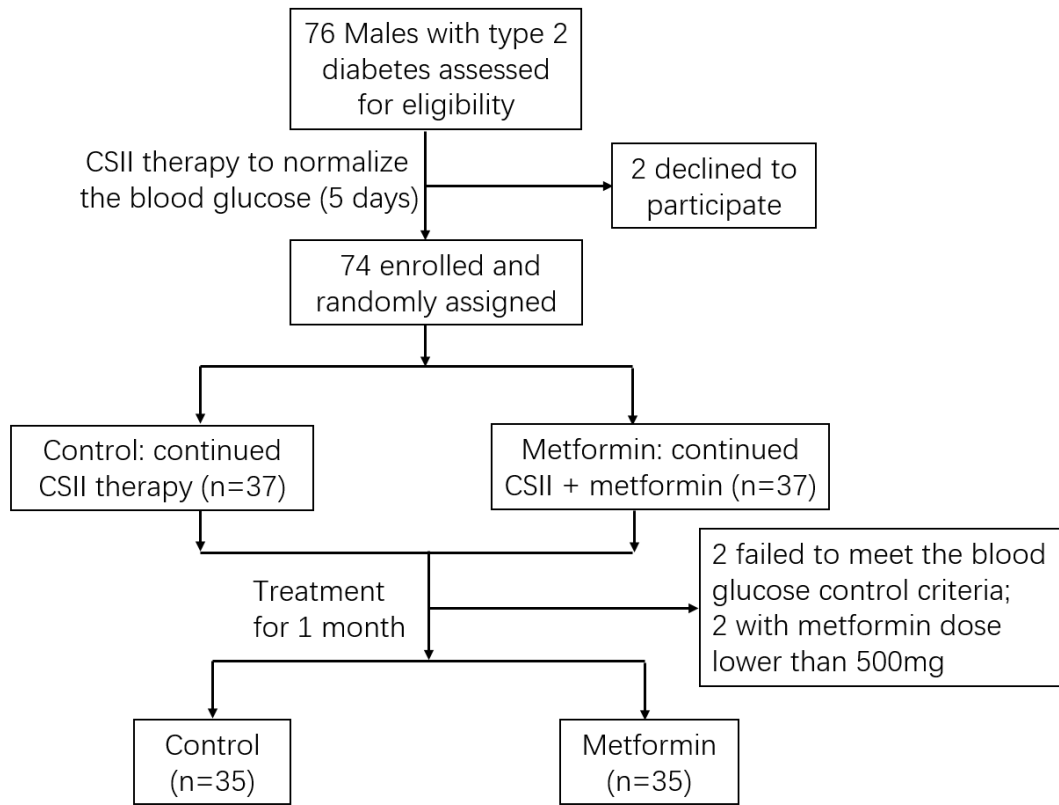


Supplementary Figure 1.



Supplementary Figure 1 Trial profile.

Supplementary Table 1. Characteristics of patients at baseline and metabolic changes before and after one-month treatment with or without metformin.

	Control (n=35)	Metformin (n=35)	<i>p</i> value
Baseline (Visit 1)			
Age (year)	44.26 (10.80)	46.51 (8.99)	0.345
Diabetes duration (day)	7 (3,15)	7 (3,30)	0.845
Body weight (kg)	76.74 (11.49)	75.73 (13.29)	0.734
BMI (kg/m ²)	25.09 (2.79)	25.61 (3.59)	0.493
HbA1c (%)	10.45 (1.19)	10.93 (1.48)	0.143
FBG (mmol/L)	11.06 (2.01)	11.54 (3.48)	0.487
Total cholesterol (mmol/L)	5.27 (0.95)	5.33(1.15)	0.824
Triglyceride (mmol/L)	1.95 (1.28,3.04)	1.82 (1.35,2.88)	0.698
HDL-c (mmol/L)	1.08 (0.80,1.25)	1.05 (0.90,1.39)	0.613
LDL-c (mmol/L)	2.74 (0.72)	2.62 (0.74)	0.492
Systolic blood pressure (mmHg)	126.26 (11.84)	123.89 (8.59)	0.341
Fasting C-peptide (ng/ml)	2.28 (1.07)	1.98 (0.91)	0.201
Fasting insulin (mU/L)	9.10 (7.35)	9.20 (5.82)	0.952
Fasting glucagon (ng/L)	119.39 (26.88)	127.13 (46.16)	0.422
HOMA2-IR	2.22 (1.07)	2.02 (0.98)	0.408
Smoking (n)	14	19	0.338
IIEF-5 score	22.0 (19.0,23.0)	21.0 (16.0,23.0)	0.276
Randomization (Visit 2)			
FBG (mmol/L)	6.86 (1.44)	6.40 (1.41)	0.208
Fasting C-peptide (ng/ml)	2.05 (1.03)	1.74 (0.79)	0.199
Fructosamine (μmol/L)	408.25(67.79)	376.25(60.17)	0.181
Body weight (kg)	76.74 (11.41)	75.76 (13.18)	0.739
HOMA2-IR	1.66 (0.87)	1.35 (0.50)	0.102
Daily insulin dose (IU)	26.11 (8.43)	25.23 (12.20)	0.731
Endpoint (Visit 3)			
FBG (nmol/L)	6.95 (1.15)	6.58 (1.05)	0.369
Fasting C-peptide (ng/ml)	2.24 (1.15)	1.98 (0.94)	0.340
Fructosamine (μmol/L)	288.10 (39.04)	272.98 (26.95)	0.344
HbA1c (%)	7.64 (0.76)	7.52 (1.30)	0.675
HOMA2-IR	1.81 (0.92)	1.66 (0.70)	0.480
Body weight (kg)	75.56 (10.62)	74.70 (11.85)	0.751
Daily insulin dose (IU)	9.7(0,22.9)	8.00 (0,20.00)	0.716
Daily metformin dose (mg)	0	1500 (1000,1500)	-
IIEF-5 score	22.5 (19.8,23.0)	21.0 (17.0,23.0)	0.347

Data are mean (SD) or median (interquartile range); BMI, body mass index; FBG, fasting blood glucose; HDL-c, high density lipoprotein cholesterol; LDL-c, Low density lipoprotein cholesterol; HOMA2-IR, Homeostasis Model Assessment 2 -insulin resistance; DKD, diabetic kidney disease; ARB, angiotensin receptor blockers; ACEI, angiotensin-converting enzyme inhibitors; TT, total testosterone; SHBG, sex hormone-binding globulin; FT, free testosterone; Bio-T, bioavailable testosterone; IIEF, international index of erectile function.

Supplementary Table 2. Testosterone levels at baseline (Visit 1), randomization (Visit 2) and endpoint (Visit 3).

	Visit 1	Visit 2	<i>p</i> value ^a	Visit 3	<i>p</i> value ^b
Total testosterone (nmol/L)					
Control	12.16 (4.80)	15.52 (5.72)	<0.001	15.38 (5.41) ^d	0.829
Metformin	11.98 (4.62)	15.19 (6.82)	<0.001	12.76 (5.43)	0.001
<i>p</i> value ^c	0.873	0.818		0.047	
Free testosterone (nmol/L)					
Control	0.19 (0.08)	0.24 (0.09)	<0.001	0.24 (0.08) ^d	0.705
Metformin	0.19 (0.08)	0.25 (0.10)	<0.001	0.20 (0.09)	0.001
<i>p</i> value ^c	0.988	0.972		0.048	
Bioavailable testosterone (nmol/L)					
Control	4.53 (1.34)	5.40 (1.60)	<0.001	5.31 (1.42) ^d	0.626
Metformin	4.50 (1.36)	5.38 (1.79)	<0.001	4.56 (1.52)	0.001
<i>p</i> value ^c	0.927	0.916		0.037	
SHBG (nmol/L)					
Control	23.27 (13.00)	31.99 (18.32)	<0.001	32.80 (17.98) ^d	0.648
Metformin	21.80 (10.03)	27.62 (12.81)	<0.001	26.49 (18.39) ^d	0.273
<i>p</i> value ^c	0.597	0.252		0.101	
Percentage of low testosterone (TT<12 nmol/L) (n/%)					
Control	21/60.00	9/25.71	0.007	10/28.57 ^e	1.000
Metformin	17/48.57	8/22.86	0.045	20/57.14	0.007
<i>p</i> value ^c	0.472	1.000		0.029	

Data are mean (SD), or number/percentage. TT, total testosterone; ^a, Visit 1 vs. Visit 2; ^b, Visit 2 vs. Visit 3; ^c, control group vs. metformin group; ^d, vs. Visit 1, *p*<0.01; ^e, vs. Visit 1, *p*<0.05.

Supplementary Table 3. Changes of testosterone levels before (Visit 2) and after treatment (Visit 3) in control and metformin group

	Control	Metformin	Estimated treatment difference (95% CI)	<i>p</i> value
Δ TT (nmol/L)	0.13 (3.64)	2.43 (3.94)	-2.29 (-4.10, -0.48)	0.014
Δ SHBG (nmol/L)	-0.81 (10.38)	1.13 (6.02)	-1.94 (-5.99, 2.11)	0.342
Δ FT (nmol/L)	0.004 (0.06)	0.05 (0.08)	-0.04 (-0.08, -0.01)	0.012
Δ Bio-T (nmol/L)	0.09 (1.08)	0.82 (1.34)	-0.73 (-1.31, -0.15)	0.014

Data are mean (SD). Δ= Visit 2- Visit 3. TT, total testosterone; SHBG, sex hormone-binding globulin; FT, free testosterone; Bio-T, bioavailable testosterone.