

## Supplementary materials

**Table S1** Identification of differential metabolic pathways in GV-H group and GV-L group in the exploratory set

Pathway_name	Pathway_id	Total	Hits	<i>P</i> value	Impact
Linoleic acid metabolism	hsa00591	28	4	0.008473	0.1842
Aminoacyl-tRNA biosynthesis	hsa00970	52	5	0.017526	0.0982
ABC transporters	hsa02010	138	9	0.019276	0.0652
Taurine and hypotaurine metabolism	hsa00430	22	3	0.025547	0.1176
Phenylalanine metabolism	hsa00360	60	5	0.030639	0.0854
Cysteine and methionine metabolism	hsa00270	63	5	0.036812	0.2089
Alanine, aspartate and glutamate metabolism	hsa00250	28	3	0.047885	0.3153

Note: Pathway\_id, ID number of target pathway in KEGG database; Total, total number of metabolites in target metabolic pathway; Hits, number of overall differential metabolites in target metabolic pathway; *P* value, *P* value of hypergeometric distribution test, the smaller *P* value, the more significant the effect of detected differential metabolites on this pathway; Impact, the effect value of metabolic pathway, indicating the effect of detected differential metabolites on the target pathway.

**Table S2** Basic characteristics and CGM parameters in GV-H and GV-L groups of the validation set

	GV-H group ( <i>n</i> = 11)	GV-L group ( <i>n</i> = 10)	<i>P</i> value
Age (years)	26.0 (19.5, 32.0)	28.5 (16.0, 32.0)	0.805
Sex (M/F)	6/5	7/3	0.477
BMI (kg/m <sup>2</sup> )	19.6 ± 2.2	19.3 ± 2.5	0.769
Duration (years)	1.0 (0.8, 8.4)	1.9 (0.7, 9.8)	0.944
Insulin (U/kg·d)	0.59 (0.50, 0.69)	0.60 (0.32, 0.73)	0.453
FBG (mmol/L)	8.4 ± 1.5	7.1 ± 1.4	0.055
2hBG (mmol/L)	15.1 (11.9, 20.9)	15.8 (11.1, 19.2)	0.753
HbA1c (%)	9.2 (6.3, 12.5)	7.5 (5.7, 8.3)	0.170
FCP (pmol/L)	83.2 (27.4, 164.0)	64.8 (16.5, 182.9)	0.915
2hCP (pmol/L)	122.4 (17.9, 229.0)	202.6 (24.6, 412.4)	0.321
TC (mmol/L)	3.9 ± 0.5	4.4 ± 1.0	0.218
TG (mmol/L)	0.71 (0.54, 0.89)	0.67 (0.40, 0.98)	0.972
HDL (mmol/L)	1.5 ± 0.3	1.7 ± 0.7	0.338
LDL (mmol/L)	2.1 ± 0.5	2.4 ± 0.9	0.438
SD (mmol/L)	4.2 (3.6, 4.7)	1.9 (1.4, 2.1)	<b>&lt;0.001</b>
MAGE (mmol/L)	9.1 (8.5, 10.6)	4.2 (3.6, 4.7)	<b>&lt;0.001</b>
CV (%)	46.2 ± 5.2	25.3 ± 6.0	<b>&lt;0.001</b>
LBGI	3.8 (3.2, 6.6)	1.8 (1.1, 3.4)	<b>0.005</b>

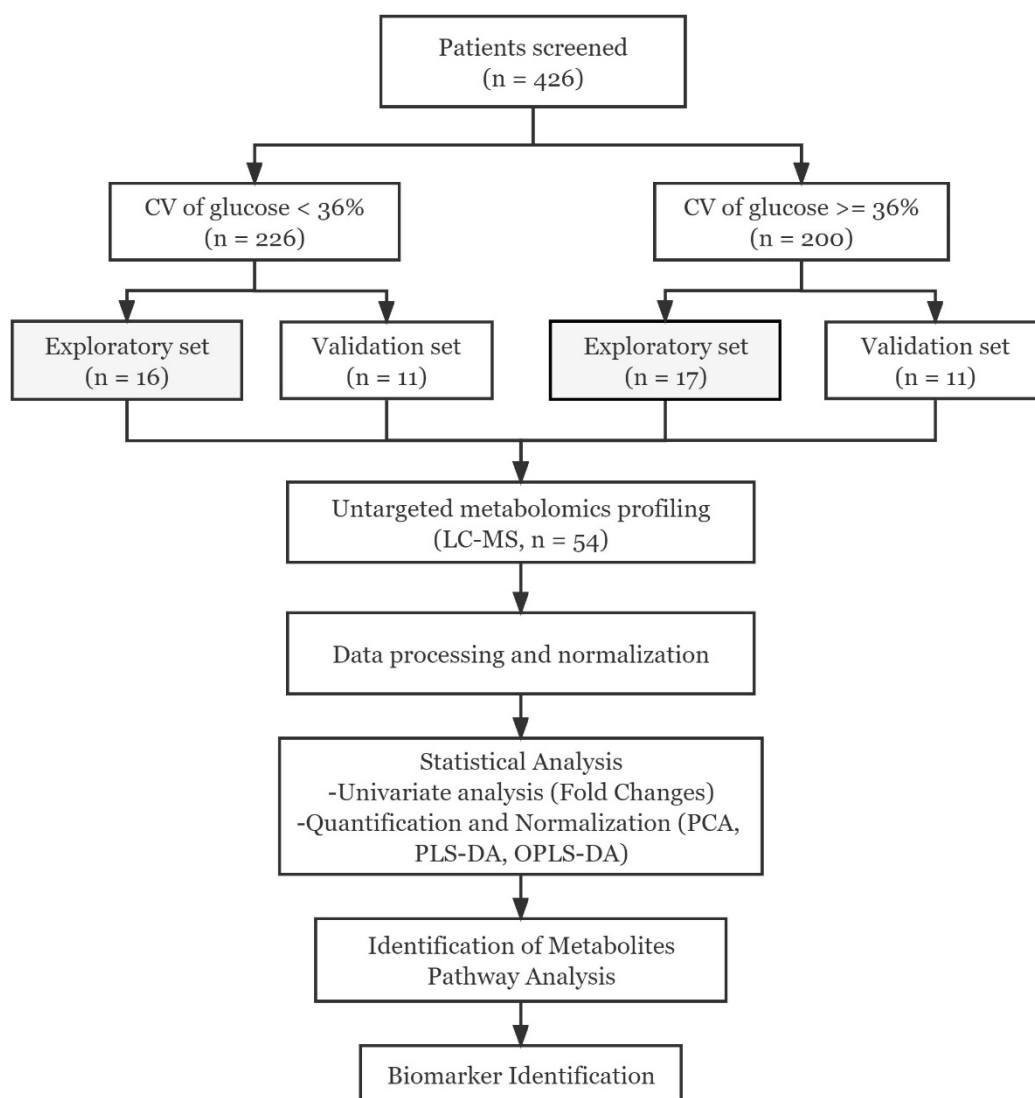
Note: Data were expressed as mean  $\pm$  SD, median (25<sup>th</sup> percentile, 75<sup>th</sup> percentile) and ratio. Abbreviations: BMI, body mass index; FBG, fasting blood glucose; 2hBG, 2-hour postprandial blood glucose; HbA1c, hemoglobin A1c; FCP, fasting C-peptide; 2hCP, 2-hour postprandial C-peptide; TC, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride; SD, standard deviation; MAGE, mean amplitude of glucose excursions; CV, coefficient of variation; LBGI, low blood glucose index.

**Table S3** Performance of candidate metabolic markers in the validation set

Metabolite	FC in the exploratory set	FC in the validation set	<i>P</i> value
Phosphatidylcholine	119.49	0.01	<0.001
3-(2-Hydroxyphenyl)propanoic acid	0.47	0.71	0.231
Riboflavin	0.51	2.11	<0.001
9,10-DHOME	0.22	5.70	<0.001
Cysteine-S-sulfate	0.16	8.70	0.002
Phenyllactate	0.48	1.60	0.360
13S-hydroxyoctadecadienoic acid	0.53	1.10	0.526
L-Cysteine	0.23	6.53	0.001
<b>Spermidine</b>	0.56	0.55	<b>0.007</b>
3-Methylthiopropionic acid	0.43	1.52	0.260
Hydrocinnamic acid	0.53	2.90	0.024
<b>Trehalose</b>	3.33	1.49	<b>0.041</b>
D-Phenylalanine	1.31	1.09	0.622
Oxoglutaric acid	1.56	0.72	0.324
2-Ketobutyric acid	1.28	0.90	0.360
Phenylethylamine	0.12	44.0	<0.001
Phthalic acid	0.02	4.66	0.001
12,13-DHOME	0.02	53.6	<0.001
D-Xylitol	2.55	0.84	0.324
<b>L-Methionine</b>	1.44	1.23	<b>0.041</b>
N-Acetyl-L-aspartic acid	1.21	0.69	0.014
L-Glutamic acid	1.28	0.70	0.833
L-Histidine	1.29	1.10	0.725
Mannitol	2.92	0.49	0.020
L-Valine	1.3	0.92	0.360

Note: *P* value represents the result of hypergeometric distribution test in the validation set.

**Figure S1**



**Figure S1. Flow chart of the comprehensive analysis of metabolomics profiles of patients with different glycemic variability**

**Table S4** Basic characteristics and CGM parameters of patients enrolled and not enrolled

	Enrolled ( <i>n</i> = 54)	Not enrolled ( <i>n</i> = 372)	<i>P</i> value
Age (years)	25.0 (15.0, 34.0)	22.0 (14.0, 35.0)	0.245
Sex (M/F)	32/22	190/182	0.167
BMI (kg/m <sup>2</sup> )	19.8 ± 2.5	20.1 ± 3.3	0.140
Duration (years)	1.2 (0.7, 6.2)	1.8 (0.4, 4.7)	0.505
Insulin (U/kg·d)	0.62 (0.48, 0.74)	0.61 (0.45, 0.76)	0.875
FBG (mmol/L)	8.1 (6.9, 10.1)	8.0 (5.4, 10.8)	0.748
2hBG (mmol/L)	16.6 (13.7, 19.7)	14.3 (11.1, 18.7)	0.026
HbA1c (%)	7.9 (6.8, 9.3)	7.6 (6.7, 9.2)	0.691
FCP (pmol/L)	55.5 (16.8, 118.9)	60.8 (16.5, 138.5)	0.081
2hCP (pmol/L)	122.2 (21.9, 228.8)	100.3 (25.7, 295.3)	0.766
TC (mmol/L)	4.2 ± 0.7	4.3 ± 1.0	0.485
TG (mmol/L)	0.69 (0.53, 0.88)	0.75 (0.56, 1.07)	0.247
HDL (mmol/L)	1.5 ± 0.5	1.5 ± 0.4	0.734
LDL (mmol/L)	2.4 ± 0.6	2.5 ± 0.9	0.715
SD (mmol/L)	3.2 (2.4, 3.9)	3.0 (2.5, 3.8)	0.746
MAGE (mmol/L)	7.0 (4.9, 8.8)	6.8 (5.2, 8.4)	0.380
CV (%)	32.3 (26.2, 45.4)	34.9 (30.0, 39.5)	0.505
LBGI	3.2 (1.3, 4.8)	2.9 (1.8, 4.5)	0.617