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Pericardial adipose tissue, cardiac structures, and cardiovascular risk factors in school-age children

Liza Toemen[1,2], Susana Santos[1,2], Arno A.W. Roest[3], Meike W. Vernooij[4], Willem A. Helbing[2,4], Romy Gaillard[1,2], and Vincent W.V. Jaddoe[1,2]*

[1]Generation R Study Group, Erasmus MC, University Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands; [2]Department of Pediatrics, Erasmus MC, University Medical Center, PO Box 22040, 3000 CA Rotterdam, The Netherlands; [3]Department of Pediatrics, Leiden University Medical Center, Postbus 9600, 2300 RC Leiden, The Netherlands; and [4]Department of Radiology and Nuclear Medicine, Erasmus MC, University Medical Center, PO Box 22040, 3000 CA Rotterdam, The Netherlands

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Aims We examined the associations of pericardial adipose tissue with cardiac structures and cardiovascular risk factors in children.

Methods and results We performed a cross-sectional analysis in a population-based cohort study among 2892 children aged 10 years (2404 normal weight and 488 overweight/obese). Pericardial adipose tissue mass was estimated by magnetic resonance imaging (MRI) and indexed on height[3]. Left ventricular mass (LVM) and left ventricular mass-to-volume ratio (LMVR) were estimated by cardiac MRI. Cardiovascular risk factors included android adipose tissue percentage obtained by Dual-energy X-ray absorptiometry, blood pressure and glucose, insulin, cholesterol, and triglycerides concentrations. Adverse outcomes were defined as values above the 75 percentile. Median pericardial adipose tissue index was 3.6 (95% range 1.6–7.1) among normal weight and 4.7 (95% range 2.0–8.9) among overweight children. A one standard deviation (1 SD) higher pericardial adipose tissue index was associated with higher LMVR [0.06 standard deviation scores, 95% confidence interval (CI) 0.02–0.09], increased odds of high android adipose tissue [odd ratio (OR) 2.08, 95% CI 1.89–2.29], high insulin concentrations (OR 1.17, 95% CI 1.06–1.30), an atherogenic lipid profile (OR 1.22, 95% CI 1.11–1.33), and clustering of cardiovascular risk factors (OR 1.56, 95% CI 1.36–1.79). Pericardial adipose tissue index was not associated with LVM, blood pressure, and glucose concentrations. The associations showed largely the same directions but tended to be weaker among normal weight than among overweight children.

Conclusion Pericardial adipose tissue is associated with cardiac adaptations and cardiovascular risk factors already in childhood in both normal weight and overweight children.

Keywords Epidemiology • Pericardial adipose tissue • Cardiovascular risk factors • Paediatrics

Introduction

Pericardial adipose tissue is a metabolically active fat depot and consists of epicardial and paracardial adipose tissue.[1] Two large prospective cohort studies in adults reported associations of larger pericardial adipose tissue volumes with the incidence of cardiovascular events, such as myocardial infarction, angina pectoris, heart failure, stroke, and death, up to a 12-year follow-up period.[2,3] Also, in adults pericardial adipose tissue seems to be associated with increased left ventricular mass (LVM) and left ventricular mass-to-volume ratio (LMVR), a measure of concentricity, higher blood pressure, higher lipid concentrations, and impaired fasting glucose.[2–4]

Cardiovascular risk factors track from childhood into adulthood, suggesting that cardiovascular disease and mortality have their origins

* Corresponding author. Tel: +31 (10) 704 3405; Fax: +31 (10) 704 4645. E-mail: v.jaddoe@erasmusmc.nl

in early life.[5–7] Whether pericardial adipose tissue contributes to development of cardiovascular risk factors from early life onwards is unknown. Studies in children suggest that epicardial adipose tissue is generally higher in obese children.[8,9] Also, studies in children suggest that greater epicardial adipose tissue is associated with larger LVM, higher blood pressure and an atherogenic lipid profile.[9–11] We hypothesized that pericardial adipose tissue is, independently of general adiposity, associated with cardiac measures and with cardiovascular risk factors from childhood onwards in both normal weight and overweight children.

We examined, in a population-based cohort study among 2892 school-aged children, the cross-sectional associations of pericardial adipose tissue measured with magnetic resonance imaging (MRI) with cardiac structures and with cardiovascular risk factors. Main outcomes included LVM and LMVR both measured with cardiac MRI (cMRI), android adipose tissue percentage obtained by Dual-energy X-ray absorptiometry, blood pressure and serum glucose, insulin, cholesterol, and triglycerides concentrations.

Methods

Design and study population

This cross-sectional study was embedded in the Generation R Study, a population-based prospective cohort study from foetal life onwards in Rotterdam, The Netherlands.[12] Childhood anthropometrics and cardiovascular risk factors were assessed at the median age of 9.9 years (95% range 9.5–11.8 years), followed by a second visit for MRI within 1.1 months (95% range 0–24.8 months). In total, 4135 singleton born children participated in the MRI substudy, of whom 2892 had measures of pericardial adipose tissue and anthropometrics and no cardiac abnormalities.[12] This lower number of pericardial adipose tissue imaging is explained by logistic issues, such as coil problems or time constraints. Of this group of children, 89% (2579) had successful cardiac measures. Missing data were mainly due to low image quality. Of the 2892 children, 72% (2069) had metabolic measures from blood samples available. Missing blood samples were mainly due to non-consent for venous puncture (flowchart, Supplementary data online, *Figure S1*). Written informed consent was obtained from all parents of participants. The study has been approved by the local medical ethics committee.

Anthropometrics and pericardial adipose tissue

All measurements were performed in a dedicated research centre according to research protocols. We measured child height and weight without shoes and heavy clothing. Height was measured to the nearest millimetre by a stadiometer (Holtain Limited, Crosswell, Crymych, UK). Weight was measured to the nearest gram using an electronic scale (SECA 888, Almere, The Netherlands), and body mass index (BMI) (kg/m^2) was calculated. We obtained sex- and age-specific BMI standard deviation scores (SDS) based on Dutch reference growth curves.[13] Children's weight status was defined according to age- and sex-specific cut-off points proposed by the International Obesity Task Force.[14] Body surface area (BSA) was calculated using the Haycock formula.[15]

Pericardial adipose tissue was measured by MRI, as described previously.[12,16] Briefly, pericardial adipose tissue imaging in short-axis orientation was performed using an electrocardiogram (ECG) triggered black-blood prepared thin slice single-shot fast spin-echo acquisition with multi-breath-hold approach. Images were analysed by the Precision Image Analysis company (PIA, Kirkland, WA, USA), using the sliceOmatic (TomoVision, Magog, Quebec, Canada) software package. Inter- and intraobserver reproducibility was calculated in 25 subjects. Interobserver mean difference was 0.0 mL [standard deviation (SD) 2.9], limits of agreement -5.6 to 5.7 mL, mean value 18.2 mL (SD 6.7), and coefficient of variation was 15.8%. Intraobserver mean difference was 0.1 mL (SD 2.0), limits of agreement -3.71 to 3.96 mL, mean value 17.8 mL (SD 6.8), and coefficient of variation was 11.0%. Pericardial adipose tissue included both epicardial- and paracardial fat directly attached to the pericardium, ranging from the apex to the left ventricular outflow tract. Fat masses were obtained by multiplying the total volumes by the specific gravity of adipose tissue, 0.9 g/mL.[17] Pericardial adipose tissue index was calculated as pericardial adipose tissue mass/height^3, the exponent was derived from a log–log regression analysis.[18]

Cardiac MRI

Cardiac measures were obtained by cMRI, as described previously.[19] Briefly, we acquired localizer images, followed by ECG gated breath-held scans for two-chamber and four-chamber views. A short-axis SSFP cine stack was then obtained with basal slice alignment with contiguous 8-mm thick slices over several end expiration breath-holds. Off-line image analyses for right and left ventricular measures on the short-axis cine stack was performed by Precision Image Analysis (Kirkland, WA, USA), using Medis QMASS software (Medis, Leiden, The Netherlands), following the guidelines of the Society for Cardiovascular Magnetic Resonance (SCMR).[20] Papillary muscle was included in the ventricular cavity. Main outcomes were LVM and LMVR. LMVR was calculated as LVM/LVEDV and considered as a marker of concentric remodelling. Secondary outcomes included right end-diastolic volume (RVEDV), right ventricular ejection fraction (RVEF), left ventricular end-diastolic volume (LVEDV), and left ventricular ejection fraction (LVEF).

Cardiovascular risk factors

Total and trunk (android) fat mass were measured using DXA (iDXA, GE-Lunar, 2008, Madison, WI, USA), and analysed with the enCORE software v.12.6.[21] Android adipose tissue percentage was calculated as android fat mass/total fat mass and used as a proxy for waist circumference. Systolic blood pressure and diastolic blood pressure were measured on the right brachial artery four times, using the validated automatic sphygmomanometer Accutorr Plus (Datascope Corporation, Fairfield, NJ, USA). We used the mean values of the last three measurements in our analyses. Non-fasting blood samples were collected to measure serum glucose, insulin, total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides concentrations. Glucose, total cholesterol, HDL cholesterol, and triglycerides concentrations were measured using the c702 module on the Cobas 8000 analyzer. Insulin was measured with electrochemiluminescence immunoassay (ECLIA) on the E411 module (Roche, Almere, The Netherlands).[22] We defined children with clustering of cardiovascular risk factors, using the previously described definition of childhood metabolic syndrome phenotype.[23] Clustering of cardiovascular risk factors means having three or more of the following components: android fat mass % ≥75th percentile, systolic or diastolic blood pressure ≥75th percentile, HDL cholesterol ≤25th percentile or triglycerides ≥75th percentile, and insulin level ≥75th percentile.[23] Percentiles were derived from the study population. We describe HDL cholesterol ≤25th percentile or triglycerides ≥75th percentile as an atherogenic lipid profile.

Covariates

Child ethnicity was classified by the countries of birth of the parents and was categorized as Dutch or non-Dutch.[12] Child sex was obtained from midwife and hospital registries at birth.

Statistical analysis

First, we compared characteristics between normal weight and overweight/obese children using one-way analysis of variance tests, Mann–Whitney *U* test and χ^2 test. Underweight children ($n = 191$) were classified as having normal weight, this clustering of weight groups did not affect our analyses. We combined overweight and obese children in one group and referred to them as overweight. Analyses were performed in the total group and in strata of normal weight ($n = 2404$) and overweight children ($n = 488$) to examine the effects and the possible interactions with BMI. Second, we used linear regression models to assess the associations of pericardial adipose tissue index with cardiac measures (LVM, LMVR, RVEDV, RVEF, LVEDV, and LVEF), and with cardiovascular risk factors (android adipose tissue percentage, systolic and diastolic blood pressures and glucose, insulin, total cholesterol, HDL cholesterol, and triglycerides concentrations). We constructed BSA-adjusted SDS for the cardiac measures using Generalized Additive Models for Location, Size and Shape (GAMLSS) in R, version 3.2.0 (R Core Team, Vienna, Austria). These models enable flexible modelling, taking into account the distribution of the outcome variable.[24] Since LMVR is usually not normalized on BSA, we created SDS as (observed value-mean)/SD. Models were adjusted for age, sex, ethnicity, and time difference between the two visits. Finally, we used logistic regression models to assess the associations of pericardial adipose tissue index with adverse outcomes (high android adipose tissue percentage, high blood pressure, high insulin concentrations, atherogenic lipid profile, and clustering of cardiovascular risk factors). The statistical interaction of pericardial adipose tissue index with childhood BMI was tested by including the product term of these variables in the models. To enable comparison of effect estimates, we created SDS for all continuous determinant and outcomes variables. We did not observe significant statistical interaction terms between child sex and pericardial adipose tissue index in relation to cardiovascular measures. Since our outcomes are correlated, we considered Bonferroni correction for multiple testing too strict. To enable interpretation of level of statistical significance, we present *P*-values as both $P < 0.05$ and $P < 0.01$. Missing data of covariates were imputed using multiple imputations. Five data sets were created and analysed together.[25] All analyses were performed using the Statistical Package for the Social Sciences version 21.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Subject characteristics

Table 1 shows that the median pericardial adipose tissue index was 3.6 (95% range 1.6–7.1) among normal weight children and 4.7

Table 1 Child characteristics

	N	Normal weight	*N*	Overweight	*P*-value
Age at MRI (years)	2404	9.9 (9.4–11.8)	488	10.0 (9.5–11.8)	0.28
Male gender, *N*	2404	1212 (50.4)	488	206 (42.2)	<0.01
Ethnicity, non-Dutch, *N*	2358	831 (35.2)	476	278 (58.4)	<0.01
Height (cm)	2404	141.1 (6.5)	488	144.3 (6.9)	<0.01
Weight (kg)	2404	32.6 (25.2–43.4)	488	45.2 (35.3–62.7)	<0.01
Body mass index (kg/m^2)	2404	16.5 (14.0–19.4)	488	21.5 (19.7–27.9)	<0.01
Pericardial adipose tissue (g)	2404	10.0 (4.5–20.7)	488	14.2 (6.4–26.7)	<0.01
Pericardial adipose tissue index (g/m^3)	2404	3.6 (1.6–7.1)	488	4.7 (2.0–8.9)	<0.01
Cardiac measures					
Right ventricular end-diastolic volume (mL)	2141	98.1 (18.5)	438	111.4 (20.8)	<0.01
Right ventricular ejection fraction (%)	2141	58.3 (4.9)	438	57.4 (4.6)	<0.01
Left ventricular end-diastolic volume (mL)	2141	98.6 (16.6)	438	110.9 (19.2)	<0.01
Left ventricular ejection fraction (%)	2141	58.4 (4.5)	438	58.3 (4.6)	0.69
Left ventricular mass (g)	2140	47.6 (9.8)	438	55.0 (10.2)	<0.01
Left ventricular mass-to-volume ratio	2139	0.49 (0.08)	438	0.50 (0.08)	<0.01
Cardiovascular measures					
Android adipose tissue (%)	2389	3.7 (2.4–6.0)	485	6.3 (3.7–8.2)	<0.01
Systolic blood pressure (mmHg)	2339	102.2 (7.5)	477	108.4 (8.1)	<0.01
Diastolic blood pressure (mmHg)	2339	58.4 (6.3)	477	60.0 (6.8)	<0.01
Glucose (mmol/L)	1727	5.3 (0.9)	341	5.2 (0.8)	0.12
Insulin (pmol/L)	1727	170.6 (33.8–564.1)	336	257.4 (49.3–830.0)	<0.01
Total cholesterol (mmol/L)	1726	4.3 (0.6)	340	4.4 (0.7)	<0.01
HDL cholesterol (mmol/L)	1728	1.5 (0.3)	341	1.3 (0.3)	<0.01
Triglycerides (mmol/L)	1723	0.91 (0.40–2.43)	338	1.15 (0.49–2.98)	<0.01
Cardiovascular risk factor clustering, *N*	1525	101 (6.6)	300	125 (41.7)	<0.01

Values are expressed as means (SD), medians (95% range), or numbers (%), based on original, non-imputed data. *P*-values obtained from analysis of variance, Mann–Whitney *U* or χ^2 tests.

Table 2 Associations of childhood pericardial adipose tissue index with cardiovascular risk factors

Cardiovascular risk factors in SDS	Total group (*N* = 2892)	Normal weight (*N* = 2404)	Overweight (*N* = 488)	*P*-value for interaction[a]
Left ventricular mass[b]	-0.01 (-0.04 to 0.03)	0.02 (-0.02 to 0.06)	-0.02 (-0.08 to 0.05)	0.02
Left ventricular mass-to-volume ratio	0.06 (0.02 to 0.09)[c]	0.04 (-0.01 to 0.09)	0.03 (-0.05 to 0.11)	0.86
Android adipose tissue percentage	0.34 (0.31 to 0.37)[c]	0.19 (0.16 to 0.22)[c]	0.12 (0.06 to 0.18)[c]	<0.01
Systolic blood pressure	0.02 (-0.02 to 0.06)	0.03 (-0.02 to 0.08)	0.00 (-0.08 to 0.08)	0.34
Diastolic blood pressure	0.01 (-0.03 to 0.05)	0.01 (-0.04 to 0.06)	0.02 (-0.07 to 0.10)	0.82
Glucose concentrations	-0.02 (-0.06 to 0.01)	-0.01 (-0.06 to 0.04)	0.01 (-0.07 to 0.08)	0.60
Insulin concentrations	0.05 (0.01 to 0.10)[d]	0.00 (-0.05 to 0.05)	0.00 (-0.10 to 0.09)	0.15
Total cholesterol concentrations	0.10 (0.05 to 0.14)[c]	0.08 (0.03 to 0.14)[c]	0.07 (-0.03 to 0.17)	0.25
HDL cholesterol concentrations	-0.06 (-0.11 to -0.02)[c]	-0.01 (-0.06 to 0.05)	0.00 (-0.10 to 0.09)	0.06
Triglycerides concentrations	0.13 (0.10 to 0.17)[c]	0.06 (0.01 to 0.12)[d]	0.16 (0.06 to 0.25)[c]	0.07

Values are linear regression coefficients (95% confidence interval). The estimates represent differences in SDS of the cardiovascular measures per increase of one SDS of childhood pericardial adipose tissue index. Models are adjusted for child age, sex, ethnicity, and time difference between measurement of anthropometrics and pericardial adipose tissue.
N, number; SDS, standard deviation scores.
[a]*P*-value for interaction represents the *P*-value of the interaction term of pericardial adipose tissue with age and gender standardized childhood BMI.
[b]Left ventricular mass was standardized on body surface area.
[c]$P < 0.01$.
[d]$P < 0.05$.

Table 3 Associations of pericardial adipose tissue index with clustering of cardiovascular risk factors

Cardiovascular measures in SDS		Total group	Normal weight	Overweight	*P*-value for interaction[a]
High android adipose tissue percentage	*N* = 2874	2.08 (1.89–2.29)[b]	1.65 (1.43–1.90)[b]	1.53 (1.19–1.97)[b]	0.87
High blood pressure	*N* = 2549	1.04 (0.95–1.12)	1.01 (0.92–1.12)	1.05 (0.89–1.24)	0.50
High insulin	*N* = 2063	1.17 (1.06–1.30)[b]	1.04 (0.91–1.19)	1.04 (0.86–1.27)	0.19
Atherogenic lipid profile	*N* = 2063	1.22 (1.11–1.33)[b]	1.06 (0.94–1.19)	1.28 (1.05–1.57)[c]	0.05
Cardiovascular risk factor clustering	*N* = 1825	1.56 (1.36–1.79)[b]	1.14 (0.91–1.44)	1.23 (0.99–1.52)	0.04

Values are odds ratio's (95% confidence interval) that reflect the risk of high (>75th percentile) android adipose tissue percentage; high (>75th percentile) systolic or diastolic blood pressure; high (>75th percentile) insulin concentration; atherogenic lipid profile (>75th percentile triglycerides or <25th percentile HDL); and the risk for having clustering of three or more risk factors, per SDS change in pericardial adipose tissue index. Models are adjusted for child age, sex, ethnicity, and time difference between measurement of cardiovascular measures and pericardial adipose tissue index.
[a]*P*-value for interaction represents the *P*-value of the interaction term of pericardial adipose tissue with age and gender standardized childhood BMI.
[b]$P < 0.01$.
[c]$P < 0.05$.

(95% range 2.0–8.9) among overweight children. As compared with normal weight children, overweight children also had a higher LVM, higher android adipose tissue percentage, higher blood pressure, higher insulin concentrations, lower HDL cholesterol concentrations, and higher triglycerides concentrations (all $P < 0.01$). Clustering of cardiovascular risk factors was observed in 6.6% of normal weight children and 41.7% of overweight children.

Pericardial adipose tissue, cardiac measures, and cardiovascular risk factors

Table 2 shows that in the full group, a one standard deviation (1 SD) higher pericardial adipose tissue index was associated with higher LMVR [0.06 SDS, 95% confidence interval (CI) 0.02–0.09] but not with LVM. A 1 SD higher pericardial adipose tissue index was associated with a 0.34 SDS (95% CI 0.31–0.37) higher android adipose tissue, a 0.05 SDS (95% CI 0.01–0.10) higher insulin concentrations, 0.10 SDS (95% CI 0.05–0.14) higher total cholesterol concentrations, -0.06 SDS (95% CI -0.11 to -0.02) lower HDL cholesterol concentrations, and 0.13 SDS (95% CI 0.10–0.17) higher triglyceride concentrations. Pericardial adipose tissue index was not associated with blood pressure and glucose concentrations. As compared to the full group, the effect estimates for the associations showed largely the same directions but were weaker among normal weight than among overweight children. Pericardial adipose tissue index was associated with lower RVEDV and LVEDV in the total group (Supplementary data online, *Table S1*).

Pericardial adipose tissue and clustering of cardiovascular risk factors

Table 3 shows that a 1 SD higher pericardial adipose tissue index was associated with increased odds of high android adipose tissue [odd ratio (OR) 2.08, 95% CI 1.89–2.29], high insulin concentrations

[OR 1.17, 95% CI 1.06–1.30], an atherogenic lipid profile [OR 1.22, 95% CI 1.11–1.33], and clustering of cardiovascular risk factors (OR 1.56, 95% CI 1.36–1.79). Pericardial adipose tissue index was not associated with high blood pressure. As compared to the full group, the associations showed largely the same directions but were weaker among normal weight children than overweight children.

Discussion

In this cross-sectional analyses embedded in a population-based cohort study, we observed that higher pericardial adipose tissue is associated with cardiac adaptations and cardiovascular risk factors already in childhood. As compared to the full group, the effect estimates for the associations showed largely the same directions but were weaker among normal weight children than among overweight children.

Interpretation of main results

Pericardial adipose tissue is associated with cardiac disease in adults.[2,26] Results from the Multi-Ethnic Study of Atherosclerosis (MESA) amongst 4234 adults showed that higher pericardial adipose tissue was associated with atherosclerotic cardiovascular events, coronary heart disease, and heart failure.[2] These associations were independent of BMI, waist circumference, and hepatic fat. Pericardial adipose tissue was also associated with atrial fibrillation.[26] Results from the Framingham Heart Study showed among 846 adults that the ratio between epicardial and body fat was associated with coronary artery disease, independent of obesity.[27] Pericardial adipose tissue was also associated with progression of coronary artery calcium, but this association was explained by BMI or visceral adiposity.[28] Findings from these studies in adults suggest that pericardial adipose tissue is associated with cardiac remodelling.[2,29] Also, pericardial adipose tissue among adults is associated with numerous cardiovascular and metabolic risk factors, such as insulin resistance, atherogenic lipid profile, hypertension, and metabolic syndrome.[4,30] Cardiovascular risk factors track from childhood into adulthood suggesting that cardiovascular disease and mortality have their origins in early life.[5–7] To the best of our knowledge, no previous studies focused on the associations of pericardial adipose tissue with cardiac structure and cardiovascular risk factors in childhood in the general population.

In this study, we examined the cross-sectional associations of childhood pericardial adipose tissue index with cardiac measures and cardiovascular risk factors among both normal weight and overweight children. We observed that both pericardial adipose tissue index and cardiac measures were larger in overweight children than in normal weight children. However, pericardial adipose tissue index was not associated with the BSA-standardized cardiac dimensions. In childhood, one of the main determinants of cardiac size is lean body mass.[31] Since we were interested in the association of pericardial adipose tissue with cardiac measures independent of body size, we used BSA-standardized measures.[32] Direct comparison with other studies is difficult since these studies used different methods to take into account body size. In adults, associations of pericardial adipose tissue have been observed with larger LVEDV and LVM.[2,29] In children, epicardial adipose tissue was associated with larger LVM, but these studies took only height and not weight into account.[8,10,11] LMVR is the ratio between LVEDV and LVM and is generally not standardized or indexed on body size. It reflects left ventricular concentricity and is associated with cardiovascular disease additional to left ventricular hypertrophy.[33] We observed that pericardial adipose tissue index was associated with increased LMVR. The absence of a similar relationship in strata of normal weight and overweight children suggests that general adiposity may at least partly explain this association.

The mechanisms by which obesity affects cardiac morphology are still unclear. A study focusing on body fat distribution shows that adults with relatively more visceral fat show a larger increase in LVM than in LVEDV, thus resulting in concentric remodelling.[34] Different depots of adipose tissue might influence cardiac morphology through different mechanisms. Visceral adipose tissue can affect cardiac morphology through endocrine and immune responses that affect cardiac morphology directly and through worsening of other cardiovascular risk factors.[35] Pericardial adipose tissue might have an additional effect, because of its direct proximity to the myocardium.[2] Obesity is associated with increased subepicardial fat, and this excess tissue can infiltrate the myocardium, changing myocardial structure.[36] In patients with coronary artery disease, perivascular adipose tissue has been shown to release inflammatory factors that could influence insulin resistance and cardiovascular functioning.[37] Pericardial fat-releasing inflammatory factors in proximity to the pulmonary vein ostia may trigger atrial fibrillation.[38] Through these pathways, increased pericardial adipose tissue could increase the risk for cardiac disease, additional to the effects of general or visceral adipose tissue.

In obese children, epicardial adipose tissue was a good indicator of visceral fat but no independent association of epicardial adipose tissue thickness with insulin resistance and metabolic syndrome was observed.[39] In line with these studies, we observed no association of pericardial fat tissue with blood pressure, nor with glucose, insulin, and HDL-cholesterol concentrations in the strata for normal weight and overweight children. In contrast to findings from a study among obese children but in line with the study among adults, we did observe associations of pericardial adipose tissue with other components of metabolic syndrome among both normal weight and overweight children.[4] A previous study among adults reported that epicardial thickness was a better predictor for coronary artery disease and metabolic syndrome among adults with a normal BMI than in adults with obesity.[40] In line with these results, we observed a stronger association of pericardial adipose tissue index with android adipose tissue percentage among normal weight children but not with the other cardiovascular risk factors. Additionally, we observed slightly stronger effect estimates for the associations of pericardial adipose tissue index with atherogenic lipid profile and cardiovascular risk clustering among overweight children. In our study, we observed the strongest association of pericardial adipose tissue index with android adipose tissue percentage. Android adipose tissue percentage is correlated to waist circumference. In line with these results, waist circumference in both adults and children correlated strongly with epicardial and pericardial adipose tissue.[2,8,41] We observed stronger associations of pericardial adipose tissue with total cholesterol and triglycerides concentrations, than of pericardial adipose tissue with other metabolic syndrome components. This difference may be explained by the differences in mechanisms underlying the associations of pericardial adipose tissue with specific risk factors. These mechanisms need to be further studied.

Based on our results, we cannot draw conclusions whether pericardial adipose tissue is merely a marker for adiposity, or leads to additional cardiovascular risk. However, we can conclude that higher pericardial adipose tissue in childhood is associated with an adverse cardiovascular risk profile on top of its association with body weight. In adults, visceral fat and pericardial adipose tissue can be reduced by a combination of diet and exercise.[42] Future studies are needed to assess the long term consequences of higher pericardial adipose tissue index and the reversibility in childhood and cardiovascular disease in later life.

Methodological considerations

Main strengths of this study are its population-based design and the large number of detailed measurements of adiposity and cardiac imaging. Some limitations need to be discussed. We did not obtain successful imaging in all participating children in this study. This could have resulted in selection bias if larger pericardial or general adipose tissue volume was related to success rate of cMRI. However, we did not observe an association between BMI and success rate of cMRI (results not shown). Since the pericardium is difficult to distinguish with our imaging method, we measured pericardial adipose tissue, which consists of both epicardial and paracardial adipose tissue. These adipose depots have different origins and might have different effects on cardiovascular disease.[43] Epicardial fat is metabolically active and can interact directly with the myocardium, whereas paracardial fat is more likely to interact with coronary arteries.[43] We collected non-fasting blood samples. This could have affected variation of glucose, insulin and triglycerides concentration and led to attenuation of any associations of pericardial adipose tissue with these outcomes.[44,45] We adjusted for some confounders, but residual confounding might be present, as in any observational study. For example, we did not have detailed information on physical activity or diet, which could have influenced the observed associations. Finally, because of the observational cross-sectional design, we could not address the causality of the associations.

Conclusion

Our results suggest that among both normal weight and obese children, higher pericardial adipose tissue is associated with cardiac adaptations and cardiovascular risk factors. Further follow-up studies are needed to assess the causality of the observed associations and to assess whether pericardial fat in childhood predicts cardiovascular disease later life independent of general adiposity markers.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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Conflict of interest: none declared.

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