

Table S1. Global amino acids profile according to DR status

	DR	Non-DR	P-value
Alanine	127.70 (38.26)	129.40 (45.43)	0.656
Arginine	10.23 (6.33-16.28)	10.63 (5.77-17.40)	0.874
Asparagine	73.40 (22.06)	78.62 (24.42)	0.012
Aspartic acid	29.47 (12.34)	30.68 (13.13)	0.276
Citrulline	21.20 (16.34-27.41)	19.64 (15.33-25.68)	0.099
Cystine	1.26 (0.88-1.68)	1.27 (0.93-1.68)	0.682
Glutamine	7.10 (5.46-9.67)	6.78 (5.00-9.20)	0.104
Glutamate	91.94 (72.13-110.65)	99.51 (81.98-122.01)	0.001
Glycine	177.97 (135.52-232.32)	206.67 (154.97-269.64)	<.001
Homocysteine	7.88 (6.56-8.56)	7.88 (6.57-8.37)	0.624
Histidine	44.01 (34.00-67.26)	52.74 (35.74-79.84)	0.007
Leucine	120.50 (40.38)	135.30 (47.56)	<.001
Lysine	147.30 (68.63)	140.3 (79.04)	0.246
Methionine	17.16 (5.39)	18.51 (6.74)	0.005
Ornithine	16.02 (11.80-23.17)	17.60 (13.36-23.73)	0.158
Proline	452.40 (189.3)	477.2 (204.5)	0.153
Serine	48.18 (41.53-58.68)	52.15 (43.78-65.26)	0.001
Threonine	25.69 (9.33)	26.52 (10.56)	0.353
Tryptophan	44.77 (12.14)	49.19 (12.14)	<.001
Valine	133.00 (33.88)	142.10 (42.22)	0.003

Abbreviations: DR, Diabetic retinopathy;

Data are mean (SD), median (IQR), or n (%).

P-value was acquired by comparing DR and Non-DR; P values were derived from independent samples Student t test for normally distributed variables or Mann-Whitney U test for skewed distributions.

Table S2. Characteristics and odds ratio of tyrosine and phenylalanine for DR risk using T2D patients chosen via propensity method

	DR	Non-DR	P-value#
Clinical characteristics			
N	162	162	
Age, years	57.8 (10.0)	58.7 (14.2)	0.487
Sex, male	89 (54.9)	86 (53.1)	0.738
Duration of DM, years	10 (7-19)	13 (6-20)	0.679
Body mass index, kg/m ²	25.1 (3.3)	24.9 (3.8)	0.639
~18.5	1 (0.6)	3 (1.9)	0.260
18.5~24.0	64 (39.5)	73 (45.1)	
24.0~28.0	66 (40.7)	50 (30.9)	
28.0~	31 (19.1)	36 (22.2)	
SBP, mmHg	145.6 (25.3)	143.7 (27.3)	0.510
HbA1c, %			
~7	15 (9.3)	17 (10.5)	0.782
7~8	16 (9.9)	18 (11.1)	
8~	64 (39.5)	69 (42.6)	
Lack	67 (41.4)	58 (35.8)	
HDL-C, mmol/L			
<1.00 in male or <1.30 in female	58 (35.8)	74 (45.7)	0.179
≥1.00 in male or ≥1.30 in female	36 (22.2)	33 (20.4)	
lack	68 (42.0)	55 (34.0)	
LDL-C, mmol/L			
<2.60	38 (23.5)	41 (25.3)	0.315
≥2.60	56 (34.6)	66 (40.7)	
lack	68 (42.0)	55 (34.0)	
Triglyceride, mmol/L			
<1.70	46 (28.4)	35 (21.6)	0.016
≥1.70	48 (29.6)	73 (45.1)	
Antidiabetic agents	68 (42.0)	54 (33.3)	0.331
Insulin	137 (84.6)	143 (88.3)	0.886
Hypotensive agents	132 (81.5)	133 (82.1)	0.736
Lipid-lowering agents	71 (43.8)	68 (42.0)	0.498
Diabetic nephropathy	63 (38.9)	69 (42.6)	0.820
Tyrosine, μmol/L	41.5 (12.4)	46.2 (15.4)	0.0029
<64	156 (96.3)	142 (87.7)	0.0068
≥64	6 (3.7)	20 (12.3)	
Phenylalanine, μmol/L	41.0 (10.2)	48.2 (14.9)	<.0001
<64	158 (97.5)	139 (85.8)	0.0002
≥64	4 (2.5)	23 (14.2)	

We selected this population through propensity score matching, with DR as dependent variable, age, sex, BMI (<18.5 kg.m-2, 18.5 kg.m-2-24.0 kg.m-2, 24.0 kg.m-2-28.0 kg.m-2 and >28.0 kg.m-2), duration of diabetes, SBP, HDL-C (<1.0mmol/L in male or <1.3mmol/L in female, ≥1mmol/L in male or ≥1.3 mmol/L in female, lack), LDL-C (<2.6mmol/L, ≥2.6 mmol/L, lack), HbA1c (<7%, 7%~8%, ≥8%, lack), triglyceride (<1.7mmol/L, ≥1.7mmol/L, lack), diabetic nephropathy, antidiabetic drugs, lipid lowering drugs and antihypertensive drugs as independent variables.

Abbreviations: DR, Diabetic retinopathy; SBP, Systolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin;

Data are mean (SD), median (IQR), or n (%).

P-value was acquired by comparing DR and Non-DR; P values were derived from independent-samples Student t test for normally distributed variables, Mann-Whitney U test for skewed distributions, Chi-square test (or fisher test if appropriate) for categorical variables.

Table S3. Odds ratio of tyrosine and phenylalanine for DR risk in subgroup chosen via propensity method

	OR	95%CI	P-value
Univariable model			
Tyr<64 vs. ≥64, μmol/L	3.66	1.43-9.38	0.007
Phe<64 vs. ≥64, μmol/L	6.53	2.21-19.4	0.001
Multivariable model			
Tyr<64 vs. ≥64, μmol/L	4.26	1.59-11.4	0.004
Phe<64 vs. ≥64, μmol/L	8.06	2.58-25.1	<0.001

Abbreviations: DR, Diabetic retinopathy; Phe, phenylalanine; Tyr, tyrosine; OR, odds ratio; CI, confidence interval.

Multivariable model was adjusted for independent variables used in propensity method as listed in Table S2.