

Visualizing coronary calcium is associated with improvements in adherence to statin therapy

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Abstract

Background: Many patients lack motivation to control cardiovascular risk factors and clinicians have long sought ways to activate apathetic patients. Despite significant and consistent data on the benefits of lipid-lowering agents to reduce cardiovascular events, adherence and utilization of these agents remains low. We evaluated whether visualization of coronary calcium would positively affect patients' adherence rates.

Methods: We evaluated patients who underwent electron beam tomography (EBT) coronary calcium evaluation at least 1 year prior with a survey questioning them about health behaviors. Patients filled out baseline and follow-up questionnaires relating to lifestyle modifications, including statin utilization, diet, exercise, tobacco cessation and vitamin/antioxidant utilization.

Results: The study population consisted of 505 individuals on statin therapy on baseline who were followed for a mean of 3 ± 2 years. Overall the statin compliance was lowest (44%) among those with CAC score in the first quartile (0–30), whereas 91% of individuals with baseline CAC score in the fourth quartile (≥ 526) adhered to statin therapy. In multivariable analysis, after adjusting for cardiovascular risk factors, age, and gender, higher baseline CAC scores were strongly associated with adherence to statin therapy.

Conclusions: In addition to risk stratification for the asymptomatic person, patients visualizing coronary artery calcium may improve utilization and adherence to lipid-lowering therapy. Outcome studies and randomized trials need to be done to quantify the true value and cost-effectiveness of this approach.

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Despite convincing data demonstrating the benefits of lipid lowering agents for both primary and secondary prevention of coronary events [1–3] these agents remain underused by high-risk patients and health-care providers [4]. Furthermore, long-term adherence to these therapies remains poor among primary prevention cohorts [5] and even among patients who survive myocardial infarction [6]. Thus, effective

interventions that improve their use and/or adherence are urgently needed [7].

We evaluated the association between electron beam tomography (EBT) coronary calcium measurement and adherence to lipid lowering therapy and lifestyle modifications among consecutive patients physician-referred to our center for evaluation of coronary atherosclerosis. We hypothesized that patient knowledge of increasing coronary artery calcium (CAC) burden would be associated with improved patient adherence to coronary risk reducing behaviors, such

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as lipid lowering therapy, exercise, diet and smoking cessation.

1. Methods

A total of 1215 consecutive asymptomatic patients referred for EBT risk assessment by their primary physician were sent a survey questioning them about health behaviors. Demographic characteristics, lifestyle behaviors including cigarette smoking, alcohol use, physical activity, diet, physician diagnosed diseases, current medications including statin utilization, vitamin/antioxidant utilization, hospitalizations and surgeries were determined using structured questionnaires. The presence and number of risk factors for a participant was calculated based on the National Cholesterol Education Program guidelines [8]. Risk factors included: males age >45 years, females >age 55 years, current cigarette smoking, history of premature coronary disease in first-degree relative, hypertension and hypercholesterolemia. Current cigarette smoking was defined as use of >10 cigarettes per day. Hypertension was defined by current use of anti-hypertensive medication or known and untreated hypertension. Hypercholesterolemia was defined as use of cholesterol lowering medication or, in the absence of cholesterol lowering medication use, as having a total serum cholesterol >240 mg/dL. Patients underwent coronary calcium scanning using the Electron Beam Tomography C150XL (GE, South San Francisco, CA), using 3 mm slices and Agatston scoring, as previously described [9]. Patients were also shown the actual scan, seeing the coronary calcium as bright white spots in their coronary arteries, describing the atherosclerosis visualized as: none, mild, moderate or severe. At the time of the original scan, we discussed scan results with patients, describing CAC as identifying underlying coronary atherosclerosis and being predictive of heart disease risk. Patients filled out a questionnaire related to risk factors, lifestyle and medication usage at baseline (time of calcium scan). The same survey was given again at follow-up, to evaluate changes in behavior or medication over the interval. A sample question from the questionnaire was “Are you currently taking a statin cholesterol-lowering agent? if so, which one”. This allowed us to assess whether those who were on statin therapy at baseline were still on statin therapy at follow-up.

Patients with baseline known cardiovascular disease (including stroke, claudication or coronary artery disease) were not included in the study. Patients experiencing an interim cardiac event (revascularization, stroke, myocardial infarction, new onset chest pain) were excluded ($n = 105$). Follow-up survey information was obtained in 981 of 1110 (88%) of patients, a mean of 3.6 ± 2 years after the baseline scan. There were no differences in the prevalence of risk factors and CAC characteristics between responders and non-responders. Since the main aim of the study was to assess compliance on statin therapy, 476/981 individuals who were

not on statin therapy were excluded from the final analyses. The study was approved by the Institutional Review Board of our institution.

2. Statistics

Categorical data are presented as number (percent), and continuous data as mean value $\pm$ S.D. Two tailed Chi-squared test and the *t*-test or Mann–Whitney rank sum test were used for analysis of categorical and continuous variables, respectively. ANOVA was used for univariate analysis of categorical variables and adherence to statin therapy across CAC quartiles. Hypertension, hypercholesterolemia, tobacco use, diabetes, age, gender, family history of premature heart disease, as well changes in behavior, such as increased physical activity, utilization of aspirin and change of diet, were variables included in the multivariable analysis using logistic regression. Risk-adjusted (i.e., controlling for cardiac risk factors) odds ratio for adherence with statins with increasing CAC quartiles were compared with lowest quartiles as well additionally with CAC scores of 1–99.9, 100–399.9 and ≥ 400 with no CAC, respectively. Higher levels of baseline risk factors are associated with increased calcification. Therefore, to control for a possible treatment bias due to higher levels of baseline cardiovascular risk factors, we further stratified the population according to presence or absence of CHD risk factors and adjusted for these risk factors in our analysis. Multiple logistic regression models were used to examine the likelihood of statin adherence with increasing baseline CAC scores in a hierarchical fashion:

- (I) adjusted for age and gender (model 1);
- (II) adjusted for age, gender, hypertension, diabetes, tobacco use and family history (model 2).

All tests of significance were two-tailed, and significance was defined at the 0.05 level or below. Data were analyzed using STATA Version 8 (Austin, TX). No external funding was utilized in this research.

3. Results

The final study population consisted of 505 individuals on statin therapy at baseline. Majority of the study population were men ($n = 413$, 82%). The mean age of the study population was 61 ± 10 years. These patients were followed for 3 ± 2 years (range 1–10 years) Patients were divided into quartiles based upon baseline CAC score (first quartile: 0–30, second quartile: 31–149, third quartile: 151–526 and fourth quartile: ≥ 527). Study participants with higher CAC were more likely to be older, hypertensive, and diabetic (Table 1). The proportion of individuals on statins at baseline increased linearly with increasing CAC quartiles (first quartile: 24%, second quartile: 46%, third quartile: 63% and fourth quartile: 74%, $p < 0.0001$), independent of baseline risk factors.

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