梅州市中医医院研究生文献汇报会（第四期）

2026 年 4 月 2 日

时间	题目	讲者
16: 00-16: 15	黄芪作为附加治疗用于 2 型糖尿病合并慢性肾脏病：一项多中心、评估者单盲、随机对照试验	杜宇乐
16: 20-16: 35	无论是否进行低碳水化合物饮食，限时饮食都能减少内脏脂肪并改善代谢综合征：一项随机试验	邓玉莹

指导老师：李佳殷、张彦中、刘舒明、张悦

第二期研究生文献汇报会（通讯员：邓玉莹）

第一节　主讲人：2025 级硕士杜宇乐

题目：黄芪作为附加治疗用于 2 型糖尿病合并慢性肾脏病：一项多中心、评估者单盲、随机对照试验

一、研究背景：

1.糖尿病肾脏疾病（DKD）是糖尿病最主要的微血管并发症，也是我国慢性肾脏病（CKD）与终末期肾病（ESRD）的首要病因。全球 20%~40% 的糖尿病患者会进展为 DKD，我国成人糖尿病患者 CKD 合并患病率约 32.36%，受累人群约 3900 万；长期高血糖介导肾脏微血管损伤与肾功能进行性下降，该病在我国透析人群中占比达 30%~44%，疾病负担沉重，是临床与公共卫生领域的重点防控方向。

2.黄芪是一味常用中草药，也是美国药典收录的食品原

料，回顾性研究与临床前研究已证实其具有肾脏保护作用，但长期前瞻性临床证据仍十分有限。

二、研究结论:

在 2 型糖尿病、2-3 期 CKD 且合并大量白蛋白尿的患者中，在标准治疗基础上联用黄芪 48 周，能显著延缓肾功能下降（eGFR 衰退），且可降低收缩压，对 UACR 无明显改善作用，同时黄芪辅助治疗的安全性良好，未增加严重不良事件风险，可作为糖尿病合并慢性肾病多学科管理的一部分。

三、研究的创新性

1.对于合并大量白蛋白尿的糖尿病肾病患者，在标准治疗基础上附加黄芪治疗 48 周，可较单纯标准治疗显著延缓 GFR 下降速度。

2.本研究是首个在人体中证实黄芪可能具有降压作用的随机对照试验。

3.研究团队的网络药理学分析显示，黄芪干预糖尿病肾病的潜在靶点也包含血压调控相关通路。

4.研究聚焦于大量白蛋白尿患者，该人群的疾病进展速度更快、同质性更高，在临床实践中也更可能寻求整合医学治疗并从中获益。

四、老师总结与点评:

这次汇报能够较为准确的解释这篇文章，理解作者的实验目的和方法，能够为自己的论文提供启发。

老师也指出了几点需要改进和深入的地方:

1. 该实验为临床实验研究，采用的是评估者单盲的方法，在临床研究中，对于同等安慰剂难以把控、对症治疗等原因，因此很难采取双盲对照实验。

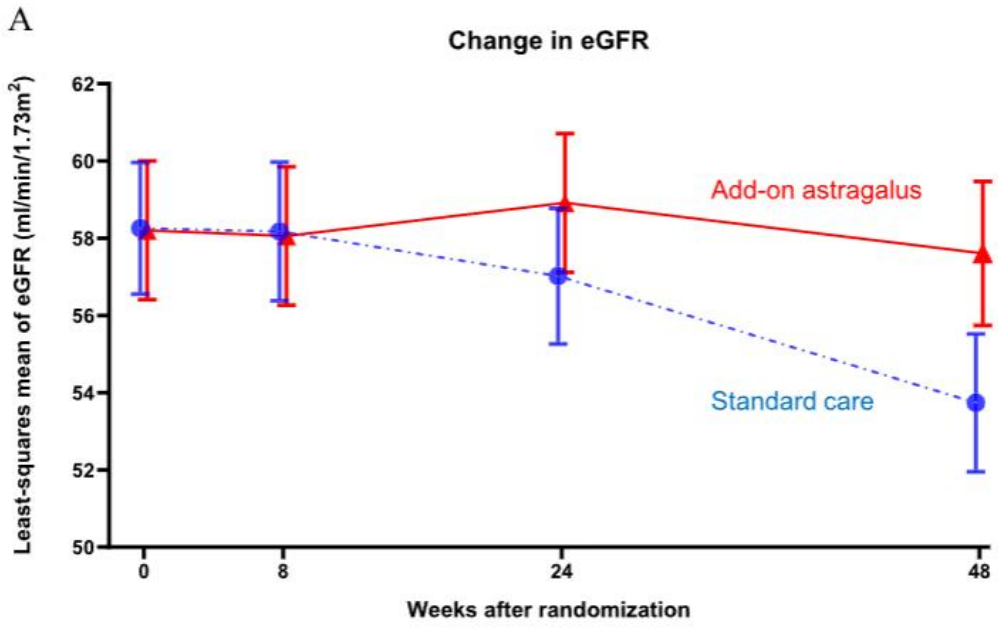
2. 关于黄芪对肾脏的保护性的机制未进行深入学习，且未思考 UACR 的关键评测标准 24 小时尿蛋白定量为什么没能列为该实验的评判标准。

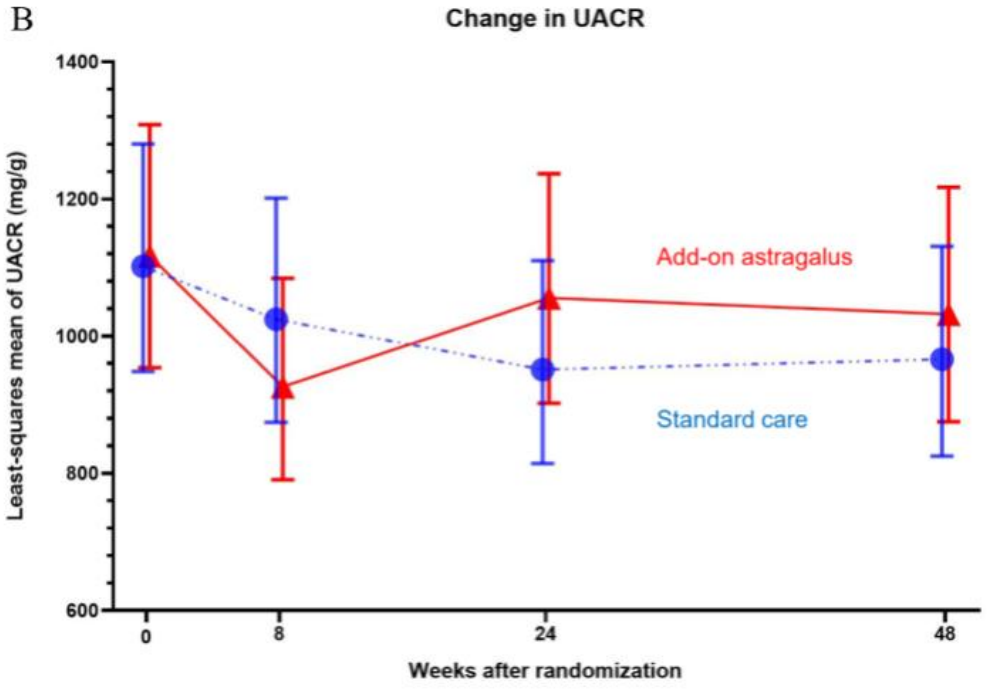
Table 1
Demographics at baseline.

	All patients (*N* = 118)	Add-on astragalus (*N* = 56)	Standard care Control (*N* = 62)
Age – years	67.9 ± 7.8	67.2 ± 7.9	68.5 ± 7.8
Female ratio – no. (%)	43 (36)	20 (36)	23 (37)
Body mass index – kg/m^2	28.0 ± 4.3	28.1 ± 4.3	27.9 ± 4.3
Hemoglobin A1c –%	7.0 ± 1.0	7.1 ± 0.9	7.0 ± 1.1
History of diabetes – years	13.4 ± 7.2	14.1 ± 8.4	12.8 ± 6.0
Smoking history			
Non-smoker – no. (%)	76 (64)	33 (59)	43 (69)
Ex-smoker – no. (%)	22 (19)	13 (23)	9 (15)
Current smoker – no. (%)	20 (17)	10 (18)	10 (16)
Average smoking duration – years	12.0 ± 18.9	14.1 ± 19.7	10.0 ± 18.1
Blood pressure – mmHg			
Systolic	152.1 ± 19.0	153.3 ± 20.8	151.1 ± 17.3
Diastolic	77.0 ± 10.0	76.4 ± 10.6	77.5 ± 9.4
eGFR – ml/min/1.73 m^2	58.0 ± 17.5	57.1 ± 16.5	58.7 ± 18.4
≥60 ml/min/1.73 m^2 – no. (%)	51 (43)	24 (43)	27 (44)
45 to <60 ml/min/1.73 m^2 – no. (%)	32 (27)	14 (25)	18 (29)
30 to <45 ml/min/1.73 m^2 – no. (%)	35 (30)	18 (32)	17 (27)
UACR – mg/g†	1105 ± 20	1183 ± 20	1039 ± 18
<100 mg/mmol – no. (%)	48 (41)	22 (39)	26 (42)
≥100 mg/mmol – no. (%)	70 (59)	34 (61)	36 (58)
Cholesterol – mmol/l			
Triglyceride	1.8 ± 0.0	2.0 ± 1.2	1.7 ± 0.9
High-density lipoprotein	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.2
Low-density lipoprotein	2.5 ± 0.7	2.5 ± 0.6	2.5 ± 0.7
Hemoglobin – g/dL	13.1 ± 1.6	12.9 ± 1.6	13.2 ± 1.6
Serum potassium – mmol/l	4.6 ± 0.4	4.6 ± 0.4	4.6 ± 0.4
Comorbidity – no. (%)			
Diabetic retinopathy	79 (67)	36 (64)	43 (69)
Coronary artery disease	5 (4)	1 (2)	4 (6)
History of stroke	7 (6)	5 (9)	2 (3)
Known peripheral artery disease	2 (2)	2 (4)	0 (0)
Congestive heart failure	0 (0)	0 (0)	(0)
Concomitant medication – no. (%)			
ACEi	52 (44)	21 (38)	31 (50)
ARB	66 (56)	35 (63)	31 (50)
Maximally tolerated dose of ACEi or ARB	105 (89)	50 (89)	55 (89)
Beta-blocker	49 (42)	20 (36)	29 (47)
Diuretic	15 (13)	7 (13)	8 (13)
Calcium channel blocker	99 (84)	46 (82)	53 (86)
Statin	92 (78)	46 (82)	46 (74)
Aspirin	16 (14)	7 (13)	9 (15)
Metformin	106 (90)	52 (93)	54 (87)
Sulfonylurea	68 (58)	28 (50)	40 (65)
Insulin	22 (19)	12 (21)	10 (16)
SGLT2i	15 (13)	8 (14)	7 (11)
DPP-4i	37 (31)	16 (29)	21 (34)
GLP-1 RA	4 (3)	4 (7)	0 (0)

Table 2
Primary and secondary outcomes.

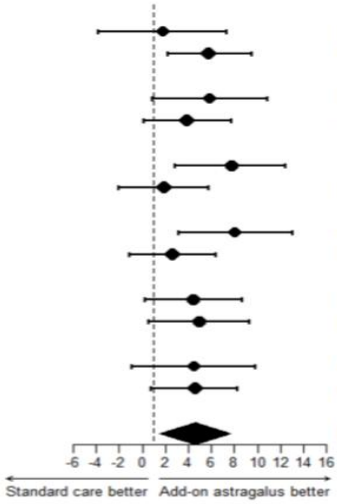
Primary outcomes*	Add-on astragalus ($N = 56$)	Standard care control ($N = 62$)		
	Adjusted mean (95 % CI)	**Adjusted mean (95 % CI)**	**Mean difference (95 % CI)**	***p***
Slope of eGFR change – ml/min/1.73m^2 per year	−0.4 (−2.6 to 1.8)	−5.0 (−7.1 to −2.9)	4.6 (1.5 to 7.6)	0.003
Slope of UACR change – per year	0.99 (0.80 to 1.22) (proportion)	0.87 (0.71 to 1.07) (proportion)	1.14 (0.85 to 1.52) (proportional difference)	0.392
Secondary outcomes				
	Adjusted mean (95 % CI)	**Adjusted mean (95 % CI)**	**Mean difference (95 % CI)**	***p***
Endpoint key outcomes*				
eGFR – ml/min/1.73 m^2	57.6 (55.7 to 59.5)	53.7 (52.0 to 55.5)	3.9 (1.3 to 6.5)	0.003
UACR – mg/g	1032 (875 to 1217)	966 (825 to 1131)	1.07 (0.85 to 1.34) (proportional difference)	0.570
Endpoint physical measurement*				
Systolic blood pressure – mmHg	140.4 (136.7 to 144.0)	148.2 (144.7 to 151.8)	−7.9 (−12.9 to −2.8)	0.003
Diastolic blood pressure – mmHg	73.3 (71.4 to 75.3)	75.7 (73.8 to 77.5)	−2.3 (−5.0 to 0.4)	0.095
Body-mass index – kg/m^2	27.8 (27.5 to 28.0)	27.8 (27.6 to 28.0)	−0.1 (−0.4 to 0.2)	0.678
Endpoint key clinical laboratory investigations*				
Serum potassium – mmol/l	4.6 (4.5 to 4.7)	4.7 (4.6 to 4.8)	−0.1 (−0.2 to 0.1)	0.285
Hemoglobin – g/dL	12.9 (12.8 to 13.1)	12.7 (12.5 to 12.8)	0.2 (0.0 to 0.5)	0.026
Hemoglobin A1c –%	7.1 (7.0 to 7.3)	7.1 (7.0 to 7.2)	0.0 (−0.2 to 0.2)	0.900
Fasting blood glucose – mmol/l	6.9 (6.5 to 7.3)	7.2 (6.8 to 7.6)	−0.3 (−0.9 to 0.2)	0.257
Plasma triglyceride – mmol/l	1.7 (1.4 to 1.9)	1.8 (1.6 to 2.0)	−0.1 (−0.4 to 0.2)	0.413
Plasma high-density lipoprotein – mmol/l	1.1 (1.1 to 1.1)	1.1 (1.1 to 1.1)	0.0 (−0.0 to 0.1)	0.575
Plasma low-density lipoprotein – mmol/l	2.3 (2.2 to 2.4)	2.4 (2.3 to 2.5)	−0.1 (−0.2 to 0.1)	0.334
Serum alkaline phosphatase – U/l	71 (69 to 74)	74 (72 to 77)	−3 (−7 to 1)	0.163
Serum alanine aminotransferase – U/l	19 (17 to 21)	21 (20 to 23)	−2 (−5 to 1)	0.126
Serum aspartate aminotransferase – U/l	19 (18 to 21)	20 (19 to 22)	−1 (−3 to 1)	0.430
Serum gamma-glutamyl transferase – U/l	33 (29 to 37)	39 (35 to 43)	−7 (−12 to −1)	0.025
Serum urea – mmol/l	8.8 (8.3 to 9.3)	9.3 (8.9 to 9.8)	−0.6 (−1.3 to 0.1)	0.112
Serum urate – µmol/l	460 (447 to 473)	432 (420 to 445)	28 (10 to 46)	0.003
Triglyceride-glucose index	9.0 (8.9 to 9.1)	9.0 (8.9 to 9.1)	−0.1 (−0.2 to 0.1)	0.349
Endpoint biomarkers*				
Serum TNF receptor 1 – pg/ml	1262.5 (1149.3 to 1375.8)	1370.5 (1262.4 to 1478.7)	−108.0 (−264.9 to 48.9)	0.177
Serum TNF receptor 2 – pg/ml	4999.3 (4612.8 to 5385.8)	5110.8 (4741.9 to 5479.6)	−111.5 (−645.9 to 423.0)	0.683
Serum TNF-alpha – pg/ml	4.0 (3.4 to 4.5)	3.7 (3.2 to 4.3)	0.2 (−0.5 to 1.0)	0.540
Serum VEGF – pg/ml	377.0 (327.7 to 426.4)	426.1 (379.0 to 473.1)	−49.0 (−117.3 to 19.2)	0.159
Serum MCP-1 – pg/ml	94.7 (87.1 to 102.3)	90.0 (82.8 to 97.2)	4.7 (−5.8 to 15.2)	0.378
Serum TGF-beta1 – ng/ml	28.5 (26.8 to 30.2)	28.7 (27.0 to 30.4)	−0.2 (−2.6 to 2.2)	0.866
Urine MCP-1-to-creatinine ratio – pg/mmol	28.2 (22.4 to 34.0)	24.9 (19.3 to 30.4)	3.3 (−4.7 to 11.4)	0.418
	n / N (%)	**n / N (%)**	**Difference –% (95 % CI)** **Hazard ratio (95 % CI)**	***p*** **(χ^2)** ***p*** **(Cox)**
Concomittant drug change†				
Increased anti-diabetic agents	18 / 55 (33)	14 / 60 (23)	9 (−7 to −26)	0.265
			1.06 (0.51 to 2.20)	0.868
Increased SGLT2i, GLP1 RA or DPP4i	11 / 55 (20)	8 / 60 (13)	7 (−7 to 21)	0.341
			2.33 (0.81 to 6.72)	0.116
Increased SGLT2i	6 / 55 (11)	4 / 60 (7)	4 (−6 to 15)	0.424
			2.50 (0.49 to 12.89)	0.273
Increased GLP1 RA	2 / 55 (4)	0 / 60 (0)	4 (−1 to 9)	0.139
			-	-
Increased DPP4i	8 / 55 (15)	4 / 60 (7)	8 (−3 to 19)	0.170
			1.66 (0.40 to 6.96)	0.486
Reduced ACEi/ARB due to hyperkalemia	5 / 55 (9)	4 / 60 (7)	2 (−8 to 12)	0.632
			0.47 (0.09 to 2.58)	0.387
Increased anti-hypertensive agents	12 / 55 (22)	10 / 60 (17)	5 (−10 to 20)	0.487
			1.73 (0.76 to 3.96)	0.193
Increased diuretics	4 / 55 (7)	4 / 60 (7)	1 (−9 to 10)	0.900
			0.58 (0.14 to 2.44)	0.462
Increased lipid-lowering drugs	6 / 55 (11)	4 / 60 (7)	4 (−6 to 15)	0.424
			1.97 (0.49 to 7.86)	0.339


A
Change in eGFR
Least-squares mean of eGFR (ml/min/1.73m²)
62
60
58
56
54
52
50
Add-on astragalus
Standard care
0
8
24
48
Weeks after randomization


B
Change in UACR
Least-squares mean of UACR (mg/g)
1400
1200
1000
800
600
Add-on astragalus
Standard care
0
8
24
48
Weeks after randomization

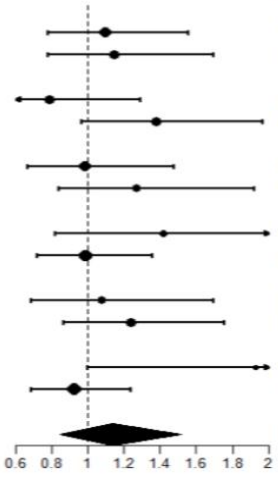
A

Subgroup	Subgroup size	Add-on astragalus	Standard care	eGFR slope difference (95% CI)	p-value
Age, years					
<65years	34	18	16	1.8 (-3.8 to 7.3)	0.53
>=65 years	84	38	46	5.8 (2.2 to 9.5)	0.002
Gender					
Female	43	20	23	5.9 (0.9 to 10.9)	0.02
Male	75	36	39	3.9 (0.1 to 7.7)	0.046
CKD stage					
Stage 2	51	24	27	7.7 (2.9 to 12.4)	0.002
Stage 3	67	32	35	1.9 (-2 to 5.8)	0.342
UACR level, mg/g					
300 to 885	48	22	26	8.1 (3.2 to 13.1)	0.001
Over 885	70	34	36	2.6 (-1.1 to 6.4)	0.169
Hemoglobin A1c, %					
Below 7	62	31	31	4.4 (0.2 to 8.7)	0.042
7 or above	56	25	31	4.9 (0.6 to 9.3)	0.027
Baseline use of DPP-4i					
User	37	16	21	4.5 (-0.9 to 9.8)	0.101
Non-user	81	40	41	4.6 (0.8 to 8.3)	0.017
All patients	**118**	**56**	**62**	**4.6 (1.5 to 7.6)**	**0.003**



B

Subgroup	Subgroup size	Add-on astragalus	Standard care	UACR slope difference (95% CI)	p-value
Age, years					
<65years	34	18	16	1.1 (0.78 to 1.56)	0.584
>=65 years	84	38	46	1.15 (0.78 to 1.7)	0.468
Gender					
Female	43	20	23	0.79 (0.48 to 1.29)	0.343
Male	75	36	39	1.38 (0.97 to 1.97)	0.071
CKD stage					
Stage 2	51	24	27	0.99 (0.67 to 1.48)	0.968
Stage 3	67	32	35	1.27 (0.84 to 1.92)	0.262
UACR level, mg/g					
300 to 885	48	22	26	1.42 (0.82 to 2.45)	0.207
Over 885	70	34	36	0.99 (0.72 to 1.36)	0.954
Hemoglobin A1c, %					
Below 7	62	31	31	1.08 (0.69 to 1.7)	0.729
7 or above	56	25	31	1.24 (0.87 to 1.76)	0.238
Baseline use of DPP-4i					
User	37	16	21	1.93 (1 to 3.71)	0.05
Non-user	81	40	41	0.93 (0.69 to 1.24)	0.603
All patients	**118**	**56**	**62**	**1.14 (0.85 to 1.52)**	**0.392**



第二节　主讲人：2025 级硕士邓玉莹

题目：无论是否进行低碳水化合物饮食，限时饮食都能减少内脏脂肪并改善代谢综合征：一项随机试验

（DOI: 10.1016/j.xcrm.2022.100777）

一、研究背景

1. 近年来我国腹型肥胖率大幅度上升，高碳水饮食与不良饮

食习惯导致中国代谢综合征（MetS）发病率攀升，其以腹型肥胖、高血压、高血糖、动脉粥样硬化血脂异常为特征，显著增加 2 型糖尿病和心血管疾病风险。

2. 代谢综合征目前的一线干预手段是通过干预生活方式来进行减重，但其长期坚持的难度具有挑战性；低碳水饮食（LCD）和限时饮食（TRE）均被证实有代谢获益，但二者及联合方案对代谢综合征患者的减重和代谢改善效果尚未被直接对比研究。
3. 中国陕西地区因其高碳水饮食、晚餐过晚、吃宵夜等不良饮食习惯使得腹型肥胖患病率接近全国平均，是研究饮食干预的代表性样本，因此本研究针对该地区代谢综合征患者开展为期 3 个月的随机试验。
4. 研究目的：本文旨在探究低碳水化合物饮食、限时饮食及其联合干预对患者体重、脂肪量和心脏代谢相关结局的影响。

二、研究结论

在不改变身体活动量的情况下，限时饮食无论是否联合低碳水化合物饮食，均能显著改善血糖、动脉粥样硬化性血脂异常和尿酸水平，从而大幅度降低代谢疾病风险；且在减重和改善腹型肥胖方面，限时饮食的效果优于低碳水化合物饮食。因此，8 小时限时饮食无论是否结合低碳水化合物饮食，均可作为改善代谢综合征的有效干预手段。

三、研究的创新性

本研究是首个直接对比低碳水化合物饮食、8 小时限时饮食及其联合干预在代谢综合征成年患者中减重效果和代谢指标改善作用的临床试验。

四、老师总结与点评

首先，这次汇报总体而言能够完整解释这篇文章，在启发方面能够对自己未来毕业课题提出具有可实行的研究方向。

老师也指出了几点需要改进和深入的地方：

1. 图表数据分析方法需要深入学习：文章中应用的线性混合模型即线性回归分析方法在文献汇报中多次提到，这是一个对于非独立性数据的处理非常重要的分析方法，希望我们能够深入学习并尝试运用该方法进行数据处理。

2. 对于各个分组定义的理解：文章中提出低碳水化合物饮食和限时饮食，每日摄取多少碳水为低碳水，限时因为为何分为早期限时饮食和晚期限时饮食，如何划分仍充分了解。

3. 文章客观数据缺少：本文饮食管控是通过线上 APP 患者自主填写而来，且具有回忆偏差性，无法证实其真实性，客观数据缺少。

总之，这次汇报对文中图表解读到位，与自身研究方向相结合并能在启发中提出对自己研究方向有益的想法，对于文章中提到的研究方法需要深入学习，并能够进行实践。

	LCD	TRE	Both	p value
Male/Female (total)	30/25 (55)	35/20 (55)	37/15 (52)	0.204
Age (years)	41.3 ± 1.4	43.0 ± 1.4	39.0 ± 1.2	0.106
Meal-eating window (hours)	10.6 ± 0.3	10.4 ± 0.3	10.7 ± 0.2	0.730
Daily carbohydrate intake (g)	324 ± 21	348 ± 16	361 ± 22	0.405
Weight (kg)	84.3 ± 2.2	84.7 ± 2.0	84.9 ± 1.8	0.979
BMI (kg/m^2)	29.3 ± 0.5	29.6 ±.5	29.0 ± 0.5	0.711
Waist circumference (cm)	96.1 ± 1.4	96.8 ± 1.2	94.7 ± 1.0	0.457
Hip circumference (cm)	105.1 ± 1.4	104.5 ± 0.9	103.7 ± 0.9	0.645
Waist-to-hip ratio (WHR)	0.92 ± 0.01	0.93 ± 0.01	0.91 ± 0.01	0.212
Body fat mass (kg)	33.9 ± 1.0	33.2 ± 0.9	32.7 ± 0.9	0.651
Body muscle mass (kg)	31.2 ± 1.0	31.6 ± 1.0	32.0 ± 0.8	0.818
Subcutaneous fat area (SFA, cm^2)	277 ± 11	270 ± 9	255 ± 9	0.307
Visceral fat area (VFA, cm^2)	92 ± 5	105 ± 5	96 ± 4	0.112
Hemoglobin A1c (HbA1c, %)	5.7 (0.6)	5.6 (0.6)	5.6 (0.8)	0.853
Fasting blood glucose (mmol/L)	5.10 (0.97)	5.05 (0.89)	5.07 (1.08)	0.763
Fasting insulin (mIU/L)	27.4 (24.7)	31.8 (24.8)	28.2 (17.7)	0.459
C-peptide (pg/mL)	1,608.8 ± 104.2	1,660.2 ± 100.1	1,651.7 ± 88.5	0.923
HOMA-IR	6.76 (9.68)	7.38 (5.90)	7.04 (6.67)	0.612
HOMA-IS	0.17 (0.17)	0.17 (0.19)	0.16 (0.12)	0.473
QUICKI	0.30 (0.04)	0.29 (0.03)	0.29 (0.03)	0.253
Uric acid (UA, μmol/L)	380 ± 13	384 ± 13	416 ± 16	0.144
Total cholesterol (mmol/L)	4.72 ± 0.14	4.76 ± 0.13	4.73 ± 0.13	0.978
LDL-c (mmol/L)	2.99 ± 0.13	3.01 ± 0.12	3.03 ± 0.12	0.974
Triglycerides (TG, mmol/L)	1.74 (1.52)	2.10 (1.55)	2.12 (2.56)	0.086
HDL-c (mmol/L)	1.13 ± 0.03	1.10 ± 0.03	1.04 ± 0.03	0.161
TG/HDL-c	1.58 (1.52)	1.84 (1.88)	2.02 (2.87)	0.044
Systolic blood pressure (mmHg)	130 ± 2	136 ± 2	131 ± 2	0.086
Diastolic blood pressure (mmHg)	82 ± 2	87 ± 2	84 ± 2	0.112

1 **Table S1. Baseline characteristics of participants**

	LCD N = 55	TRE N = 55	Both N = 52	p value
Drug treatment (number, n%)				0.252
Hypotensive drugs	9 (16.4)	12 (21.8)	5 (9.6)	
Lipid-lowering drugs	2 (3.6)	4 (7.3)	0 (0.0)	
Urate-lowering drugs	3 (5.5)	3 (5.5)	5 (9.6)	
Oral hypoglycemic drugs	8 (14.5)	2 (3.6)	4 (7.7)	
Insulin	2 (3.6)	2 (3.6)	1 (1.9)	
Complicating metabolic disease (number, n%)				0.539
Hypertension	12 (21.8)	17 (30.9)	8 (15.4)	
Coronary heart disease	2 (3.6)	2 (3.6)	1 (1.9)	
Arthrolithiasis	4 (7.3)	3 (5.5)	6 (11.5)	
Type 2 diabetes	8 (14.5)	3 (5.5)	6 (11.5)	

Table 2. Change in body composition and metabolic risk factors after 3 months intervention among participants

		LCD		TRE		Both		p value for pairwise comparison		
		N = 55	p value	N = 55	p value	N = 52	p value	LCD vs. TRE	LCD vs. Both	TRE vs. Both
Days of adherence (days)	–	55.5 ± 3.5	–	65.9 ± 3.0	–	57.7 ± 3.1	–	0.024	0.631	0.059
Willingness to continue the diet (n/total, %)	–	46/47 (98)	–	43/44 (98)	–	36/44 (82)	–	0.962	0.010	0.014
Meal-eating window (hours)	Follow-up	10.0 ± 0.3	–	6.5 ± 0.3	–	6.8 ± 0.3	–	–	–	–
	Δ	−0.6 ± 0.3	0.075	−3.9 ± 0.4	< 0.001	−3.9 ± 0.4	< 0.001	< 0.001	< 0.001	0.992
Daily carbohydrate intake (g)	Follow-up	149 ± 12	–	327 ± 15	–	140 ± 11	–	–	–	–
	Δ	−175 ± 22	< 0.001	−21 ± 14	0.137	−221 ± 20	< 0.001	< 0.001	0.125	< 0.001
Weight [a] (kg)	1 M Follow-up	83.0 ± 2.2	–	82.6 ± 2.1	–	82.1 ± 1.8	–	–	–	–
	1 M Δ	−1.7 ± 0.3	< 0.001	−2.4 ± 0.4	< 0.001	−2.6 ± 0.4	< 0.001	0.116	0.082	0.768
	2 M Follow-up	82.2 ± 2.2	–	81.4 ± 2.0	–	80.5 ± 1.8	–	–	–	–
	2 M Δ	−2.5 ± 0.3	< 0.001	−3.7 ± 0.4	< 0.001	−4.2 ± 0.4	< 0.001	0.015	0.002	0.347
	3 M Follow-up	82.3 ± 2.4	–	81.2 ± 2.2	–	80.2 ± 1.8	–	–	–	–
	3 M Δ	−2.2 ± 0.3	0.213	−3.4 ± 0.4	0.323	−5.0 ± 0.4	0.028	0.013	<0.001	0.004
BMI (kg/m^2)	Follow-up	28.3 ± 0.4	–	28.1 ± 0.4	–	27.2 ± 0.4	–	–	–	–
	Δ	−0.9 ± 0.2	< 0.001	−1.4 ± 0.3	< 0.001	−1.8 ± 0.2	< 0.001	0.098	0.003	0.280
Waist circumference (cm)	Follow-up	93.6 ± 1.6	–	92.7 ± 1.5	–	91.4 ± 1.4	–	–	–	–
	Δ	−2.4 ± 1.1	0.035	−4.2 ± 1.0	< 0.001	−3.3 ± 1.2	0.008	0.248	0.603	0.563
Hip circumference (cm)	Follow-up	102.3 ± 0.9	–	103.0 ± 0.9	–	100.9 ± 1.0	–	–	–	–
	Δ	−2.7 ± 0.8	0.001	−1.5 ± 0.7	0.046	−2.8 ± 0.9	0.002	0.263	0.945	0.267
Waist-to-hip ratio (WHR)	Follow-up	0.91 ± 0.01	–	0.90 ± 0.01	–	0.90 ± 0.01	–	–	–	–
	Δ	−0.01 ± 0.01	0.421	−0.04 ± 0.01	< 0.001	−0.01 ± 0.01	0.493	0.023	0.994	0.033
Body fat mass (kg)	Follow-up	31.9 ± 0.9	–	31.9 ± 0.9	–	29.8 ± 0.9	–	–	–	–
	Δ	−2.0 ± 0.4	< 0.001	−1.3 ± 0.6	0.028	−3.0 ± 0.5	< 0.001	0.301	0.103	0.041
Body muscle mass (kg)	Follow-up	31.3 ± 1.0	–	31.1 ± 0.9	–	31.5 ± 0.8	–	–	–	–
	Δ	0.1 ± 0.2	0.524	−0.5 ± 0.3	0.046	−0.5 ± 0.2	0.064	0.048	0.064	0.893
Subcutaneous fat area (SFA, cm^2)	Follow-up	253 ± 12	–	245 ± 10	–	231 ± 10	–	–	–	–
	Δ	−23 ± 5	< 0.001	−24 ± 8	0.003	−24 ± 8	0.006	0.927	0.988	0.949
Visceral fat area (VFA, cm^2)	Follow-up	98 ± 6	–	92 ± 5	–	86 ± 4	–	–	–	–
	Δ	6 ± 5	0.277	−13 ± 5	0.008	−10 ± 3	0.006	0.009	0.016	0.548
Hemoglobin A1c (HbA1c, %)	Follow-up	5.7 (0.6)	–	5.6 (0.6)	–	5.6 (0.7)	–	–	–	–
	Δ	0.0 (0.3)	0.404	0.0 (0.3)	0.385	−0.1 (0.4)	0.021	0.928	0.126	0.157
Fasting blood glucose (mmol/L)	Follow-up	5.22 (1.11)	–	4.76 (1.01)	–	5.01 (1.23)	–	–	–	–
	Δ	0.07 (0.81)	0.820	−0.18 (0.65)	0.024	−0.21 (0.96)	0.048	0.102	0.113	0.739
Fasting insulin (mIU/L)	Follow-up	23.7 (19.4)	–	26.5 (20.3)	–	18.2 (20.8)	–	–	–	–
	Δ	−3.1 (10.4)	< 0.001	−3.3 (12.7)	< 0.001	−5.5 (14.4)	< 0.001	0.394	0.319	0.781

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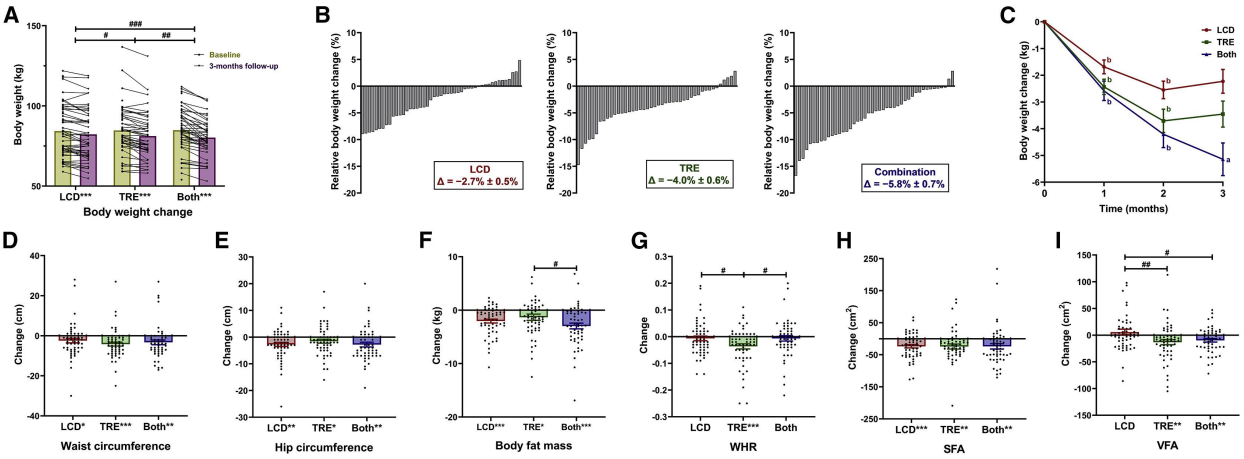
Table 2. *Continued*

		LCD		TRE		Both		p value for pairwise comparison		
		N = 55	p value	N = 55	p value	N = 52	p value	LCD vs. TRE	LCD vs. Both	TRE vs. Both
C-peptide (pg/mL)	Follow-up	1,424.1 ± 85.2	-	1,416.3 ± 80.3	-	1,332.7 ± 71.0	-	-	-	-
	Δ	−184.6 ± 47.6	< 0.001	−243.9 ± 66.0	0.001	−319.1 ± 67.8	< 0.001	0.468	0.104	0.429
HOMA-IR	Follow-up	4.64 (4.70)	-	5.73 (4.39)	-	4.17 (4.41)	-	-	-	-
	Δ	−1.15 (2.99)	< 0.001	−1.04 (4.53)	< 0.001	−2.16 (4.82)	< 0.001	0.427	0.049	0.258
HOMA-IS	Follow-up	0.23 (0.29)	-	0.22 (0.42)	-	0.29 (0.21)	-	-	-	-
	Δ	0.03 (0.12)	< 0.001	0.04 (0.25)	< 0.001	0.10 (0.20)	< 0.001	0.421	0.042	0.245
QUICKI	Follow-up	0.31 (0.04)	-	0.30 (0.04)	-	0.31 (0.04)	-	-	-	-
	Δ	0.01 (0.02)	0.001	0.01 (0.03)	< 0.001	0.02 (0.03)	< 0.001	0.144	0.004	0.157
Uric acid (UA, μmol/L)	Follow-up	363 ± 14	-	345 ± 12	-	364 ± 12	-	-	-	-
	Δ	−17 ± 11	0.125	−40 ± 9	0.001	−51 ± 13	< 0.001	0.146	0.039	0.259
Total cholesterol (mmol/L)	Follow-up	4.91 ± 0.15	-	4.79 ± 0.14	-	4.87 ± 0.15	-	-	-	-
	Δ	0.19 ± 0.12	0.112	0.03 ± 0.17	0.866	0.14 ± 0.13	0.289	0.432	0.777	0.603
LDL-c (mmol/L)	Follow-up	3.27 ± 0.14	-	3.14 ± 0.14	-	3.33 ± 0.15	-	-	-	-
	Δ	0.28 ± 0.13	0.042	0.13 ± 0.14	0.343	0.30 ± 0.13	0.026	0.447	0.929	0.389
Triglycerides (TG, mmol/L)	Follow-up	1.30 (0.94)	-	1.60 (1.64)	-	1.40 (1.59)	-	-	-	-
	Δ	−0.15 (1.20)	0.052	−0.30 (1.36)	0.006	−0.51 (2.01)	< 0.001	0.363	0.011	0.160
HDL-c (mmol/L)	Follow-up	1.16 ± 0.03	-	1.13 ± 0.03	-	1.13 ± 0.03	-	-	-	-
	Δ	0.03 ± 0.03	0.288	0.02 ± 0.03	0.442	0.09 ± 0.02	< 0.001	0.869	0.136	0.109
TG/HDL-c	Follow-up	1.20 (1.20)	-	1.49 (1.54)	-	1.30 (1.33)	-	-	-	-
	Δ	−0.02 (1.20)	0.244	−0.30 (1.59)	0.024	−0.59 (2.13)	< 0.001	0.265	0.003	0.094
Systolic blood pressure (mmHg)	Follow-up	130 ± 3	-	137 ± 2	-	131 ± 2	-	-	-	-
	Δ	1 ± 2	0.770	1 ± 2	0.635	1 ± 2	0.719	0.923	0.979	0.914
Diastolic blood pressure (mmHg)	Follow-up	81 ± 2	-	85 ± 2	-	80 ± 2	-	-	-	-
	Δ	−1 ± 1	0.313	−2 ± 1	0.144	−5 ± 2	0.005	0.823	0.140	0.178



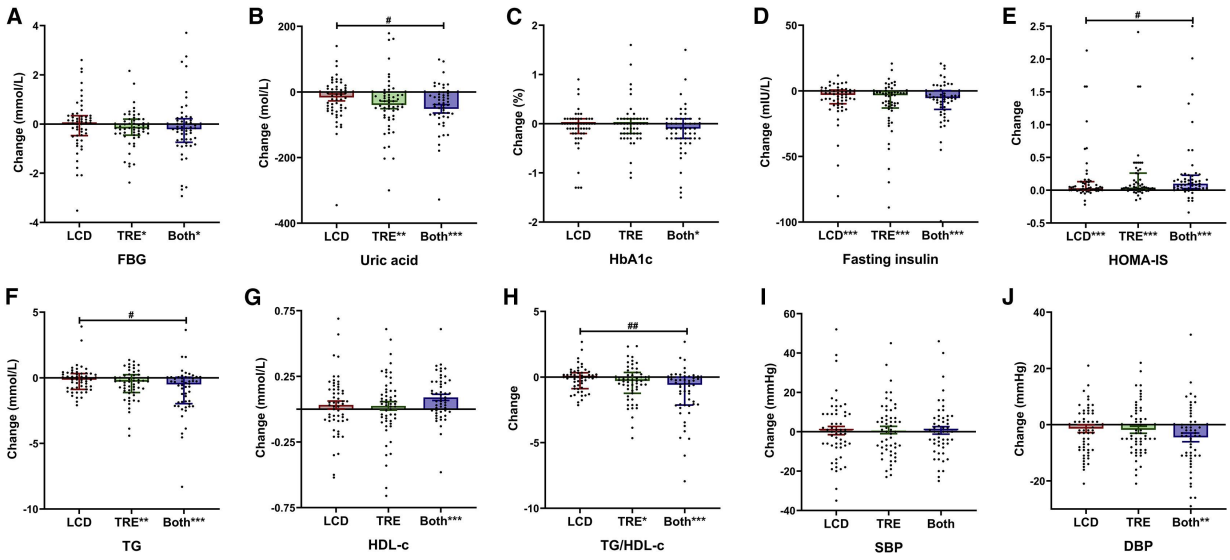


Table 3. Adverse effects among participants

	LCD N = 55	TRE N = 55	Both N = 52	p value
Adverse effects (number, n%)	-	-	-	0.232
Constipation	0 (0.0)	1 (1.8)	3 (5.8)	-
Dizziness	0 (0.0)	1 (1.8)	2 (5.8)	-
Insomnia	3 (5.5)	0 (0.0)	1 (1.9)	-
Dry mouth	1 (1.8)	0 (0.0)	1 (1.9)	-
Alopecia	0 (0.0)	0 (0.0)	1 (1.9)	-