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Evidence for contemporary arterial stiffening in obese children and adolescents using pulse wave velocity: A systematic review and meta-analysis

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ABSTRACT

Introduction: Pulse wave velocity (PWV) and augmentation index (AI) may provide information on future cardiovascular risk. Reports are conflicting on whether obese children show evidence of raised PWV and AI.

Methods: Systematic review and meta-analysis of published studies using EMBASE, Web-of-Science and PUBMED databases for studies reporting PWV and AI in obese versus non-obese controls(<age 18 years). Studies were pooled in meta-analyses to generate weighted mean differences (WMD) using random effects methodology. Analyses were repeated by method, quality grade and anatomical region.

Results: 383 studies were found in initial searches and 81 were assessed in detail; 14 studies (6677 total participants, 1120 obese and 5557 non-obese) were suitable for meta-analysis for PWV, and 5 studies (728 participants obese and 317 non-obese) for AI. Across all studies, obese children had higher PWV than non-obese children (WMD 0.45(95% confidence interval 0.10 to 0.81 ms^{-1})). This difference was not significant when only studies with low/medium risk of bias were included. Obese subjects had higher PWV measured directly at the carotid (WMD 0.51 (0.35–0.67 ms^{-1})) and aorta (WMD 1.33 (0.36–2.31)). No significant differences were found for AI. Heterogeneity was high in all analyses(I^2 > 90% in PWV and AI meta-analyses).

Conclusion: There is moderate evidence that obese children have increased arterial stiffening, especially in central arteries. This supports concerns about future CVD risk in obese children. Developing effective obesity interventions must remain a health priority.

1. Introduction

Rising child and adolescent obesity internationally [1–5] has raised concerns regarding high future cardiovascular disease (CVD) risk in this generation; yet prediction of adult outcomes for contemporary obese children is challenging [6,7]. As pathological arterial processes begin in childhood and adolescence [8,9], one approach is to search for demonstrable, contemporaneous evidence of arterial stiffness [10,11]. Two potentially useful proxies for arterial stiffness are pulse wave velocity (PWV) and the Augmentation Index (AI) [12–14]. PWV is a derived gradient velocity calculated from non-invasive measures of pulse waveforms at two separate peripheral loci (within an artery or between arteries e.g. carotid and radial) and the distance between them (with greater PWV a proxy for greater arterial stiffness). AI is derived from pulse waveforms at an arterial site, calculated by the difference in the augmented and forward waves in an arterial waveform, divided by the overall pulse pressure of the waveform (with greater AI a proxy of greater arterial stiffening). PWV in particular has been shown to be reliably reproducible [14,15] and to predict future CVD mortality in adults [16,17] as well as degree of arterial plaques [18], with evidence poorer for AI [19,20].

The evidence that obese children have higher arterial stiffness is inconsistent. Studies investigating differences in PWV and AI in obese and healthy weight children have reported conflicting findings [11,21]. We therefore conducted a systematic review and meta-analysis to evaluate associations between obesity and PWV and AI in children and adolescents.

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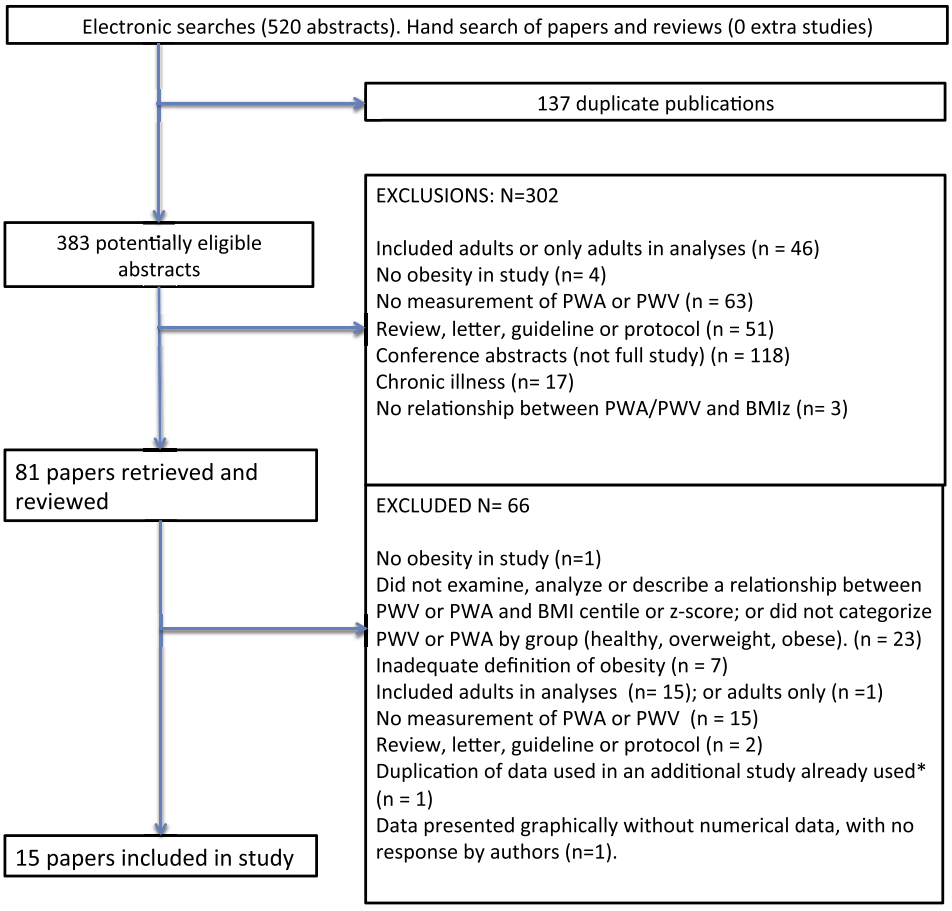

Fig. 1. Summary of search results.

2. Methods

2.1. Data sources and search strategy

A systematic search using PRISMA guidelines was performed to identify studies that compared PWV and/or AI in both obese and non-obese children (<age 18). We searched PubMed, Embase and Web of Science electronic databases in September 2014 (see Supplementary table one for search terms). Inclusion criteria were: 1) studies measuring PWV and/or AI at any site; 2) participants < age 18 years; 3) use of accepted criteria to define childhood obesity. Exclusion criteria were: 1) genetic, syndromic or endocrine causes of obesity; 2) Studies of participants with chronic illness which might independently affect arterial stiffness 3) Studies using self-reported BMI.

2.2. Selection of studies and data extraction

Two reviewers (LH and AR) screened abstracts for inclusion separately, adjudicated by a third researcher (RV). Potentially eligible studies were independently reviewed by LH and AR and data extracted and adjudicated by a third researcher (RV). Reviews and retrieved studies were hand-searched for additional eligible studies. Where inadequate information was provided, primary authors were contacted. Translations of non-English language studies were sought from authors or interpreters used.

2.3. Assessment of study quality

We graded studies for bias risk using a method used in a previous review [22] as low, medium risk or high risk of bias, combining domains from the Cochrane Collaboration guidelines [23] (inadequate blinding of outcome assessment, incomplete outcome data, and selective reporting) with two additional domains - "inappropriate measurement methods" (split into a. suitability and b. reliability) and "use of an unrepresentative sample". A priori standards were agreed (see Supplementary Table Two). Where it was not possible to grade as low or high bias, a medium risk was assigned. Although each study was assessed in each category, an overall bias assignment was assigned based on the highest risk score across all categories. Studies were independently assessed for bias by LH and AR, and adjudicated by RV.

2.4. Analysis

Individual studies were pooled for meta-analysis using STATA version 13 (StataCorp, Texas, USA). As arterial stiffening is potentially influenced by a number of factors, we made an a priori decision to use a random effects model (DerSimonian & Laird method [24]). Weighted mean differences (WMD) (with 95% confidence intervals) were calculated for a) all site arterial stiffness and b) by site (carotid-femoral, carotid-radial), to examine for differences by region measured. In studies with multiple measures over time, we used baseline data. Medians and ranges provided in some studies were used to estimate means and standard deviations using published formulae [25]. Sensitivity analyses assessed findings by risk