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**Total body fat, abdominal fat, body fat distribution and surrogate markers for health related to adipocyte fatty-acid-binding protein (FABP4) in children**

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**Running title:** Adipocyte fatty-acid-binding protein and markers for health

**Abstract**

**Objective:** To assess possible relationships between Adipocyte fatty-acid-binding protein (FABP4) and total body fat, abdominal fat, body fat distribution, aerobic fitness, blood pressure, cardiac dimensions and the increase in body fat over 2 years in a community sample of children.

**Methods:** Cross-sectional study in a community sample of 170 (92 boys and 78 girls) children aged 8-11 years. Total fat mass (TBF) and abdominal fat (AFM) were measured by Dual-energy x-ray absorptiometry (DXA). Total body fat was also expressed as percentage of total body mass (BF%), and body fat distribution was calculated as AFM/TBF. Maximal oxygen uptake ($VO_{2PEAK}$) was assessed by indirect calorimetry during a maximal exercise test and scaled to body mass. Systolic and diastolic blood pressure (SBP and DBP) and pulse pressure (PP) were measured. Echocardiography was performed. Left atrial size (LA) was measured and left ventricular mass (LVM) was calculated. A follow-up DXA scan was available in 152 children (84 boys and 68 girls). Frozen serum samples were analyzed for FABP4.

**Results:** Partial correlations, with adjustment for sex, between FABP4 versus ln TBF, ln BF%, ln AFM, AFM/TBF and $VO_{2PEAK}$ were ($r=0.69$, 0.68, 0.69, 0.49 and -0.39, $P<0.05$ for all). Moreover, SBP, PP, LVM and LA were also weekly correlated with FABP4 ($r=0.23$, 0.22, 0.28 and 0.21, $P<0.05$ for all). Correlations between FABP4 versus increase in TBF and AFM over 2 years were 0.29 and 0.26, $P<0.05$, for both (Increase in percent body fat or change in fat distribution were not correlated).

**Conclusion:** Findings from this community-based cohort of young children shows that increased body fat and abdominal fat, more abdominal body fat distribution, low fitness, more LVM and increased LA, increased SBP and PP were all associated with increased levels of

FABP4. Increase in total body fat and abdominal fat over 2 years were also associated with increased levels of FABP4.

## Introduction

Obesity, whether it is total, abdominal or expressed as body fat distribution represents a known risk factor for disease in adults (1). Moreover, the prevalence of obesity among children and adolescents is increasing (2,3), which represents a future public health concern. Obese children and adolescents have an increased risk of developing adult obesity (4), and are more likely to experience significant short- and long-term health problems (5,6). Overweight and obesity in adolescence have been shown to be associated with increased cardiovascular mortality in adulthood (7,8). It is therefore important to investigate different mechanisms of obesity in detail, also in young subjects. Adipose tissue is increasingly regarded as an endocrine organ. Adipokines are biologically active factors secreted from the adipose tissue that have both local and systemic effects. Adipocyte fatty acid binding protein (FABP4) is a sparsely investigated adipokine. It is mainly produced and secreted from adipocytes into the bloodstream and has a wide range of effects ranging from weight-control, metabolism to formation of atherosclerosis (9). In adults, FABP4 has been shown to be elevated in patients with obesity, cardiovascular diseases or metabolic syndrome (9). Moreover, FABP4 has been associated with development of metabolic syndrome and increased cardiovascular morbidity and mortality (9). FABP4 has also been investigated in young subjects. A few case-control studies have shown that FABP4 is elevated in obese children compared to normal weight children (10-14), but this is not the case in all studies (15). Weight loss (10,12) and nutritional counselling and supplementation with encapsulated fruit and vegetable juice concentrate have been shown to decrease FABP4 levels (14). However, data in unselected young populations are scarce. We are aware of only two studies that have investigated relations between FABP4 and markers for obesity, and the effect of change in body composition over time in unselected population of children (16,17). The primary purpose of this investigation was, in a community sample of children, to explore potential relationships between FABP4 levels versus total body

fat, abdominal fat, body fat distribution, and also changes in body fat and abdominal fat over 2 years. The secondary aim was investigate potential relationships between surrogate markers for impaired health such as aerobic fitness, blood pressure, and cardiac dimensions.

## Material and methods

### Subjects

The study population was recruited among children at four different schools in Malmö, Sweden. The schools were all situated in socially homogeneous middle-class areas with inhabitants of essentially non-immigrant origin. All 477 children (boys = 259, girls = 218) attending third or fourth grade were invited to participate in the study. Out of these 477 children 248 accepted the invitation (boys = 140, girls = 108), and 172 children gave consent to give blood sample. Blood samples and a complete data set of other variables were available for 170 children (92 boys and 78 girls) giving an inclusion frequency of 36%. A **2-year** follow-up DXA scan was available in 152 children (84 boys and 68 girls). A separate study of height and weight of all invited children from the general health data registered by the school nurses showed no significant differences in height, body mass or BMI between the children that chose to participate and those who did not (18). Written informed consent was obtained from the parents of all participating children. The regional ethics committee Lund, Sweden, approved the study (LU 243-01).

### Anthropometric measures

Anthropometric measures were performed at baseline and at the follow-up measurement (2.0±0.1, mean±SD) years later. Total body height was measured to the nearest 1 cm using a fixed stadiometer (Hultafors AB, Hultafors, Sweden) and total body mass was measured to the nearest 1 kg with a standardized scale (Avery Berkel model HL 120, Avery Weigh-Tronix

Inc, Fairmont, MN, USA). The children were dressed in light clothing. Puberty status was assessed by self-evaluation according to Tanner (19).

**Dual-energy x-ray absorptiometry (DXA)**

Body composition was measured by DXA total body scan (DPX-L version 1.3z, Lunar, Madison, WI, USA), both at baseline and at the follow-up measurement. This method uses two beams of low-energy X-rays that are collected by the external detector after attenuation by the body tissue through which they have passed. Soft tissue is resolved by use of mass attenuation coefficients derived from tissue-equivalent standards for fat-free and fat tissue. Pediatric software was used for children with a weight below 30 kg. Daily calibration of the machines was carried out with the Lunar phantom. One research technician performed all measurements and software analyses. Total body fat mass (TBF), total lead body mass (LBM) and abdominal fat (AFM) were quantified. Percent body fat (BF%) was calculated as percentage of total body mass. Body fat distribution was calculated as AFM/TBF. Studies have shown that DXA provides accurate measurements of fat mass, including regional fat mass (20).

**Measurement of aerobic fitness**

Maximal oxygen uptake ($VO_{2PEAK}$) was determined by a maximum exercise test at the baseline. The test was performed on an electrically braked bicycle ergometer (Rodby rhc, model RE 990, Rodby Innovation AB, Karlskoga, Sweden). Expired gas was sampled continuously via a mixing chamber and analyzed for the concentration of $O_2$ and $CO_2$ (Sensor Medics 2900, SensorMedics Inc, Yorba Linda, CA, USA). Measurements were obtained every 20 s during 2 min at rest and during exercise with progressively increasing work load to volitional exhaustion. All children, regardless of gender, fitness, height and body mass, used

the same protocol with an initial workload of 30 Watt (W) and an increase of 15 W per minute. Maximum heart rate (max HR) and maximum respiratory exchange ratio (RER) were recorded. $VO_{2PEAK}$ was determined as the highest value during the last minute of exercise and scaled to both body mass (ml/min/kg) and to LBM (ml/min/LBM), which has been shown to be a body fat independent way of expressing fitness (21). The exercise test was considered acceptable if it met one of the following criteria: RER ≥ 1.0, max HR >90% of predicted value or signs of intense effort (e.g. hyperpnoea, facial flushing or inability to keep adequate revolutions/min (53-64)) (22).

**Blood pressure**

A Dinamap paediatric vital signs monitor (model XL, Critikron Inc., Tampa, FL, USA) was used to measure systolic blood pressure (SBP), and diastolic blood pressure (DBP) in the seated position after 15 minutes of rest (23). The mean of three measurements was used in all analyses. Pulse pressure (PP) was calculated as SBP-DBP.

**Echocardiography**

Echocardiographic examination was performed with subjects in the left lateral supine position using Sonos 2500 (Philips Inc, Eindhoven, the Netherlands) or Aspen (Acuson Inc, Mountain View, CA, USA) equipment. Studies were performed with 2-dimensional guided M-mode echocardiography obtained in the parasternal short and long-axis views, in accordance with the American Society of Echocardiography (ASE) recommendations (24). The following variables were measured: End-diastolic left ventricular diameter (LVDD), left atrial end-systolic diameter (LA), end-diastolic inter-ventricular septum thickness (IVS), and end-diastolic posterior wall thickness (PW). Left ventricular mass (LVM) was calculated using the

ASE convention: LVM = 0.83 x [(LVDD + IVS + PW)$^3$ - LVDD$^3$] + 0.6 (measurements in cm) (24). Both LVM and LA were indexed for height (25-27).

**Blood samples**

Non-fasting venous serum sample were drawn from 172 children and stored at –70C until analysis. The samples were collected in conjunction with the DXA measurement. FABP4 was analyzed by the Proximity Extension Assay technique using the Proseek Multiplex CVD 96x96 reagents kit (Olink Bioscience, Uppsala, Sweden) at the Clinical Biomarkers Facility, Science for Life Laboratory, Uppsala, as previously described (28,29). The variance for intra-assay variation and inter-assay variation were 12% and 14%, respectively. Data are presented as arbitrary units (AU). Values can be transformed to actual concentrations using transforms on the Olink Bioscience website. There is, however, an approximation in this transformation. Two samples were excluded due to technical problems at the analysis.

**Statistical Analyses**

All analyses were made in Statistica 12 (StatSoft Inc, Tulsa, OK, USA). The descriptive data are presented as means ± SD. Differences in anthropometric data between boys and girls were tested using Student's t-test. Distribution of body fat measurements and abdominal fat were skewed and therefore normalized by natural logarithm (ln). Partial correlations for all children, with adjustment for sex, between FABP4 and ln TBF, ln AFM, AFM/TBF, $VO_{2PEAK}$ SBP, DBP, PP, LVM, LA and increase in TBF, AFM, BF% or change AFM/TBF were assessed by regression analyses. In the regression analyses used to assess the relations between FABP4 and increase in TBF or AFM, increase in TBF or AFM entered as dependent variables and FABP4 levels, sex and Tanner stage change during follow-up as independent variables. One-way ANCOVA analyses, with adjustment for sex, were used to investigate

significant differences in FABP4 levels between the different tertiles of TBF, BF%, AFM, or AFM/TBF and also for different quartiles of increase in TBF or AFM. A value of $P < 0.05$ was regarded as statistically significant.

**Results**

Complete data set was available for 170 (92 boys and 78 girls) of 248 children, and a follow-up DXA scan was available in 152 children (84 boys and 68 girls). The children that did not consent to give a blood sample were slightly younger than those who gave consent (9.6±0.6 vs. 9.9±0.6 years, P=0.002), no other differences were found in anthropometric, fitness or DXA data between those children who were part of the final study group at baseline and those who were not (data not shown). Those children who did not participate in the follow-up were slightly younger at baseline than those who did (9.7±0.6 vs. 9.9±0.6 years, P=0.005). There were no differences in anthropometric, fitness or DXA data between those who participated in the follow-up and those who did not (data not shown). At baseline **three** girls were Tanner stage 2, all other children Tanner stage 1. The distribution of Tanner score at follow-up were; (N for stage 1 = 18, stage 2 = 63, stage 3 = 49, stage 4 = 22). At baseline, there were no significant gender differences except girls had higher TBF, BF%, AFM and FABP4 levels. Boys had higher fitness and LVM. At follow-up there were no differences in increase of body fat measurement except that boys had a higher increase in BF%. Girls had higher Tanner score at follow-up. Summary of baseline and follow-up data are displayed in table 1. Regression analyses indicated rather strong relationships between FABP4 levels versus baseline body fat measurements and fitness. Moreover, weak relationships were observed between FABP4 levels versus SBP, PP, LVM and LA. Weak relationships were observed between FABP4 and increase in TBF or AFM, but not for increase in percent body fat or change in fat distribution. The partial correlations were slightly higher between FABP4 versus

increase in TBF or AFM when change in Tanner stage during follow-up was adjusted for, than those with just sex adjustment (R=0.33 vs. 0.29 and 0.29 vs. 0.26). Summary of partial correlations is displayed in table 2. There were significant differences in FABP4 levels between the different tertiles of TBF, BF%, AFM, or AFM/TBF (figure 1), and also for different tertiles of increase in TBF or AFM (figure 2).

**Discussion**

This is, to our knowledge, the first community-based report in young children showing that increased, objectively measured, body fat and abdominal fat, and increased ratio of abdominal body fat are all closely correlated with increased levels of FABP4. Also, increase in total body fat and abdominal fat over 2 years were associated with increased levels of FABP4. In addition, surrogate markers for impaired health such as low fitness, more left ventricular mass and increased left atrial size, increased systolic blood pressure and pulse pressure were all associated with increased levels of FABP4.

We are not aware of any other study in children that have investigated potential relations between FABP4 levels and a multitude of other measurements. Some case-control studies have shown that FABP4 is elevated in obese children compared to normal weight children (10-14), whereas one case-control study did not find any differences (15). We are aware of only two studies in unselected children that have attempted to investigate relationships between FABP4 and different measures of body fat (16,17). In a cross-sectional analysis Yun et al. reported data from 161 Korean children (80 boys and 81 girls) aged 9 years old (16). They found correlations (all sex adjusted) between FABP4 versus BMI and waist circumference (r=0.58 and r=0.51), which are slightly lower than our findings for TBF and AFM from DXA scan (r=0.70 and r=0.69). There were, however, similarities between their

correlations for BMI (r=0.58) and ours for BMI (r=0.66). Moreover, children with values of FABP4 in the higher quartiles had slightly higher SBP, but no differences were found for DBP, which parallel our findings. In our extended analysis we also found moderate to weak relationships between FABP4 and other surrogate markers for health such as fitness, left ventricular mass, left atrial size and pulse pressure, which has previously not been investigated. There was one striking difference; we found clear sex differences in the FABP4 level whereas Yun et al. did not. One reasonable explanation could be the higher BMI for the Korean boys (BMI 18.6 versus our 17.5). In a longitudinal study Choi and co-workers investigated 159 Korean boys, aged 9 years at baseline (17). FABP4 levels at baseline had a weak correlation with increase in BMI and waist circumference over 3 years (r=0.18 and r=0.27, both $p<0.05$). Yet again, this is very similar to our findings for increase in TBF or AFM from DXA scan (r=0.29 and r=0.26, both $p<0.05$).

The exact mechanisms behind others and our findings are at large not known. FABP4 is mainly produced and secreted from adipocytes into the bloodstream and therefore the findings in our and previous studies of a close correlation between FABP4 and different body fat measurements is not surprising. Also, our findings of weak relations between FABP4 levels and increase in total body fat or abdominal fat over 2 years are in agreement with both human and animal studies that have shown that FABP4 plays a role in weight control (9,10,12,17). A novel finding of our study is the moderately strong relationship between FABP4 and fitness, scaled to body mass. This relationship is probably driven by body fat, as they diminished when fitness was scaled to LBM. The mechanisms behind the weak relationships between LVM, LA, PP and SBP versus FABP4 could be direct or indirect through body fat. There have been previous speculations about possible molecular or cellular mechanisms behind increased LVM and LA in obesity. These include elevated lipid, lipoprotein, leptin, insulin,

adipokines, angiotensin-converting enzyme, and angiotensinogen levels, which may in part act directly on the myocytes or connective tissue matrix, or more likely through the vascular system (5,30). Elevated blood pressure leads to thickened walls of the left ventricle. The thickened walls of the left ventricle become stiffer which leads to diastolic dysfunction and impaired filling in diastole. This impairment leads to increased filling pressure and in turn pressure exposure and subsequent enlargement of the LA. In addition, there may be possible prenatal and/or a postnatal programming effect because both birth weight and parental body composition have been shown to influence obesity level (5), and consequently increase in blood pressure, LVM and LA size. Neither parental body composition nor subject's birth weight were included in the analysis because we did not have access to such data.

Major strengths of the present investigation are the urban community-based sample, the multitude of measurements, and objective measurement of body fat by DXA. Although DXA measurement of fat mass is a much more accurate estimate of adiposity than anthropometric measurements (e.g. BMI), DXA is only capable of measuring total abdominal fat, and is not able to differentiate between intra-visceral and extra-visceral fat. The inclusion frequency in this study of 52% might be considered somewhat low. A complete data set was available in no more than 36% (170 out of 477 invited children). However, a separate study of anthropometric data from all children that received an invitation to participate in the study showed no significant differences in height, body mass or BMI between the children that chose to participate and those who did not (18). Moreover, there were no major differences (except a slight age difference) in baseline measurements between those who gave consent to give a blood sample and those who participated in the follow-up versus those who did not. This suggests that the final study group is fairly representative. Further, population mean may be affected by selective dropout, but associations in the data material tend to be robust to

dropout as long as variation in the subgroup is similar to the whole group. A potential major limitation of the present study was the non-fasting blood samples. Whether FABP4 levels are affected by food intake or not is to our knowledge not known although some information was provided by Jahn et al. who investigated 18 metabolic syndrome subjects and 16 controls, aged 18–60 years (31). In that study FABP4 levels after overnight fasting were compared with values 2 hours after a high fat breakfast meal and difference of approximately 20% in FABP4 levels were seen between the two extremes. It is reasonable to assume that the children in our study represented a broad spectrum of post-prandial times. The introduced error is probably in the magnitude of 10% which is similar to the the variance for intra-assay variation or inter-assay variation for the FABP4 measurement. Another limitation of the present study is the fact that there was no information on the children's dietary patterns, which obviously have a correlation to increased total body fat (32,33). Neither was parental aspects accounted for. It has been shown that overweight parents are more likely to have overweight children (34).

**Conclusions**

Findings from this community-based cohort of young children shows that increased body fat, abdominal fat and higher ration of abdominal body fat, low fitness, more left ventricular mass and larger left atrial size, increased systolic blood pressure and pulse pressure were all associated with increased levels of FABP4. Increase in total body fat and abdominal fat over 2 years were also associated with increased levels of FABP4.

**Contributions**

All authors participated in the conception and design of the study. MD, MKK, PW, LBA and OT responsible for acquisition of data. All authors participated in analysis and interpretation of data and all authors have approved the final manuscript.

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**Conflicts of interest**

The authors declare that they have no conflicts of interest.

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**Table 1.** Display of age, anthropometric, fitness and Tanner statistics (± SD) for baseline and follow-up measurements. Total body fat (TBF), abdominal fat (AFM), lean body mass (LBM), maximum heart rate (Max HR), respiratory exchange ratio (RER), systolic blood pressure (SBP), diastolic blood pressure (DBP), adipocyte fatty-acid-binding protein (FABP4).

| **Variable** | **Boys (n=92)** | **Girls (n=78)** | **P-value** |
|---|---|---|---|
| **Baseline** | | | |
| Age (yrs) | 10.0±0.6 | 9.8 ± 0.6 | 0.03 |
| Height (cm) | 141±7 | 141±7 | 0.69 |
| Body mass (kg) | 35.2±7.4 | 34.6±6.6 | 0.57 |
| BMI (kg/m$^2$) | 17.5±2.6 | 17.4±2.7 | 0.90 |
| Total body fat (kg) | 6.2±4.6 | 8.0±4.6 | 0.01 |
| Percent body fat (%) | 16.1±8.3 | 22.0±8.5 | <0.001 |
| Abdominal fat (kg) | 2.3±2.0 | 3.2±2.2 | 0.01 |
| Fat distribution (AFM/TBF) | 0.36±0.04 | 0.37±0.05 | 0.09 |
| Fitness (ml/min/kg) | 42±7 | 36±6 | <0.001 |
| Fitness (ml/min/LBM) | 55±7 | 51±7 | <0.001 |
| Max HR (b/min) | 189±14 | 184±16 | 0.03 |
| RER | 1.0 ± 0.1 | 1.0 ± 0.1 | 0.64 |
| SBP (mm Hg) | 104±8 | 104±9 | 0.75 |
| DBP (mm Hg) | 60±5 | 60±6 | 0.48 |
| Pulse pressure (mm Hg) | 44±8 | 43±7 | 0.29 |
| Left ventricular mass (g/m) | 53.9±12.0 | 48.3±11.3 | 0.002 |
| Left atrial diameter (mm/m) | 19.9±2.4 | 19.5±2.0 | 0.22 |
| FABP4 (AU) | 1.86±0.55 | 2.12±0.54 | 0.003 |
| Tanner stage score | 1.0 ± 0.0 | 1.0 ± 0.2 | 0.06 |
| | | | |
| **Follow-up** | **Boys (n=84)** | **Girls (n=68)** | |
| Age (yrs) | 11.9±0.6 | 11.8±0.6 | 0.16 |
| Height (cm) | 152±8 | 153±8 | 0.31 |
| Body Mass (kg) | 43.2±8.6 | 43.9±9.1 | 0.62 |
| BMI (kg/m$^2$) | 18.5±2.8 | 18.6±3.2 | 0.97 |
| Increase in TBF (kg) | 2.1±2.6 | 2.2±2.4 | 0.95 |
| Increase in AFM (kg) | 1.0±1.2 | 1.1±1.5 | 0.48 |
| Increase in percent body fat (%) | 1.4±4.0 | 0.0±3.8 | 0.03 |
| Change in fat distribution | 0.02±0.03 | 0.03±0.15 | 0.32 |
| Tanner stage score | 2.3±0.9 | 2.7±0.8 | 0.007 |

**Table 2.** Partial correlations, sex adjusted, between adipocyte fatty acid-binding protein versus different baseline measurements and change in body fat measurements at follow-up. Lean body mass (LBM). * Indicates significant (P<0.05) correlation.

| **Variable** | **n=170** |
|---|---|
| **Baseline** | |
| Age | -0.02 |
| Height | 0.16* |
| Body mass | 0.59* |
| BMI | 0.66* |
| ln Total body fat (TBF) | 0.70* |
| ln Percent body fat | 0.68* |
| ln Abdominal fat (AFM) | 0.69* |
| Fat distribution (AFM/TBF) | 0.49* |
| Fitness (ml/min/kg) | -0.39* |
| Fitness (ml/min/LBM) | 0.07 |
| Systolic blood pressure | 0.23* |
| Diastolic blood pressure | 0.04 |
| Pulse pressure | 0.23* |
| Left ventricular mass | 0.28* |
| Left atrial diameter | 0.21* |
| | |
| **Follow-up** | **n=152** |
| Increase in TBF (kg) | 0.29* |
| Increase in AFM (kg) | 0.26* |
| Increase in percent body fat | -0.09 |
| Change in fat distribution | 0.04 |

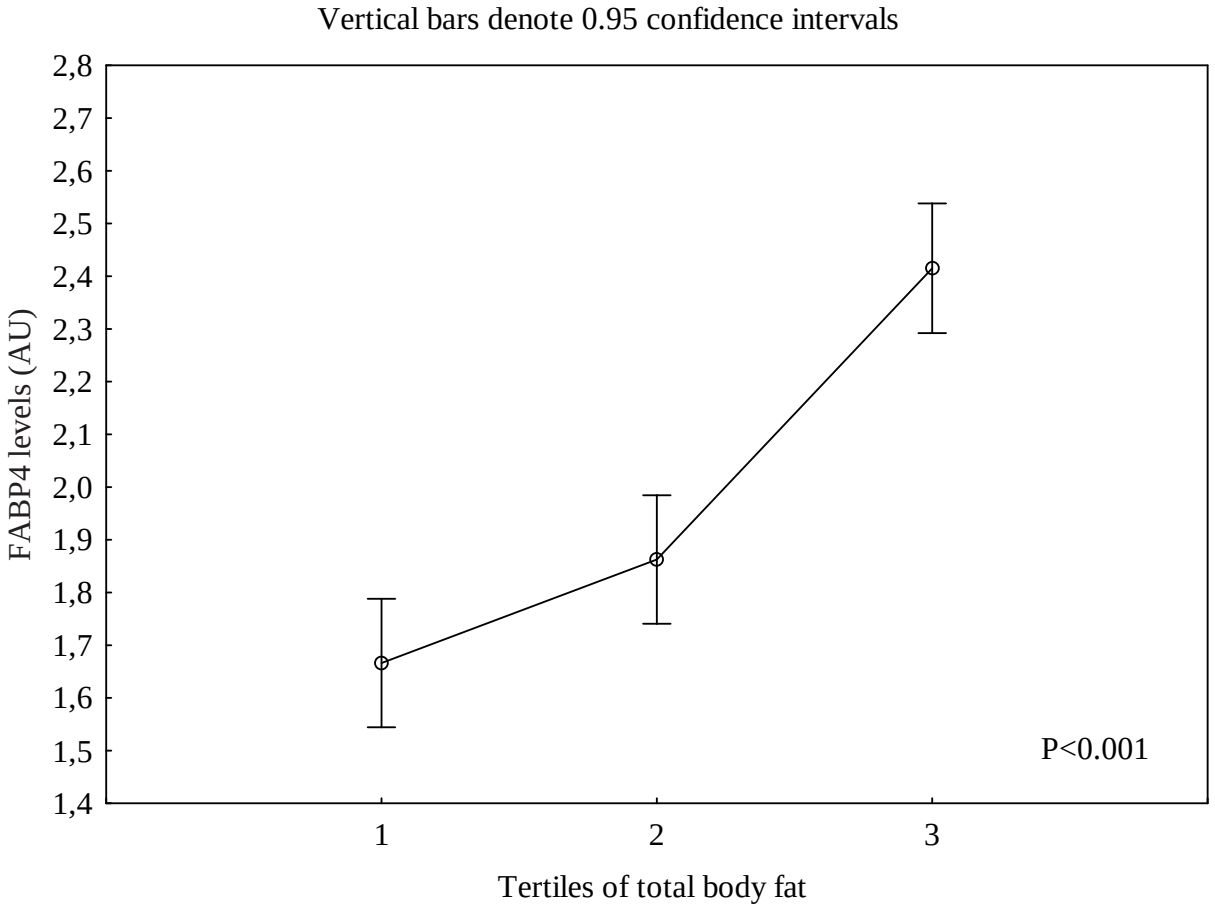
## Figure legends

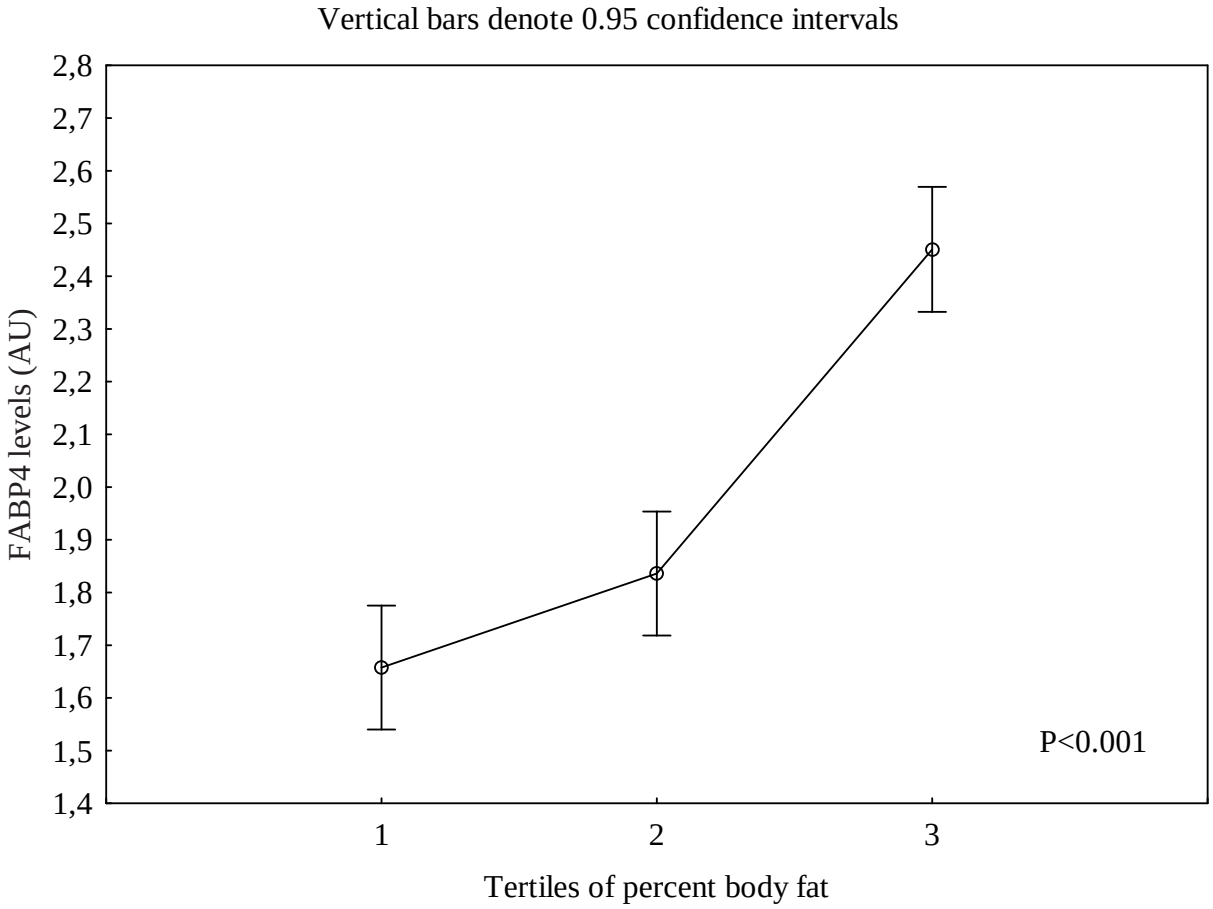
### Figure 1

Adipocyte fatty acid-binding protein (FABP4) levels (±95% confidence intervals) in boys and girls, with adjustment for sex, between the different tertiles (1=lowest, 3=highest) of total body fat (TBF) (A), percent body fat (B), abdominal fat (AFM) (C), and fat distribution (AFM/TBF) (D).

### Figure 2

Adipocyte fatty acid-binding protein (FABP4) levels (±95% confidence intervals) in boys and girls, with adjustment for sex, between the different tertiles (1=lowest, 3=highest) of increase in total body fat (A) or abdominal fat (B).


Vertical bars denote 0.95 confidence intervals
2,8
2,7
2,6
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertiles of total body fat


Vertical bars denote 0.95 confidence intervals
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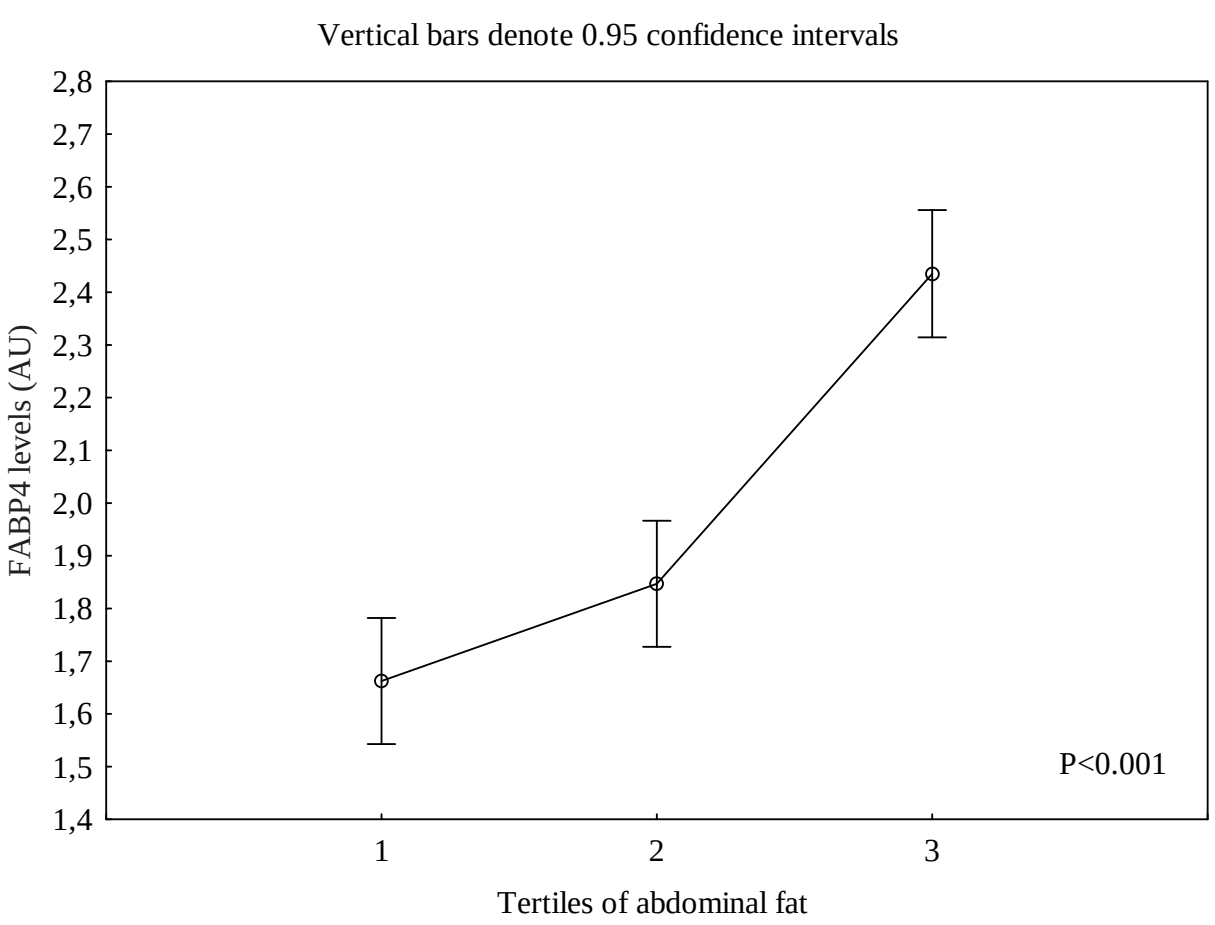
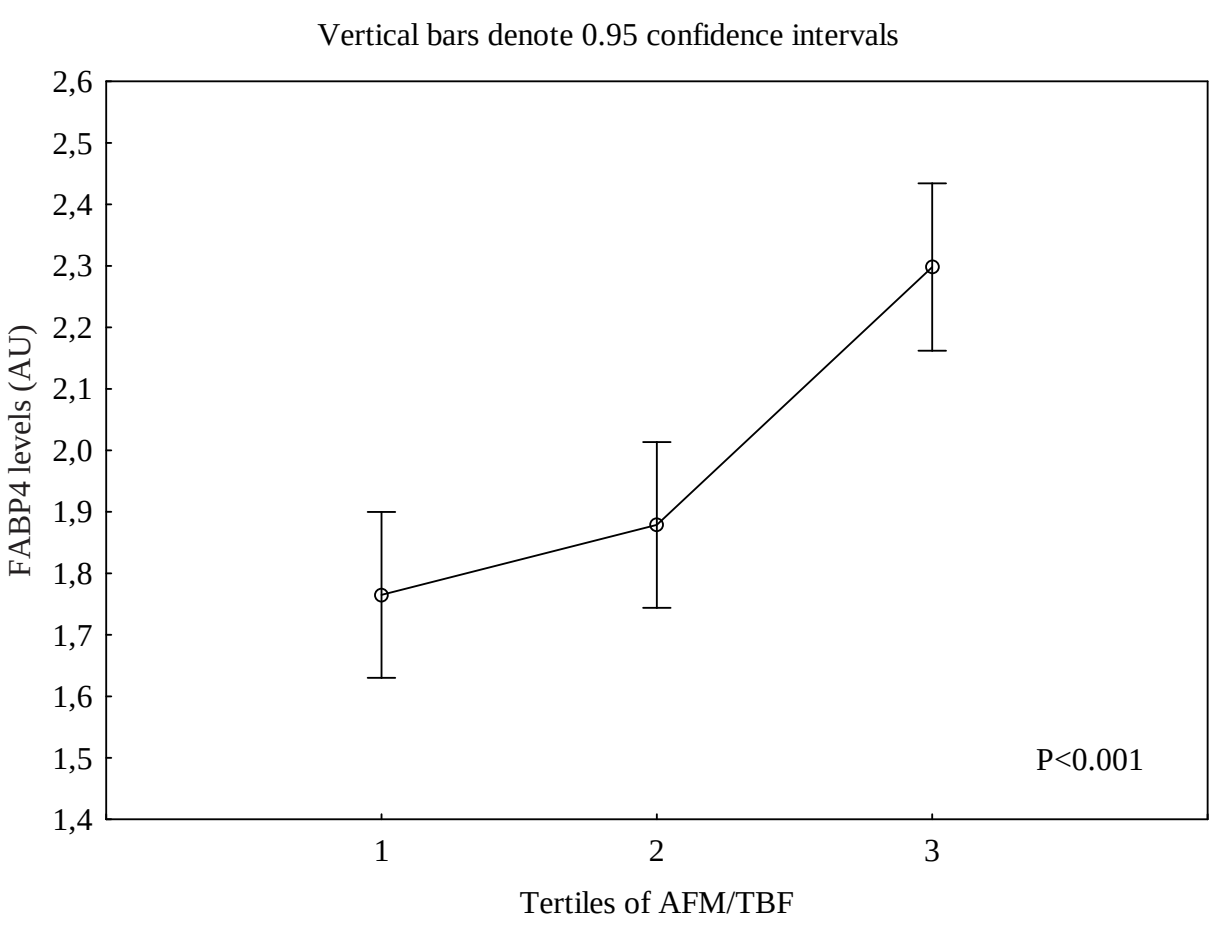
2,7
2,6
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertiles of percent body fat


Vertical bars denote 0.95 confidence intervals
2,8
2,7
2,6
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertiles of abdominal fat


Vertical bars denote 0.95 confidence intervals
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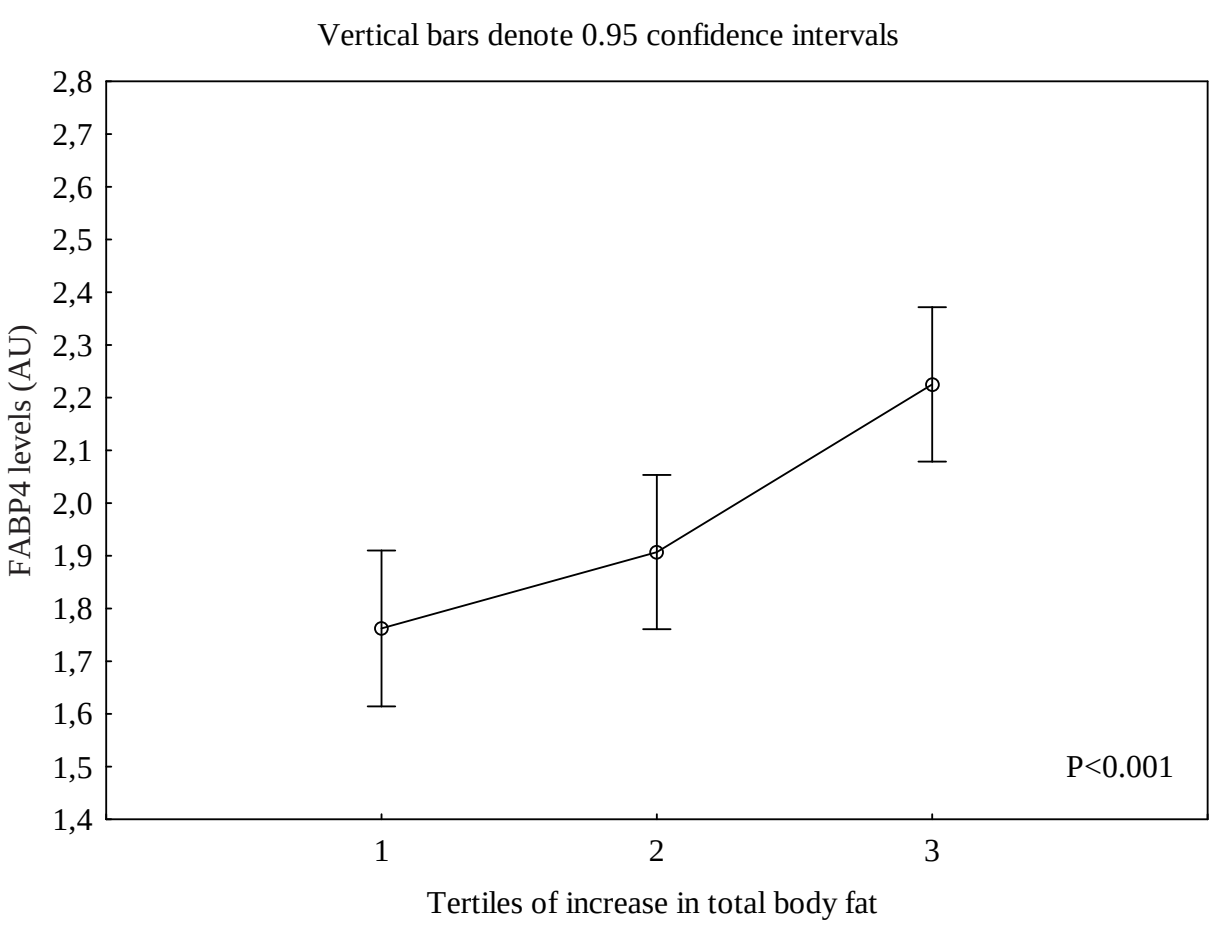
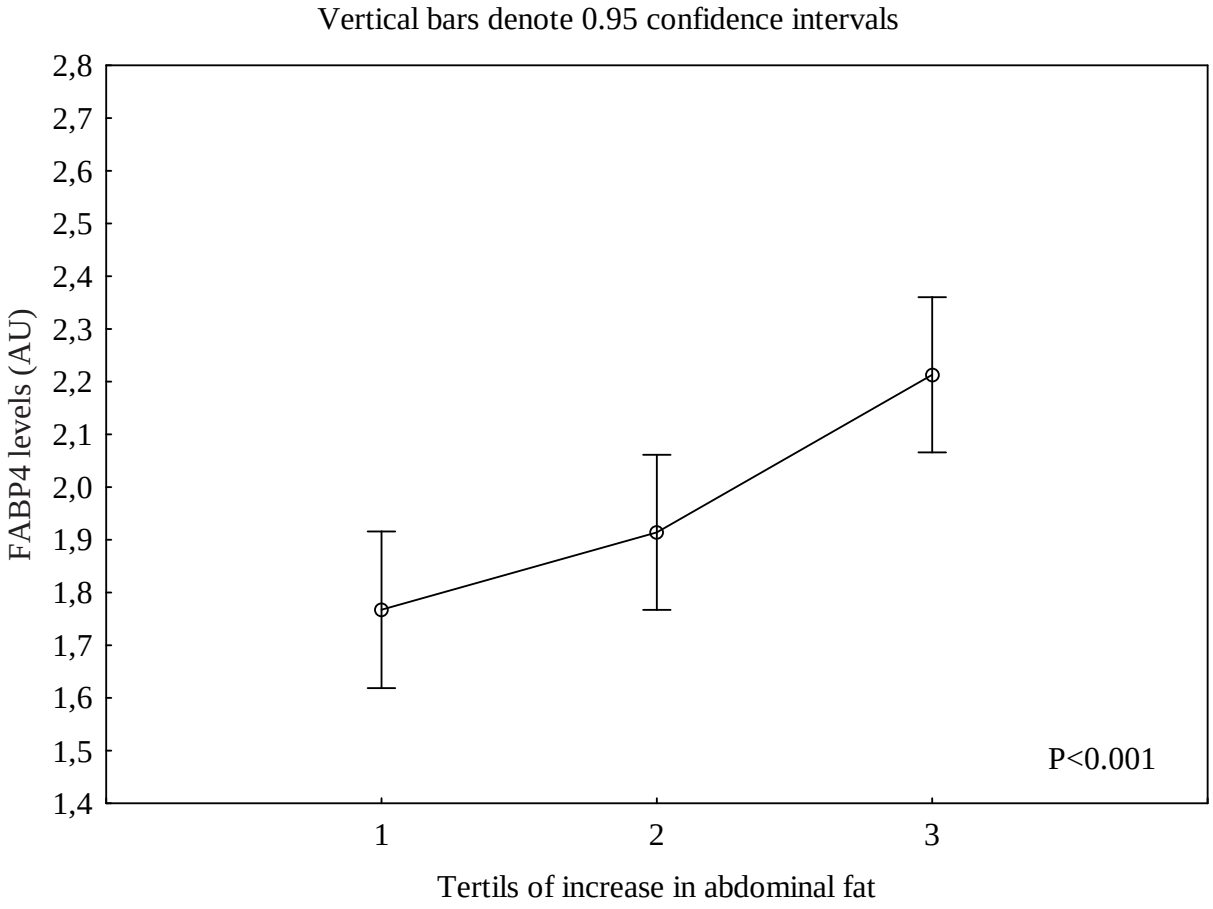
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertiles of AFM/TBF


Vertical bars denote 0.95 confidence intervals
2,8
2,7
2,6
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertiles of increase in total body fat


Vertical bars denote 0.95 confidence intervals
2,8
2,7
2,6
2,5
2,4
2,3
2,2
2,1
2,0
1,9
1,8
1,7
1,6
1,5
1,4
FABP4 levels (AU)
P<0.001
1
2
3
Tertils of increase in abdominal fat