higher CAC scores (1–99, 23.4%; 100–399, 30.8%; ≥ 400 , 33.6%; $P < 0.001$ for trend). In addition to being a robust risk stratification tool, a higher rate of adherences with statin therapy was observed in patients with higher CAC scores. *Coron Artery Dis* 26:225–230 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

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Keywords: adherence, cardiac computed tomography, coronary artery calcium, statin use, weight loss

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Introduction

Cardiovascular disease (CVD) currently consumes 17% of the national health budget [1]. In a place where health expenditures and BMIs are the highest in the world, CVD has recently grown at an average annual rate of 6%. Based merely on demographic changes in the population, the prevalence of CVD will increase by nearly 10% and related costs will triple in the next 20 years. Although the mortality rate due to coronary artery disease (CAD) has indeed decreased, the prevalence of cardiovascular risk factors including obesity continues to increase in a startling manner that actually makes the above estimates conservative.

Although weight loss and statin therapy have been validated as beneficial means for the prevention of coronary heart disease [2–5], it remains challenging to motivate compliance with lipid-lowering medications [6] and

changes in cardiovascular risk behaviors resulting in weight loss [7]. Specifically, in addition to HmGCoA inhibitors being underused by healthcare providers [6], only one-third of high-risk primary care patients are taking needed medications for dyslipidemia and patient adherence commonly falls below 50% [4]. Furthermore, less than 15% of American adults and children engage in exercise regularly. This demonstrates the utilization of behaviors that can result in weight loss remains poor at large [4]. With only a mild fraction of total cardiovascular risk burden truly being alleviated, effective interventions for the enhancement of adherence to statin therapy and compliance with lifestyle behavioral modifications are urgently needed [8].

Coronary artery calcium (CAC) scanning by cardiac computed tomography (CCT) is used for the detection of subclinical CAD and serves as a tool for accurate

measurement of cardiovascular risk [9–11]. This use of computed tomography (CT) scanning may enhance motivation for using lipid-lowering medications and optimizing modifiable cardiovascular risk factors through patient knowledge of increasing CAC burden [12]. We examined the effects of visualizing CAC on patient adherence to statin medications and weight loss. We hypothesized that higher CAC scores would be associated with increased patient adherence to lipid-lowering therapy and greater weight loss.

Methods

Patients

Chest CT scans were performed on asymptomatic patients from 1995 to 2012 at a University-Affiliated Disease Prevention Center in Torrance, California to examine the extent of atherosclerotic calcification in the coronary arteries. This clinical population of participants was either physician or self-referred as a supplement to their preventive healthcare.

CCT scans were performed at the first clinic visit (baseline) and at a subsequent visit, and all participants completed a detailed health history questionnaire that collected information on demographics, diabetes, hypertension, smoking, alcohol consumption, diet, exercise, and family history of coronary heart disease at that time. Blood pressure was obtained by automated oscillometry after the patient rested for 5 min in a seated position.

Imaging

Either an Imatron C-150 (General Electric, San Francisco, California, USA) or GE 64 slice was utilized to perform the scans used to obtain images of each patient's heart. Scans proceeded down from the level of the carina to the level of the diaphragm to encompass the entire coronary tree. Contiguous slices of each participant's heart were obtained, each of which were 3 mm thick. Cardiac tomographic imaging was electrocardiographically triggered at 75% of the R–R interval to avoid motion artifacts. Imaging of the heart was conducted during one breath hold at end inspiration.

Coronary calcification was defined as a minimum plaque area of 1.00 mm^2 (≥ 3 pixels) with a density of 130 Hounsfield units or more. Quantitative measures of calcium scores were determined according to the technique explained by Agatston *et al.* [13]; this calcium scoring was performed by either a CT technician or physician trained in the methodology outlined above, blinded to all clinical information. This method has been previously described in detail.

Consultation

Before leaving the CT center, patients were shown his/her CT images and a detailed discussion was taken describing the location, presence and severity of atherosclerosis on their scan. Patients were made aware that

CAC identifies underlying coronary atherosclerosis and is associated with incident heart disease. The patients followed up with a physician who reviewed the results of the CT scan, discussed the risk factors associated with CAC, and made recommendations for risk reduction based on the patient's CAC score. The recommendations for risk reduction included nutritional advice, exercise suggestions, and smoking cessation recommendations (if pertinent) and compliance with medications.

Behavioral assessment

An average of 4.2 ± 3.2 years after the baseline clinic visit, patients revisited the clinic for a subsequent scan and completed a detailed health history questionnaire that collected information on demographics, diabetes, hypertension, smoking, alcohol consumption, diet, exercise, and family history of coronary heart disease at that time. Blood pressure was obtained by automated oscillometry after the patient rested for 5 min in a seated position.

Prospective determination of statin utilization

Medications for the treatment of cardiovascular risk were neither specifically recommended nor provided under the study protocol. Participants and their referring physician were provided with the CAC score; however, pharmacotherapy was neither endorsed nor prescribed by the study. After the baseline visit, participants returned to the care of their primary care providers who determined all subsequent clinical management. At the follow-up visit, statin use was ascertained by the study personnel.

Statistical analysis

Dyslipidemia was defined either by total cholesterol to HDL ratio of more than 5, or by self-report of current use of prescription cholesterol-lowering medications. Participants were grouped into either never, former, or current smokers.

The outcome variables for this study were compliance with statin use on a background history of dyslipidemia and different health behavior changes potentially made after receiving CCT scan results and the physician consultation: which may have had an impact on weight loss. The primary predictor variables were presence and extent of CAC, with covariates of age, sex, premature sibling and parent heart disease, hypertension, dyslipidemia, diabetes, and ethnicity.

Statistics

The statistical methods addressed two specific aims: (a) to assess the effect of behavioral lifestyle changes (weight loss) in patients who underwent serial CAC scoring with electron beam computerized tomography or CCT; (b) to assess the effect of statin medication compliance based on coronary artery calcification. The initial step of the analysis focused on clinical and epidemiological characteristics of participants. Descriptive statistics are presented

Table 1 Characteristics of study population

	Participants (%)
Number	2608
Age (years)	58±8
Males	72
Hypertension	51
Tobacco use	14
Diabetes	7
Family history of premature CHD	69

CHD, coronary heart disease.

as counts and percentages for categorical data and mean and SDs for continuous variables. In the second step, Cox proportional hazards models were applied to estimate the association of weight loss with coronary artery calcification based on age, sex race, BMI and traditional CVD risk factor adjusted relative risks and 95% confidence intervals (CIs). Given that CAC scores do not fit normal distribution, the CACs were log-transformed. The outcome variables for this study were compliance with statin use on a background history of dyslipidemia and different health behavior changes potentially made after receiving CCT scan results and the physician consultation: which may have had an impact on weight loss. For univariate analyses, continuous variables were compared with a *t*-test for independent groups, and categorical variables were compared with the χ^2 -test. We conducted multivariable logistic regression for the dependent variables of medication (statin). Independent variables in this analysis included coronary risk variables as specified by the NCEP, CAC-identified as categorically present or absent, and other variables of interest with possible impact on medication-taking behavior. Specifically, we controlled for diabetes, hypertension, smoking, alcohol consumption, diet, exercise, and family history of coronary heart disease, along with race-ethnicity and age and sex. Weight was modeled as a continuous variable over follow-up. In the third model, relative risk regression was used to model the effect of statin therapy in patients who underwent serial CAC scoring. All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, North Carolina, USA).

Results

The study population with data regarding statin compliance consisted of 2608 individuals (72% men, mean age 58±8 years) who were followed for a mean of 4.1±3.2 years after an initial CAC scan. Characteristics are outlined in Table 1. Overall, statin compliance was lowest (27.4%) among those with CAC=0, and gradually increased with higher CAC scores (1–99, 39.2%; 100–399, 53.6%; ≥400, 58.8%; *P*<0.001 for trend) (Table 2). In multivariable regression analysis, there is a dose–response relationship between increasing CAC score and adherence to statin therapy. In the group that had statin compliance compared with those who were not compliant, the

Table 2 Statin compliance for cohort based on baseline calcium score

CAC score	Patients with hyperlipidemia (n)	Statin compliance [n (%)]
0	514	141 (27.4)
1–100	779	305 (39.2)
100–400	580	311 (53.6)
>400	735	432 (58.8)

CAC, coronary artery calcium.

P<0.001 for trend of values.

Table 3 Percent of participants losing weight in cohort based on baseline calcium score

CAC score	Patients with weight (n)	Weight loss [n (%)]
0	212	42 (19.8)
1–100	312	73 (23.4)
100–400	224	69 (30.8)
>400	330	111 (33.6)

CAC, coronary artery calcium.

mean CAC score was 30% higher (95% CI 0.2–0.3, *P*<0.001) after being adjusted for age, sex, and race. In logistical regression analysis, those with CAC score of 1–99, 100–400, and >400, as compared with those with a score of 0, were 1.7 (95% CI 1.3–2.1, *P*<0.05), 3.1 (95% CI 2.4–3.9, *P*<0.01), and 3.8 (95% CI 2.0–3.5, *P*<0.001) fold, respectively, more likely to adhere to statin therapy when adjusted for age sex and race (Table 3).

In the group analyzed for weight loss, the study population consisted of 1078 individuals (68% men, mean age 60±8 years) who were followed for a mean of 4.1±3.2 years after an initial CAC scan. Overall, behavioral modification resulting in weight loss was lowest (19.8%) among those with CAC=0, and gradually increased with higher CAC scores (1–99, 23.4%; 100–399, 30.8%; ≥400, 33.6%; *P*<0.001 for trend) (Table 3). In multivariable regression analysis, there is a dose–response relationship between increasing CAC score and weight loss. In logistical regression analysis, those with CAC score of 1–99, 100–400, and >400, as compared with those with a score of 0, were 1.2 (95% CI 0.8–1.9, *P*=not significant), 1.8 (95% CI 1.2–2.8, *P*<0.001), and 2.1 (95% CI 1.4–3.1, *P*<0.001) fold, respectively, more likely to lose weight when adjusted for age, sex, and race (Table 4).

Discussion

Our study is the largest study performed demonstrating the effects of CAC scanning were significantly associated with improved compliance with cardiovascular risk-reducing behaviors. Specifically, patients showing greater CAC were more likely to adhere to statin medications and to lose weight. This suggests visualization of the CT scan and knowledge of CAC score, in addition to a brief consultation, may motivate changes in cardiovascular risk behaviors which persist over 4 years.

Table 4 Logistic regression of statin compliance and weight loss for CAC score groups

OR (95% CI)	Statin compliance		Weight loss	
	Unadjusted model	Adjusted model ^a	Unadjusted model	Adjusted model ^a
CAC score				
0	Reference	Reference	Reference	Reference
1–100	1.7 (1.3, 2.2)***	1.6 (1.3, 2.1)***	1.2 (0.8, 1.9)	1.1 (0.7, 1.7)
100–400	3.1 (2.4, 3.9)***	2.7 (2.1, 3.6)***	1.8 (1.2, 2.8)**	1.4 (0.9, 2.2)
> 400	3.8 (3.0, 4.8)***	3.1 (2.4, 4.1)***	2.1 (1.4, 3.1)***	1.4 (0.8, 2.2)

CAC, coronary artery calcium; CI, confidence interval; OR, odds ratio.

^aAdjusted by age, sex, and race.

** $P < 0.01$; *** $P < 0.001$.

Baseline CAC score was an independent predictor of both statin compliance and weight loss at follow-up. With the average CAC score being 30 and 40% higher in groups that had statin adherence and weight loss in comparison with those groups not showing corresponding risk-reducing behaviors, we believe that a change in patient perception of health status after a CT scan was the motivating factor for lifestyle behavior modifications. In this case, visualizing and knowledge of CAC may serve as a ‘teachable moment’ that influences patient choices and behavior [7,14]. These effects may reflect how not only the presence but also the extent of CAC burden, and thus perhaps the extent of perceived risk, was significantly associated with the likelihood of medication adherence or weight loss. This tendency for high-risk patients to demonstrate increased adherence has been reported. Large studies have shown a pattern of increased adherence rates to statins in patients with a higher severity of cardiac disease [15,16].

Prior studies

The current study lends support to the findings of various studies that have demonstrated a significant association between the effects of CAC screening and statin therapy adherence [12,14,17,18]. Kalia *et al.* [14] examined 505 asymptomatic individuals and determined adherence was lowest (44%) among those in the first quartile of CAC scores (0–30) and highest (91%) among those in the fourth quartile (≥ 526). A study reported by Taylor *et al.* [17], investigating a community-based cohort of 1640 asymptomatic men aged 40–50 years, found that detection of CAC is independently associated with a three-fold to seven-fold greater likelihood of statin and aspirin utilization at follow-up. Our current data are highly concordant to that of the study by Taylor and colleagues in which they found CAC was strongly and independently associated with statin use (odds ratio 3.53; 95% CI 2.66–4.69), whereas we found 3.1–3.8-fold increased use with increasing CAC scores. In an examination of 208 symptomatic individuals, LaBounty *et al.* [18] also demonstrated a significant association between CAD severity and risk-reducing behaviors, including adherence to lipid-lowering therapy. In comparison, the current study utilized a relatively large and heterogeneous sample (2100, 72% men) of adults aged an

average of 58 years, with over 4-year follow-up. This may make for better generalization to a larger asymptomatic population.

Despite extensive evidence validating the use of CT to detect subclinical coronary atherosclerosis, there is relatively limited knowledge of the extent of its effects on motivating individuals to initiate lifestyle behavioral changes. Considering the limited investigations of cardiovascular risk factor management following CAC screening, the current study is distinguished even more by monitoring weight loss as opposed to simply related behaviors, such as diet and exercise. The significant association between weight loss and higher baseline CAC scores may indicate an even stronger benefit of coronary calcium determination using CT. This is an important matter to consider in light of the fact that weight loss of 15% or more of body weight, when accompanied by other dietary and lifestyle interventions, drastically reduces cardiovascular risk up to 45% [19]. Furthermore, recording of weight at both baseline and follow-up provide a more verifiable and valid change in comparison with self-reported behaviors like diet and exercise.

The results of this study contradict those of a randomized study by O’Malley and colleagues that indicate the effects of CAC screening on electron beam computerized tomography were not a significant motivating factor for changes in modifiable cardiovascular risk behaviors. However, that study was limited in several aspects, the most notable being a sample of primarily young military personnel with a mean age of only 42 years and a very low prevalence of modifiable cardiovascular risk factors [20]. Also, a vast majority of the participants had scores of zero, so the potential motivation of a positive score is lost. This relatively young, healthy, and asymptomatic population may have insufficiently demonstrated behavioral change since it is perceived risk as well as knowledge of disease that presumably drives this behavioral modification. This is highly consistent with the participants in our study with scores of zero, who exhibited less behavioral changes than those with documented subclinical atherosclerosis. Further, in the study by O’Malley and colleagues, even though only 18% of participants had CAC present, there was a trend toward improvement in behavioral modification, but obviously underpowered to assess this small cohort.

Study limitations

Being both observational and retrospective, this study had several inherent limitations. First of all, it lacked a randomized control population for comparison with the CT-tested population. However, because withholding scan results from patients would be unethical, we must use large, observational studies to determine association between CAC and compliance [14]. Furthermore, a very low prevalence of changes among patients with no CAC serves as an internal comparison that suggests it was CAC results, as opposed to referral bias, serving as the motivating factor for improved compliance. Second, generalizability may be applied to only self-referred or physician-referred patients. Being comprised of perhaps health-conscious individuals more likely to routinely seek health prevention and improvement, this sample may not be representative of the population at large. Third, self-reported behavior in regards to statin therapy adherence was subjective and non-quantitative, thereby limiting ability to precisely quantify effects. Several studies have shown that self-reported medication compliance tends to be overestimated and suffer from recall bias [15,21]. On the other hand, self-reported adherence does provide vital information to clinical response in therapy [22]. Fourth, it was not addressed whether patients with high CAC scores and at high risk were subsequently managed more aggressively by their primary care physicians. Motivation for adherence and weight loss may have been influenced by lifestyle changes initiated by patients or physicians, rather than solely the effects of CAC screening. Regardless, the study demonstrated a significant association between behavior modification and risk severity. Some evidence indicates that these lifestyle behavioral changes initiated after screening for cardiovascular risk factors tend to diminish over time. However, our study, with over 4 years of follow-up, shows high persistence. In addition, the study by Taylor *et al.* [17] demonstrated increasing compliance over 6 years of follow-up.

A randomized trial of patients undergoing CAC versus no CAC also demonstrated improvement in behaviors, with a graded improvement with increasing CAC scores associated with increased compliance and change in CVD risk factors. In the largest randomized study to assess CAC, the Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research (EISNER) study [23], adults who underwent CAC testing met individually with a nurse to see sample images and receive counseling on risk factor modification. After 4 years, compared with the no-scan group, the scan group showed a net favorable change in systolic blood pressure ($P=0.02$), low-density lipoprotein cholesterol ($P=0.04$), and waist circumference for those with increased abdominal girth ($P=0.01$), and tendency to weight loss among overweight patients ($P=0.07$). Within the scan group, increasing baseline CAC score was associated with a dose-response improvement in systolic and diastolic blood

pressure ($P<0.001$), total cholesterol ($P<0.001$), low-density lipoprotein cholesterol ($P<0.001$), triglycerides ($P<0.001$), weight ($P<0.001$), and Framingham Risk Score ($P<0.003$).

Conclusion

Our study suggests that determination of coronary calcium using CT may not only be useful in diagnosing coronary atherosclerosis, but also in improving patient compliance with beneficial behavioral changes. Considering that HmGCoA are still substantially underused by patients at higher risk [6] and that lowering the prevalence of obesity is the most urgent matter in preventing CAD [4], our findings showing significantly increased adherence among high-risk patients as a result of CAC visualization are an important matter to consider when formulating prevention strategies. Our study along with previous smaller trials are concordant, demonstrating increasing scores associated with increasing adherence of lifestyle and medications to improve cardiac health. This strongly supports the incremental use of CAC scanning, not only for risk stratification in asymptomatic persons, but also to improve behavioral changes known to improve cardiovascular outcomes. In this study, higher CAC scores were associated with higher rate of adherence with statin therapy. Further studies elucidating the mechanism of this benefit need to be performed.

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Conflicts of interest

Dr Budoff has a conflict of interest, as he is a consultant for General Electric. For the remaining authors there are no conflicts of interest.

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