Lipidomic Profiling Reveals Distinct Differences in Plasma Lipid Composition in Overweight or Obesity Adolescence Student

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Abstract

Introduction The relationship between dyslipidemia and obesity has been widely reported, but the global lipid profiles associated with the development of obesity remain to be clarified, especially in the East Asia teenage population.

Methods Mass spectrometry coupled with liquid chromatography was applied to detect the global lipidome in the fasting plasma from 90 Chinese adolescence, including 30 obesity adolescents, 30 overweight adolescents, and 30 adolescents with normal body mass index (BMI). All participants were performed anthropometric measurement by using InBody 770. Clinical biochemical indicators were measured by Cobas Elecsys 601.

Results Both qualitative and quantitative analyses revealed a gradual change in plasma lipid features with obesity students exhibiting characteristics close to overweight students, but they differed significantly from students with normal. The levels of triglyceride (TG), 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin were up-regulated in obesity group, while phosphatidylcholine (PC), phosphatidylethanolamine (PE), LysoPC, LysoPE, and Phosphatidylinositol (PI) were significantly down-regulated in obesity group than in control and overweight individuals. Then conducted venn diagram and selected 8 significant metabolites from the 3 paired comparisons. Most of the selected features significantly correlated with anthropometric measurement.

Conclusions: The altered plasma lipidome in Chinese obesity and overweight students suggests that lipid features may play important role in the pathogenesis of obesity and that such features may provide a basis for evaluating risk and monitoring obesity development.

Background

The prevalence of obesity and metabolic syndrome can now be observed in both adults and young people. These phenomena affect 380 million children and adolescents worldwide [1]. Childhood obesity have a significant impact on both physical and psychological health [2]. Sahoo et al reported that childhood obesity not only can affect children's physical health, social and emotional well-being, but also self-esteem. Moreover, childhood obesity could lead to metabolic, pulmonary, orthopedic, neurological, cardiovascular, hepatic, and menstrual disorders [3]. WHO defines adolescence as a period of growth and development between the ages of 10 and 19 years after childhood and before adulthood.

It is believed that adolescent and childhood obesity have reached epidemic levels [1], and about 17% children are facing obesity problem in the United States [2]. The increased prevalence of overweight and obesity in children and adolescents observed in several countries, as weight gain is an independent predictor for metabolic syndrome development although not seen in all obese individuals. Metabolic syndrome is defined as the presence of a combination of risk factors for cardiovascular disease and type 2 diabetes, including obesity, dyslipidemia, hypertension and glucose intolerance [4]. This condition, although more frequent in adults, can manifest at early ages [5, 6]. Therefore, early diagnosis of possible

obesity and timely control interventions have a beneficial effect on the health of adults and the prevention of cardiovascular diseases.

By comparing the metabolomics characteristics of obesity, Newgard et al. further revealed resistance-related BCAA-related metabolite characteristics, and the accompanying specific increase in C3 and C5 carnitine levels indicates an increase in BCAA catabolism [7]. Longitudinal lipidomics studies in children have shown that maternal obesity increases the risk of offspring obesity, which is a long-term change in plasma ceramide levels [8]. To study the changes of metabolites in blood lipids by lipidomics, caloric restriction and improvement of metabolic syndrome following fish oil intake were predicted, and potential lipid metabolites were identified [9]. Pawelzik et al. performed lipidomic analysis of urine samples from obese people and identified the relationship between urinary prostaglandin levels and obesity-related dyslipidemia, abdominal obesity, and insulin resistance [10].

Conventional data-dependent acquisition (DDA) mass spectrometry (MS) mode has been widely used in lipidomic studies, where parameters are detected to minimize duplicate precursor ions and can be optimized to identify complex lipid molecules [11]. However, DDA performance has some inherent limitations, such as limited dynamic range, bias against highly abundant ions, and long duty cycles with increasing sample complexity. A data independent acquisition (DIA) strategy was recently developed to alleviate the limitations of the DDA model [12], it improves detection sensitivity and analytical reproducibility. However, the independent data acquisition method is not easy to apply by lipidomics, because the annotation of MS features and the estimation of false discovery rate in large and complex lipid data sets require more sophisticated software and integrated reference databases [13].

Here, we conducted nontargeted lipidomics analysis of 90 Chinese adolescence students, including 30 obesity students, 30 overweight students, and 30 students with normal BMI, using DIA-based liquid chromatography–tandem mass spectrometry (LC-MS/MS). By using statistical business and in-house software to analyze highly complex data sets, we demonstrate that compared with overweight and normal students, obese students in China have significant changes in lipids in plasma. In addition, we identified several lipid characteristics, including TG, 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin, PC, PE, LysoPC, LysoPE, and PI, which are potential indicators for predicting obesity risk.

Material And Methods

Study population

Nighty teenagers from junior middle school took part in the study (Beijing 9th Middle School, aged between 12 and 13). All the participants signed informed consent with all the measurement in this research which they have to complete. The volunteers with serious diseases and special diet or weight change (> 2.5 kg in one month) were excluded. The trial was approved by the Ethic Committee at the Lu-

he Hospital affiliated Capital Medical University. All participants were included with no change of their eating habits and their habits related to the physical activity.

Data collection and anthropometric measurement

The participants had to take anthropometric measurement by using InBody 770 (InBody Co. Ltd., Seoul, Republic of Korea). We evaluated the collected data from the anthropometric measurements statistically and graphically in Microsoft Office Excel 2010 (Los Angeles, CA, USA). In this study, blood was allowed to coagulate at 4℃ and serum was separated by centrifugation for 15 min at 3,000 rpm. Serum TSH, FT4 and FT3 were tested with an electrochemiluminescence immunoassay (ECLIA) using an Abbott Architect I2000 (Abbott Diagnostics, Abbott Park, IL, USA). Clinical biochemical indicators were measured by Cobas Elecsys 601 (Roche Diagnostics, Switzerland). According to individual BMI values, they were divided into 3 group: values between 16–20 kg/m^2 are control group, values between 20–26 kg/m^2 are overweight group, values between 26–37 kg/m^2 are obesity group. To delineate global lipidomic profiles in Chinese overweight and obesity adolescence, BMI and body fat percent together with the corresponding clinical and phenotypic data were collected from 3 groups in Beijing, China (Additional file 1).

Liquid chromatography–tandem mass spectrometry (LC-MS/MS)

Lipids were extracted from individual plasma samples and then injected into the mass instrument in both positive and negative modes, with pooled extraction quality control (QC) samples at certain intervals. In this project, advanced mass spectrometer Xevo G2-XS QTOF (Waters, UK) is used for mass spectrometry data collection, and commercial software PROGENESIS QI (Version 2.2) (Waters, UK) and independently developed metabonomics R software package metaX are used for statistical analysis of mass spectrometry data, wherein metabolite identification is based on databases HMDB and LipidMaps [14]. Univariate and multivariate analyses were conducted using R statistics software to identify and evaluate the significant metabolites among the groups.

Metabolites extraction method

40 μL of each sample was added to the corresponding 96-well plate; 120 μL of pre-cooled isopropyl alcohol was added, shaken and mixed for 1 min, and then placed in a refrigerator at -20 ℃ for 2 h or overnight; centrifuged 4000 g at 4 ℃ for 30 min; Placed it in a new 96-well plate and diluted it with 225 μL of lipid complex solution (isopropanol: acetonitrile: water = 2: 1: 1); taked 20 μL of each sample and mixed it into QC sample; taked 60 μL of supernatant Transfer to a 96-well microtiter plate, sealed the label, and tested on the machine.

LC-MS parameters

All samples were acquired by the LC-MS system followed machine orders. Firstly, all chromatographic separations were performed using an ultra-performance liquid chromatography (UPLC) system (Waters, UK). An ACQUITY UPLC CSH C18 column (100 mm*2.1 mm,1.7 μm, Waters□UK) was used for the separation. The column oven was maintained at 55 ℃. The flow rate was 0.4 mL/min and the mobile

phase consisted of solvent A (ACN: H2O = 60:40, 0.1% formate acid and 10 mM ammonium formate) and solvent B (IPA: ACN = 90:10, 0.1% formate acid and 10 mM ammonium formate). Gradient elution conditions were set as follows: 0 ~ 2 min，40–43% phase B; 2.1 ~ 7 min，50–54% phase B; 7.1–13 min, 70–99% phase B; 13.1–15 min, 40% phase B. The injection volume for each sample was 10 μL.

Mass spectrometer description

A high-resolution tandem mass spectrometer Xevo G2 XS QTOF (Waters, UK) was used to detect metabolites eluted form the column. The Q-TOF was operated in both positive and negative ion modes. For positive ion mode, the capillary and sampling cone voltages were set at 3.0 kV and 40.0 V, respectively. For negative ion mode, the capillary and sampling cone voltages were set at 2 kV and 40 V, respectively. The mass spectrometry data were acquired in Centroid MSE mode. The TOF mass range was from 100 to 2000 Da in positive mode and 50 to 2000 Da in negative mode. And the survey scan time was 0.2 s. For the MS/MS detection, all precursors were fragmented using 19–45 eV, and the scan time was 0.2 s. During the acquisition, the LE signal was acquired every 3 s to calibrate the mass accuracy. Furthermore, in order to evaluate the stability of the LC-MS during the whole acquisition, appropriate standards were run and a quality control sample (Pool of all samples) was also acquired after every 10 samples.

Results

Assessment of clinical characteristics and plasma lipidomic features

The clinical information including physiological and anthropometric indicators of the individuals included in this cohort is summarized in Table 1. The participants were divided into three groups according to their BMI values. The level of SBP, Waist-hip ratio, fat mass, body fat percent and visceral fat area were significantly higher in both overweight and obesity individuals than in control group, with obesity participants exhibiting higher values compared with overweight individuals (Kruskal-Wallis test, $P < 0.001$).

We evaluated both coverage and reproducibility of the non-targeted lipidomic data on our sample. Using Progenesis QI 2.0 and metaX, the non-targeted metabolomics analysis yielded 51135 positive ion mode (Additional file 2) and 8988 negative ion mode (Additional file 3).

Overweight and obesity-related features

Because of the observed effects of obesity on lipid profiles, we performed a blocked Kruskal-Wallis test, using obesity group as the blocking factor, followed by Dunn's hoc test for paired comparisons. As shown in Additional file 4 and 5, 876 in positive and 544 in negative features displayed gradually up-regulated among the 3 groups. Also, there are 1081 in positive and 353 negative features showed down-regulated in Additional file 6 and 7. Of these, there are lipid or lipid-like compounds, also including organooxygen

compounds, amino acids, peptides, and analogues, benzyl alcohols, glycerophospholipids and triacylglycerol. As shown in Fig. 1, paired comparisons revealed that 460 features (290 features in Additional file 8 positive and 170 features in Additional file 11 in negative) exhibited significant differences between control and obesity group, whereas 231 and 244 features (Additional file 9 and 12, Additional file 10 and 13 in both positive and negative, respectively) showed obvious differences between overweight versus control group and obesity group, respectively ($P < 0.05$). Of these significant changed metabolites, we screened out eight (six positive and two negative) metabolites with significant differences in expression among the three groups. The number of variables distinguishing overweight and obesity suggested that changes in a large fraction of the lipid profiles in overweight and obesity were shared, implying that compared with control group, the overweight and obesity group shares similar metabolites.

To quantify the differential features among the 3 groups, all detected features were assessed using criteria: 1) variable importance of the projection (VIP) > 1.0 estimated by partial least squares discriminant analysis (PLS-DA); 2) fold change in mass intensity ≥ 1.2 or ≤ 0.83; 3) $P < 0.05$.

Table 1

Basic characteristics of three groups in the study.

Variables	Control (n = 30)	Overweight (n = 30)	Obesity (n = 30)	P value [b]	Obesity vs Overweight [c]	Obesity vs Control [c]	Overweight vs Control [c]
Gender (female %), no. (%) [a]	18 (60.00)	16 (53.33)	14 (46.67)	0.594	——	——	——
Age, year	12.50 ± 0.51	12.73 ± 0.45	12.77 ± 0.47	0.058	0.958	0.072	0.132
BMI, Kg/m^2	17.49 ± 1.41	23.76 ± 1.00	29.89 ± 3.17	< 0.0001	< 0.0001	< 0.0001	< 0.0001
SBP, mmHg	111.93 ± 9.77	120.27 ± 7.18	123.13 ± 6.23	< 0.0001	< 0.0001	< 0.0001	0.339
DBP, mmHg	68.13 ± 6.77	68.73 ± 4.68	70.07 ± 7.10	0.477	0.69	0.46	0.927
TG, mmol/L	0.88 ± 0.36	1.08 ± 0.67	1.12 ± 0.61	0.207	0.964	0.225	0.342
CHO, mmol/L	4.16 ± 0.76	4.03 ± 0.80	4.34 ± 0.77	0.297	0.268	0.631	0.796
HDL, mmol/L	1.39 ± 0.29	1.24 ± 0.22	1.22 ± 0.20	0.015	0.885	0.018	0.061
LDL, mmol/L	2.32 ± 0.53	2.35 ± 0.61	2.71 ± 0.66	0.031	0.069	0.048	0.987
Waist-hip ratio	0.79 ± 0.03	0.85 ± 0.04	0.91 ± 0.05	< 0.0001	< 0.0001	< 0.0001	< 0.0001
FBG, mmol/L	5.52 ± 0.37	5.56 ± 0.42	5.60 ± 0.42	0.740	0.907	0.718	0.933
Fat mass, Kg	9.00 ± 3.33	19.70 ± 4.05	28.82 ± 6.96	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Body fat percent, %	19.86 ± 6.06	31.63 ± 5.44	38.00 ± 6.60	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Viseral fat area, cm^2	38.78 ± 14.26	88.76 ± 24.86	138.81 ± 39.78	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Values are given as mean ± SD or number of individuals (%). BMI: body mass index; SBP: systolic pressure; DBP: diastolic pressure; TG: triglyceride; CHO: cholesterol; HDL: high density lipoprotein; LDL: Low density lipoprotein; FBG: fast blood glucose.

a P value of chi-square test.

b P value of Kruskal–Wallis test.

c P-value of Dunn's post hoc test.

Comparision between control and overweight, overweight and obesity, and cntrol and obesity using random forest classifier and ROC curve

As the qualitative and quantitative analyses revealed significant differences in the metabolites levels between the 3 groups and indicated a gradual change from control to obesity via overweight, we investigated if the metabolites could predict risk of further obesity development. To assess this possibility, we used a random forest classifier.

As illustrate in Fig. 1, 8 metabolites were generated. The relationships among the 3 groups were analyzed by random forest classifier and receiver operating characteristic (ROC) curve. Figure 2A-C showed that an area under the ROC curve (AUC) is 61.90% (95% confidence interval (CI) = 42.00–85.60%), 62.80% (95% CI = 21.50–86.50%), 74.30% (95% CI = 56.00–91.00%) between control and overweight, overweight and obesity, and control and obesity in down-regulated both positive and negative ion mode. For up-regulated, the AUC is 59.70% (95% CI = 19.50–82.50%), 65.40% (95% CI = 34.10–75.50%), 72.10% (95% CI = 49.00–93.50%) in Fig. 2D-F. Together, these results indicate that the lipidomic profiles are regulated in a complex manner during development of overweight and obesity.

(A-F) ROC and AUC for validation set with Control and Overweight, Overweight and 0besity, and Control and Overweight, respectively. The model was trained using decreased and increased intensity of the detected features from positive and negative ion mode

in the training set among control, overweight and obesity (n = 30).

The level of selected metabolites in control, overweight and obesity groups

As illustrated in Fig. 1, 8 metabolites were selected from both positive and negative ion mode lipidomic profiling. Then the expression of selected metabolites was shown in Fig. 3. Figure 3A and Fig. 3B indicated that 6.10_861.5490 m/z and 1.82_480.3095 m/z in negative ion mode were gradually decreased in control, overweight and obesity groups. Figure 3D and Fig. 3H exhibited 1.11_396.2412 m/z and10.13_949.7263 m/z in selected positive ion mode were gradually increased in control, overweight and obesity groups. However, 4.86_902.5761 m/z was gradually decreased in Fig. 3E, 4.84_530.4012n and 4.96_546.3962n peaked in overweight group (Fig. 3F-G). In summary, the development of obesity may go through the process of overweight in most cases, but it may directly develop into obesity through the alterations of some lipid metabolites.

(A) and (B) showed negative ion modes level in control, overweight and obesity groups. (C-G) showed positive ion modes level in control, overweight and obesity groups.

Correlations between selected metabolites with clinical parameters

In the body of overweight and obese people, metabolism is inevitably changed. Hence, the metabolites were also changed. To investigate the relationship between selected metabolites and clinical parameters, we performed a correlation analysis between them. As shown in Fig. 4A, 6.10_861.5490 m/z was negatively with BMI, visceral fat area, body fat percent, and waist/hip ratio. 1.82_480.3095 m/z was negatively with BMI, visceral fat area, body fat percent, and waist/hip ratio, but positively with triglyceride in Fig. 4B. 4.84_530.4012n was negatively with total cholesterol (CHO) in Fig. 4C. 1.11_396.2412 m/z was positively with BMI, visceral fat area, and waist/hip ratio in Fig. 4D. 4.86_902.5761 m/z was negatively with BMI, but positively with triglyceride. (Fig. 4E) 10.13_949.7263 m/z was positively with BMI, visceral fat area, waist/hip ratio, triglyceride, and body fat percent.

1. 6.10_861.5490 m/z was negatively with BMI, visceral fat area, body fat percent, waist/hip ratio, and HDL. (B) 1.82_480.3095 m/z was negatively with BMI, visceral fat area, body fat percent, and waist/hip ratio. (C) 4.84_530.4012n was negatively with cholesterol. (D) 1.11_396.2412 m/z was positively with BMI, visceral fat area, body fat percent, and waist/hip ratio. (E) 4.86_902.5761 m/z was negatively with BMI, but positively with triglyceride. (F) 10.13_949.7263 m/z was positively with BMI, body fat percent, visceral fat area,
2. FT3, waist/hip ratio, and triglyceride.

Phospholipids phosphatidylcholine (PC) and phosphatidylethanolamine (PE) are the two most abundant phospholipid species in eukaryotic cells [15]. Lysophosphatidylcholine (LysoPC), an important signaling molecule and fatty acid carrier, constitutes 5–20% of total plasma phospholipids [16]. Phosphatidylinositol (PI) plays an important role in cell morphology, metabolic regulation, signal transduction and various physiological functions. 1.82_480.3095 m/z was annotated as PC (15:0/0:0), PE (18:0/0:0), LysoPC (15:0), and LysoPE (0:0/18:0). 6.10_861.5490 m/z was annotated as PI (14:0/22:2(13Z, 16Z))- PI (22:2(13Z,16Z)/14:0) (Additional file 3). 1.11_396.2412 m/z was annotated as 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin; 4.86_902.5761 m/z was annoted as PI (18:0/20:5 (5Z,8Z,11Z,14Z,17Z)); 10.13_949.7263 m/z was annoted as TG (20:4 (5Z,8Z,11Z,14Z) /20:3(5Z,8Z,11Z) /18:3 (9Z,12Z,15Z)). The levels of TG, 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin were up-regulated in obesity group, while PC, PE, LysoPC, LysoPE, and PI were significantly down-regulated in obesity group than in control and overweight individuals (Additional file 2).

Discussion

Due to the increased prevalence of obesity in children and adolescents, various studies have been conducted to discover which associations and risk factors increase the likelihood of obesity in children. Although it is still difficult to fully grasp all the risk factors related to obesity, it is of great significance to control and prevent obesity by combining diet, exercise, physiological factors and psychological factors [2]. The short-term and long-term effects of obesity on children's health are a major issue due to adverse psychological and health consequences [17]. Potential negative psychological outcomes are depressive symptoms, poor body image, low self-esteem, risk of eating disorders, and behavioral and learning

problems; negative health consequences include insulin resistance, type 2 diabetes, asthma, hypertension, and nonalcoholic steatohepatitis [17, 18]. Obese children are more likely to become obese adults, and therefore increase their risk of multiple diseases before they even reach puberty [18].

The human lipidomic profile reflects lipid metabolism, including the early phase of pathophysiological changes associated with diseases. Wang et al. observed a significant reduction in the levels of five lysophosphatidylcholines (LPC) species (LPC18:2, LPC18:1, LPC20:2, LPC20:1, and LPC20:0) in the obese group compared with the normal-weight group [19]. In addition, lower total LPC, LPC18:0, LPC18:2, and LPC20:4 levels were measured in obese and obese subjects with type 2 diabetes than in nonobese adults. A difference in the LPC profile was not observed between obese individuals and obese subjects with type 2 diabetes [20]. Moreover, Wallace et al. reported associations between the levels of several LPC species, BMI, and inflammatory markers [21]. The authors identified higher levels of LPC14:0 and LPC18:0 and a lower concentration of LPC18:1 in obese subjects compared with lean subjects [22].

Obesity can be estimated in several ways: Body mass index (BMI), the ratio of weight to squared height [23], is used as the most common indicator of obesity. It is convenient and simple, but it can cause changes in cardiovascular and metabolic performance between individuals, but there are alternative methods of body fat distribution. Higher WHR indicates more intraperitoneal cavity and is associated with a higher risk of type 2 diabetes, cardiovascular disease and mortality [24]]. At the same time, waist circumference can also be used. Similar to WHR [25], it is considered a more direct and reliable method. Generally, body fat percentage (BFP) is a method in the body to measure the ratio of adipose tissue to lean meat and water [26], and most are determined using bioelectrical impedance. BFP is not related to BMI, it is associated with an increase in all-cause mortality, and it is generally suggested to estimate obesity better than BMI [27]. Therefore, this study aimed at Chinese teenagers, a group with relatively stable diet and lifestyle, carried out a lipidomics study to observe the development process of obesity and to screen out some biochemical indicators for predicting obesity.

In the present study, the levels of TG, 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin were up-regulated in obesity group, while PC, PE, LysoPC, LysoPE, and PI were significantly down-regulated in obesity group than in control and overweight individuals. 1.82_480.3095 m/z was annotated as PC (15:0/0:0), PE (18:0/0:0), LysoPC (15:0), and LysoPE (0:0/18:0). 6.10_861.5490 m/z was annotated as PI (14:0/22:2(13Z, 16Z))- PI (22:2(13Z,16Z)/14:0) (Additional file 3). According to the Fig. 1, eight metabolites generated only in 1.11_396.2412 m/z was annotated as 18-Hydroxycortisol, Isohumulinone A, and 11-Dihydro-12-norneoquassin; 4.86_902.5761 m/z was annoted as PI (18:0/20:5 (5Z,8Z,11Z,14Z,17Z)); 10.13_949.7263 m/z was annoted as TG (20:4 (5Z,8Z,11Z,14Z) /20:3(5Z,8Z,11Z) /18:3 (9Z,12Z,15Z)) (Additional file 2). These data suggested that the development of obesity may does not have to be through overweight, and it may develop directly to obesity due to some changes in lipid metabolism.

There are also some limitations in our study. First of all, it was a cross-sectional study which only addressed the alterations of lipidomic profiling in normal, overweight and obesity students. Furthermore,

subjects were selected into groups just according to BMI rather than selected randomly, therefore, this can produce selection bias. In addition, there is a small sample study. So based on the above limitations, more large-scale population studies are still needed in the future investigation.

Conclusions

In summary, the altered plasma lipidome in Chinese obesity and overweight students suggests that lipid features may play important role in the pathogenesis of obesity and that such features may provide a basis for evaluating risk and monitoring obesity development.

Abbreviations

BMI: body mass index; SBP: systolic pressure; DBP: diastolic pressure; TG: triglyceride; CHO: cholesterol; HDL: high density lipoprotein; LDL: Low density lipoprotein; FBG: fast blood glucose. PC: phosphatidylcholine; PE: phosphatidylethanolamine; PI: phosphatidylinositol; DDA: data-dependent acquisition; DIA: data-independent acquisition; LC-MS/MS: liquid chromatography-tandem mass spectrometry; MS: mass spectrometry; UPLC-MS: ultra-performance liquid chromatography–mass spectrometry; VIP: variable importance of the projection.

Declarations

Ethical Approval and Consent to participate

All the participants signed informed consent with all the measurement in this research, and the trial was approved by the Ethic Committee at the Beijing Luhe Hospital affiliated Capital Medical University.

Consent for publication

All authors agree to publish this article in the journal of Lipids in Health and Disease.

Availability of data and material

The author has produced the original data described in the manuscript, which can be obtained free of charge by any scientist who wants to use it, without violating the confidentiality rules of the participants.

Competing interests

The authors declare that they have no conflict of interests.

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Authors' contributions

LyY performed data analysis and interpretation and wrote the first draft of the manuscript. RlY conducted the research and contributed to data interpretation and writing and editing the manuscript. DZ is the chief investigator of the trial and planned and designed the study, obtained funding, oversaw data collection and analysis, and contributed to data interpretation and writing and editing the manuscript. KY takes responsibility for data integrity and accuracy. All authors meet the ICMJE criteria for authorship, and have approved the final version of the manuscript.

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Conflicts of interest

The authors declare that they have no conflict of interests.

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Figures

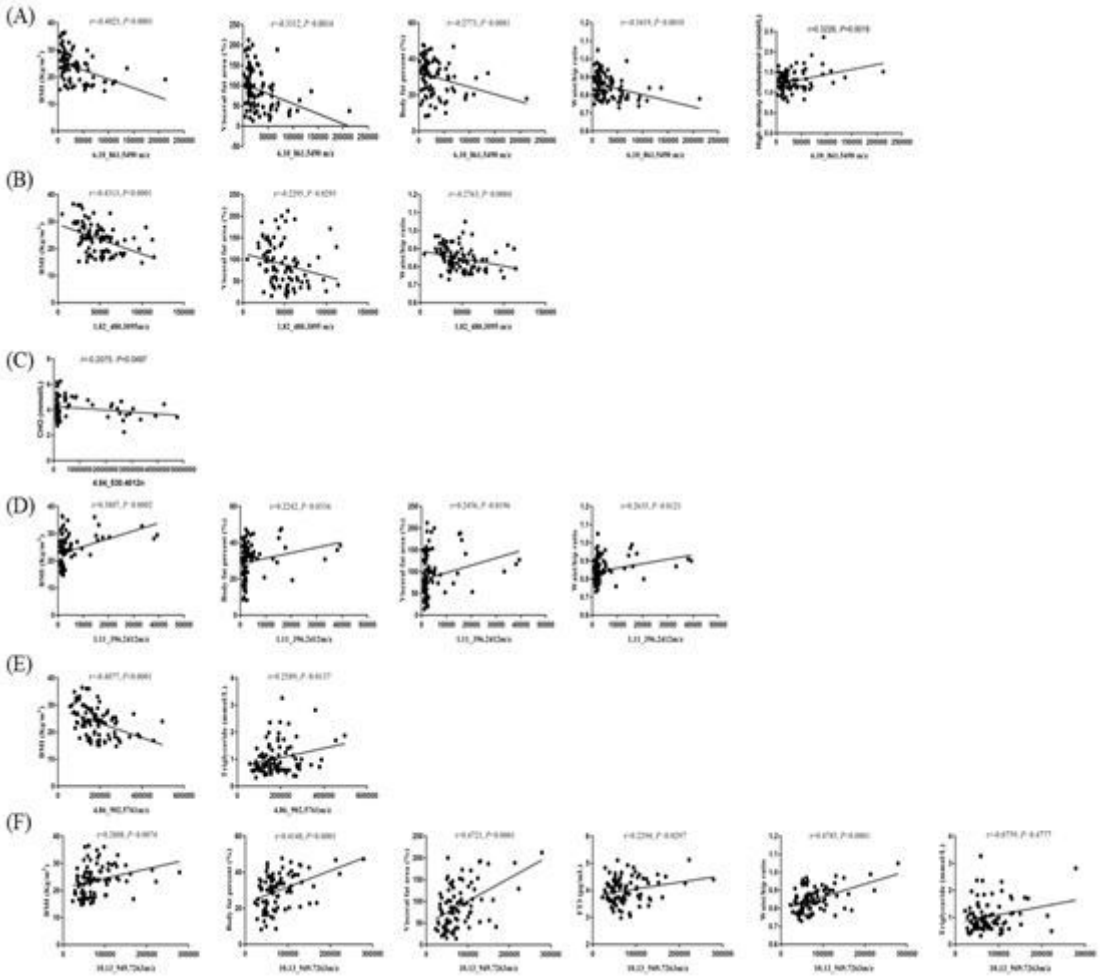

Figure 1

Correlation between clinical parameters and selected features. (A) 6.10_861.5490m/z was negatively with BMI, visceral fat area, body fat percent, waist/hip ratio, and HDL. (B) 1.82_480.3095m/z was negatively with BMI, visceral fat area, body fat percent, and waist/hip ratio. (C) 4.84_530.4012n was negatively with cholesterol. (D) 1.11_396.2412m/z was positively with BMI, visceral fat area, body fat percent, and waist/hip ratio. (E) 4.86_902.5761m/z was negatively with BMI, but positively with triglyceride. (F) 10.13_949.7263m/z was positively with BMI, body fat percent, visceral fat area, (B) FT3, waist/hip ratio, and triglyceride.

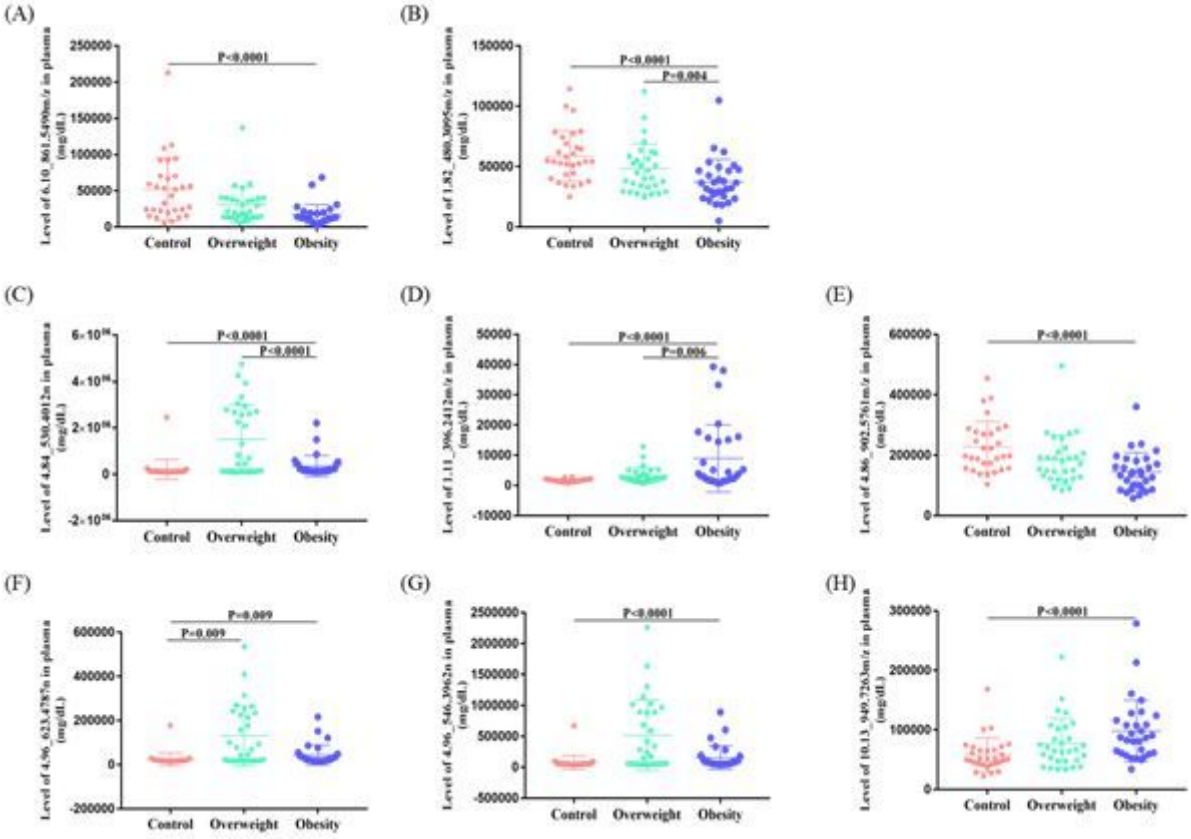

Figure 2

Level of selected metabolites in control, overweight and obesity groups. (A) and (B) showed negative ion modes level in control, overweight and obesity groups. (C-G) showed positive ion modes level in control, overweight and obesity groups.

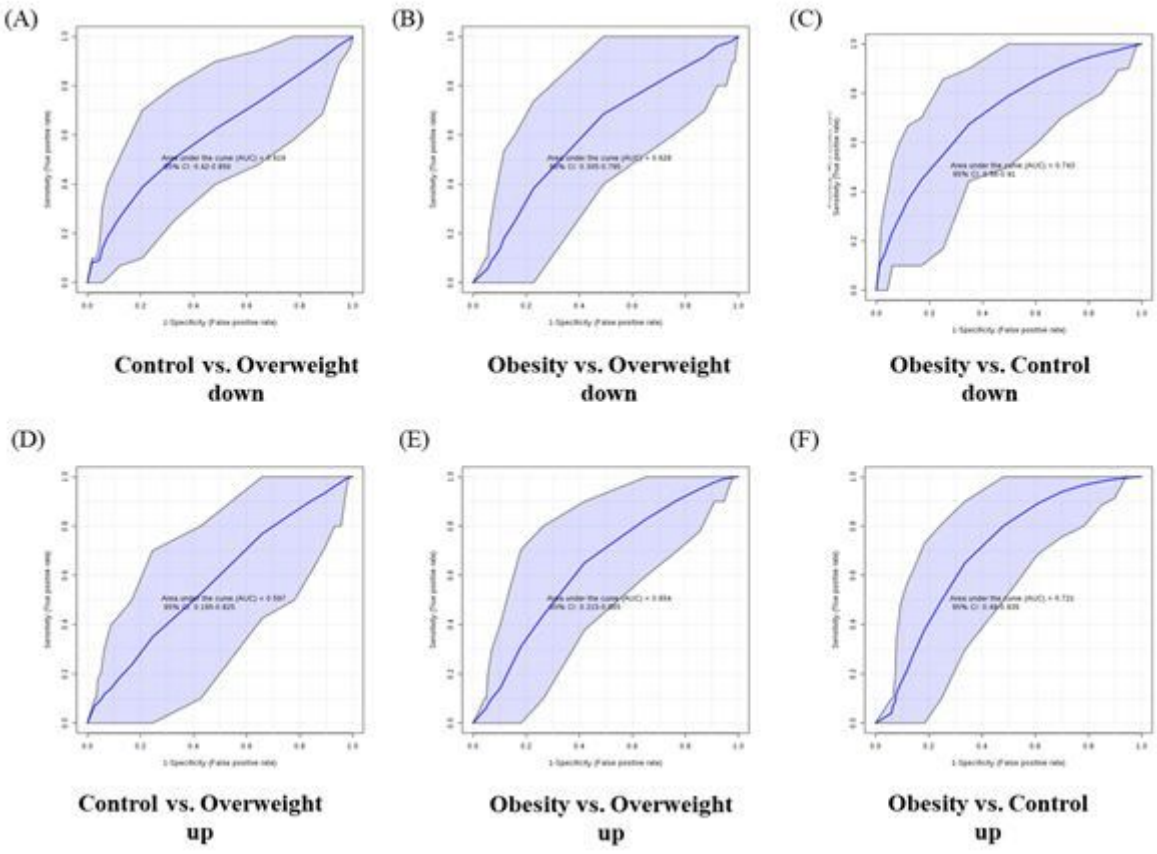

Figure 3

Receiver operating characteristic curve and area under the ROC curve in the training set.

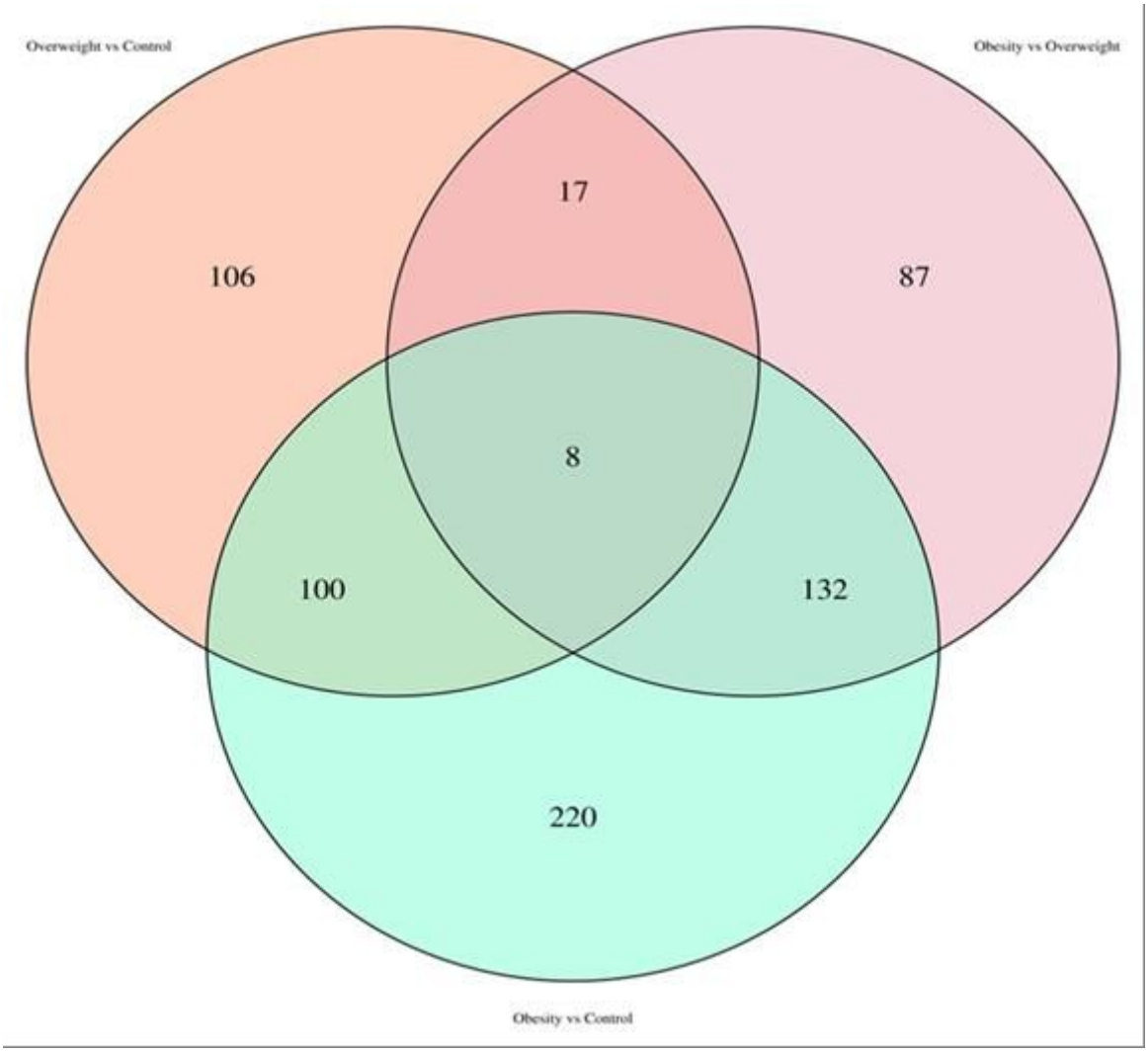

Figure 4

Venn diagram of significant metabolites from the 3 paired comparisons. Venn diagram depicting the number of significant metabolic features from 3 paired comparisons (the direction of change was ignored, P < 0.05, Dunn's post hoc test).

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