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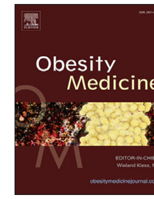

Original research

Which body composition measures are associated with cardiovascular function and structure in adolescence?

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ABSTRACT

Background: Quantifying relationships between non-invasive body composition and comprehensive adolescent cardiovascular phenotypes could aid clinicians in identifying adolescents at increased cardiovascular risk.
Aims: To assess (1) cross-sectional associations between body composition and cardiovascular function and structure, and (2) determine whether cardiovascular variation is better predicted by combined than individual body composition measures.
Methods: Participants- 202 adolescents (mean age 15.1 years, SD 0.6) from a community-based cohort. *Measures*- Body composition ‘exposures’: BMI/waist z-score, fat/lean mass indices. Cardiovascular ‘outcomes’: systolic/diastolic blood pressure, augmentation index, pulse wave velocity, carotid intima-media thickness, and arteriole-to-venule ratio. *Analysis*- Adjusted regression models to determine associations. R^2 values to determine relative predictiveness of models.
Results: A one-unit increase in BMI/waist z-scores and fat/lean mass indices was associated with increased systolic blood pressure (2.5 mmHg (95%CI:0.9–4.0); 1.9 mmHg (95%CI:0.5–3.4); 0.5 mmHg (95%CI:0.0–1.1); 1.4 mmHg (95%CI:0.4–2.3)) and augmentation index (2.9% (95%CI:1.2–4.6); 2.0% (95% CI:0.4–3.6); 1.0% (95%CI:0.4–1.6); 1.9% (95%CI:0.9–2.9)). Statistically significant differences were not observed for other cardiovascular outcomes. The R^2 value of combined models was marginally higher than individual models for all cardiovascular outcomes.
Conclusions: In adolescence, body composition was associated with some functional outcomes but not readily-measurable structural change, implying that associations may not be evident until at least young adulthood. Combined measurements provide limited additional advantage to the clinician above BMI alone.

1. Introduction

Childhood adiposity is an established risk factor for adult cardiovascular disease (CVD) (Must et al., 1992; Baker et al., 2007). This relationship could be explained by adiposity tracking from childhood into adulthood (Singh et al., 2008), with adult obesity leading to functional and structural changes known to precede CVD. Alternatively, childhood adiposity could have an immediate effect on cardiovascular function and structure, directly contributing to the known childhood variation in these parameters. Reducing childhood adiposity across the entire population would be even more urgent if shown to contribute to end-organ pathology within youth. With the advent of technologies that can accurately measure, in population samples, multiple aspects of both body composition and developing cardiovascular function and structure, this is now possible.

With regard to functional measures, high blood pressure has long been associated with adverse cardiovascular outcomes

Abbreviations: CVD, cardiovascular disease; PEAS, Parent Education and Support program; SEIFA, Socioeconomic Indexes of Disadvantage; SBP, systolic blood pressure; DBP, diastolic blood pressure; AIx, augmentation index; PWV, pulse wave velocity; cIMT, carotid intima-media thickness; aIMT, aortic intima-media thickness; AVR, arteriole-to-venule ratio.

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(Franklin and Wong, 2013). More recently, the focus has shifted to non-invasive measures of arterial stiffness as predictors of adverse cardiovascular health. For example, in a community-based sample of 10 year olds carotid-femoral pulse wave velocity, one measure of arterial stiffness, was positively associated with adiposity measured using body mass index (BMI), waist circumference, and percentage body fat (Sakuragi et al., 2009). Carotid intima-media thickening and retinal microvascular abnormalities, including arteriolar narrowing and venule widening, provide objective measurements of macro- and micro-vascular morphology respectively and thence an indication of an individual's structural vascular health (Chambless et al., 1997; Li et al., 2013). To our knowledge, no studies have yet investigated this comprehensive range of cardiovascular functional and structural variables *simultaneously* in adolescents to assess timing aspects of developing cardiovascular health known to increase the likelihood of later CVD.

While various brief, non-invasive measures of body composition are already widely used in community settings, it remains unclear whether these are strongly associated with cardiovascular health and, if so, which is/are most predictive. BMI, a widely used proxy for childhood adiposity (Juonala et al., 2011; Bell et al., 2013), is associated with blood pressure in childhood (6–13 years) (Bell et al., 2007). In adolescence (11–17 years) it also correlates with carotid artery hypertrophy, a precursor to atherosclerosis, measured with both aortic and carotid intima-media thickness (Dawson et al., 2009). However, BMI neither differentiates central adiposity (a known predictor of increased adult cardiovascular risk), nor accounts for differences in body composition that may be crucial to cardiovascular outcomes. Increased waist circumference strongly predicts children's cardiovascular risk factors, including hypertension (Savva et al., 2000; Watts et al., 2008). Bioelectrical impedance yields more comprehensive indices of body composition, including fat and lean mass indices (Kyle et al., 2003), which also predict hypertension in children (Weber et al., 2014). However, whether waist or fat/lean indices predict cardiovascular outcomes better than BMI alone remains inconclusive (Savva et al., 2000; Watts et al., 2008; Kyle et al., 2003; Weber et al., 2014; Lawlor et al., 2010).

Previous studies investigating associations between adiposity and cardiovascular risk have focussed predominantly on individuals categorised as overweight and/or obese (I'Allemand et al., 2008; Charakida et al., 2012; Cote et al., 2015). To draw conclusions about the nature (i.e. linear vs. non-linear) of relationships between body composition and cardiovascular health, individuals across the entire range of body composition must be sampled. Few studies have explored these associations in community samples. In one community sample of children (6–13 years) enriched for overweight and obesity, associations between BMI z-score and blood pressure were linear; however, curvilinear associations with other cardiovascular risk factors, e.g. plasma triglycerides, were observed (Bell et al., 2007). Empirically determining the nature of relationships between adiposity and developing cardiovascular phenotypes, including whether there are threshold effects, could aid clinicians in identifying which adolescents are at the greatest risk of poor cardiovascular outcomes in contemporary communities.

With increased portability of both body composition and cardiovascular measurements, it is now possible to investigate how multiple aspects of body composition, including lean mass index, are associated singly or jointly with a comprehensive set of cardiovascular functional and structural measurements in adolescence. Our long-running PEAS Kids Growth Study provided an opportunity to do so in a community sample of 14–17 year olds. For this paper, we aimed to assess (1) cross-sectional associations of body composition with comprehensive functional and structural (micro- and macro-vascular) cardiovascular phenotypes, and (2) determine whether cardiovascular variation is better predicted by combined than individual body composition measures.

2. Methods

2.1. Study design, recruitment and follow-up: overview of the PEAS study

The PEAS Kids Growth Study is a longitudinal cohort study based in Melbourne, Australia. Detailed information about study recruitment is described elsewhere (Wake et al., 2006). Briefly, parents of all first-born newborns born (June 1998–February 1999 and July 1999–February 2000) in three local government areas (one low, one medium and one high level of social advantage) were invited by their Maternal and Child Health nurse to take part in the Parent Education and Support (PEAS) study. PEAS tested the efficacy of brief, evidence-based support for common issues faced by parents in the first two years of their child's life (Wake et al., 2006). As measured outcomes at 2 years were similar in intervention and control groups, participants were combined from 4 years onwards into a single longitudinal cohort renamed the PEAS Kids Growth Study.

Subsequent data collection occurred during periods important for healthy growth and development including follow-up at six-monthly intervals during the period of adiposity rebound (4–6.5 years), a single follow-up at pre-adolescence (average age 10 years), and the most recent follow-up during adolescence (average age 15 years). The Human Research Ethics Committee at The Royal Children's Hospital approved all phases of the study prior to commencement (HREC 28135).

2.2. Overview of procedures for the adolescent follow-up (this study)

Cross-sectional data from the adolescent follow-up of the PEAS Kids Growth Study comprised the dataset for this paper. Between February–October 2014, all enrolled study families residing in Victoria, Australia ($n = 261$), were invited to participate. Parents completed written consent and a questionnaire prior to their appointment (1.5 h at Melbourne's Royal Children's Hospital, or a shorter 1 h home visit). At the appointment, the child completed consent, a questionnaire and a brief physical assessment.

2.3. Measurements

Table 1 provides a detailed description of body composition 'exposures' and cardiovascular functional and structural 'outcomes'. For logistical reasons, cardiovascular micro- and macro-vascular structure measurements were only performed on those able to attend Melbourne's Royal Children's Hospital ($n = 109$). Potential confounders identified *a priori* included child age, gender, height, neighborhood and family socioeconomic status (measured with Socioeconomic Indexes of Disadvantage (Adhikari, 2006) and maternal education respectively) and puberty status (Petersen et al., 1988), as all have previously been found to be associated with both adiposity and cardiovascular outcomes.

2.4. Data analysis

To assess cross-sectional associations of body composition with comprehensive functional and structural (micro- and macro-vascular) cardiovascular phenotypes *(Aim 1),* adjusted linear