·热带皮肤病研究专栏·

寻常痤疮患者血清脂质代谢组学分析

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摘要：目的 分析中重度痤疮患者与健康对照之间血清脂质代谢组学差异，了解痤疮患者血清脂质代谢特征。**方法** 2019年5月—2020年4月于西南医科大学附属医院皮肤科采集30例中重度痤疮患者血清，同时收集30例年龄、性别、体质量指数匹配的健康对照者血清，采用液相色谱-串联质谱法（liquid chromatograph mass spectrometer, LC-MS）进行血清脂质代谢组学分析。采用偏最小二乘法判别分析（partial least squares discrimination analysis, PLS-DA）对差异表达的脂质代谢物进行多变量统计分析。通过京都基因与基因组百科全书（Kyoto encyclopedia of genes and genomes, KEGG）数据库筛选两组间具有显著差异的代谢途径。利用Mann-Whitney *U*检验方法计算差异代谢产物。采用Spearman相关性分析，分析血清PC（18:2e/20:2）浓度和痤疮严重程度相关性。**结果** PLS-DA结果显示，痤疮患者血清脂质代谢物组成与健康对照呈明显分离趋势，在差异最显著的前30种脂质代谢产物中，痤疮患者组有4种三酰甘油（triacylglycerol, TG）、2种甘油二酯（diacylglycerol, DG）、6种磷脂酰胆碱（phosphatidylcholine, PC）、1种甲基化磷脂酰胆碱（methylated phosphatidylcholine, MePC）、2种鞘磷脂（sphingomyelin, SM）、2种磷脂酰肌醇（phosphatidylinositol, PI）、2种糖基神经酰胺[单己糖神经酰胺（monohexosyl ceramide, Hex1Cer）、二己糖神经鞘氨醇（dihexosyl ceramide, Hex2Cer）]、2种心磷脂（cardiolipin, CL）水平升高（$P<0.05$）。1种DG、2种脑磷脂（cephalin, LPE）、1种二甲基磷脂酰乙醇胺（dimethylphosphatidylethanolamine, dMePE）、1种二甲基磷脂酸（bismethyl phosphatidic acid, BisMePA）、3种磷脂酰乙醇胺（phosphatidyl ethanolamine, PE）、1种神经酰胺（ceramide, Cer）水平降低（$P<0.05$），大部分属于磷脂类代谢产物。Spearman相关性分析显示，血清PC（18:2e/20:2）浓度和痤疮严重程度呈正相关（$r=0.456$, $P=0.004$）。KEGG富集功能分析显示差异脂质代谢产物主要富集的代谢途径包括：鞘脂信号通路、胆固醇代谢、胰岛素抵抗、甘油磷脂代谢，其中，鞘脂信号通路可能发挥着重要作用。**结论** 痤疮患者与健康对照间血清脂质代谢存在明显差异，脂代谢紊乱可能与痤疮的发病相关，但其分子机制仍需进一步的实验探究。

关键词：寻常痤疮；脂类代谢；脂质组学

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Metabolomics analysis of serum lipids in patients with acne vulgaris

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Abstract: Objective To analyze and compare the differences in serum lipid metabolomics between patients with moderate to severe acne and healthy controls to understand the characteristics of serum lipid metabolism in acne patients. **Methods** Serum samples were collected from 30 patients with moderate to severe acne and 30 healthy controls matched for age, gender and body mass index in the Department of Dermatology, the Affiliated Hospital of Southwest Medical University from May 2019 to Apr. 2020. Serum lipid metabolomics was analyzed by liquid chromatography-tandem mass spectrometry. Partial least squares discriminant analysis (PLS-DA) was used for multivariate statistical analysis of differentially expressed lipid metabolites. The metabolic pathways with significant differences between the two groups were screened by Kyoto Encyclopedia of Genes and Genomes (KEGG) database. Using Mann-Whitney U test to calculate differential metabolites. Spearman correlation analysis was used to analyze the correlation between serum PC (18:2e/20:2) concentration and acne severity. **Results** The PLS-DA results showed that the composition of serum lipid metabolites in acne patients was significantly separated from that in healthy controls. Of the top 30 lipid metabolites with the most significant differences, four kinds of triglycerides (TG), two kinds of diglycerides (DG), six kinds of phosphatidylcholine (PC), one kind of MePC, two kinds of sphingomyelin (SM), two kinds of phosphatidylinositol (PI), two kinds of ceramide (monohexosyl ceramide, Hex1Cer;

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dihexosyl ceramide, Hex2Cer), two cardiolipin (CL) were found to be increased in the acne group (P<0.05). The levels of one kind of DG, two kinds of lysophosphatidyl ethanolamines (LPE), one kind of dimethylphosphatidyl ethanolamine (dMePE), one kind of bismethyl phosphatidic acid (BisMePA), three kinds of phosphatidyl ethanolamine (PE) and one kind of ceramide were found to be decreased in the acne group (P<0.05), and most of them belonged to phospholipid metabolites. Spearman correlation analysis showed that serum PC (18:2e/20:2) concentration was positively correlated with acne severity (r=0.456, P=0.004). KEGG enrichment function analysis revealed that the differential lipid metabolites were primarily enriched in metabolic pathways such as sphingolipid signaling pathway, cholesterol metabolism, insulin resistance, glycerophospholipid metabolism, among which the sphingolipid signaling pathway may play an important role. **Conclusion** There are significant differences in serum lipid metabolism between acne patients and healthy controls. Lipid metabolism disorders may be related to the pathogenesis of acne, but it's molecular mechanism still needs further experimental exploration.

Keywords: Acne vulgaris; lipid metabolism; lipidomics

寻常痤疮(acne vulgaris, AV)是一种发生于毛囊皮脂腺单位的慢性炎症性皮肤病[1],累及约85%的12~25岁人群[2],是青少年最常见的皮肤病之一[3]。本病常表现为损容性外观,可对患者生活质量、自尊心和情绪产生负面影响,并增加其焦虑、抑郁和自杀念头的风险[4-7]。虽然目前普遍认为,痤疮的发病与皮脂大量分泌、痤疮丙酸杆菌繁殖、免疫炎症反应等有关,但是其机制仍未完全阐明。研究显示,痤疮患者常伴发肥胖、胰岛素抵抗、代谢综合征等代谢性疾病[8-10],亦有文献报道痤疮患者血清总胆固醇(total cholesterol, TC)、低密度脂蛋白(low-density lipoprotein, LDL)、三酰甘油(triacylglycerol, TG)水平升高[11-12]。但是系统脂质代谢与痤疮发病的关系及潜在机制并不清楚,痤疮患者是否存在系统脂质代谢的问题还需要进一步分析。因此,本研究拟采用色谱-串联质谱法(liquid chromatograph mass spectrometer, LC-MS)分析对痤疮患者及健康对照血清脂质组学进行检测及差异分析,揭露痤疮患者血清脂质代谢特征,为阐明脂质代谢在痤疮发生发展中的作用机制提供新的思路。

1 资料与方法

1.1 一般资料 2019年5月—2020年4月于西南医科大学附属医院门诊部招募符合寻常痤疮诊断标准[13]、未经治疗的寻常痤疮患者30例,采用痤疮综合分级系统(global acne grading system, GAGS)[14]对入组患者的病情严重程度进行评估,将其分为轻度(1~18)、中度(19~30)、重度(31~38)和极重度(≥39)。同时面向社会招募30例18~30岁的健康人作为对照组。记录入组者性别、年龄、体质量指数(body mass index, BMI)等一般人口学资料及GAGS评分。

1.2 纳入标准 诊断为中重度寻常痤疮的患者,年龄18~30岁,BMI 18~25 kg/cm^2,6个月内未系统应用任何药物,自愿签署本试验知情同意书。

1.3 排除标准 有精神疾患者;伴有严重的心、肝、肾功能不全或合并其他严重的内科疾病、肿瘤患者;妊娠期、哺乳期妇女;患者不能配合治疗或不能定期随访。

1.4 血清样本采集及检测 受试者入组时采集2 mL空腹静脉血于非抗凝管中,20~25 ℃静置30 min,以3 000 r/min(离心半径为10 cm)离心15 min获得血清样本,储存于-80 ℃冰箱中。采用全自动生化检测仪(Synchron LX-20, Beckman Coulter, USA)测定空腹静脉血中的丙氨酸转氨酶(alanine aminotransferase, ALT)、天冬氨酸转氨酶(aspartate aminotransferase, AST)、血糖(bloodglucose, Glu)、TC、TG、LDL、高密度脂蛋白(high-density lipoproteins, HDL)、空腹胰岛素(fasting insulin, INS)的水平。根据ELISA试剂盒(美国Promega)的说明进行测量。通过稳态模型的胰岛素抵抗指数(homeostasis model assessment for insulin resistance, HOMA-IR)评估胰岛素抵抗情况。采用LC-MS分析血清中脂质代谢组学变化。

1.5 血清脂质代谢组学分析

1.5.1 样本处理 取200 μL血清样本于EP管中,加入80 μL甲醇和400 μL甲基叔丁基醚(MTBE),涡旋混匀30 s后,超声提取30 min(5 ℃,40 kHz)。将样品静置于-20 ℃,30 min后高速离心(13 000 r/min,离心半径为10 cm,4 ℃)15 min。移取350 μL上清液,在真空浓缩仪中干燥,100 μL复溶液(异丙醇∶乙腈=1∶1)复溶。涡旋混匀 30 s后,冰水浴中40 kHz超声5 min。高速离心(13 000 r/min,离心半径为10 cm,4 ℃)5 min后,移取80 μL上清液至带内插管的进样小瓶中上机分析。

1.5.2 色谱-质谱(LC-MS分析)条件 本次LC-MS分析的仪器平台为Thermo公司的超高效液相色谱串联傅里叶变换质谱UPLC-Q Exactive系统。

色谱条件:2 μL样本经BEH C18色谱柱(100 mm×2.1 mm i.d., 1.7 μm)分离后进入质谱检测。流动相A为10 mmol/L乙酸铵50%乙腈水溶液(含0.1%甲酸),流动相B为2 mmol/L乙酸铵乙腈/异丙醇/水(10/88/2)(含0.02%甲酸)。分离梯度:0~4 min,流动相A从线性65%降至40%,流动相B从线性35%升至60%;4~12 min,流动相A从线性40%降至15%,流动相B线性

从60%升至85%；12~21 min，流动相A从线性15%降至0%，流动相B线性从85%升至100%；21~24 min，流动相A维持0%，流动相B维持100%；24.0~24.1 min，流动相A线性从0%升至65%，流动相B线性从100%降至35%；24.1~28 min，流动相A线性线性维持65%，流动相B线性线性维持35%。流速为0.40 mL/min，柱温为40 ℃。

质谱条件：样品质谱信号采集采用正负离子扫描模式，质量扫描范围：200~2 000 m/z。离子喷雾电压，正离子电压3 000 V，负离子电压3 000 V，鞘气60 psi，辅助加热气20 psi，离子源加热温度370 ℃，20~60 V循环碰撞能。

1.5.3 脂质组学多元统计分析 采用R软件（R4.1.1版本）进行偏最小二乘判别分析（partial least squares-discriminant analysis, PLS-DA）多元统计分析，根据*VIP*值及*t*检验结果，筛选出*VIP*≥1，*P*<0.05的差异代谢物。利用KEGG（Kyoto Encyclopedia of Genes and Genomes）数据库（kegg_v2021.09.18）对差异代谢物进行通路富集分析，预测差异脂质代谢产物参与的代谢途径。

1.6 统计学分析 应用SPSS 20.0统计学软件分析处理数据。符合正态分布的计量数据采用均数±标准差表示，采用卡方检验评估性别差异；两两组间比较，符合正态分布及方差齐性的资料采用*t*检验，不同时满足则采用Mann-Whitney *U*检验分析；采用Spearman相关性分析，分析血清PC（18:2e/20:2）浓度和痤疮严重程度相关性。*P*<0.05为差异有统计学意义。

2 结 果

2.1 两组一般资料比较 纳入30例痤疮患者中男性23例，女性7例，年龄（20.650±3.110）岁，BMI（20.590±1.878）kg/m^2；对照组30例，男性24例，女性6例，年龄（25.400±2.644）岁，BMI（20.086±1.615）kg/m^2。痤疮组和对照组性别、BMI之间差异无统计学意义（*P*>0.05）。对照组年龄高于患者组（*P*<0.05），但所有入组者年龄均符合纳入标准年龄区间要求。痤疮患者与健康对照组ALT、AST、HOMA-IR、INS、Glu、HDL、LDL、TG、TC差异均无统计学意义（*P*>0.05）。见表1。

2.2 脂质组学分析 送检的60例血清标本中，最终一共检测到1 023个可定量的峰，去掉假阳性和噪音后，最后测到258种脂质代谢产物。PLS-DA分析显示，健康对照与痤疮患者间的代谢产物组成之间无论是阴离子还是阳离子，均表现为明显的离散趋势，表明两组血清样本的脂质代谢物组成具有显著差异（图1A、图1B）。进一步对PLS-DA建立的阴、阳离子模型进行置换检验，结果表明模型无过拟合的问题，具有良好的可靠性和有效性（图1C~图1D）。

2.3 痤疮患者与健康对照差异脂质代谢产物比较 设*P*值<0.05，差异倍数值（fold change, FC）>1/*FC*<1以及*VIP*≥1为条件，筛选差异代谢物。两组之间共筛选到191个差异有统计学意义的脂质代谢产物。表2展示了两组间差异最显著的前30种脂质代谢产物及统计学数值。与健康对照组相比，痤疮患者组有4种TG、2种甘油二酯（diacylglycerol, DG）、6种磷脂酰胆碱（phosphatidylcholine, PC）、1种甲基化磷脂酰胆碱（methylated phosphatidylcholine, MePC）、2种鞘磷脂（sphingomyelin, SM）、2种磷脂酰肌醇（phosphatidylinositol, PI）、2种糖基神经酰胺[单己糖神经酰胺（monohexosyl ceramide, Hex1Cer）、二己糖神经鞘氨醇（dihexosyl ceramide, Hex2Cer）]、2种心磷脂（cardiolipin, CL）水平升高（*P*<0.05）。1种DG、2种脑磷脂（cephalin, LPE）、1种二甲基磷脂酰乙醇胺（dimethylphosphatidylethanolamine, dMePE）、1种二甲基磷脂酸（bismethyl phosphatidic acid, BisMePA）、3种磷脂酰乙醇胺（phosphatidyl ethanolamine, PE）、1种神经酰胺（ceramide, Cer）水平降低（*P*<0.05）。其中TG（4:0/6:0/10:1）、TG（6:0/6:0/10:4）差异最大。

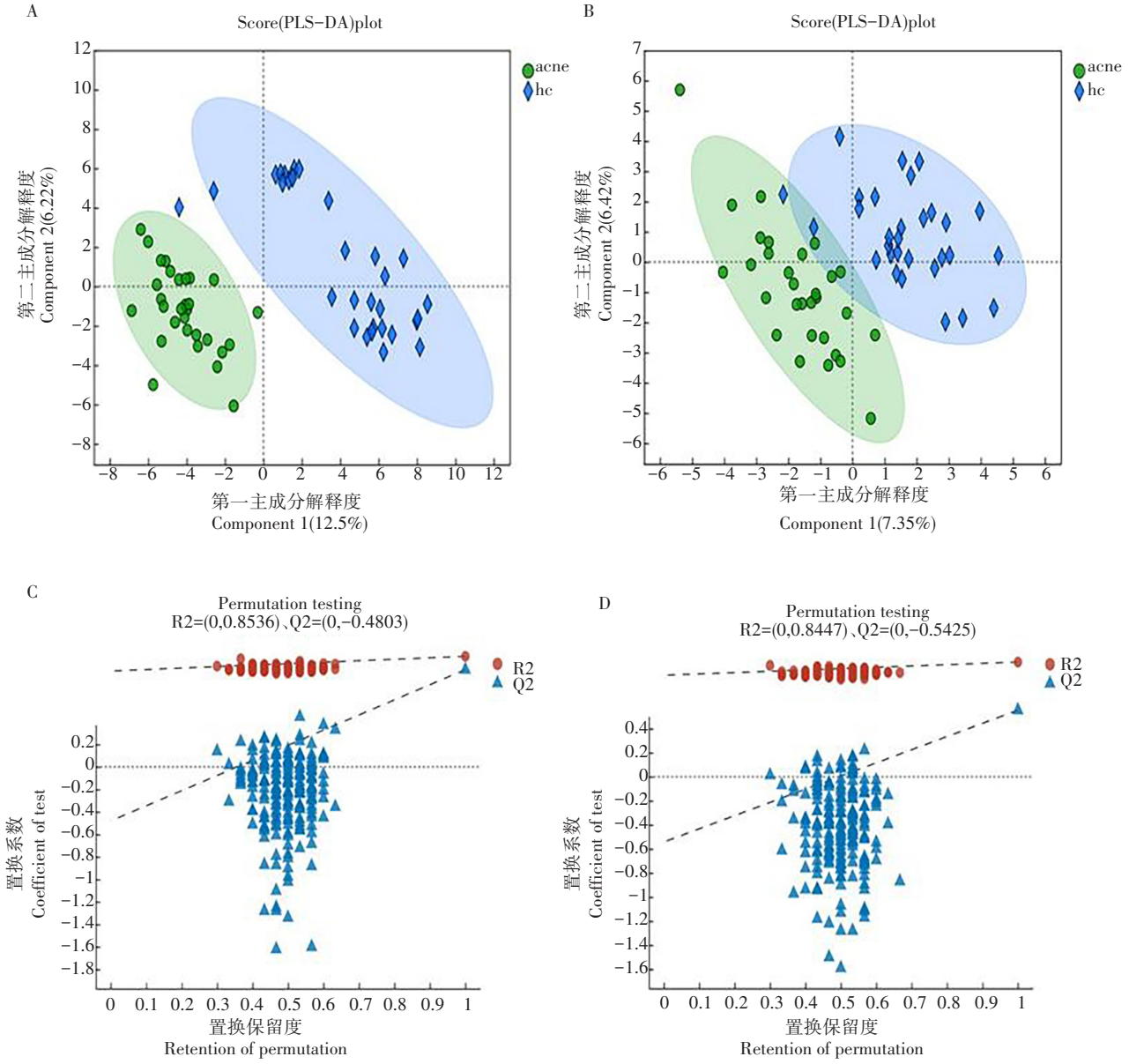
表1 寻常痤疮患者与健康对照的临床资料

Table 1 Clinical data of patients with acne vulgaris and healthy control

项目 Program	健康对照 Healthy control	痤疮患者 Acne vulgaris	*Z*	*P*
年龄/岁 Age/Year	25.400±2.644	20.650±3.110	−4.780	0.001
BMI/(kg·m^{-2})	20.086±1.615	20.590±1.878	−0.886	0.375
性别（男/女）Gender (male/female)	24/6	23/7		0.754
AST/(U·L^{-1})	20.180±3.980	19.705±6.659	−1.262	0.207
ALT/(U·L^{-1})	20.800±9.793	15.658±10.485	−1.830	0.072
HOMA-IR	1.612±0.667	1.440±0.741	−0.925	0.355
INS/(μU·mL^{-1})	7.853±2.983	6.792±3.331	−1.333	0.183
Glu/(mmol·L^{-1})	4.594±0.385	4.707±0.296	−1.239	0.215
HDL/(mmol·L^{-1})	1.426±0.267	1.431±0.323	−0.345	0.730
LDL/(mmol·L^{-1})	2.299±0.361	2.162±0.603	−1.074	0.283
TG/(mmol·L^{-1})	0.954±0.434	0.802±0.299	−1.153	0.249
TC/(mmol·L^{-1})	3.985±0.463	3.814±0.605	−1.294	0.196
GAGS得分 GAGS score		27.875±4.950		

注：BMI. 体质指数；AST. 天冬氨酸转氨酶；ALT. 丙氨酸转氨酶；HOME-IR. 胰岛素抵抗指数；INS. 空腹胰岛素；Glu. 血糖；HDL. 高密度脂蛋白；LDL. 低密度脂蛋白；TG. 三酰甘油；TC. 总胆固醇；GAGS. 全球痤疮分级系统。Note: BMI. Body mass index; AST. Aspartate aminotransferase; ALT. Alanine aminotransferase; HOMA-IR. Homeostasis model assessment for insulin resistance; INS. Fasting insulin; Glu. Bloodglucose; HDL. High density lipoprotein; LDL. Low density lipoprotein; TG. Triglyceride; TC. Total cholesterol; GAGS. Global acne grading system.

2.4 痤疮患者与健康对照差异代谢物KEGG富集分析 KEGG富集通路富集分析显示，健康对照和痤疮患者之间明显差异的代谢途径包括：产热作用、鞘脂信号通路、脂肪细胞脂肪分解的调节、坏死性凋亡、脂质与动脉粥样硬化、脂肪消化吸收、胆固醇代谢、糖尿病并发症中的AGE-RAGE信号通路、胰岛素抵抗、甘油磷脂代谢等信号通路。其中产热作用信号通路在两组中的富集程度最明显，其次是鞘脂信号通路。见图2。



注：A. 阳离子模型得分图；B. 阴离子(1B)模型得分图；C. PLS-DA阳离子模型置换检验；D. PLAS-DA阳离子模型置换检验。R2Y(cum)和Q2(cum)是模型验证参数，分别表示模型可解释度和模型可预测度。样本的阳离子模型系数：Q2为0.866(cum)、R2Y(cum)为0.984；阴离子模型系数：Q2(cum)为0.554、R2Y(cum)为0.954，以上系数均大于0.5，接近1，表明模型预测能力高，模型的拟合度较好。Note: A. Cationic model score chart; B. Anionic model score chart; C. PLS-DA cationic model permutation test; D. Anion model permutation test; R2Y (cum) and Q2 (cum) are model validation parameters, which represent model interpretability and model predictability, respectively. The coefficient of cation model of samples was Q2 0.866 (cum) and R2Y 0.984 (cum). The cation model coefficients of the sample were 0.866 (cum) for Q2 and 0.984 for R2Y (cum). The anion model coefficients: Q2 (cum) is 0.554, R2Y (cum) is 0.954, and the above coefficients are greater than 0.5, close to 1, indicating that the model had high predictive ability and good fitting degree.

图1 PLS-DA分析及其阴、阳离子模型置换检验

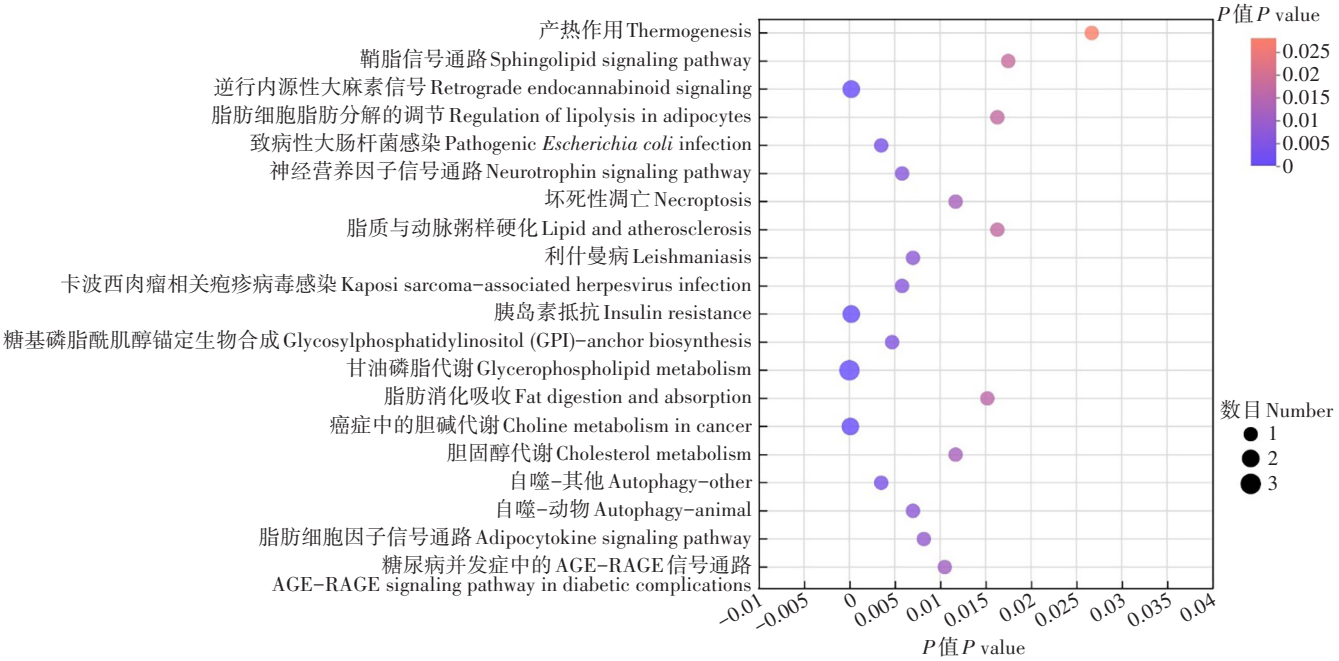
Fig.1 PLS-DA analysis and permutation test of anion and cation models

表2 血清差异脂质代谢产物比较

Table 2 Comparison of serum differential lipid metabolites

脂质代谢产物 Metabolite	*VIP*_PLS-DA	*FC*(Acne/HC)	*P*	脂质代谢产物 Metabolite	*VIP*_PLS-DA	*FC*(Acne/HC)	*P*
BisMePA(18:2e/18:2)	2.096	0.944	<0.001	PC(18:0e/16:0)	2.41	1.091	<0.001
Cer(m17:0/25:0+O)	3.050	0.923	<0.001	PC(18:2e/20:2)	2.524	1.102	<0.001
CL(24:0/18:0/20:4/18:2)	2.388	1.044	<0.001	PC(20:1/20:4)	2.624	1.098	<0.001
CL(24:0/18:0/20:4/20:4)	3.544	1.067	<0.001	PC(6:0/22:6)	2.936	1.136	<0.001
DG(10:0/11:2)	4.102	1.338	<0.001	PE(14:1e/22:6)	2.534	0.927	<0.001
DG(18:1/22:6)	3.391	0.695	<0.001	PE(17:0/22:6)	2.999	0.896	<0.001
DG(9:0/11:2)	4.372	1.368	<0.001	PE(17:1/20:4)	2.876	0.923	<0.001
dMePE(16:1e/16:0)	2.254	0.960	<0.001	PI(16:2e/19:0)	2.691	1.088	0.004
Hex1Cer(t18:0/23:4)	2.012	1.069	<0.001	PI(18:1e/17:0)	2.132	1.052	0.009
Hex2Cer(d14:0/22:6)	2.089	1.041	0.001	SM(d18:1/22:0)	2.149	1.063	<0.001
LPE(16:1e)	1.704	0.974	0.008	SM(d20:1/23:4)	2.388	1.089	<0.001
LPE(18:2e)	2.191	0.961	0.002	TG(15:0/6:0/12:1)	2.31	1.125	<0.001
MePC(20:4e/23:1)	2.508	1.109	<0.001	TG(4:0/6:0/10:1)	7.262	7.581	<0.001
PC(12:0e/18:1)	2.393	1.115	<0.001	TG(4:0/9:0/10:1)	2.954	1.171	<0.001
PC(16:1/18:2)	2.099	1.073	<0.001	TG(6:0/6:0/10:4)	7.309	5.474	<0.001

注：BisMePA. 二甲基磷脂酸；Cer. 神经酰胺；CL. 心磷脂；DG. 甘油二酯；dMePE. 二甲基磷脂酰乙醇胺；Hex1Cer. 单己糖神经酰胺；Hex2Cer. 二己糖神经鞘氨醇；LPE. 脑磷脂；MePC. 甲基化磷脂酰胆碱；PC. 磷脂酰胆碱；PE. 磷脂酰乙醇胺；PI. 磷脂酰肌醇；SM. 鞘磷脂；TG. 三酰甘油。Note: BisMePA. Bismethyl phosphatidic acid; Cer. Ceramide; CL. Cardiolipin; DG. Diacylglycerol; dMePE. Dimethylphosphatidylethanolamine; Hex1Cer. Monohexosyl ceramide; Hex2Cer. Dihexosyl ceramide; LPE. Cephalin; MePC. Methylated phosphatidylcholine; PC. Phosphatidylcholine; PE. Phosphatidyl ethanolamine; PI. Phosphatidylinositol; SM. Sphingomyelin; TG. Triacylglycerol.



注：横坐标为富集显著性*P*值，*P*值越小在统计学上就越有显著意义，一般*P*值小于0.05认为该功能为显著富集项；纵坐标为KEGG通路；气泡颜色由红到紫表示*P*依次降低；气泡越大，说明富集到该通路上的代谢物数目越多。Note: The abscissa is the enrichment significance *P* value; the smaller the *P* value, the more statistically significant it is, and the *P* value of less than 0.05 is considered as a significant enrichment term; Ordinate is KEGG pathway; The color of bubbles from red to purple indicates that the *P* value decreases in turn. The larger the bubble, the greater the number of metabolites enriched to the pathway.

图2 痤疮患者与健康对照差异代谢物KEGG富集分析气泡图

Fig. 2 KEGG enrichment analysis bubble map in acne patients and healthy controls

3 讨 论

据报道，系统脂质代谢可以动态影响皮肤皮脂组成，如脂质过氧化物的增加在脂蛋白代谢、炎症反应、表皮细胞增殖、分化和皮脂腺细胞增殖、凋亡中发挥作用[9,15]。众所周知，皮脂分泌增加是参与痤疮发病的主要因素之一，那么是否可以反推，痤疮患者的系统脂质代谢可能发生了异常呢?有文献表明，痤疮患者的血清TC、TG、LDL、HDL及胆固醇比健康对照显著升高[11-12]，但亦有研究显示痤疮患者和健康对照的脂质谱参数值并无差异[16]。本研究发现痤疮患者与健康对照TC、TG、LDL和HDL临床检测亦无差异，这可能跟本研究样本量小，及对入组患者BMI的严格控制有关。另外，临床检测方法的敏感性不够也可能是导致以上结果的原因之一。因此本研究进一步采用敏感性更好的脂质代谢组学检测方法，结果发现痤疮患者与健康对照脂质代谢产物差异显著。

在差异代谢产物中，PC、MePC、CL、PE、LPE、dMePE均属于磷脂类物质。PC是生物膜的组成部分，其生物合成和降解被认为是细胞周期过程所必需的，其合成缺陷是细胞凋亡的标志[17]。通过胞质磷脂酶A2（cPLA2）的作用去除sn-2位置的PC脂肪酸链导致LPC的形成[18]。LPC是一种生物活性溶血磷脂，在体外对各种免疫细胞（例如单核细胞，巨噬细胞，T淋巴细胞和中性粒细胞）具有刺激作用[19]。通过与TLR2和TLR4受体结合，LPC可以激活NF-κB，p38MAPK和JUN信号通路。这些途径的激活可以诱导IL-1β和IL-8等促炎因子的产生[20]。而IL-1β及IL-8都是参与痤疮发生发展中必不可少的促炎细胞因子[21]。甚至有研究证明，升高的PC和LPC可能通过触发TLR2和TLR4介导的信号通路来诱导炎症因子的产生，从而参与痤疮的发病机制[22]。同时，本研究中，Spearman相关性分析显示，血清PC（18:2e/20:2）浓度和痤疮严重程度呈正相关（r=0.456, P=0.004）。进一步验证了升高的PC可能与痤疮的发病有关。

KEGG富集信号通路显示痤疮患者鞘脂信号通路明显上调。在表皮中，鞘脂具有参与维持皮肤屏障功能、调节角质细胞增殖分化过程的重要作用。许多与皮肤屏障受损有关的皮肤病，如银屑病、特应性皮炎和鱼鳞病的发生发展，都与表皮鞘脂的组成和代谢改变有关[23]。有报道指出，轻中度痤疮患者与健康对照之间的鞘脂含量存在显着差异[24]。本研究亦提示，痤疮患者血清鞘磷脂[SM（d18:1/22:0）、SM（d20:1/23:4）]浓度相比对照组明显升高，与既往报道一致[25]。但血清鞘磷脂在痤疮发生发展中的分子机制仍需进一步实验验证。同时，本研究亦发现痤疮患者胆固醇代谢通路异常。众所周知，角鲨烯是胆固醇生物合成途径中的中间产物。在皮脂腺细胞中，促角鲨烯生成的酶即角鲨烯合酶的表达和/或活性增加;而参与角鲨烯转化为胆固醇的酶，如角鲨烯-2,3-环氧酶和氧化角鲨烯环化酶却受到抑制[15]，这可能与角鲨烯在皮脂腺细胞中积聚有关。研究表明，角鲨烯氧化产物即过氧化角鲨烯可能通过消耗谷胱甘肽介导细胞毒性，同时致粉刺增加[26]。

综上，本研究结果显示痤疮患者血清脂代谢紊乱，其血清差异脂质代谢产物与疾病的发生发展关系密切，但具体的分子机制仍需进一步的实验验证。

伦理审查与知情同意　本研究依据《赫尔辛基准则》开展，所有患者及健康志愿者均签署知情同意书，本试验已经得到了西南医科大学附属医院伦理委员会批准（批准号：KY2020115; KY2019139）。

益冲突声明　所有作者声明不存在利益冲突

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