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The Prognostic Importance of Weight Loss in Coronary Artery Disease: A Systematic Review and Meta-analysis

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Abstract

Objective: To assess the prognostic impact of weight loss on clinical outcomes in patients with coronary artery disease (CAD).

Methods: We performed a systematic review and meta-analysis of the prognostic effects of weight loss in patients with CAD on a composite outcome of all-cause mortality, cardiovascular mortality, and major adverse cardiac events considering studies published between January 1, 1964, and August 8, 2013. We considered weight loss "intentional" when it occurred in the presence of programmed therapeutic lifestyle changes and "observational" when no such intervention was specified.

Results: We searched 1218 abstracts, of which 12 studies with 14 cohorts met the inclusion criteria. A total of 35,335 patients (mean age, 64 years; 72% male; body mass index [BMI], 30; 3.2 years of follow-up) were included. Overall, weight loss was associated with a greater risk of the composite outcome (relative risk [RR], 1.30; 95% CI, 1.00-1.69; P=.05). However, heterogeneity was high (I^2=90%) and was substantially explained by weight loss intentionality. Presumed intentional weight loss (4 cohorts) was associated with improved outcomes (RR, 0.67; 95% CI, 0.56-0.80; P<.001), whereas observational weight loss (10 cohorts) was associated with worsened outcomes (RR, 1.62; 95% CI, 1.26-2.08; P<.001; interaction P<.001).

Conclusion: Whereas observational weight loss is associated with increased adverse cardiovascular events, intentional weight loss is associated with lower clinical events. These results suggest that the underlying mechanism of weight loss (ie, intentional or unintentional) affects its impact on subsequent risk in persons with known CAD.

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Obesity is an independent risk factor for coronary artery disease (CAD).[1,2] Consequently, an initial 10% body weight loss is recommended in American Heart Association and American College of Cardiology practice guidelines for patients with CAD who are overweight or obese, with the goal of achieving a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) less than 25.[3] These recommendations are primarily based on the consistent beneficial effects of weight loss on intermediate-risk markers such as hypertension,[4] diabetes control,[5] metabolic syndrome,[6] and blood lipid levels.[7] It is generally thought that such improvements will lead to improved long-term outcomes.[8,9]

However, weight loss is not uniformly associated with improved long-term outcomes. Specifically, it is well-established that among general adult patients, weight loss can be an important risk marker for the subsequent development of cancer, diabetes, or other life-threatening systemic illness,[10-12] particularly when the weight loss is unintentional. Even patients with intentional weight loss do not always have improved long-term cardiovascular outcomes.[13,14] In addition, the recent Action for Health Diabetes (Look AHEAD) study found that patients with diabetes randomized to receive a lifestyle intervention designed for purposeful weight loss did not have improved long-term outcomes.[15]

To further complicate the issue, several studies have suggested that in patients with

CAD, weight loss seems to be associated with worse long-term survival.[16,17] Reasons for this association are unclear but may be rooted in the obesity paradox, a finding in which obese patients with CAD have better long-term survival compared with their normal-weight counterparts.[18] Consequently, this set of controversial findings casts doubt on current clinical practice guidelines and leaves clinicians with substantial uncertainty regarding the value of weight loss in patients with CAD.

We undertook a systematic review and meta-analysis to summarize the literature, explore possible reasons for these conflicting results, and guide future research on the long-term effects of weight loss on prognosis in patients with CAD. We specifically hypothesized that weight-loss intentionality might be an important discriminator between studies that show harmful vs beneficial effects of weight loss in patients with CAD.

METHODS

Data Sources and Searches

We performed a literature search for all articles that included (1) patients with clinical CAD, (2) measures of achieved weight loss/change, (3) comparison with a non—weight-loss group, and (4) long-term clinical outcomes. We identified potentially relevant articles through a search of PubMed and EMBASE between January 1, 1964, and August 8, 2013, using a search strategy developed with the assistance of a medical librarian (Supplemental Appendix 1; available online at http://www.mayoclinicproceedings.org). Web of Science was searched (March 1, 2008, to March 1, 2013) for meeting abstracts from cardiology, endocrinology, and obesity society meetings. Bibliographies of selected articles were reviewed for additional potentially relevant articles. Because no individual patient data were analyzed, ethical approval was not required.

Study Selection

In mixed populations, we required that greater than 50% of the cohort have documented CAD and the remainder be at high risk with another form of vascular disease or diabetes. If the population was less than 50% CAD, we included studies only if the CAD subgroup outcomes were reported and analyzed separately. We required that each analysis directly assess the impact of achieved weight loss on outcomes as well. We also required that the study account for weight change due to medications (such as a sibutramine) present in the original randomized trial. We included studies regardless of the study sample's baseline BMI or proportion classified as overweight or obese.

We excluded studies evaluating children, cardiac cachexia, heart failure not directly preceded by a CAD diagnosis or event, bariatric surgery, and isolated diabetes, isolated peripheral vascular disease, or isolated cerebrovascular disease in which CAD was not a comorbidity. We excluded all reviews, commentaries, letters to the editor, and non-English abstracts.

Data Extraction and Quality Assessment

Two of us (Q.R.P., J.P.R.-E.) independently reviewed all the titles, abstracts, and selected full-text articles. Data abstraction was performed by Q.R.P. and verification by J.P.R.-E. All disagreements were resolved by F.L.-J. When not reported directly, data for meta-analysis were estimated from reported outcomes. Missing data were obtained from study authors as needed.

Quality assessment was performed in duplicate (Q.R.P. and J.P.R.-E.) and used the Newcastle-Ottawa quality assessment scale for cohort studies.[19] Although some studies were originally randomized controlled trials testing pharmacologic interventions, the weight-loss studies were uniformly secondary or ad hoc analyses and as such were treated as cohorts for the purpose of quality assessment. We noted which studies reported evaluating, controlling, or adjusting for the effects of age, smoking status, sex, and preexisting cancer diagnosis or cancer development on their outcomes. We considered secondary analyses of randomized controlled trials and cardiac rehabilitation studies to be at risk for selection bias.

Data Synthesis and Analysis

We predefined a 5% body weight loss as the primary predictor. Because not all studies used this definition, we further classified studies into low, medium, and high weight loss, with weight loss definitions of less than 2.5%, 2.5% to 4.9%, and 5% or greater body weight loss, respectively. We considered a 5-kg threshold to be approximately equivalent to a 5% body weight change.