

Supplementary Table 1. Elution gradient of mobile phase.

Gradient time (min)	A%	B%	Flow velocity (mL/min)	Gradient change
0.0	5.0	95.0	0.4	1300.0
3.0	20.0	80.0	0.4	1300.0
6.5	50.0	50.0	0.4	1300.0
12.5	85.0	15.0	0.4	1300.0
17.5	100.0	0.0	0.4	1300.0
23.3	100.0	0.0	0.4	1300.0

Supplementary Table 2. Characteristics of the participants and serum biochemical parameters.

		FO+D (n=23)		FO (n=27)		CO (n=24)		
		Mean \pm SD	<i>P</i> ^a	Mean \pm SD	<i>P</i> ^a	Mean \pm SD	<i>P</i> ^a	<i>P</i> ^b
Age, y		56.87 \pm 15.29		54.41 \pm 16.72		54.54 \pm 15.38		0.623
Female, n		12		11		12		
BMI (kg/m ²)	Day 0	26.29 \pm 2.33	0.886	27.51 \pm 4.29	0.815	26.46 \pm 2.36	0.665	0.873
	Day 90	26.33 \pm 2.54		27.38 \pm 3.27		26.72 \pm 2.71		0.667
	Change	0.04 \pm 0.64		-0.13 \pm 1.96		0.25 \pm 0.82		0.581
Dietary intakes								
Energy (kcal)	Day 0	1924.99 \pm 580.83	0.152	2649.16 \pm 796.03	0.361	2040.75 \pm 583.58	0.252	0.863
	Day 90	2546.03 \pm 1222.61		2475.50 \pm 829.21		2275.93 \pm 714.69		0.380
	Change	621.04 \pm 982.41		-173.66 \pm 984.77		235.18 \pm 659.04		0.307
Carbohydrate (g/d)	Day 0	221.81 \pm 54.30	0.330	332.11 \pm 113.23	0.071	248.26 \pm 90.73	0.715	0.647
	Day 90	294.49 \pm 155.44		267.45 \pm 79.41		271.91 \pm 118.65		0.614
	Change	72.68 \pm 155.16		-64.66 \pm 110.23		23.65 \pm 124.04		0.444
Lipid (g/d)	Day 0	82.81 \pm 36.70	0.206	101.02 \pm 34.13	0.744	80.90 \pm 25.87	0.990	0.725
	Day 90	106.49 \pm 62.78		111.83 \pm 55.76		94.80 \pm 36.84		0.467
	Change	23.68 \pm 37.61		10.81 \pm 59.15		13.90 \pm 36.95		0.569
Protein (g/d)	Day 0	73.12 \pm 31.55	0.300	100.54 \pm 43.94	0.823	79.26 \pm 24.22	0.105	0.774
	Day 90	102.42 \pm 69.36		99.82 \pm 52.38		81.36 \pm 26.85		0.205
	Change	29.30 \pm 62.31		-0.71 \pm 42.73		2.10 \pm 28.46		0.103
Cholesterol (mg/d)	Day 0	195.91 \pm 143.41	0.387	193.94 \pm 152.06	0.611	192.72 \pm 93.46	0.167	0.956
	Day 90	156.84 \pm 136.73		161.49 \pm 130.50		156.79 \pm 133.02		0.995
	Change	-38.03 \pm 106.51		-32.44 \pm 104.59		-35.93 \pm 142.22		0.960
Saturated lipids (g/d)	Day 0	19.38 \pm 7.22	0.668	22.42 \pm 10.31	0.685	22.19 \pm 6.75	0.612	0.240
	Day 90	21.15 \pm 9.48		23.74 \pm 10.72		22.66 \pm 9.72		0.622
	Change	1.78 \pm 10.40		1.03 \pm 12.21		0.46 \pm 11.02		0.682
Blood biomarkers								
ALT (U/L)	Day 0	26.91 \pm 13.42	0.113	31.59 \pm 29.27	0.182	28.63 \pm 27.11	0.577	0.821
	Day 90	20.30 \pm 7.79		26.15 \pm 19.12		28.29 \pm 27.03		0.173
	Change	-6.61 \pm 10.14		-5.44 \pm 19.20		-0.33 \pm 0.26		0.047
AST (U/L)	Day 0	22.87 \pm 7.55	0.243	26.67 \pm 8.70	0.615	21.42 \pm 5.35	0.885	0.546
	Day 90	19.78 \pm 3.89		22.41 \pm 6.69		22.04 \pm 8.92		0.272
	Change	-3.09 \pm 5.93		-1.26 \pm 4.96		0.63 \pm 3.49		0.010
GGT (U/L)	Day 0	34.52 \pm 34.51	0.222	31.44 \pm 24.77	0.917	28.92 \pm 18.68	0.828	0.476
	Day 90	23.26 \pm 20.26		25.48 \pm 12.36		29.58 \pm 22.94		0.183
	Change	-11.26 \pm 32.45		-5.96 \pm 18.57		0.67 \pm 8.17		0.064
Glucose (mmol/L)	Day 0	6.38 \pm 1.99	0.583	5.71 \pm 1.16	0.076	6.01 \pm 1.21	0.327	0.417
	Day 90	6.47 \pm 1.93		6.09 \pm 1.20		6.20 \pm 0.94		0.518
	Change	0.09 \pm 0.58		0.38 \pm 0.36		0.19 \pm 0.71		0.588
TAG (mmol/L)	Day 0	1.71 \pm 0.76	0.050	2.55 \pm 1.55	0.095	1.76 \pm 0.73	0.452	0.917
	Day 90	1.36 \pm 0.70		1.76 \pm 0.62		1.87 \pm 1.40		0.074
	Change	-0.35 \pm 0.84		-0.78 \pm 1.12		0.11 \pm 1.02		0.128
TC (mmol/L)	Day 0	5.32 \pm 1.14	0.583	4.83 \pm 1.03	0.729	5.02 \pm 0.96	0.386	0.338
	Day 90	5.26 \pm 1.19		4.79 \pm 1.14		5.22 \pm 0.80		0.915
	Change	-0.07 \pm 0.96		-0.04 \pm 0.91		0.20 \pm 0.62		0.287
HDL-C (mmol/L)	Day 0	1.24 \pm 0.26	0.312	1.03 \pm 0.24	0.616	1.18 \pm 0.36	0.726	0.515
	Day 90	1.30 \pm 0.28		1.06 \pm 0.25		1.23 \pm 0.39		0.479
	Change	0.05 \pm 0.11		0.03 \pm 0.14		0.04 \pm 0.18		0.828
LDL-C (mmol/L)	Day 0	3.64 \pm 1.05	0.583	2.96 \pm 0.99	0.616	3.31 \pm 0.84	0.523	0.267
	Day 90	3.61 \pm 1.10		3.13 \pm 1.14		3.48 \pm 0.73		0.685
	Change	-0.03 \pm 0.66		0.17 \pm 0.98		0.17 \pm 0.72		0.395
Insulin (pmol/L)	Day 0	13.21 \pm 2.86	0.021	13.56 \pm 1.93	0.012	13.50 \pm 2.35	0.364	0.692
	Day 90	11.60 \pm 1.56		12.50 \pm 2.38		12.87 \pm 2.13		0.040
	Change	-1.61 \pm 1.99		-1.06 \pm 2.27		-0.63 \pm 1.52		0.091
HOMA-IR	Day 0	3.71 \pm 1.22	0.410	3.48 \pm 0.13	0.952	3.59 \pm 0.82	0.869	0.685
	Day 90	3.37 \pm 1.10		3.55 \pm 1.07		3.59 \pm 0.75		0.463
	Change	-0.34 \pm 0.71		0.07 \pm 0.97		-0.00 \pm 0.53		0.142

Serum inflammatory biomarkers

IL-1 β (ng/L)	Day 0	22.98 \pm 32.16	0.379	29.21 \pm 29.43	0.164	23.36 \pm 23.88	0.194	0.984
	Day 90	20.62 \pm 26.78		24.56 \pm 34.00		20.23 \pm 26.47		0.954
	Change	-6.85 \pm 7.28		-3.65 \pm 7.51		1.06 \pm 5.71		< 0.001
IL-6 (ng/L)	Day 0	8.97 \pm 11.13	0.750	7.56 \pm 9.92	0.029	6.99 \pm 8.45	0.224	0.499
	Day 90	8.54 \pm 10.60		8.48 \pm 8.66		7.98 \pm 7.96		0.835
	Change	-0.43 \pm 1.93		0.92 \pm 2.33		1.00 \pm 2.88		0.049
TNF- α (pg/L)	Day 0	435.03 \pm 380.53	0.009	422.95 \pm 468.96	0.004	390.80 \pm 312.57	0.003	0.705
	Day 90	259.09 \pm 420.66		294.26 \pm 439.84		243.25 \pm 300.67		0.887
	Change	-167.24 \pm 102.11		-106.47 \pm 150.90		-22.56 \pm 90.62		< 0.001

P^a is for the differences between the baseline and endpoint of intervention by a paired Wilcoxon rank sum test. P^b is for the differences between three groups by a generalized linear model. Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; GGT, gamma-glutamyl transpeptidase; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IL-1 β , interleukin-1 β ; IL-6, interleukin-6; LDL-C, low-density lipoprotein cholesterol; TAG, triacylglycerol; TC, total cholesterol; TNF- α , tumor necrosis factor- α .

Supplementary Table 3. Summary of parameters from OPLS-DA models for discriminating serum metabolite profiling before and after intervention

Group	R^2Y	Q^2Y
FO+D	0.948	0.720
FO	0.974	0.847
CO	0.960	0.634

Supplementary Table 4. Metabolites changed significantly between day 90 and day 0 in FO+D group.

Metabolite	Retention time (rt, min)	Experimental m/z ([M+H] ⁺)	Calculated m/z	Molecular Formula	VIP scores	Fold change
(5R,6Z,8E,10E,14Z)-5,20,20-trihydroxy-12-oxoicosa-6,8,10,14-tetraenoic acid	0.603	367.1903	366.2042	C ₂₀ H ₃₀ O ₆	2.51	0.37
Zucchini factor B	4.331	664.3977	663.4288	C ₄₄ H ₅₇ NO ₄	2.39	0.36
9-[(3,7-Dimethyl-2,6-octadienyl)oxy]-7H-furo[3,2-g]benzopyran-7	4.473	339.1580	338.1518	C ₂₁ H ₂₂ O ₄	2.55	0.36
Oxidized phosphatidylglycerol (prostaglandin J2/i-12:0)	4.689	745.3942	744.4214	C ₃₈ H ₆₅ O ₁₂ P	3.60	3.49
N-Eicosapentaenoyl Phenylalanine	4.819	450.2568	449.2930	C ₂₉ H ₃₉ NO ₃	3.33	0.36
Estrone glucuronide	4.941	447.2189	446.1941	C ₂₄ H ₃₀ O ₈	3.11	3.24
1-Hydroxyrutacridone epoxide	5.426	340.1188	339.1107	C ₁₉ H ₁₇ NO ₅	2.22	0.44
p-Hydroxyphenylethylbiguanide	5.799	222.1369	221.1277	C ₁₀ H ₁₅ N ₅ O	3.54	0.26
Homocholic acid	6.916	423.3501	422.3032	C ₂₅ H ₄₂ O ₅	8.16	4.96
3b-Hydroxy-17-(1h-1,2,3-triazol-1-yl)androsta-5,16-diene	6.987	340.2418	339.2311	C ₂₁ H ₂₉ N ₃ O	3.79	0.42
Cholylhistidine	10.085	546.3325	545.3465	C ₃₀ H ₄₇ N ₃ O ₆	2.15	3.37
Oxidized phosphatidylcholine (22:5)	10.200	600.3789	599.3223	C ₃₀ H ₅₀ NO ₉ P	2.05	2.06
Monoacylglyceride (20:4)	10.264	379.2912	378.2770	C ₂₃ H ₃₈ O ₄	2.06	19.47
Oxidized ceramide (d18:0/ prostaglandin F1 alpha)	10.581	656.4668	655.5387	C ₃₈ H ₇₃ NO ₇	2.54	9.45
Oxidized phosphatidic acid (36:4)	11.148	697.4813	696.4730	C ₃₉ H ₆₉ O ₈ P	3.83	0.45
Goyaglycoside h	11.184	815.4804	814.4715	C ₄₂ H ₇₀ O ₁₅	2.55	0.34
Oxidized phosphatidic acid (39:4)	11.690	755.5204	754.5149	C ₄₂ H ₇₅ O ₉ P	2.61	5.23
Acylcarnitine (22:6)	11.836	472.3956	471.3349	C ₂₉ H ₄₅ NO ₄	2.26	0.44
Lysophosphatidylethanolamine (20:4)	12.217	502.2976	501.2855	C ₂₅ H ₄₄ NO ₇ P	4.13	6.55
3-hydroxytridecanoyl carnitine	12.332	374.2856	373.2828	C ₂₀ H ₃₉ NO ₅	6.93	6.21
Lysophosphatidylcholine (22:5)	12.461	570.4320	569.3481	C ₃₀ H ₅₂ NO ₇ P	6.07	7.61
Oxidized phosphatidylinositol (36:4)	12.687	873.5186	872.5133	C ₄₅ H ₇₆ O ₁₆	2.38	0.38
Diadenosine hexaphosphate	13.113	996.9140	995.9809	C ₂₀ H ₃₀ N ₁₀ O ₂₅ P ₆	3.24	0.18
Phosphatidic acid (38:8)	13.330	717.4503	716.4417	C ₄₁ H ₆₅ O ₈ P	3.13	30.29
1,2-Dipalmitoyl-rac-glycero-3-phosphoethanolamine	13.361	692.5035	691.5152	C ₃₇ H ₇₄ NO ₈ P	2.37	0.47
N-arachidonylethanolamine	14.048	334.2970	333.3032	C ₂₂ H ₃₉ NO	2.38	0.38
Oxidized phosphatidic acid (40:2)	14.316	789.5606	788.5567	C ₄₃ H ₈₁ O ₁₀ P	4.18	3.50
Lysophosphatidylcholine (24:0)	14.317	608.4482	607.4577	C ₃₂ H ₆₆ NO ₇ P	3.14	2.14
Diacylglycerol (prostaglandin J2/10:0)	14.461	563.3740	562.3870	C ₃₃ H ₅₄ O ₇	8.85	10.45
Oxidized phosphatidylinositol (prostaglandin J2/22:3)	14.524	981.5739	980.5626	C ₅₂ H ₈₅ O ₁₅ P	4.12	0.26
Pyrohyperforin	14.554	535.3775	534.3709	C ₃₅ H ₅₀ O ₄	3.36	0.41
Cholylmethionine	14.557	540.3362	539.3281	C ₂₉ H ₄₉ NO ₆ S	15.39	2.16
Oxidized phosphoglycerophosphate (33:1)	14.683	969.6252	968.6119	C ₄₉ H ₉₄ O ₁₄ P ₂	4.08	0.26
Oxidized phosphatidylcholine (44:7)	14.691	920.6500	919.6302	C ₅₂ H ₉₀ NO ₁₀ P	2.59	2.25
Phosphatidylethanolamine (36:3)	15.095	726.5429	725.5359	C ₄₁ H ₇₆ NO ₇ P	2.92	10.71
3b,18b-3-Methoxy-11-oxo-12-oleanen-30-oic acid	15.173	485.3616	484.3553	C ₃₁ H ₄₈ O ₄	2.20	0.45
Oxidized ceramide (d16:1/6-keto prostaglandin F1 alpha)	15.290	624.4595	623.4761	C ₃₆ H ₆₅ NO ₇	2.61	2.36
Oxidized phosphatidic acid (28:4)	15.295	601.3864	600.3427	C ₃₁ H ₅₃ O ₉ P	2.25	0.38
N-Nervonoyl Alanine	15.861	438.3590	437.3869	C ₂₇ H ₅₁ NO ₃	2.06	0.38
Oxidized phosphatidylcholine (35:4)	15.924	800.5443	799.5363	C ₄₃ H ₇₈ NO ₁₀ P	2.06	0.34
Phosphatidylinositol (36:3)	16.016	861.5591	860.5415	C ₄₅ H ₈₁ O ₁₃ P	4.38	3.58
N-[(Z)-1,3-Dihydroxyoctadec-4-en-2-yl]-6-[(4-nitro-2,1,3-benzoxadiazol-7-yl)amino]hexanamide	16.114	576.3649	575.3683	C ₃₀ H ₄₉ N ₅ O ₆	3.43	2.78

Oxidized phosphatidylglycerol (36:1)	16.128	809.5538	808.5466	C ₄₂ H ₈₁ O ₁₂ P	3.39	0.20
Diacylglycerol (37:5)	16.262	677.4811	676.4914	C ₄₀ H ₆₈ O ₈	2.23	0.34
Dimethylphosphatidylethanolamine (40:8)	16.332	816.5502	815.5465	C ₄₇ H ₇₈ NO ₈ P	3.18	0.24
Oxidized phosphatidylcholine (37:5)	16.342	808.5494	807.5414	C ₄₅ H ₇₈ NO ₉ P	3.92	0.29
Lysophosphatidylcholine (22:1)	16.440	578.3948	577.4107	C ₃₀ H ₆₀ NO ₇ P	2.78	0.37
Oxidized phosphatidylcholine (33:3)	16.614	758.5391	757.5258	C ₄₁ H ₇₆ NO ₉ P	4.06	0.43
Phosphatidylcholine (38:8)	17.009	802.5042	801.5309	C ₄₆ H ₇₆ NO ₈ P	4.12	26.15
Sphingosylphosphorylcholine	17.172	992.6939	464.3379	C ₂₃ H ₄₉ N ₂ O ₅ P	3.92	0.26
		[2M+ACN+ Na] ²⁺				
Phosphatidylethanolamine (31:0)	17.306	678.5294	677.4996	C ₃₆ H ₇₂ NO ₈ P	2.59	0.17
Oxidized phosphatidylethanolamine (42:10)	17.660	828.5228	827.5101	C ₄₇ H ₇₄ NO ₉ P	2.08	0.44
Oxidized phosphatidylserine (24:3)	18.043	666.3442	665.3167	C ₃₀ H ₅₂ NO ₁₃ P	7.01	2.26
N-Cyclopropyl-trans-2-cis-6-nonadienamide	18.290	194.1452	193.1467	C ₁₂ H ₁₉ NO	3.40	0.25
Phosphatidylethanolamine (34:1)	18.946	718.5366	717.5309	C ₃₉ H ₇₆ NO ₈ P	2.32	5.86
Oxidized phosphatidic acid (34:1)	19.112	673.4774	672.4730	C ₃₇ H ₆₉ O ₈ P	2.68	4.62
Oxidized phosphatidylcholine (35:3)	19.942	786.5739	785.5571	C ₄₃ H ₈₀ NO ₉ P	2.17	0.37

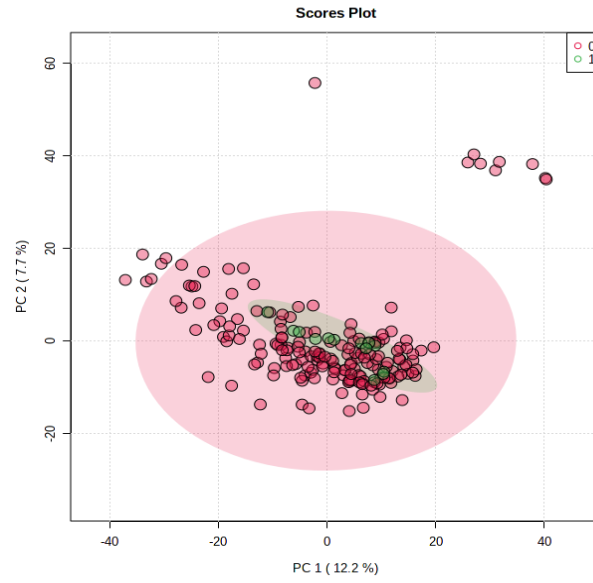
Supplementary Table 5. Metabolites changed significantly between day 90 and day 0 in FO group.

Metabolite	Retention time (rt, min)	Experimental m/z ([M+H] ⁺)	Calculated m/z	Molecular Formula	VIP scores	Fold change
(5R,6Z,8E,10E,14Z)-5,20,20-trihydroxy-12-oxoicosa-6,8,10,14-tetraenoic acid	0.603	367.1903	366.2042	C ₂₀ H ₃₀ O ₆	2.21	0.43
Zucchini factor B	4.331	664.3977	663.4288	C ₄₄ H ₅₇ NO ₄	2.14	0.40
9-[(3,7-Dimethyl-2,6-octadienyl)oxy]-7H-furo[3,2-g][1]benzopyran-7-one	4.473	339.1580	338.1518	C ₂₁ H ₂₂ O ₄	2.15	0.44
Oxidized phosphatidylglycerol (prostaglandin J2/i-12:0)	4.689	745.3942	744.4214	C ₃₈ H ₆₅ O ₁₂ P	3.02	2.87
Estrone glucuronide	4.941	447.2189	446.1941	C ₂₄ H ₃₀ O ₈	2.83	3.08
Moguisteine	5.280	340.1198	339.1140	C ₁₆ H ₂₁ NO ₅ S	3.14	0.45
p-Hydroxyphenylethylbiguanide	5.799	222.1369	221.1277	C ₁₀ H ₁₅ N ₅ O	4.60	0.13
Homocholic acid	6.916	423.3501	422.3032	C ₂₅ H ₄₂ O ₅	7.09	3.69
3b-Hydroxy-17-(1h-1,2,3-triazol-1-yl)androsta-5,16-diene	6.987	340.2418	339.2311	C ₂₁ H ₂₉ N ₃ O	3.55	0.42
Cholyhistidine	10.085	546.3325	545.3465	C ₃₀ H ₄₇ N ₃ O ₆	2.05	3.00
Monoacylglyceride (20:4)	10.264	379.2912	378.2770	C ₂₃ H ₃₈ O ₄	2.18	18.43
Cochliobolin A	10.265	401.2723	400.2614	C ₂₅ H ₃₆ O ₄	2.18	3.94
Oxidized ceramide (d18:0/ prostaglandin F1 alpha)	10.581	656.4668	655.5387	C ₃₈ H ₇₃ NO ₇	2.48	8.87
Oxidized phosphatidylethanolamine (16:0)	10.935	790.5222	789.5156	C ₄₁ H ₇₆ NO ₁₁ P	3.39	16.50
Goyaglycoside h	11.184	815.4804	814.4715	C ₄₂ H ₇₀ O ₁₅	2.44	0.30
Oxidized phosphatidic acid (39:4)	11.690	755.5204	754.5149	C ₄₂ H ₇₅ O ₉ P	2.44	4.35
Lysophosphatidylethanolamine (20:4)	12.217	502.2976	501.2855	C ₂₅ H ₄₄ NO ₇ P	4.27	5.44
3-hydroxytridecanoyl carnitine	12.332	374.2856	373.2828	C ₂₀ H ₃₉ NO ₅	6.83	6.12
Lysophosphatidylcholine (22:5)	12.461	570.4320	569.3481	C ₃₀ H ₅₂ NO ₇ P	5.74	5.30
Oxidized phosphatidylinositol (36:4)	12.687	873.5186	872.5133	C ₄₅ H ₇₆ O ₁₆	2.04	0.45
Diadenosine hexaphosphate	13.113	996.9140	995.9809	C ₂₀ H ₃₀ N ₁₀ O ₂₅ P ₆	3.24	0.18
Phosphatidic acid (38:8)	13.330	717.4503	716.4417	C ₄₁ H ₆₅ O ₈ P	3.31	14.50
Oxidized phosphatidylethanolamine (38:5)	14.032	780.5176	779.5101	C ₄₃ H ₇₄ NO ₉ P	2.38	0.49
N-arachidonylethanolamine	14.048	334.2970	333.3032	C ₂₂ H ₃₉ NO	2.00	0.46
Oxidized phosphatidic acid (40:2)	14.316	789.5606	788.5567	C ₄₃ H ₈₁ O ₁₀ P	3.61	2.88
Diacylglycerol (prostaglandin J2/10:0)	14.461	563.3740	562.3870	C ₃₃ H ₅₄ O ₇	10.41	11.57
Oxidized phosphatidylinositol (prostaglandin J2/22:3)	14.524	981.5739	980.5626	C ₅₂ H ₈₅ O ₁₅ P	4.76	0.17
Pyrohyperforin	14.554	535.3775	534.3709	C ₃₅ H ₅₀ O ₄	3.08	0.41
Cholylmethionine	14.557	540.3362	539.3281	C ₂₉ H ₄₉ NO ₆ S	17.59	2.94
Oxidized phosphoglycerophosphate (33:1)	14.683	969.6252	968.6119	C ₄₉ H ₉₄ O ₁₄ P ₂	4.92	0.15
Oxidized phosphatidylcholine (44:7)	14.691	920.6500	919.6302	C ₅₂ H ₉₀ NO ₁₀ P	2.59	2.25
Oxidized phosphatidylethanolamine (40:7)	14.771	804.5190	803.5101	C ₄₅ H ₇₄ NO ₉ P	3.80	2.95
Phosphatidic acid (38:3)	14.886	727.5219	726.5200	C ₄₁ H ₇₅ O ₈ P	5.59	3.12
Phosphatidylethanolamine (36:2)	14.937	728.5610	727.5516	C ₄₁ H ₇₈ NO ₇ P	4.53	2.96
Phosphatidylethanolamine (36:3)	15.095	726.5429	725.5359	C ₄₁ H ₇₆ NO ₇ P	3.49	17.55
Lysophosphatidylethanolamine (22:0)	15.156	538.3743	537.3794	C ₂₇ H ₅₆ NO ₇ P	2.07	2.88
Alpha-Tocopherol phosphate	15.227	511.3757	510.3474	C ₂₉ H ₅₁ O ₅ P	2.09	0.50
Oxidized ceramide (d16:1/6-keto prostaglandin F1 alpha)	15.290	624.4595	623.4761	C ₃₆ H ₆₅ NO ₇	2.49	2.49
12-[Methyl-(4-nitro-2,1,3-benzoxadiazol-7-yl)amino]octadecanoic acid	15.393	477.2985	476.2999	C ₂₅ H ₄₀ N ₄ O ₅	3.48	2.02
Phosphatidylinositol (36:3)	16.016	861.5591	860.5415	C ₄₅ H ₈₁ O ₁₃ P	4.65	6.86
N-[(Z)-1,3-Dihydroxyoctadec-4-en-2-yl]-6-[(4-nitro-2,1,3-benzoxadiazol-7-yl)amino]hexanamide	16.114	576.3649	575.3683	C ₃₀ H ₄₉ N ₅ O ₆	3.19	2.32
Diacylglycerol (37:5)	16.262	677.4811	676.4914	C ₄₀ H ₆₈ O ₈	2.11	0.32
Dimethylphosphatidylethanolamine (40:8)	16.332	816.5502	815.5465	C ₄₇ H ₇₈ NO ₈ P	3.09	0.20
Oxidized phosphatidylcholine (37:5)	16.342	808.5494	807.5414	C ₄₅ H ₇₈ NO ₉ P	3.68	0.27

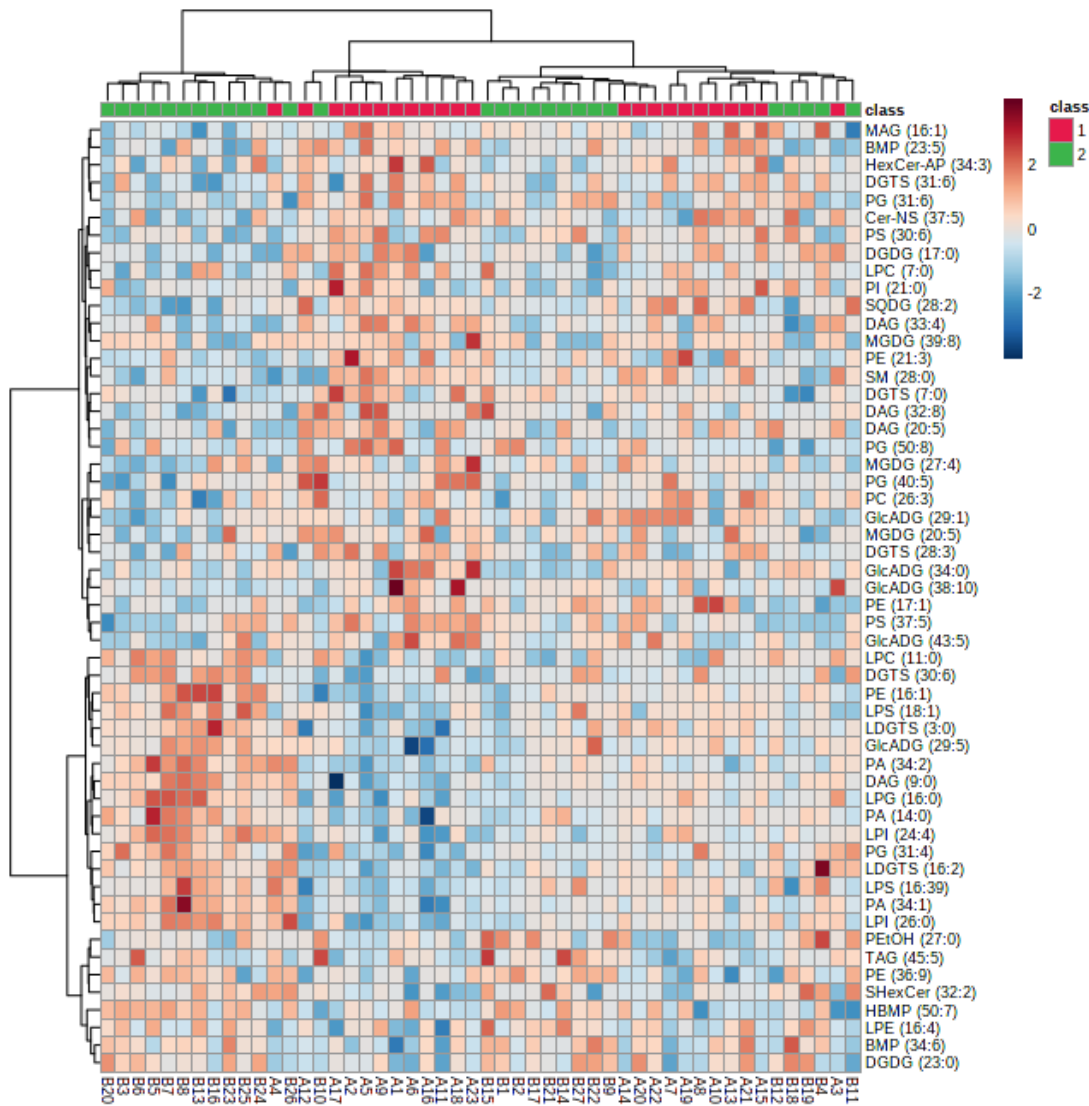
Lysophosphatidylcholine (22:1)	16.440	578.3948	577.4107	C ₃₀ H ₆₀ NO ₇ P	2.43	0.39
Oxidized phosphatidylcholine (33:3)	16.614	758.5391	757.5258	C ₄₁ H ₇₆ NO ₉ P	3.69	0.45
Phosphatidylcholine (38:8)	17.009	802.5042	801.5309	C ₄₆ H ₇₆ NO ₈ P	3.56	10.22
Sphingosylphosphorylcholine	17.172	992.6939	464.3379	C ₂₃ H ₄₉ N ₂ O ₅ P	4.90	0.14
		[2M+ACN+Na] ²⁺				
Phosphatidylethanolamine (31:0)	17.306	678.5294	677.4996	C ₃₆ H ₇₂ NO ₈ P	2.49	0.14
Oxidized phosphatidylglycerol (36:1)	17.341	809.5573	808.5466	C ₄₂ H ₈₁ O ₁₂ P	4.50	0.15
Oxidized phosphatidylcholine (35:3)	17.415	786.5635	785.5571	C ₄₃ H ₈₀ NO ₉ P	2.28	2.85
Oxidized phosphatidylserine (24:3)	18.043	666.3442	665.3167	C ₃₀ H ₅₂ NO ₁₃ P	10.27	5.41
N-Cyclopropyl-trans-2-cis-6-nonadienamide	18.290	194.1452	193.1467	C ₁₂ H ₁₉ NO	4.31	0.14
Phosphatidylethanolamine (34:1)	18.946	718.5366	717.5309	C ₃₉ H ₇₆ NO ₈ P	2.29	4.84
Oxidized phosphatidic acid (34:1)	19.112	673.4774	672.4730	C ₃₇ H ₆₉ O ₈ P	2.50	3.82
Oxidized phosphatidylcholine (35:3)	19.942	786.5739	785.5571	C ₄₃ H ₈₀ NO ₉ P	2.00	0.41

Supplementary Table 6. Metabolites changed significantly between day 90 and day 0 in CO group.

Metabolite	Retention time (rt, min)	Experimental m/z ([M+H] ⁺)	Calculated m/z	Molecular Formula	VIP scores	Fold change
N-Nervonoyl Methionine	3.842	498.3845	497.3903	C ₂₉ H ₅₅ NO ₃ S	2.55	0.48
Dimethylphosphatidylethanolamine (40:8)	4.818	814.5469	813.5520	C ₄₇ H ₇₆ NO ₈ P	3.61	0.35
Oxidized phosphatidylcholine (34:1)	4.819	792.5662	791.5676	C ₄₂ H ₈₂ NO ₁₀ P	4.58	0.50
Phosphatidic acid (44:4)	4.821	837.6189	836.6295	C ₄₉ H ₈₉ O ₈ P	2.29	0.40
Lysophosphatidylcholine (14:0)	9.033	468.2875	467.3012	C ₂₂ H ₄₆ NO ₇ P	2.24	7.17
Lysophosphatidylethanolamine (22:6)	9.754	526.2716	525.2855	C ₂₇ H ₄₄ NO ₇ P	2.03	3.35
Lysophosphatidylethanolamine (20:4)	9.814	502.2712	501.2855	C ₂₅ H ₄₄ NO ₇ P	2.53	6.35
Lysophosphatidylcholine (20:4)	9.854	544.3179	543.3325	C ₂₈ H ₅₀ NO ₇ P	4.19	2.49
Cochliobolin A	10.310	401.2738	400.2614	C ₂₅ H ₃₆ O ₄	4.23	3.55
N-Desisopropyl Pentisomide	11.122	278.2346	277.2154	C ₁₆ H ₂₇ N ₃ O	2.46	4.98
7-[(1S,2R,3R,4R)-3-(3-Hydroxy-4-phenylpent-1-enyl)-7-oxabicyclo[2.2.1]heptan-2-yl]hept-5-enoic acid	11.588	385.2385	384.2301	C ₂₄ H ₃₂ O ₄	5.25	8.86
C9-acylcarnitine	12.050	302.2321	301.2253	C ₁₆ H ₃₁ NO ₄	2.89	5.49
Oxidized phosphatidylglycerol (prostaglandin D1/12:0)	12.818	765.4528	764.4476	C ₃₈ H ₆₉ O ₁₃ P	2.39	0.49
Oxidized phosphatidylcholine (33:3)	14.819	758.5377	757.5258	C ₄₁ H ₇₆ NO ₉ P	4.49	0.39
Oxidized phosphatidylserine (32:4)	15.667	744.3940	743.4373	C ₃₈ H ₆₆ NO ₁₁ P	2.30	4.04
N-(2R-Hydroxytricosanoyl)-2S-amino-1,3S,4R-octadecanetriol	15.921	670.6140	669.6271	C ₄₁ H ₈₃ NO ₅	2.31	0.27
Oxidized phosphatidylcholine (46:7)	16.287	948.6818	947.6615	C ₅₄ H ₉₄ NO ₁₀ P	2.00	0.32
Oxidized phosphatidylcholine (44:6)	16.336	904.6537	903.6353	C ₅₂ H ₉₀ NO ₉ P	2.29	0.33
Phosphatidylcholine (40:7)	16.435	816.6053	815.5829	C ₄₈ H ₈₂ NO ₇ P	2.51	0.35
Phosphatidylcholine (35:2)	16.480	772.5839	771.5778	C ₄₃ H ₈₂ NO ₈ P	2.49	0.36
Oxidized phosphatidylcholine (37:5)	17.487	810.5695	809.5571	C ₄₅ H ₈₀ NO ₉ P	3.71	0.15
Oxidized phosphatidylcholine (37:5)	17.617	810.5681	809.5571	C ₄₅ H ₈₀ NO ₉ P	3.98	0.18
3-O-Sulfogalactosylceramide (d36:2)	17.693	806.5391	805.5374	C ₄₂ H ₇₉ NO ₁₁ S	3.28	0.24
3-O-Sulfogalactosylceramide (d34:1)	17.927	780.5256	779.5217	C ₄₀ H ₇₇ NO ₁₁ S	2.14	0.16
Phosphatidylserine (40:10)	17.961	828.4884	827.4737	C ₄₆ H ₇₀ NO ₁₀ P	2.23	0.38
Oxidized phosphatidylethanolamine (40:7)	17.795	806.5361	805.5258	C ₄₅ H ₇₆ NO ₉ P	2.42	0.43
Oxidized phosphatidylethanolamine (38:6)	18.004	780.5208	779.5101	C ₄₃ H ₇₄ NO ₉ P	2.16	0.15

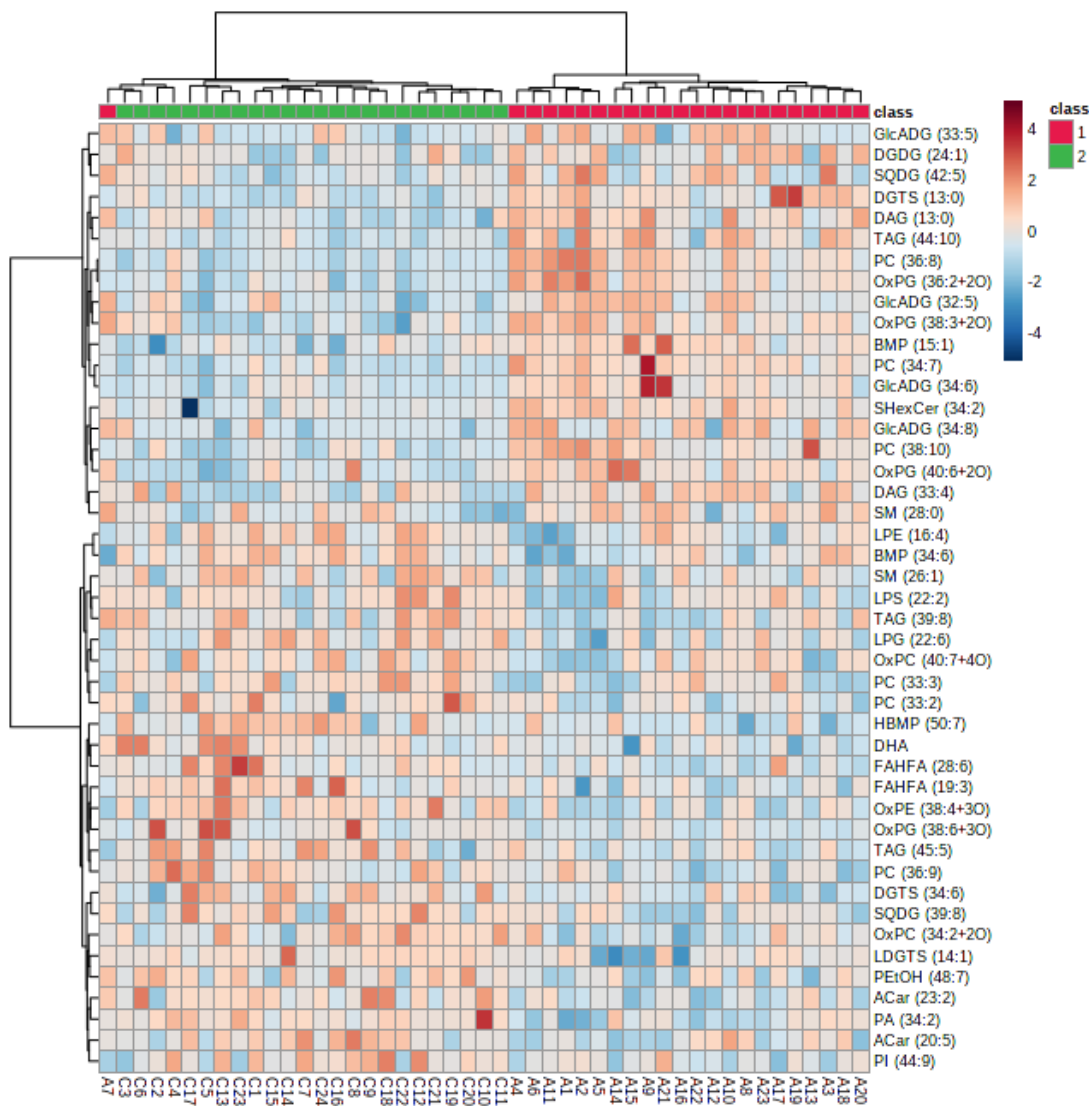


Supplementary Figure 1. PCA score plot of QC samples. 0 represents serum samples, 1 represents QC samples.



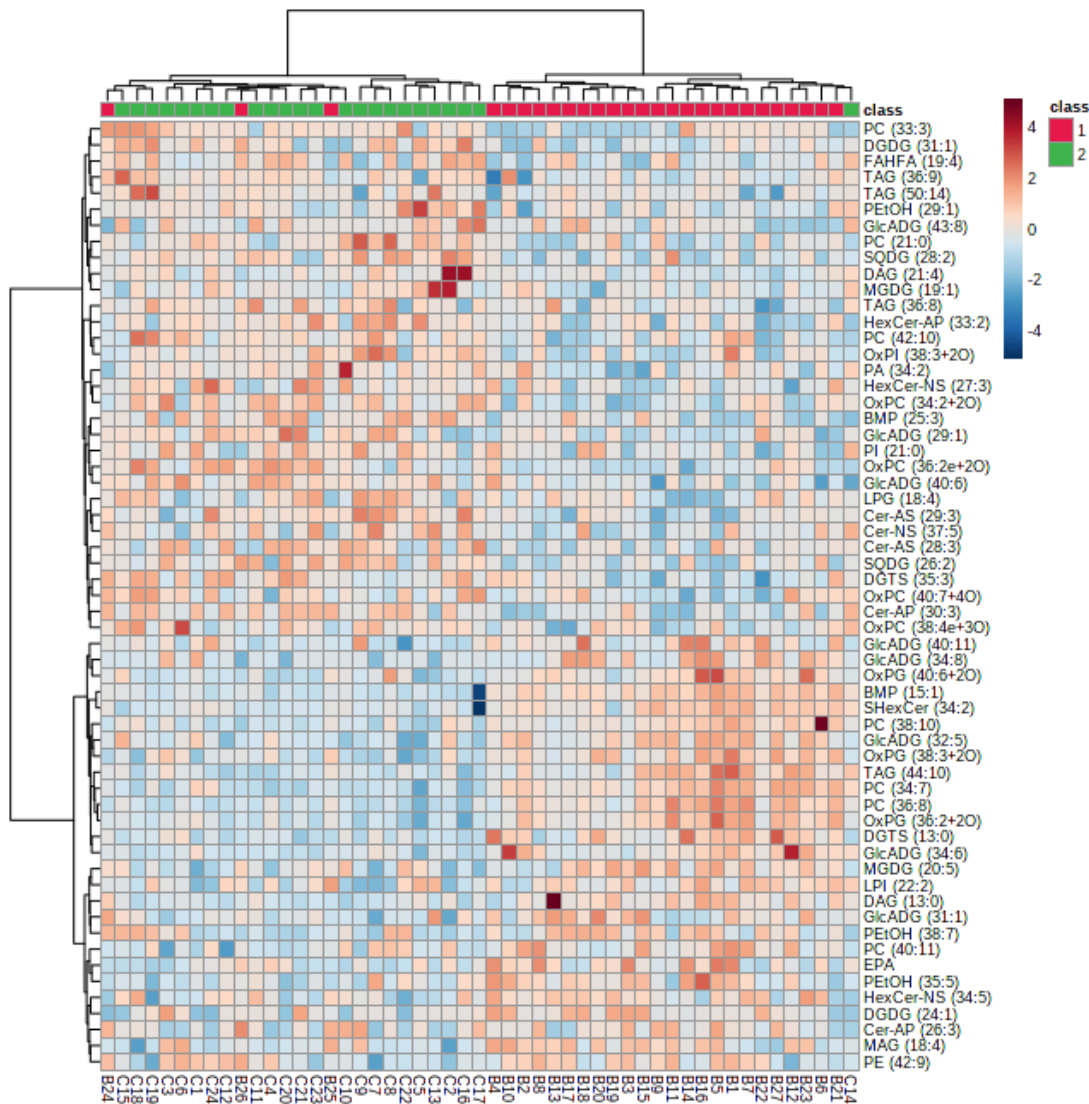
Supplementary Figure 2. Hierarchical clusters of significant metabolites between FO+D and FO groups, 1 represents FO+D group, 2 represents FO group.

Abbreviations: BMP, bis monoacylglycerol phosphate; Cer-NS, ceramide-non-hydroxy fatty acid/sphingosine; DAG, diacylglycerol; DGDG, digalactosyldiacylglycerol; DGTS, diacylglycerol-N-trimethylhomoserine; GlcADG, glucuronosyldiacylglycerol; HBMP, human bone morphogenetic protein; HexCer-AP, hexosylceramides-alpha-hydroxy fatty acid/phytosphingosine; LDGTS, lysodiacylglyceryltrimethyl homoserines; LPC, lysophosphatidylcholine; LPE, lysophosphatidylethanolamide; LPG, lysophosphatidylglycerol; LPI, lysophosphatidylinositol; LPS, lysophosphatidylserine; MAG, monoacylglycerol; MGDG, monogalactosyl-diacylglycerol; PA, phosphatidic acid; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PEtOH, Phosphatidylethanol; PG, phosphatidylglycerol; PI, phosphatidylinositol; PS, phosphatidylserine; SHexCer, sulfatides hexosylceramide; SM, sphingomyelin; SQDG, sulfoquinovosyl-diacylglycerol; TAG, triglyceride.



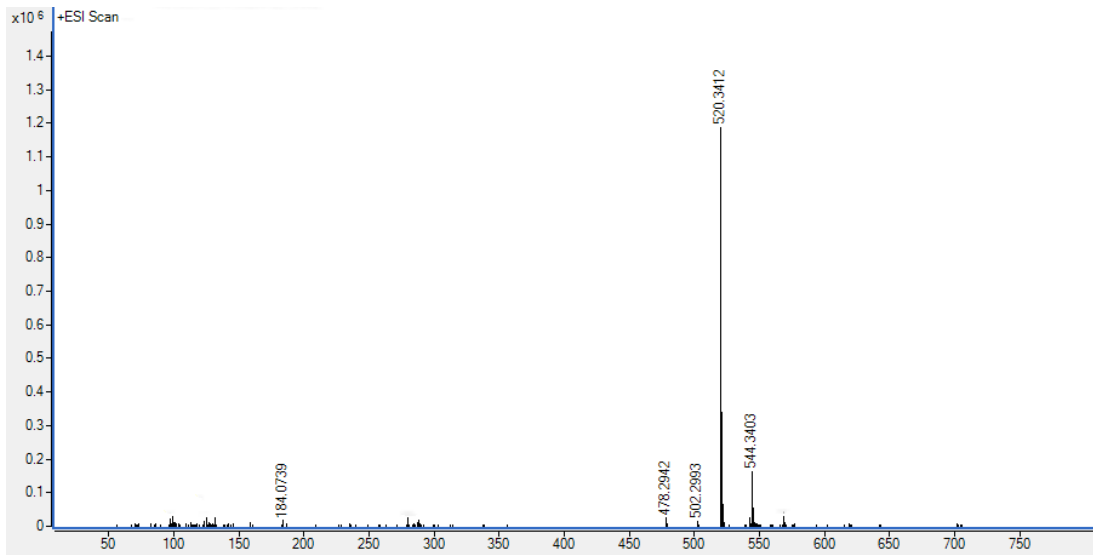
Supplementary Figure 3. Hierarchical clusters of significant metabolites between FO+D and CO groups, 1 represents FO+D group, 2 represents CO group.

Abbreviations: ACar, acylcarnitine; BMP, bis monoacylglycerol phosphate; DAG, diacylglycerol; DGDG, digalactosyldiacylglycerol; DGTS, diacylglycerol-N-trimethylhomoserine; DHA, docosahexaenoic acid, FAHFA, fatty acyl esters of hydroxy fatty acid; GlcADG, glucuronosyldiacylglycerol; HBMP, human bone morphogenetic protein; LDGTS, lysodiacylglyceryltrimethyl homoserines; LPE, lysophosphatidylethanolamide; LPG, lysophosphatidylglycerol; LPS, lysophosphatidylserine; OxPC, oxidized phosphatidylcholine; OxPE, oxidized phosphatidylethanolamine; OxPG, oxidized phosphatidylglycerol; PA, phosphatidic acid; PC, phosphatidylcholine; PEtOH, Phosphatidylethanol; PI, phosphatidylinositol; SHexCer, sulfatides hexosylceramide; SM, sphingomyelin; SQDG, sulfoquinovosyl-diacylglycerol; TAG, triglyceride.

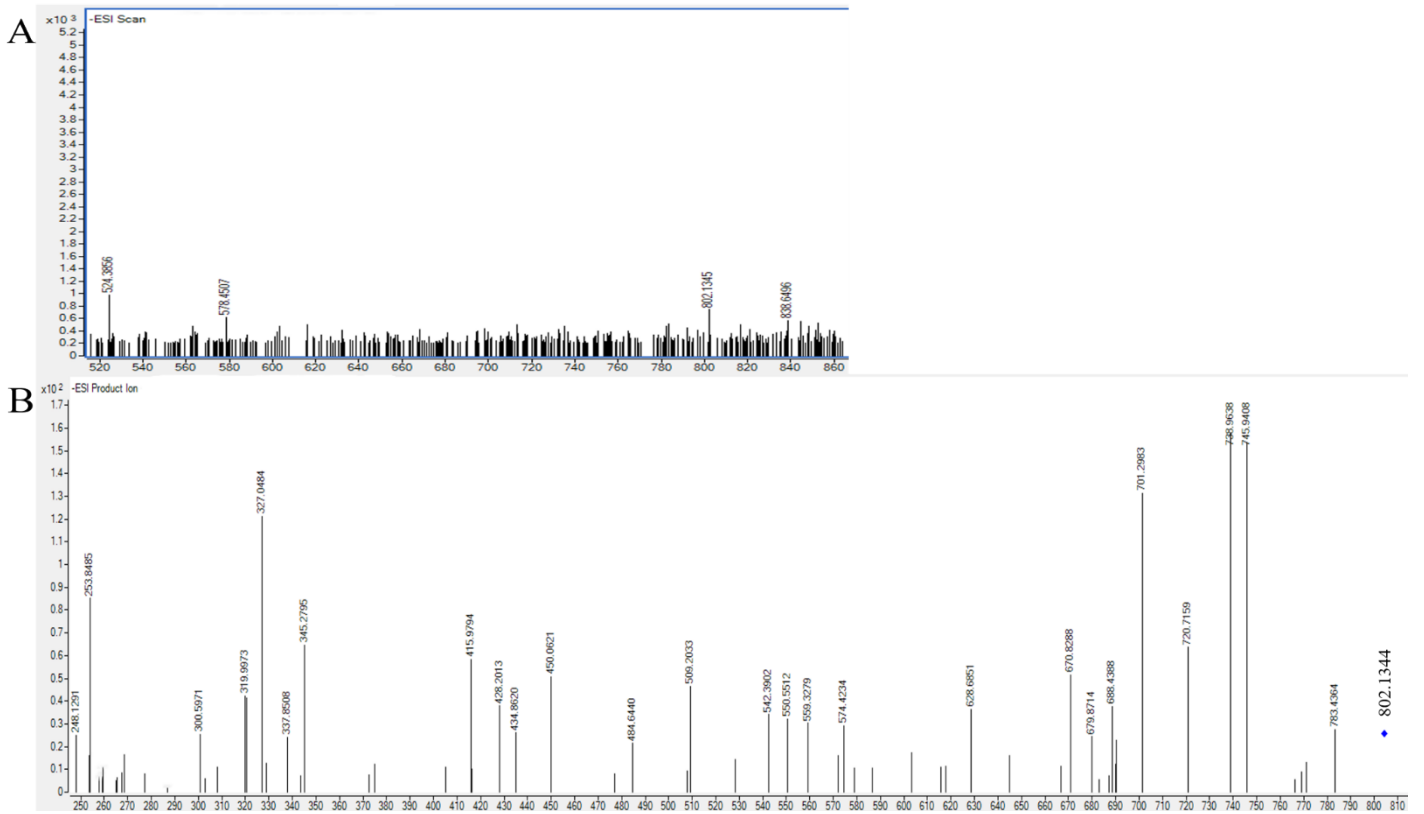


Supplementary Figure 4. Hierarchical clusters of significant metabolites between FO and CO groups, 1 represents FO group, 2 represents CO group.

Abbreviations: BMP, bis monoacylglycerol phosphate; Cer-AP, ceramide-alpha-hydroxy fatty acid/phytosphingosine; Cer-AS, ceramide-alpha-hydroxy fatty acid/sphingosine; Cer-NS, ceramide-non-hydroxy fatty acid/sphingosine; DAG, diacylglycerol; DGDG, digalactosyldiacylglycerol; DGTS, diacylglycerol-N-trimethylhomoserine; EPA, eicosapentaenoic acid; FAHFA, fatty acyl esters of hydroxy fatty acid; GlcADG, glucuronosyldiacylglycerol; HexCer-AP, hexosylceramides-alpha-hydroxy fatty acid/phytosphingosine; HexCer-NS, hexosylceramides-non-hydroxy fatty acid/sphingosine; LPG, lysophosphatidylglycerol; LPI, lysophosphatidylinosito; MAG, monoacylglycerol; MGDG, monogalactosyl-diacylglycerol; OxPC, oxidized phosphatidylcholine; OxPG, oxidized phosphatidylglycerol; OxPI, oxidized phosphatidylinositol; PA, phosphatidic acid; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PEtOH, Phosphatidylethanol; PI, phosphatidylinositol; SHexCer, sulfatides hexosylceramide; SQDG, sulfoquinovosyl-diacylglycerol; TAG, triglyceride.



Supplementary Figure 5. Targeted LC-MS/MS spectrometry of PC (38:7) in [M+H]⁺ mode.



Supplementary Figure 6. Mass spectrogram (A) of PC (38:7) and targeted LC-MS/MS spectrometry of PC (16:1/22:6) (B) in [M-H]⁻ mode.