Supplemental materials

The Cre/CysC ratio can predict muscle composition and is associated with glucose disposal ability and macrovascular disease in patients with type 2 diabetes

Qing Yang,[1]* Mei Zhang,[2]* Peng Sun,[1] Yanying Li, [2] Huichao Xu, [1] Kejun Wang, [1] Hongshan Shen, [1] Bo Ban[2], Fupeng Liu[2]

1. Department of Nutrition, Affiliated Hospital of Jining Medical University, Jining, Shandong, China.
2. Department of Endocrinology, Affiliated Hospital of Jining Medical University, Jining, Shandong, China.

Yang Q, *et al. BMJ Open Diab Res Care* 2022; 9:e002430. doi: 10.1136/bmjdrc-2021-002430

Method of the 100 g steamed bun test

Islet β-cell function was assessed using the 100 g steamed bun test. The test was performed between 7:30 and 10:30 a.m. after an overnight fast of at least 12 h. The levels of serum blood glucose and C-peptides were measured during fasting and 30, 60, 120, and 180 min after eating 100 g steamed bread within 10 mins.

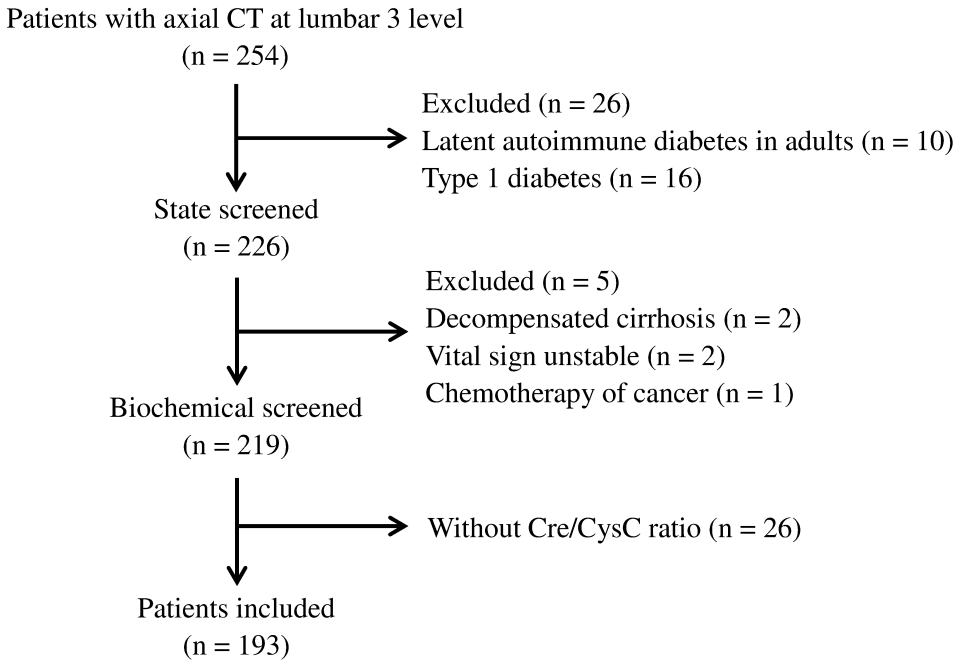
Diagnostic criteria of diabetic complications

Diabetic peripheral neuropathy: Diabetic peripheral neuropathy refers to peripheral nerve dysfunction-related symptoms or signs in diabetic patients that cannot be attributed to other causes. Asymptomatic patients must be diagnosed by physical examination or neuroelectrophysiological examination.

Diabetic nephropathy: Diabetic nephropathy is diagnosed by elevated urinary albumin excretion and reduced eGFR in the absence of other primary causes of kidney damage. Albuminuria was defined as an albumin/creatinine ratio of 30 mg/g or higher. The eGFR was calculated using the Modification of Diet in Renal Disease Study equation or the Cockcroft–Gault formula and regarded as reduced if the value was less than 90 (ml/min/1.73 m^2).

Diabetic retinopathy: Diabetic retinopathy was diagnosed according to the international clinical grading standard for diabetic retinopathy by an ophthalmologist who specializes in diabetic retinopathy.

Lower-extremity arterial disease: Lower-extremity arterial disease was diagnosed if the patients had a resting ABI $\leqslant$0.90. For patients who experienced discomfort upon moving and had a resting ABI $\geqslant$0.90, lower-extremity arterial disease was also diagnosed if the ABI decreased by 15–20% after a treadmill test.



Supplemental figure 1. The screening process for patients enrolled in this study.

Supplemental table 1. Correlations between skeletal composition and clinical factors.

	SMI			MMA		
Variable	**Total (n = 193)**	**Male (n = 114)**	**Female (n = 79)**	**Total (n = 193)**	**Male (n = 114)**	**Female (n = 79)**
Age (years)	-0.288***	-0.226*	-0.119	-0.481***	-0.416***	-0.492***
Duration (months)	-0.134	-0.175	0.063	-0.234**	-0.165	-0.251
BMI (kg/m^2)	0.505***	0.594***	0.402***	-0.178*	-0.117	-0.435***
WHR	0.286***	0.098	0.275*	-0.149*	-0.214	-0.302**
Creatinine (mg/L)	0.382***	0.153	-0.032	0.132	0.007	-0.143
Cystatin C (mg/L)	-0.046	-0.163	-0.154	-0.234**	-0.287**	-0.310**
Cre/CysC	0.375***	0.234*	0.131	0.378***	0.337***	0.223*
Albumin (g/L)	0.250	0.273**	0.180	0.163*	0.101	0.167
BUN (mmol/L)	0.095	0.010	0.092	0.051	0.011	0.025
TG (mmol/L)	0.144*	0.058	0.123	0.171*	0.159	0.102
TCH (mmol/L)	-0.099	-0.080	-0.037	-0.067	0.122	-0.150
HDL (mmol/L)	-0.248**	-0.038	-0.088	-0.165*	-0.087	-0.037
LDL (mmol/L)	-0.139	-0.040	-0.034	-0.156*	0.040	-0.227*
HbA1c (%)	0.061	0.160	0.158	0.016	0.158	-0.079
FBG (mmol/L)	-0.172*	-0.221*	0.093	-0.083	-0.055	0.009
FCP (ng/ml)	0.185*	0.055	0.148	0.047	0.030	-0.084
HOMA2%B	0.284***	0.206*	0.121	0.082	-0.014	0.001
HOMA2%S	-0.223**	-0.192	-0.151	-0.016	-0.141	0.213
HOMA2 IR	0.126	0.021	0.181	0.016	0.020	-0.061
Hypertension	(-1.20, 3.76)	(-0.29, 4.73)	(-3.72, 1.81)	(-3.86, -0.01)	(-4.46, -0.02)*	(-4.98, 1.28)
CV disease	(-5.31, 0.02)	(-2.96, 2.87)	(-4.87, 0.72)	(-5.78, -1.36)**	(-5.19, -0.20)*	(-6.32, -0.02)*
DPN	(-2.14, 3.67)	(-2.95, 3.02)	(-1.54, 4.86)	(-3.90, 0.64)	(-4.34, 0.83)	(-5.16, 2.14)

LEAD	(-3.14, 1.85)	(-1.16, 3.92)	(-5.49, -0.05)*	(-3.19, 0.71)	(-3.38,1.28)	(-4.33, 2.01)
DN	(-1.41, 3.60)	(0.27, 5.31)*	(-3.21, 2.33)	(-4.20, -0.33)*	(-5.19, -0.50)*	(-4.23, 2.06)
DR	(-4.07, 1.83)	(-4.43, 1.88)	(-1.77, 4.43)	(-2.96, 1.66)	(-4.00, 1.52)	(-2.54, 4.54)
SMI (cm^2/m^2)	1.000	1.000	1.000	0.409***	0.276**	0.208
MMA (HU)	0.409***	0.276**	0.208	1.000	1.000	1.000
FMI (cm^2/m^2)	0.101	0.349***	0.220	-0.481***	-0.355***	-0.567***

Correlations are shown with the coefficient r or 95% Cl of the mean difference between the patients with complications and without. Abbreviations: Cre/CysC, creatinine-to-cystatin C ratio; BUN, blood urea nitrogen; TG, triglycerides; TCH, total cholesterol; HDL, high-density lipoproteins; LDL, low-density lipoproteins; FBG, fasting blood glucose; FCP, fasting C-peptide; CV, cardiovascular; DPN, diabetic peripheral neuropathy; LEAD, lower-extremity arterial disease; DN, diabetic nephropathy; DR, diabetic retinopathy; SMI, skeletal muscle index; MMA, mean skeletal muscle attenuation; FMI, fat mass index. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Supplemental table 2. Multiple stepwise linear regression analysis of factors associated with the SMI and MMA in males and females.

Variable	Male			Female	
	Beta (95% CI)	**p value**	**Variables**	**Beta (95% CI)**	**p value**
SMI			**SMI**		
BMI	1.28 (0.95, 1.61)	<0.001	BMI	0.78 (0.43,1.12)	<0.001
Age	-0.10 (-0.18, -0.01)	0.022	Age	-0.15 (-0.28, 0.03)	0.019
MMA			**MMA**		
Age	-0.17 (-0.25, -0.09)	<0.001	Age	-0.28 (-0.40, 0.15)	<0.001
DN	-2.67 (-4.62, -0.72)	0.008	BMI	-0.66 (-1.00, 0.31)	<0.001
Cre/CysC	0.60 (0.11, 1.09)	0.016	LDL	-2.17 (-3.55, -0.78)	0.003
			Albumin	0.26 (0.01, 0.51)	0.040

Adopted factors: age, BMI, WHR, Cre/CysC, creatinine, albumin, high-density lipoproteins, HOMA2%B, HOMA2%S, fasting blood glucose and fasting C-peptide for the SMI; age, duration, BMI, WHR, Cre/CysC, cystatin C, albumin, triglycerides, high-density lipoproteins, low-density lipoproteins, hypertension, cardiovascular disease and diabetic nephropathy for the MMA. R^2 = 0.382 for the SMI and 0.270 for the MMA in males. R^2 = 0.220 for the SMI and 0.443 for the MMA in females. Cre/CysC, creatinine-to-cystatin C ratio; SMI, skeletal muscle index; MMA, mean skeletal muscle attenuation; DN, diabetic nephropathy; LDL, low-density lipoprotein.

Supplemental table 3. Multiple stepwise linear regression analysis of factors associated with glucose at 120 min and 180 min.

Variable	Beta (95% CI)	p value
120 min		
HOMA2%B	-0.04 (-0.05, -0.02)	<0.001
Cre/CysC	-0.46 (-0.69, -0.23)	<0.001
BMI	-0.18 (-0.31, -0.05)	0.008
Duration	0.01 (0.00, 0.01)	0.014
HbA1c	0.30 (0.07, 0.54)	0.012
Creatinine	0.27(0.01, 0.53)	0.042
180 min		
HOMA2%B	-0.05 (-0.06, -0.04)	<0.001
Cre/CysC	-0.49 (-0.74, -0.25)	<0.001
Sex	-1.90 (-2.92, 0.87)	<0.001
Creatinine	0.41 (0.12, 0.70)	0.006
HbA1c	0.40 (0.15, 0.65)	0.002
Duration	0.01 (0.00, 0.02)	0.013

Adopted factors: sex, age, duration, BMI, diabetic peripheral neuropathy, diabetic retinopathy, Cre/CysC, creatinine, albumin, total cholesterol, low-density lipoproteins, HbA1c, HOMA2%B and skeletal muscle index. R^2 = 0.462 for 120 min and 0.552 for 180 min glucose levels.