Supplementary Table 1. Clinical characteristics of ECC patients.

Characteristics	Controls (n=60)	Patients (n=60)
Sex (F/M)	30/30	32/28
Age	43±4	44±5
BMI(kg/m2)	24.39±2.38	24.43±2.91
HBsAg (negative/positive)	negative	positive
ALT (U/L)	18.25±6.31	32.85±7.01
AST (U/L)	15.99±7.35	34.28±9.09
ALP(U/L)	54.21±12.03	74.36 ± 17.23
Bilirubin (total) (mg/dl)	0.78±0.32	1.47±0.47
Albumin (g/dl)	1.59±0.36	3.72±1.09
Serum CEA (ng/ml)	3.39±1.07	6.01±1.72

Supplementary Table 2. Differential metabolites in ECC identified by LC/ESI-Q/TOF-MS in positive and negative ion mode.

No.	VIP	Rt (min)	Ion Form	Formula	Metabolite Name	Trend
1	16.0495	4.55	$[M+H]^+$	170.1819	3-Methylhistidine	↓
2	15.3307	4.45	$[M+H]^+$	193.1236	Citric acid	↑
3	15.3086	3.87	$[M+H]^+$	112.1015	Cytosine	↓
4	15.9796	1.06	$[M+H]^+$	176.1846	Indoleacetic acid	↑
5	17.7435	4.23	$[M+H]^+$	196.1723	Salicyluric acid	↓
6	13.3484	1.01	$[M+H]^+$	150.2119	L-Methionine	↓
7	14.1206	4.72	$[M+H]^+$	120.0758	Aminomalonic acid	↑
8	30.8734	8.46	$M+H]^+$	133.1147	Glutaric acid	↑
9	11.8028	6.76	$M+H]^+$	393.5717	Ursodeoxycholic acid	↓
10	14.6432	3.01	$M+H]^+$	175.1978	N-Acetylornithine	↑
11	11.7141	6.21	$[M-H]^-$	157.1153	Allantoin	↑
12	10.1821	9.38	$[M-H]^-$	464.6225	Glycocholic acid	↑
13	10.3943	3.42	$[M-H]^-$	110.1456	Histamine	↓
14	12.0588	4.63	$[M-H]^-$	167.1462	Homogentisic acid	↑
15	16.2448	8.47	$[M-H]^-$	207.2147	L-Kynurenine	↓
16	10.6578	3.49	$[M-H]^-$	88.0936	Sarcosine	↓
17	17.7802	3.06	$[M-H]^-$	87.0626	Pyruvic acid	↑
18	15.0201	2.88	$[M-H]^-$	124.1466	Taurine	↑
19	15.0308	9.42	$[M-H]^-$	130.1139	Methylsuccinic acid	↑

No. was the number of metabolites from S- and VIP-score plots constructed from the supervised OPLS-DA analysis of urine. VIP is variable importance in the project and its value of above 5.00 showing high relevance for explaining the differences of sample groups. $[M+H]^+$, positive ion form; $[M-H]^-$, negative ion form.

Supplementary Table 3. Metabolic pathway analysis with MetPA.

No.	Pathway Name	Total	Expected	Hits	Raw p	Impact
1	Citrate cycle (TCA cycle)	20	0.15787	2	0.010308	0.15351
2	Taurine and hypotaurine metabolism	20	0.15787	2	0.010308	0.35252
3	Arginine and proline metabolism	77	0.60781	3	0.021091	0.01083
4	Histidine metabolism	44	0.34732	2	0.045868	0.0382
5	Primary bile acid biosynthesis	47	0.371	2	0.051686	0.01668
6	Glycine, serine and threonine metabolism	48	0.37889	2	0.053683	0.04973
7	Glyoxylate and dicarboxylate metabolism	50	0.39468	2	0.057759	0.00326
8	Cysteine and methionine metabolism	56	0.44204	2	0.070614	0.05455
9	Tyrosine metabolism	76	0.59992	2	0.11913	0.04285
10	Alanine, aspartate and glutamate metabolism	24	0.18945	1	0.17396	0
11	Pantothenate and CoA biosynthesis	27	0.21313	1	0.19357	0
12	Valine, leucine and isoleucine biosynthesis	27	0.21313	1	0.19357	0.02173
13	Glycolysis or Gluconeogenesis	31	0.2447	1	0.21903	0.0953
14	Pentose phosphate pathway	32	0.2526	1	0.22528	0
15	Vitamin B6 metabolism	32	0.2526	1	0.22528	0.01914
16	Pyruvate metabolism	32	0.2526	1	0.22528	0.18254
17	Terpenoid backbone biosynthesis	33	0.26049	1	0.23148	0
18	Ubiquinone and other terpenoid-quinone biosynthesis	36	0.28417	1	0.24979	0.0709
19	Nitrogen metabolism	39	0.30785	1	0.26769	0
20	Butanoate metabolism	40	0.31575	1	0.27356	0.08516
21	Nicotinate and nicotinamide metabolism	44	0.34732	1	0.29662	0
22	Phenylalanine metabolism	45	0.35521	1	0.30228	0
23	Ascorbate and aldarate metabolism	45	0.35521	1	0.30228	0.01617
24	Lysine degradation	47	0.371	1	0.31346	0.06505
25	Fatty acid metabolism	50	0.39468	1	0.32992	0
26	Pentose and glucuronate interconversions	53	0.41836	1	0.346	0
27	Pyrimidine metabolism	60	0.47362	1	0.38211	0.02127
28	Aminoacyl-tRNA biosynthesis	75	0.59202	1	0.45324	0
29	Tryptophan metabolism	79	0.6236	1	0.47085	0.0478

Note: Total is the total number of compounds in the pathway; the Hits is the actually matched number from the user uploaded data; the Raw p is the original p value calculated from the enrichment analysis; the Impact is the pathway impact value calculated from pathway topology analysis.
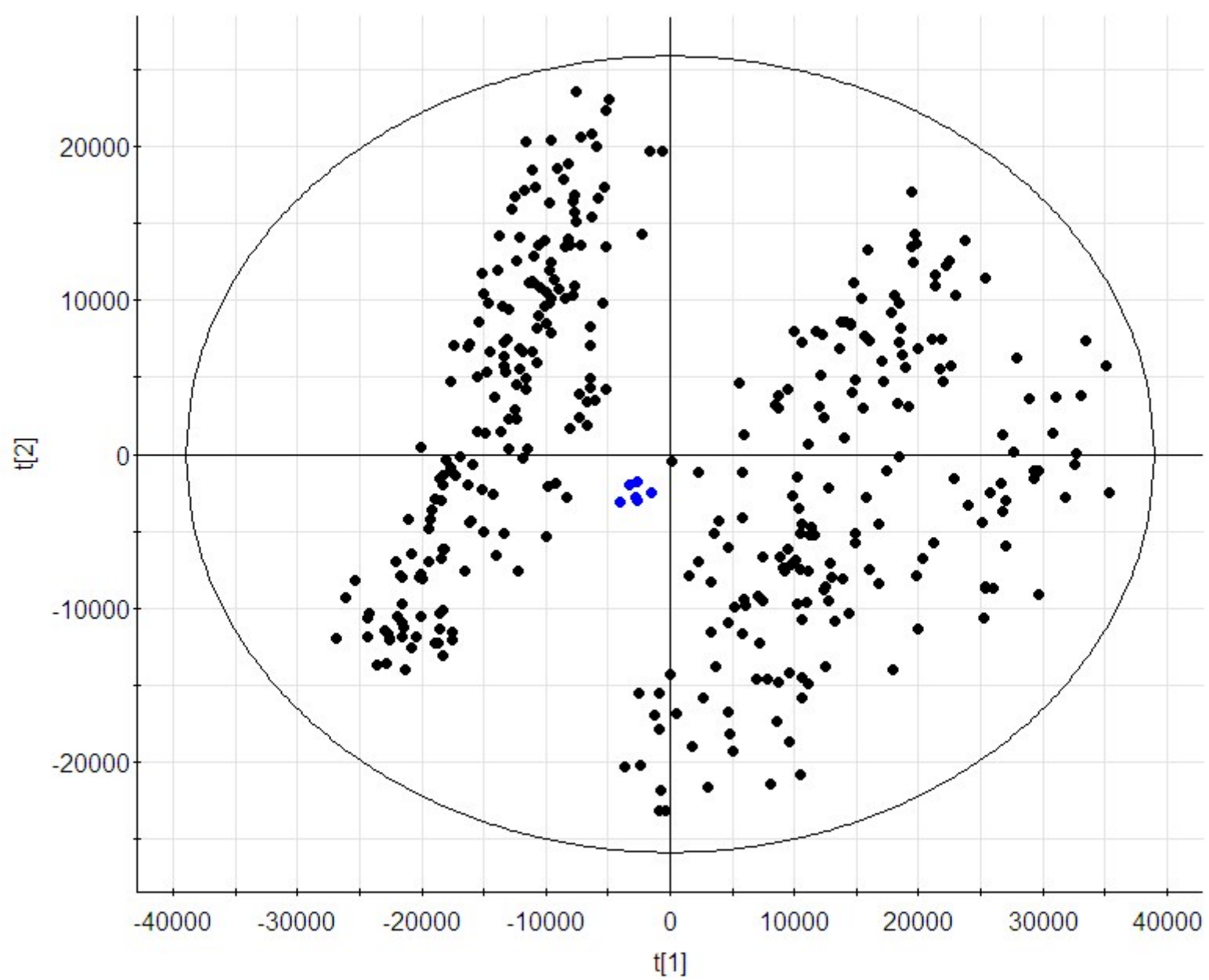
Fig. S1 The score plot of principal component analysis of QC samples using UPLC-Q-TOF/MS. Black dot present urine samples, and samples in blue box present samples.