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The Identification of Calcified Coronary Plaque Is Associated With Initiation and Continuation of Pharmacological and Lifestyle Preventive Therapies:

A Systematic Review and Meta-Analysis

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Abstract

OBJECTIVES—The aim of this study was to assess the odds of initiation or continuation of pharmacological and lifestyle preventive therapies in patients with nonzero versus zero coronary artery calcium (CAC) score detected on cardiac computed tomography.

BACKGROUND—Detection of calcified coronary plaque could serve as a motivational tool for physicians and patients to intensify preventive therapies.

METHODS—We searched PubMed, EMBASE (Excerpta Medica database), Web of Science, Cochrane CENTRAL (Cochrane central register of controlled trials), ClinicalTrials.gov, and the International Clinical Trials Registry Platform for studies evaluating the association of CAC scores with downstream pharmacological or lifestyle interventions for prevention of cardiovascular disease. Pooled odds ratios (ORs) of downstream interventions were obtained using the DerSimonian and Laird random effects model.

RESULTS—After a review of 6,256 citations and 54 full-text papers, 6 studies (11,256 participants, mean follow-up time: 1.6 to 6.0 years) were included. Pooled estimates of the odds of aspirin initiation (OR: 2.6; 95% confidence interval [CI]: 1.8 to 3.8), lipid-lowering medication

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initiation (OR: 2.9; 95% CI: 1.9 to 4.4), blood pressure–lowering medication initiation (OR: 1.9; 95% CI: 1.6 to 2.3), lipid-lowering medication continuation (OR: 2.3; 95% CI: 1.6 to 3.3), increase in exercise (OR: 1.8; 95% CI: 1.4 to 2.4), and dietary change (OR: 1.9; 95% CI: 1.5 to 2.5) were higher in individuals with nonzero CAC versus zero CAC scores, but not for aspirin or blood pressure–lowering medication continuation. When assessed within individual studies, these findings remained significant after adjustment for baseline patient characteristics and cardiovascular risk factors.

CONCLUSIONS—This systematic review and meta-analysis suggests that nonzero CAC score, identifying calcified coronary plaque, significantly increases the likelihood of initiation or continuation of pharmacological and lifestyle therapies for the prevention of cardiovascular disease. (J Am Coll Cardiol Img 2017;10:833–42)

Keywords

cardiovascular prevention; coronary calcium score; meta-analysis

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The presence of calcified coronary plaque detected on cardiac computed tomography has been shown to be a strong predictor of future major adverse cardiovascular events among asymptomatic individuals, and it offers incremental risk stratification beyond traditional risk factors and risk scores endorsed by national guidelines (1–3). Coronary artery calcium (CAC) testing offers the potential to promote more aggressive pharmacological and lifestyle therapies among individuals with an elevated CAC score who are thus at increased risk for adverse cardiovascular events (4–6).

A meta-analysis by Whelton et al. (7) examined 4 randomized controlled trials (RCTs) to investigate the impact of CAC screening on risk factor modification (7). They found a nonsignificant trend toward reduction in blood pressure, lipid levels, and smoking cessation among individuals who had a CAC scan compared with those who were managed by standard care (7). However, in the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) study (8), when these findings were evaluated within the group that had a CAC scan, there was a significant increase in the initiation of aspirin (ASA), lipid lowering medication (LLM), and blood pressure–lowering medication (BPLM) among individuals with a nonzero CAC score (8). This would imply that having an abnormal CAC score, rather than merely undergoing the scan, accounts for behavioral changes.

Prior observational studies have similarly suggested a correlation between the presence of CAC and initiation of ASA, LLM, and BPLM as well as increased exercise and dietary changes (9,10). However, to our knowledge, no studies have summarily evaluated the impact of presence versus absence of CAC on cardiovascular preventive therapies. As such, we conducted a systematic review and meta-analysis to evaluate the impact of nonzero versus zero CAC scores on initiation and continuation of pharmacological and lifestyle therapies for prevention of cardiovascular disease.

METHODS

The systematic review and meta-analysis was conducted and reported in accordance with recommendations of the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) Group (11).

DATA SOURCES AND SEARCH STRATEGY

We performed a systematic search of published data using PubMed, EMBASE (Excerpta Medica database), Web of Science, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, and the International Clinical Trials Registry Platform from their inception through November 21, 2016. We used free text and medical subject headings terms to represent CAC and preventive therapies, including ASA, BPLM, LLM, smoking, exercise, dietary changes, and weight loss. We set no limitations on age, type of study, or language. The search strategy is shown in the Online Appendix.

STUDY SELECTION

Studies that evaluated the influence of CAC scores on downstream lifestyle modifications or medication usage for primary prevention of cardiovascular disease were eligible for inclusion. After removing duplicates, 2 independent reviewers excluded articles that were not relevant to the study and identified papers of interest based on titles and abstracts. Full-text reviews of relevant papers were then performed to identify eligible studies. References of the included papers were also screened to identify other potential papers of interest. Any disagreements on study inclusion or exclusion were adjudicated by the senior author (R.B.).

DATA EXTRACTION AND QUALITY ASSESSMENT

Two reviewers (A.G. and R.V.) independently extracted data from the included studies. If a study of interest had evaluated the effect of CAC score on preventive lifestyle or pharmacological therapies, but the categorization of CAC score was such that data on patients with zero versus nonzero CAC could not be extracted, then the corresponding author was contacted to provide data in zero versus nonzero CAC categories for inclusion in the meta-analysis. Such a study was excluded only if the corresponding author was unable to complete the data request. If multiple publications existed from the same cohort of patients or their subsets, we extracted data from multiple papers if different outcomes of interest were reported in separate publications.

For each study, the baseline characteristics, as detailed in Table 1, and outcomes of interest stratified by patients who had zero versus nonzero CAC scores were extracted. We also recorded all unadjusted and adjusted odds ratios (ORs), which evaluated the association of an outcome across CAC groups, and the corresponding covariates used for statistical adjustment. The Newcastle-Ottawa scale was used to assess the quality of individual studies.

DATA SYNTHESIS AND STATISTICAL ANALYSIS

The primary aim of our analysis was to quantify the OR of preventive interventions following CAC testing in the nonzero versus zero CAC groups. We used OR and 95% confidence interval (CI) as a measure of effect size. The DerSimonian and Laird random-

effects model was used to pool the ORs across studies for each outcome of interest (12). Unadjusted ORs from all included studies were pooled to obtain a crude estimate of association. Adjusted ORs, when reported, were recorded from the most complete multivariable models used by each original study. Heterogeneity was assessed using the Cochrane Q chi-square test and the I^2 statistic to calculate the percentage of total variation in study estimates due to heterogeneity as opposed to sampling variation. I^2 >50% was considered as significant heterogeneity.

Publication bias was assessed using a contour-enhanced funnel plot, Egger's linear regression test, and fail-safe N to calculate the number of missing studies that would bring the p value of the pooled effect estimate above an alpha level of 0.05. Shift of OR by imputation of missing studies that would create symmetry in a funnel plot was also examined to assess the robustness of pooled estimates to publication bias. Sensitivity analysis of pooled effect estimate was performed for outcomes with 3 or more studies after excluding 1 study at a time. Meta-regression was performed to evaluate the effect of follow-up duration on the study findings for outcomes with more than 3 studies. For all analyses, a 2-tailed p value <0.05 was considered statistically significant. Pooling of estimates, heterogeneity testing, and Forest plots were created using Review Manager (RevMan) version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Sensitivity analyses, meta-regression, and publication bias assessment were performed in Comprehensive Meta-Analysis version 3 (Biostat, Englewood, New Jersey).

RESULTS

STUDY SELECTION

Our literature search strategy identified 6,256 unique papers. After exclusions (Figure 1), we identified 8 eligible papers for inclusion in the meta-analysis (4,5,8–10,13–15). A total of 7 studies were observational in design and 1, the EISNER study (8), was an RCT investigating CAC scanning versus standard care. For the purposes of our analysis, the CAC arm alone was used. Three other RCTs, investigating the impact of CAC scanning versus standard care alone, did not stratify the results of the CAC arm by the presence or absence of CAC, and were therefore excluded (16–18).

Of the 7 observational studies eligible for inclusion, 1 study provided point estimates of association without measures of variance (4) and 3 studies presented results in a format from which estimates of association for zero versus nonzero CAC could not be obtained (5,9,13). The corresponding authors for these 4 studies were contacted to obtain additional unpublished data: 2 of them (9,13) provided the total number of patients in both nonzero and zero CAC groups as well as the proportion of patients in each group who achieved outcomes of interest, allowing for calculation of crude effect estimates; the remaining 2 studies (4,5) could not provide original data (length of time since their respective publications was ≥10 years) and thus were excluded from the analysis. The patient population in the study by Kalia et al. (13) represented a subset of the population in the study by Orakzai et al. (10), but both studies were included in the analysis as they reported different outcomes—LLM continuation in the study by Kalia et al. (13) and ASA initiation, increased exercise, and

dietary change in the study by Orakzai et al. (10). A total of 6 eligible studies were included in the analysis.

CHARACTERISTICS OF INCLUDED STUDIES

The 6 studies included were published from 2006 to 2011 and collectively enrolled 11,256 patients (Table 1).

Enrollment and patient population—The method of enrollment varied from self-referrals (15), primary care physician referrals (10,13,15), volunteer active duty men participating in the Prospective Army Coronary Calcium project (14), volunteers in a large longitudinal cohort study (MESA [Multi-Ethnic Study of Atherosclerosis]) (9), and recruitment from a large tertiary care medical center for a clinical trial (8). The mean age across studies ranged from 43 to 65 years. All studies examined populations that were predominantly Caucasian except for the MESA study (9), which was multiethnic in nature.

Method of counseling—The method of counseling patients post-CAC scan varied between studies, and relied on physicians (10,13,15), technologists (10,13), or nurse practitioners (8), or was left up to the patients and their primary care providers (9,14). The MESA study disclosed the results to the subjects and then to the primary care provider only if the patient consented (76% consented) (9). Another study disclosed the CAC score to the participant and primary care provider, but made no specific recommendation on medication or lifestyle changes (14). Some studies emphasized showing the CAC images to the patient while educating them that the presence of CAC identified coronary atherosclerosis and increased heart disease risk (8,10,13,15).

Method of follow-up—Follow-up methods varied between the studies and included mailed (10,13,15) or telephone-based surveys (14) versus in-person follow-up visits (8,9). Among the studies that conducted follow-up with surveys, 1 study verified reported medication use via the electronic health record (14). The mean follow-up time ranged from 1.6 to 6.0 years.

INITIATION OF PREVENTIVE PHARMACOLOGICAL THERAPY

Pooled estimates of the odds of ASA initiation (OR: 2.6; 95% CI: 1.8 to 3.8), LLM initiation (OR: 2.9; 95% CI: 1.9 to 4.4), and BPLM initiation (OR: 1.9; 95% CI: 1.6 to 2.3) were significantly higher in the nonzero CAC group than the zero CAC group (Figure 2). Only unadjusted estimates were available for pooling of nonzero versus zero CAC groups.

Orakzai et al. (10) showed a 2.6× to 3.0× greater odds of ASA initiation in patients with increasing CAC score categories compared with zero CAC score after adjustment for age, sex, diabetes, hypertension, hyperlipidemia, smoking status, and family history of coronary artery disease (CAD). Nasir et al. (9) also showed a trend toward increased relative risk (RR) for the initiation of pharmacological therapy with increasing CAC score categories after adjustment for age, sex, race, MESA site, low-density lipoprotein cholesterol, diabetes, hypertension, systolic blood pressure, body mass index, smoking status, income, education, and health insurance: ASA initiation (RR: 1.3; 95% CI: 1.0 to 1.7), LLM initiation (RR: 1.5;

95% CI: 1.1 to 2.2), and BPLM initiation (RR: 1.6; 95% CI: 1.1 to 2.2) among individuals with CAC >400 versus those with CAC = 0, irrespective of whether they met respective national guidelines recommendation to be on preventive pharmacological therapies at baseline. Taylor et al. (14) reported similar results and found that among patients in whom baseline low-density lipoprotein cholesterol at study entry was not a goal, as per National Cholesterol Education Program Adult Treatment Panel III (19), there was a significantly higher proportion of statin initiation in the nonzero CAC group compared with the zero CAC group (55.0% vs. 31.1%; $p < 0.001$). A study by Uretsky et al. (20) showed that reporting of incidental CAC in inpatients on chest computed tomography performed for noncardiac reasons led to a small increase in aspirin (5%) and statin (4%) initiation at the time of discharge, although these changes were not statistically significant.

CONTINUATION OF PREVENTIVE PHARMACOLOGICAL THERAPY

Pooled estimates of the odds of continuation of preventive pharmacological therapy in the nonzero CAC group compared with the zero CAC group were significantly higher for LLM continuation (OR: 2.3; 95% CI: 1.6 to 3.3) but not for ASA continuation (OR: 1.3; 95% CI: 0.8 to 2.2) or BPLM continuation (OR: 1.4; 95% CI: 0.9 to 2.2), as shown in Figure 3. Although most studies defined continued use of medication based on patient reported use at the end of the study period, Taylor et al. (14) defined continuation as “persistent use” of the medication at each of the 6 annual follow-up visits. This strict definition of continued use, as well as having the longest duration of follow-up, may have attenuated the effect size reported by Taylor et al. (14) on ASA and LLM continuation by CAC groups in comparison to other studies.

In addition, although in the study by Rozanski et al. (8) there was a 44% increase in the odds of ASA continuation among the nonzero CAC group versus the zero CAC group, this comparison was limited by a small sample size with a wide and nonsignificant CI (Figure 3). Among the studies that reported significant unadjusted effect estimates, adjusted effect estimates were not available for nonzero versus zero CAC groups. Nasir et al. (9) reported a trend toward increased RR for continuation of pharmacological therapy with increasing CAC score category after adjustment for age, sex, race, MESA site, low-density lipoprotein cholesterol, diabetes mellitus, hypertension, systolic blood pressure, body mass index, smoking status, income, education, and health insurance: ASA continuation (RR: 1.1; 95% CI: 1.0 to 1.3), LLM continuation (RR: 1.1; 95% CI: 1.0 to 1.2), and BPLM continuation (RR: 1.1; 95% CI: 1.0 to 1.1) for those with CAC >400 versus CAC = 0. Kalia et al. (13) also found an increased OR of LLM continuation with increasing quartiles of CAC score after adjustment for age, sex, diabetes, hypertension, tobacco use, and family history of CAD (OR: 9.3; 95% CI: 4.1 to 20.8 comparing the fourth quartile of CAC score [CAC ≥526] vs. first quartile [CAC = 0 to 30]). Similarly, another study by Kalia et al. (21) showed significantly higher rates of statin compliance in patients with hyperlipidemia with increasing CAC score categories compared with those with zero CAC after a mean follow-up of 4.1 years (statin use in group with CAC ≥400: 59% vs. CAC = 0: 28%). However, this study did not provide any data on baseline statin use and thus was not included in our meta-analysis.

LIFESTYLE INTERVENTIONS

Pooled estimates of the odds of increase in exercise (OR: 1.8; 95% CI: 1.4 to 2.4) and dietary change (OR: 1.9; 95% CI: 1.5 to 2.5) were significantly higher in patients with nonzero CAC score than those with zero CAC score (Figure 4). Schwartz et al. (15) reported adjusted OR for an increase in exercise (OR: 1.8; 95% CI: 1.0 to 3.2) and dietary change (OR: 1.7; 95% CI: 1.1 to 2.8) for the nonzero versus zero CAC group after adjustment for age, sex, body mass index, diabetes, hypertension, dyslipidemia, and family history of heart disease. Orakzai et al. (10) showed a trend for increased odds of lifestyle interventions with increasing CAC scores after adjustment for age, sex, diabetes, hypertension, hyperlipidemia, smoking status, and a family history of CAD: increase in exercise (OR: 2.0; 95% CI: 1.3 to 3.3) and dietary change (OR: 2.7; 95% CI: 1.6 to 4.3) for CAC ≥400 versus CAC = 0. Although the effect of CAC on smoking cessation and weight loss could not be meta-analyzed due to the lack of more than 1 study reporting these outcomes along with their variance in nonzero versus zero CAC groups, individual studies examined these outcomes by CAC score. Rozanski et al. (8) showed no effect of nonzero versus zero CAC on smoking cessation (OR: 0.7; 95% CI: 0.3 to 1.8). Similarly, Wong et al. (4) also reported no effect of nonzero versus zero CAC on smoking cessation (RR: 2.0; $p > 0.05$, no measure of variance reported). Rozanski et al. (8) reported no significant change in weight from baseline to follow-up after CAC testing (change in weight: 1 lb [25th to 75th percentile: −5 to 8 lbs] in CAC = 0 group; −3 lbs [25th to 75th percentile: −10 to 3 lbs] in CAC ≥400 group). Similarly, Wong et al. (4) reported no significant weight loss in nonzero versus zero CAC groups (RR: 1.67; $p > 0.05$, no measure of variance reported), and Sandwell et al. (5) found no significant difference in the proportion of people who lost weight on follow-up among those with a low CAC score (CAC = 0 to 10) versus those with high CAC score (CAC >400).

RISK OF BIAS, HETEROGENEITY, AND SENSITIVITY ANALYSIS

The Newcastle-Ottawa scale for cohort studies was used to examine study quality for each study included in the meta-analysis (Online Table 1). There were only small differences in study quality across studies as assessed by this scale, with most studies of intermediate quality. Statistical heterogeneity was present across studies for many of the outcomes (Figures 2 to 4). The heterogeneity, especially for pharmacological therapy initiation and lifestyle interventions, was mainly in the magnitude of effect, as most studies had the same direction of effect.

To account for statistical heterogeneity, the Der-Simonian and Laird random effects model was used for pooling of results. In addition, sensitivity analysis was performed for outcomes with 3 or more studies by creating pooled estimates of effect after excluding 1 study at a time. Sensitivity analysis showed minimal change in the magnitude of each estimate and no change in the direction of results, supporting the robustness of our pooled results (Online Figure 1).

The potential sources of heterogeneity were variations in sample size (n = 505 to 6,814), study populations (from army physicals to patients from a tertiary care academic medical center), variation in proportion of patients with zero CAC versus nonzero CAC (zero CAC

group size: 12.7% to 77.6% of participants), and whether patients were shown their CAC scan, as well as variation in clinical characteristics of study populations including mean age; sex; and baseline prevalence of hypertension, diabetes, and dyslipidemia (Table 1).

Variation in the mean duration of follow-up (range 3 to 6 years) was another potential source of heterogeneity. The odds for initiation of preventive pharmacological therapy in the nonzero versus the zero CAC group tended to be higher in studies with a longer duration of follow-up, whereas the odds for continuation of preventive pharmacological therapy in nonzero versus zero CAC patients tended to be lower in studies with longer follow-up (Figures 2 and 3). To further evaluate this association of effect with follow-up duration, a meta-regression was performed for the outcomes of interest with at least 4 studies (ASA initiation and LLM continuation). It did not show a statistically significant linear effect of mean duration of follow-up on log odds of ASA initiation or LLM continuation (Online Figure 2).

There was no evidence of publication bias in any of the outcomes with 3 or more studies as assessed using Egger's linear regression test, fail-safe N, and shift of OR after imputation of missing studies (Online Table 2, Online Figure 3).

DISCUSSION

In this systematic review and meta-analysis, we found a 2- to 3-fold increase in the odds for initiation of ASA, LLM, and BPLM among individuals found to have CAC versus those with no CAC. We also found a >2-fold increase in LLM continuation among those with CAC. With respect to lifestyle interventions, we found a 2-fold increase in the odds of implementing favorable exercise or dietary changes when CAC was detected.

The association of calcified coronary plaque with the downstream use of preventive therapies in our study does not, in itself, imply causation. For instance, patients with CAC are more likely to have cardiovascular risk factors and tend to be older. In these patients, risk factors, independently or in combination with CAC findings, may have influenced the use of preventive therapies. Some of the individual studies included in our analysis reported that increased odds of initiation or continuation of preventive therapies persisted following adjustment for baseline risk factors. However, due to limited availability and heterogeneity of the available adjusted estimates, we were unable to pool the adjusted data. Even among the individual studies that reported adjusted estimates, there were differences in the CAC score categories used as well as the covariates used for adjustment. Nevertheless, when examining individual studies, there was a significant increase in preventive interventions with increasing CAC score category, even after adjustment for baseline patient characteristics and cardiovascular risk factors. This effect of coronary plaque detection on behavioral modification and associated increased use of preventive therapies is also consistent with results on studies that used coronary computed tomography angiography for plaque evaluation (22,23). The studies included in meta-analysis did not investigate what proportion of the difference between zero versus nonzero CAC groups is due to stopping of the therapy in individuals with no CAC. However, these studies were performed before the

accumulation of evidence on zero CAC as a negative CV risk factor and thus, it is less likely that in these studies therapy was stopped directly as a result of the zero CAC score.

Our study also showed that the presence of CAC increased the odds of exercise and dietary change. However, the individual studies included in the meta-analysis did not find a subsequent effect of presence versus absence of CAC on weight loss. Rozanski et al. (8) reported a significant increase in the odds of exercising in the nonzero CAC group but reported no significant change in weight from baseline to follow-up at 4 years after CAC scan (change in weight: 1 lb [25th to 75th percentile: −5 to 8 lbs]; in CAC = 0 group, −3 lbs [25th to 75th percentile: −10 to 3 lbs] in CAC ≥400 group). A large study by Kalia et al. (21) that investigated the motivational effects of CAC scores on weight loss with a follow-up period of 4.1 ± 3.2 years after an initial CAC scan reported a significant increase in the proportion of patients with measurable weight loss in groups with higher CAC scores compared with those with zero CAC. These findings suggest that knowledge of CAC scores could promote behavioral modifications that result in weight loss; however, more studies are needed to confirm this effect.

An area of concern in advocating the use of CAC scanning among asymptomatic patients is the risk of downstream testing and increases in health care costs. In an RCT of CAC scan versus no scan, Rozanski et al. (8) found no increased risk of downstream stress testing (34.6% vs. 33.9%; p = 0.7), cardiac catheterization (3.3% vs. 2.9%; p = 0.7), coronary revascularization (2.3% vs. 1.8%; p = 0.5), or procedure costs ($904 vs. $712; p = 0.6) in the CAC scan versus no-scan groups after 4 years of follow-up. Even when considering the potential cost of downstream testing for incidental extracardiac findings on CAC scans, a Markov analysis from MESA showed robust cost-effectiveness of CAC testing in intermediate-risk patients compared with established risk-assessment guidelines (2,24).

STUDY LIMITATIONS

This is a meta-analysis of observational studies and, as such, it has inherent limitations. First, the pooled estimates of effect for nonzero versus zero CAC were unadjusted. Although the adjusted estimates of effect for CAC score categories in individual studies showed an increase in the odds of initiation or continuation of preventive therapies with increasing CAC score category, there remains the potential for residual or unmeasured confounding. Second, although our study did not examine unpublished data, we did not find any evidence of publication bias using Egger’s linear regression test or fail-safe N. Although there was a small number of studies in each outcome, imputation of “negative” studies did not change the meaning or direction of our results. Third, there is potential for reporting bias due to the use of surveys for follow-up in some of the included studies. Despite statistical heterogeneity across studies and the risk of bias of individual studies, sensitivity analyses indicated the robustness of our results.

CONCLUSIONS

In summary, this systematic review and meta-analysis suggests that the identification of coronary atherosclerosis by coronary calcium scanning significantly increases the likelihood

of initiation or continuation of pharmacological and lifestyle therapies for prevention of cardiovascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

For a description of the search strategy as well as supplemental tables and figures, please see the online version of this paper.

ABBREVIATIONS AND ACRONYMS

ASA	aspirin
BPLM	blood pressure lowering medication
CAC	coronary artery calcium
CAD	coronary artery disease
CI	confidence interval
LLM	lipid lowering medication
OR	odds ratio
RCT	randomized controlled trial
RR	relative risk

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE

Identification of coronary atherosclerosis, a calcium score >0, significantly increases the odds of initiation or continuation of pharmacological and lifestyle therapies for prevention of cardiovascular disease. Coronary calcium score, obtained via a simple low-radiation noncontrast computed tomographic scan, could be considered in patients who are eligible for preventive pharmacological therapies, if knowledge of CAC >0 would be used to intensify preventive therapies. Such intensification of therapy may be most relevant among patients who prefer to avoid pharmacotherapy if CAC score = 0.

TRANSLATIONAL OUTLOOK

Additional studies are needed in how to best integrate the results provided by CAC testing with other clinical data to inform individuals and providers regarding their risk in a method that will promote effective pharmacological and lifestyle changes for the reduction of cardiovascular disease.

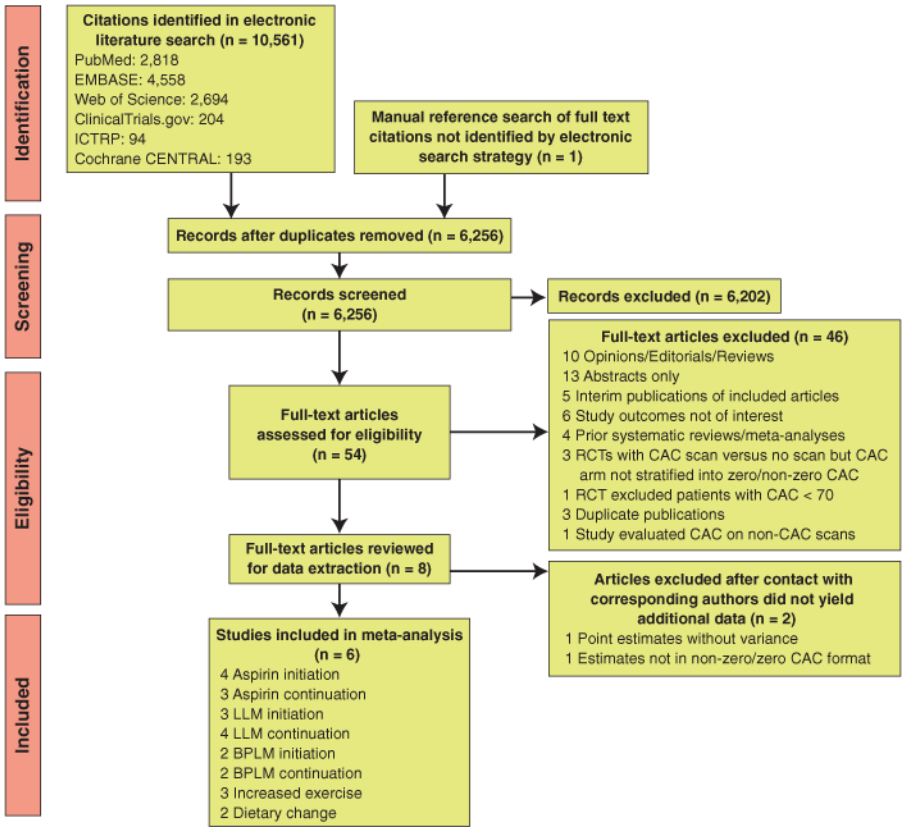

FIGURE 1.

PRISMA Flow Diagram

BPLM = blood pressure lowering medication; CAC = coronary artery calcium; CENTRAL = Cochrane central register of controlled trials; EMBASE = Excerpta Medica database; ICTRP = International Clinical Trials Registry Platform; LLM = lipid-lowering medication; PRISMA = preferred reporting items for systematic reviews and meta-analysis; RCT = randomized controlled trial.

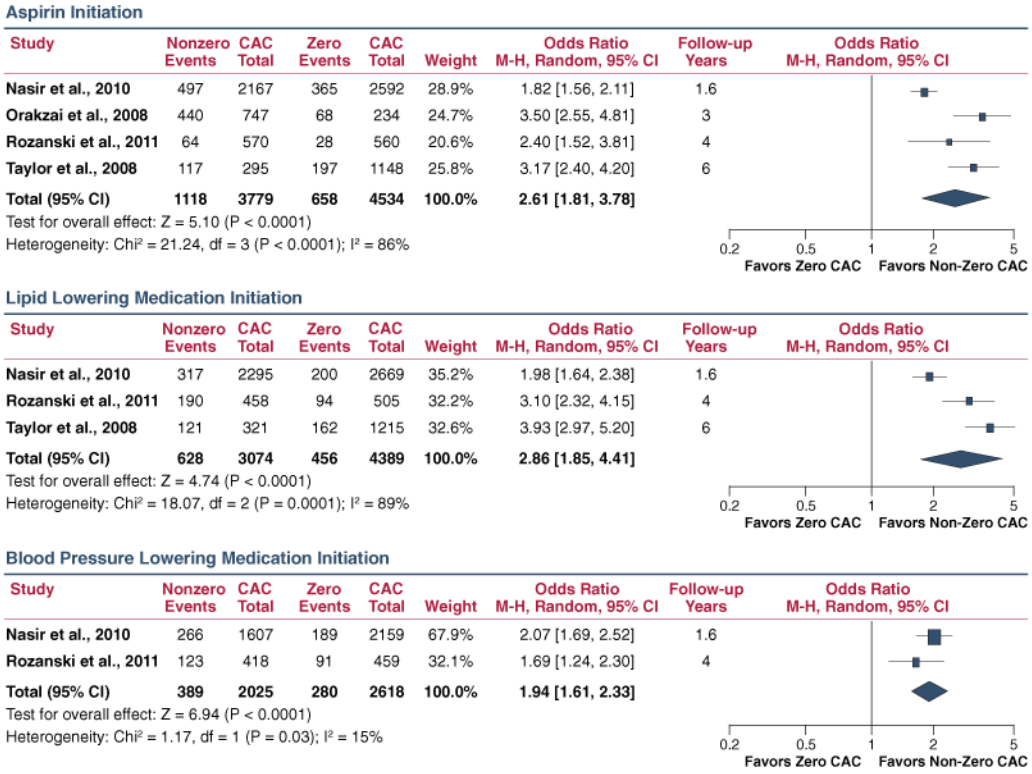

FIGURE 2.

Forest Plots and Pooled Odds Ratios for Initiation of Pharmacological Preventive Therapies

CAC = coronary artery calcium; CI = confidence interval; M-H = Mantel-Haenszel.

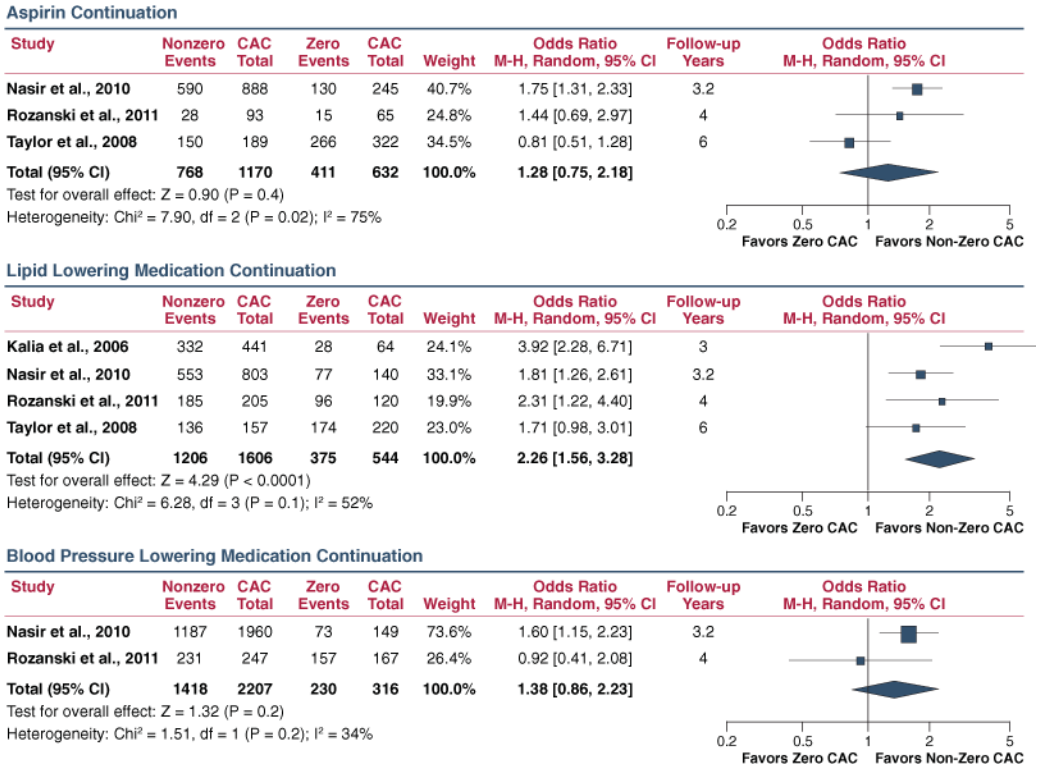

FIGURE 3.

Forest Plots and Pooled Odds Ratios for Continuation of Pharmacological Preventive Therapies

Abbreviations as in Figure 2.

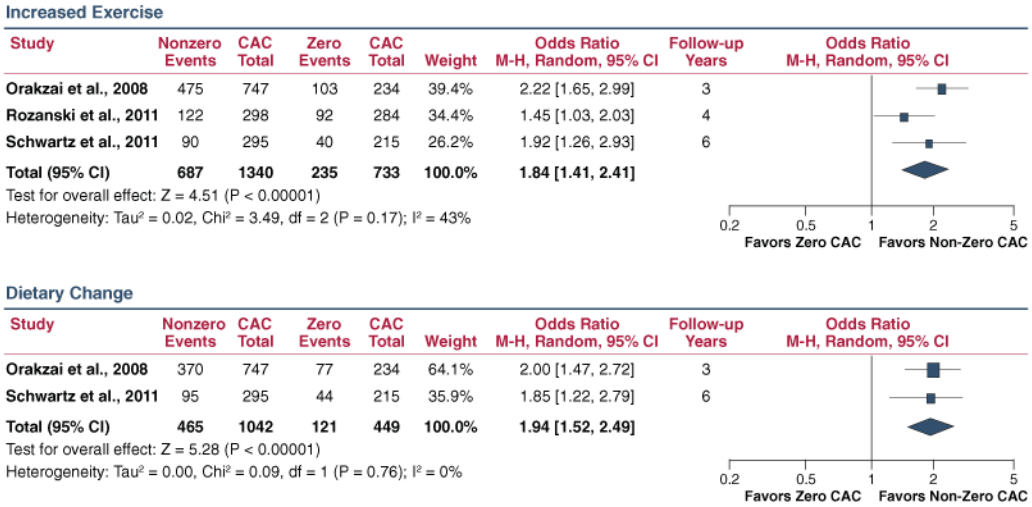

FIGURE 4.

Forest Plots and Pooled Odds Ratios for Lifestyle Preventive Therapies

Abbreviations as in Figure 2.

TABLE 1

Baseline Characteristics of the Studies Included in the Meta-Analysis

First Author (Ref. #), Year	N	Mean Follow-Up, yrs	Patient Enrollment	Referral Reason	Zero CAC, %	Patients Shown CAC Scan	Mean Age, yrs	Women, %	DM/HTN/HLD, %	Baseline Medication Use: ASA/LLM/ BPLM, %
Kalia et al. (13), 2006	505	3	Physician referral	CAD screening	12.7	Yes	60.8	18.0	7.0/43.5/–	–/51.8/–
Orakzai et al. (10), 2008	981	3	Physician referral	CAD screening	24.0	Yes	60.0	22.0	–/–/–	–/–/–
Taylor et al. (14), 2008	1,640	6	Active duty army men	Research	77.6	No	42.9	0.0	0.8/30.8/–	12.0/5.7/–
Nasir et al. (9), 2010	6,814	1.6 (Initiation) 3.2 (Continuation)	Community recruitment	Research	50.0	No	62.0	52.6	14.4/44.8/–	25.3/16.3/37.3
Rozanski et al. (8), 2011	1,311	4	Tertiary care hospital	Research	48.1	Yes	58.6	47.5	8.1/57.4/78.6	12.2/25.4/32.3
Schwartz et al. (15), 2011	510	6	Physician or self-referral	CAD screening	42.2	Yes	64.5	38.2	2.8/43.9/35.1	–/–/–

All studies had a prospective cohort study design except Rozanski et al. (8), in which we extracted data from CAC scan arm of a randomized controlled trial. All studies enrolled asymptomatic patients without clinical cardiovascular disease.

ASA = aspirin; BPLM = blood pressure–lowering medication; CAC = coronary artery calcium; CAD = coronary artery disease; DM = diabetes mellitus; HLD = hyperlipidemia; HTN = hypertension; LLM = lipid lowering medication; Ref = reference number.