METABOCATEGORIESLOMIC ANALYSIS OF PATIENTS WITH CKD 3-5 IN DIFFERENT OF TRADITIONAL CHINESE MEDICINE

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INTRODUCTION AND AIMS: Chronic kidney disease (CKD) is public health problem worldwide. It is very popular using traditional Chinese medicine theory for the diagnosis and treatment of CKD in China. Chinese medicine theory defines some physical symptoms and signs as a corpus and classifies different categories. These categories can help understand the progression of CKD by patients themselves and help physicians evaluate the status of patients promptly. This study used metabolomics anlysis to find the biomarker of patients with CKD 3-5 stage in different categories of traditional Chinese medicine.

METHODS: 60 patients with CKD 3 to 5 and 30 healthy volunteers were recruited. The patients divided to two groups(qi-deficieny and yang-deficieny categories) with Chinese medicine theory by experts according the guideline of Chinese medine, while volunteers as control group. 30 patients were divided into qi-deficieny group, others were divided into Yang-deficieny group. We collected the blood from each patients and volunteers, and detected biochemical parameters and metabolomic analysis. The serum samples and seven blood mix samples (quality control samples) were prepared with deproteinization and filtration, 200μL solution with each sample was used to the analyse machine with a Ultra Performance Liquid Chromatography (UPLC) system coupled online to a Time-of-Flight mass spectrometry (TOF-MS). The parameters consisted of pumping 100% acetonitrile through the pump heads and UPLC column for a minimum of 30 min at a flow rate of 0.4 mL・min^{-1} and a column temperature of 40 °C. The MS source (sample cone and baffle components) was cleaned by sonication in 50/40/10 methanol/water/formic acid for 15 min. All the raw data files were preprocessing with MarkerView software and statistical analysis of metabolomics was using SIMCA-P 11.5 software .

RESULTS: There was no significant difference in age, gender and clinical biochemical parameters(creatinine, Uric Acid, albumin, triglyceride, cholestenone, low density lipoprotein, high density lipoprotein). The PLS-DA model (Figure 1) was presented the different metabolic distribution in different groups. The potential biomarker showed in Table 1.
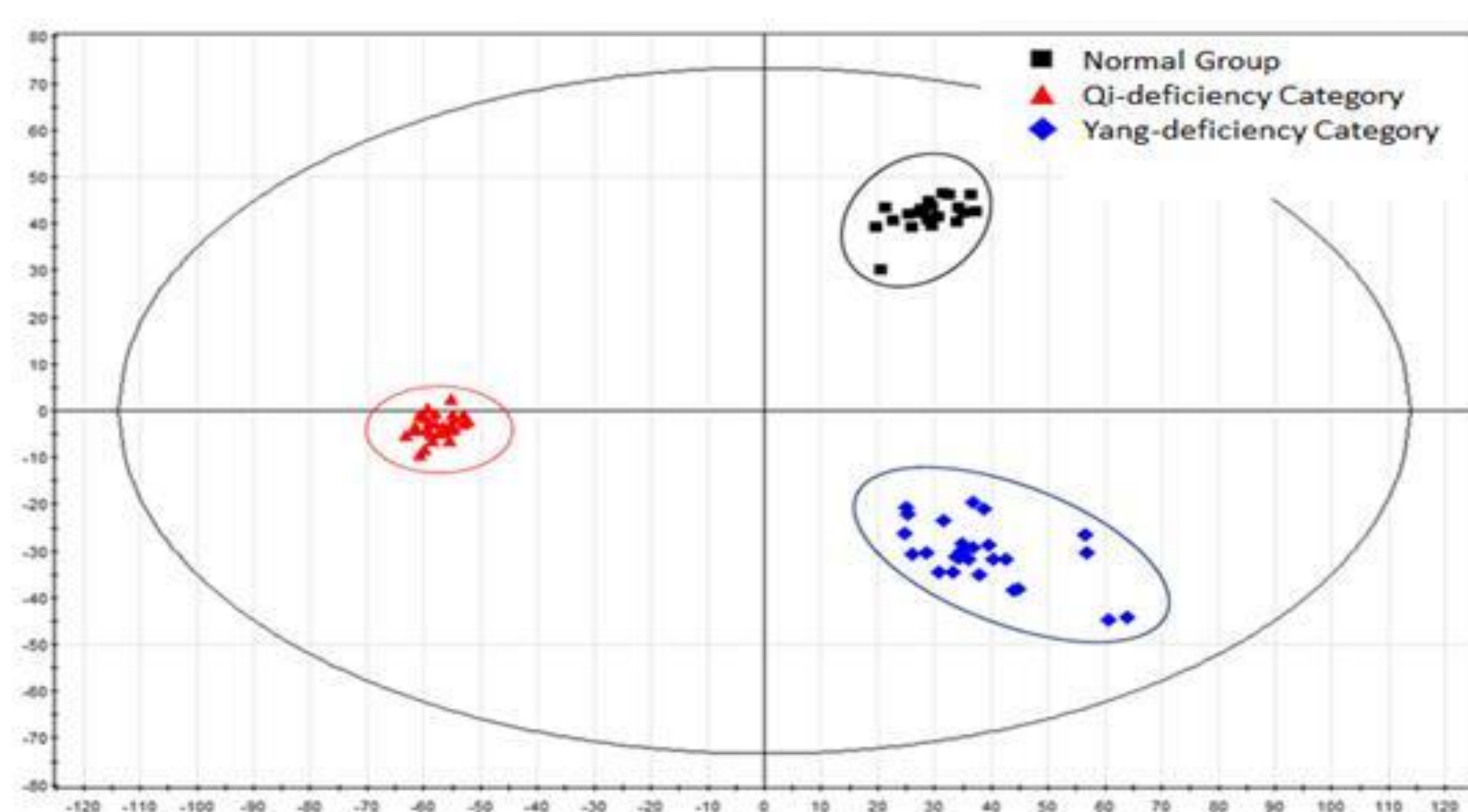

Fig. 1 PLS-DA score plot in each group

Table 1 potential bio-markers

No.	Rt	m/z	Ion	Formula	Identified potential biomarker
1	26.01	312.3292_26.01	[M+ACN+H]+	$C_{18}H_{38}O$	Octadecanol▲
2	12.27	272.2418_12.27	[M+ACN+H]+	$C_{13}H_{28}NO_2$	Capryloylcholine▲
3	22.93	257.2363_22.93	[M+H]+	$C_{14}H_{28}NO_2$	9-Decenoylcholine▲
4	24.98	318.2809_24.98	[M+H]+	$C_{18}H_{39}NO_3$	Phytosphingosine▲
5	25.47	540.5042_25.47	[M+H]+	$C_{33}H_{65}NO_4$	Hexacosanoylcarnitine▲
6	27.49	356.3336_27.49	[M+ACN+H]+	$C_{18}H_{34}O_4$	12,13-DHOME▪
7	20.43	256.2472_20.43	[M+ACN+H]+	$C_{14}H_{30}O$	Tetradecanol▪
8	28.03	218.2000_28.03	[M+H]+	$C_9H_{19}N_3O_3$	γ-glutamyl-L-putrescine▲
9	28.69	230.2326_28.69	[M+H]+	$C_{12}H_{23}NO_3$	N-Decanoylglycine▲
10	21.18	304.2466_21.18	[M+H]+	$C_{14}H_{25}NO_6$	Pimelylcarnitine▲
11	29.09	171.0892_29.09	[M+H]+	$C_8H_{10}O_4$	3,4-Dihydroxyphenylglycol▪
12	26.55	594.5463_26.55	[M+H]+	$C_{38}H_{69}NO_3$	Ceramide (d18:1/20:0)▪
13	24.99	280.2482_24.99	[M+ACN+H]+	$C_{16}H_{24}O_3$	Terpenylisovalerate▪
14	20.85	283.2644_20.85	[M+H]+	$C_{18}H_{34}O_2$	Oleic acid▪
15	20.85	282.2607_20.85	[M+H]+	$C_{18}H_{33}O_2$	Petroselinic acid▪

Note: ▲: Potential bio-markers for Qi-deficiency Category. ▪: Potential bio-markers for Yang-deficiency Category

According the metabolic pathways in PubChem and KEGG. databases , we can know that the potential bio-markers is relevant to lipids, amino acids, linoleic acids and sphingolipids four metabolic pathways.

CONCLUSIONS: The results indicated that there are significant metabolomics differences in patients with CKD 3-5 stage in different categories of traditional chinese medicine. The potential bio-markers is relevant to lipids, amino acids, linoleic acids and sphingolipids four metabolic pathways.