Meta-Analysis of the Effects of Lifestyle Modifications on Coronary and Carotid Atherosclerotic Burden

Sunny Jhamnani, MD[a,b,*], Dhavalkumar Patel, MD[a,c], Layla Heimlich, MSILS[a], Fred King, MSLS[a], Brian Walitt, MD[a], and Joseph Lindsay, MD[a]

Lifestyle modifications are the crux of atherosclerotic disease management. The goal of this study was to determine the effectiveness of diet and exercise in decreasing coronary and carotid atherosclerotic burden. Randomized controlled trials examining the effects of intensive lifestyle measures on atherosclerotic progression in coronary and carotid arteries as measured by baseline and follow-up quantitative coronary angiogram and ultrasonographic carotid intimal-medial thickness (CIMT), respectively, were included. Studies were excluded if the intervention additionally included a medication. MEDLINE, EMBASE, CINAHL, Cochrane Controlled Trials Registers, reports, and abstracts from major cardiology meetings were searched by 2 researchers independently and verified by the primary investigator. Standardized mean difference (SMD) with 95% confidence intervals (CIs) was calculated using random-effects model. Publication bias and heterogeneity were assessed. Fourteen trials were included. Seven used quantitative coronary angiogram, and 7 used CIMT; 1,343 lesions in 340 patients in the coronary group and 919 patients in the carotid group were analyzed. Overall, lifestyle modifications were associated with a decrease in coronary atherosclerotic burden in percent stenosis by −0.34 (95% CI −0.48 to −0.21) SMD, with no significant publication bias and heterogeneity ($p = 0.21$, $I^2 = 28.25$). Similarly, in the carotids, there was a decrease in the CIMT, in millimeter, by −0.21 (95% CI −0.36 to −0.05) SMD and by −0.13 (95% CI −0.25 to −0.02) SMD, before and after accounting for publication bias and heterogeneity ($p = 0.13$, $I^2 = 39.91$; $p = 0.54$, $I^2 = 0$), respectively. In conclusion, these results suggest that intensive lifestyle modifications are associated with a decrease in coronary and carotid atherosclerotic burden. **(Am J Cardiol 2015;115:268−275)**

Diet and exercise are the cornerstones in atherosclerotic disease management. Guidelines for secondary prevention of atherosclerotic disease from committees like the American Heart Association/American College of Cardiology Foundation[1] and the European Society of Cardiology[2] include dietary modifications and regular exercise. However, patient adherence to this is spotty at best. Several studies have shown that dietary modifications and regular exercise reduce cardiovascular events, mortality, and morbidity.[3−5] Demonstration that these lifestyle changes, in addition to reducing clinical events, reduce the likelihood of the progression of atherosclerotic disease should strengthen the argument for adherence. However, to date, randomized controlled trials (RCTs) designed to establish the beneficial effects of these measures on atherosclerotic disease progression have not been convincing. Small sample sizes in these trials appear to have led conflicting results. As an attempt to overcome these shortcomings, this study was undertaken to critically examine the effectiveness of intensive lifestyle modifications on atherosclerotic disease progression by a systematic review and quantify them using meta-analytical tools. We decided to focus our study on the coronary and carotid arteries as they are known to hold important prognostic value for cardiac cerebrovascular events and overall morbidity and mortality.

Methods

Only RCTs comparing the efficacy of lifestyle measures, that is, diet and/or exercise versus usual care, were identified by a systematic search. Two independent researchers searched MEDLINE, EMBASE, CINAHL, and Cochrane Controlled Trials Register for eligible studies. Studies from 1946 (MEDLINE) or 1947 (EMBASE) or earliest time frame available (CINAHL, Cochrane Controlled Trials Register) to third week of March 2014 were included. Search terms included: “diet,” “exercise,” “lifestyle,” “risk factors,” “health behavior,” “food habits,” “exercise therapy,” “lifestyle change,” “behavior modification,” “risk factor reduction,” “risk factor modification,” “arteriosclerosis,” “carotid artery diseases,” “carotid artery thrombosis,” “coronary disease,” “angiography,” “carotid intima thickness,” “plaque thickness,” “gensini,” “stenosis,” “coronary artery,” “carotid artery,” and “atherosclerotic burden.” Abstracts and unpublished studies from major cardiology meetings were reviewed. Lastly, references of relevant peer-reviewed publications were evaluated. PRISMA guidelines were

[a]MedStar Georgetown University Hospital/Washington Hospital Center, MedStar Washington Hospital Center, Washington, District of Columbia; [b]Division of Cardiology, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut; and [c]Division of Cardiology, Department of Medicine, Virginia Commonwealth University Medical Center, Richmond, Virginia. Manuscript received September 1, 2014; revised manuscript received and accepted October 17, 2014.

See page 274 for disclosure information.

*Corresponding author: Tel: (203) 785-6484; fax: (203) 785-6506.
E-mail address: sunny.jhamnani@yale.edu (S. Jhamnani).

0002-9149/14/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2014.10.035

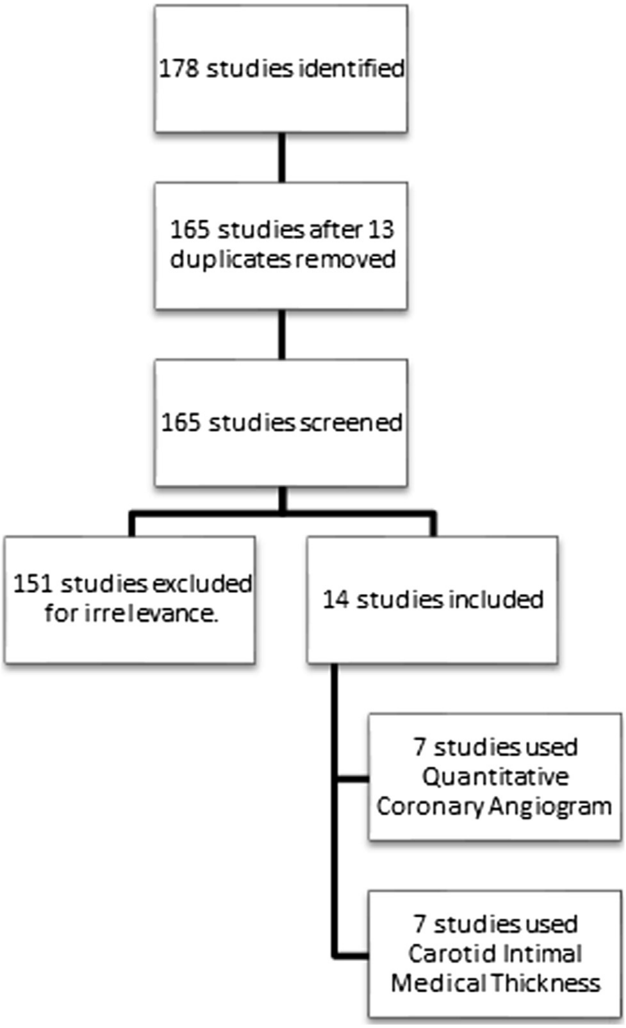

Figure 1. Flow diagram of studies identified and included.

used.[6] Institutional review board approval was not required because of the nature of the study.

We included only studies that (1) were prospective controlled trials, in which patients were randomized to diet and/or exercise alterations or usual care; (2) in the methods, clearly reported subject selection process, interventions, and follow-up; (3) included baseline and follow-up data on quantitative coronary angiograms (QCAs) or carotid intimal-medial thickness (CIMT) or both. Usual care in the trials entailed patients being left at their own discretion or their physician's advice and not being enrolled into an active diet and/or exercise program that the trial offered. Studies were excluded if they were not RCTs or if subjects received a medication along with diet and/or exercise as their intervention. Investigators were contacted to obtain additional data or verify data. Studies meeting all inclusion and no exclusion criteria were reviewed. Two individual investigators (SJ and DP) independently used the Jadad's system to assess for the quality of the studies.[7] Discrepancies were resolved by consensus.

Relevant data from the RCTs including year of study, characteristics of subjects, details of intervention, and imaging procedures were collected by 1 investigator and verified by another. Total number of patients and coronary lesions in intervention and control groups were reported. Data regarding QCA and CIMT were collected at baseline and follow-up. When available, clinical outcomes were recorded to complement the review; although if unavailable, they were not actively sought as this was not the theme of this study.

Studies were grouped based on the imaging tool used, that is, QCA and CIMT. Outcome of interest was change in QCA and CIMT. Follow-up imaging was conducted after the intervention ended. Compliance to the intervention was recorded as reported in the individual studies. In our meta-analysis, we report overall changes by QCA and CIMT in percent stenosis and millimeter, respectively, with reference to the standardized mean difference (SMD).

Comprehensive Meta-analysis software (version 2, 2005; Biostat, Englewood, New Jersey) was used for analysis. To assess publication bias, funnel plots were drawn and assessed for asymmetry. Statistical heterogeneity was also calculated, and $p < 0.1$ was considered as statistically significant heterogeneity. Fixed- and random-effect models were used to determine overall effect of lifestyle modification.

Results

Our initial search provided us with 178 citations (EMBASE: 16, MEDLINE: 138; CINAHL: 24, Cochrane: 0). After removing duplicate and irrelevant citations, there were 14 studies that met the inclusion and exclusion criteria (Figure 1): 7[8−14] used QCA, whereas 7[15−21] used CIMT. Table 1 outlines their characteristics. Of the QCA studies, 5 used diet and exercise as the intervention[8,10,12−14] and 2 diet only.[9,11] Meanwhile, in the CIMT studies, 3 examined both diet and exercise as the intervention,[16,17,19] 3 included only exercise,[15,20,21] and 1 diet only.[18] In studies using diet and exercise as their intervention,[8,10,12−14,16,17,19] an equal emphasis was laid on diet and exercise. The interval between baseline and follow-up imaging ranged from 6 months to 6.5 years, with a mean of 2.5 and 3 years for QCA and CIMT studies, respectively. Duration of intervention was similar to the interval between baseline and follow-up imaging in all studies expect 1,[16] in which the participants had lifestyle modifications for 2.7 years before the baseline CIMT study. Thus, duration of intervention ranged from 3 months to 9 years, with a mean of 2.5 and 3.4 years for QCA and CIMT studies, respectively. A total of 1,343 lesions in 340 patients were followed by QCA and 919 patients, with CIMT. Table 2 compares baseline and follow-up QCA and CIMT measurements in both groups.

Jadad's scoring was used to evaluate for the quality of the studies (Table 1). Because of the nature of the imaging techniques used, blinding of study participants and physicians was not always possible. For this reason, all studies lost 2 points. Thus, overall Jadad scores were low. It is, however, noteworthy that image acquisition and/or analysis of reading was performed in a blinded fashion in 11[8−10,12−15,17−19,21] reports. In addition to this, details on study criteria, changes in weight, body mass index, lipids, blood pressure, medications, and smoking patterns were sought and reported in Supplementary Table 1. All studies apart from 1 QCA[9] and CIMT[17] study were associated with decreases in