



Effect of weight loss induced by energy restriction on measures of arterial compliance: A systematic review and meta-analysis



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ABSTRACT

Aim: To conduct a systematic review and meta-analysis of clinical trials involving adults, to determine the effect of weight loss induced by energy restriction with or without exercise, anti-obesity drugs or bariatric surgery on measures of arterial stiffness and compliance.

Methods: A systematic search of Pubmed, EMBASE, MEDLINE and the Cochrane Library was conducted to find intervention trials (randomised/non-randomised) that aimed to achieve weight loss and included the following outcome measures: cardio-ankle vascular index (CAVI), direct measures of area/diameter related to pressure change (including β -stiffness index, brachial or carotid artery compliance, aortic, carotid or brachial artery distensibility and strain), measures derived from peripheral pulse wave analysis (including augmentation index, augmentation pressure, distal oscillatory, proximal capacitive and systemic compliance) and pulse pressure. Data were analysed using Comprehensive Meta Analysis V2 using random effects analysis. Standardised mean difference (SMD) is reported with negative values indicating an improvement.

Results: A total of 43 studies, involving 4231 participants, were included in the meta-analysis. Mean weight loss was approximately 11% of initial body weight. Weight loss improved CAVI (SMD -0.48 ; $p = 0.04$), β -stiffness index (SMD $= -0.98$; $p = 0.001$), arterial compliance (SMD $= -0.61$; $p = 0.0001$) and distensibility (SMD -1.10 ; $p = 0.005$), distal oscillatory compliance (SMD $= -0.41$; $p = 0.03$), proximal capacitive compliance (SMD -0.66 ; $p = 0.009$), systemic arterial compliance (SMD -0.71 ; $p = 0.003$) and reflection time (SMD -0.51 ; $p = 0.001$). Augmentation index, strain, augmentation pressure and pulse pressure were not significantly changed with weight loss.

Conclusion: Weight loss induced by energy restriction improves some measures of arterial compliance and stiffness.

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1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide [1]. Globally the prevalence of obesity has more than doubled since 1980 [2]. Obesity increases the risk of CVD by approximately two fold [3]. Longer exposure to adiposity in adulthood has been shown to have a cumulative adverse effect on

cardiovascular risk factors in later life but individuals that lose weight in adulthood have a more favourable cardiovascular risk profile than those that have never lost weight, even if weight loss is not maintained [4]. Bariatric surgery reduces cardiovascular events [5]. However, moderate weight loss has not been shown to reduce cardiovascular endpoints in randomised controlled trials, despite an improvement in cardiovascular risk factors [6,7]. Arterial stiffening is a risk factor for CVD [8,9] and overweight and obesity is associated with increased stiffening [10] and a reduction in arterial compliance [11,12].

Arterial stiffness is defined as a reduction in the capacity of an artery to expand and contract in response to a given pressure change and can be measured in many different ways [13]. Compliance, distensibility and strain are direct measures of arterial area/diameter related to a given pressure change [14]. In a stiff artery change in the area/diameter per pressure change is reduced.

Abbreviations: BMI, Body Mass Index; CAVI, Cardio-ankle Vascular Index; CKD, Chronic Kidney Disease; CVD, Cardiovascular Disease; GB, Gastric Banding; GBP, Gastric Bypass; PWV, Pulse Wave Velocity; SMD, Standardised Mean Difference; SOS, Swedish Obesity Study; VBG, Vertical Banded Gastroplasty.

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The consequence of increased stiffness is an increase in the propagation of the pressure wave through the vasculature. This can be measured by pulse wave velocity (PWV) and pulse wave analysis parameters including augmentation index. In healthy arteries, the speed of the forward pressure wave is low and therefore the reflected wave arrives back at the aortic root during diastole. However, when arteries stiffen the speed of the forward pressure wave increases and the reflected wave arrives back at the central arteries earlier adding to the forward wave and augmenting systolic pressure [15].

Reduced arterial compliance measured by distensibility is associated with increased risk of CVD and all-cause mortality [16]. In addition, increased arterial stiffness determined by augmentation index and PWV increases the risk of a cardiovascular event and total mortality [8,9].

We have previously shown in a meta-analysis of 20 studies that modest weight loss is associated with an improvement in PWV, the gold standard for determining arterial stiffness [17]. However, often other indices of arterial stiffness are measured and there has been no quantitative assessment of the effect of weight loss on these measures [12]. The aim is to conduct a meta-analysis of intervention trials (with or without a no weight loss control group) to determine the effect of weight loss achieved with an energy restricted diet with or without exercise, anti-obesity drugs or bariatric surgery on cardio-ankle vascular index (CAVI), direct measures of area/diameter related to pressure change (including β -stiffness index, brachial or carotid artery compliance, aortic, carotid or brachial artery distensibility and strain), measures derived from peripheral pulse wave analysis (including augmentation index, augmentation pressure, distal oscillatory, proximal capacitive and systemic compliance) and pulse pressure.

2. Methods

2.1. Search strategy

A systematic literature search was conducted, from the index date of each database through to March 2014 using PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>, since 1966), EMBASE (<http://embase.com>, since 1947), MEDLINE (<http://www.nlm.nih.gov/bsd/pmresources.html>, since 1946) and the Cochrane Library (<http://www.thecochranelibrary.com>, since 1951) to identify all of the intervention trials that have investigated the effect of weight loss on measures of arterial compliance and arterial stiffness. See Table S1 for the search terms that were used. Reference lists of the identified publications were searched for additional relevant articles. Authors were not contacted to identify additional studies. The search was restricted to studies published in English involving humans. The search was conducted by two independent researchers (KSP and NL).

2.2. Selection criteria

The search strategy was developed to identify all of the intervention trials that had investigated the effect of weight loss achieved by an energy restricted diet with or without exercise, anti-obesity drugs or bariatric surgery on arterial compliance or arterial stiffness. We have recently published a meta-analysis on the effect of weight loss on PWV [17] and so trials reporting on PWV will not be reported on in this paper despite being included in the systematic review. Intervention trials investigating the effect of weight loss achieved with an energy restricted diet with or without exercise, anti-obesity drugs or bariatric surgery on measures of arterial compliance and stiffness in adults 18 years or older were included. Studies identified by the search strategy were screened

by the title and abstract and excluded if they were not relevant to the research question. The full text article of studies that were not excluded based on the title or abstract were obtained and assessed against the inclusion criteria. Studies were excluded if weight loss was primarily achieved with physical activity or weight or body mass index (BMI) was not reported pre or post intervention. There was no limit on the duration of the intervention; where measurements were provided for a number of time points during the intervention period, data from the greatest time since baseline were used.

2.3. Outcomes

Outcomes included were CAVI, direct measures of area/diameter related to pressure change (including β -stiffness index, brachial or carotid artery compliance, aortic, carotid or brachial artery distensibility and strain), measures derived from peripheral pulse wave analysis (including augmentation index, augmentation pressure, distal oscillatory, proximal capacitive and systemic compliance) and pulse pressure. A description of each of these measurements is included in the online-only Data Supplement.

2.4. Data extraction

The data were extracted for each identified publication and entered by two independent researchers (KSP and NL) and cross-verified. Authors were contacted for additional information not reported in the publication. The demographic characteristics of the study population and details of the study protocol and methodology were also extracted from the included studies. For studies with multiple treatment arms, treatments that did not meet the inclusion criteria were excluded.

2.5. Critical appraisal

The Newcastle-Ottawa Scale [18] was used to assess the quality of the studies. Briefly studies are given a score out of 9 based on selection of the study groups, comparability of the groups, and ascertainment of the outcome.

2.6. Statistical analysis

Statistical analysis was conducted using Comprehensive Meta Analysis V2 (Eaglewood, NJ 07631). Data is reported as standardised mean difference (SMD) and 95% confidence intervals. For all group comparisons significance was set at $p < 0.05$. Most studies did not have a control group and therefore the change from baseline was used. When there was a control group this was used for comparison. Treatment effects were pooled when a study had two treatment arms or contributed data for more than one measure included in a category. A study could contribute data for more than one measurement in different categories. Treatment effects were determined by calculating the SMD with negative values indicating improvement in the outcome measurement for consistency i.e. if a positive change in the outcome measure indicates improvement the values were inverted so that a negative SMD was reflective of improvement. Random effects analysis was used. Heterogeneity between studies was examined by chi-square tests for significance, and measured inconsistency (I^2) $>50\%$ indicated substantial heterogeneity [19]. To explore the sources of heterogeneity subgroup analysis was performed with $p < 0.05$ indicating a significant between group difference. For continuous study characteristics (e.g. age, weight loss, sample size, study duration and baseline arterial stiffness/compliance measure) the median value for each arterial stiffness/compliance measurement category was used as the cut

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