Online-Only Supplemental Material

The non-linear relationship between psoas cross-sectional area and body mass index: A new observation and its insights into diabetes remission after Roux-en-Y gastric bypass

Supplement Appendix

Study Procedures

This was a single-center, open-label study approved by the institutional review board of the Shanghai Jiao Tong University Affiliated Sixth People's Hospital. All patients provided informed consent after being made aware of the treatment standards for T2DM and the risks and benefits of the surgery. Inclusion criteria were as follows: diagnosis of T2DM according to the 1999 World Health Organization criteria, aged 18–67 years, BMI of 25.5–50.0 kg/m^2, fasting C-peptide >1ng/mL, and the peak to fasting value >2. We excluded patients with scoliosis, anemia, poor compliance, pregnancy, type 1 diabetes mellitus, mental disorders, latent autoimmune diabetes, malignancy, and previous gastrointestinal surgery. All subjects included in this study underwent abdominal MRI examination, which was part of the study protocol.

Between February 2011 and August 2020, 553 patients met the above inclusion criteria of the study. Based on the exclusion criteria, 19 patients were excluded from the study. Moreover, we excluded 33 of these patients from the analysis as they did not undergo preoperative MRI examination. Therefore, a total of 501 patients (mean age, 41.5 [SD, 12.8] years; mean baseline BMI, 34.0 [SD, 5.4] kg/m^2; 58.5% females) were enrolled in the cross-sectional study. In the longitudinal study, we focused solely on the 186 patients (mean age 47.3±11.9 years, range from 24–67 years; mean BMI 31.0±3.3 kg/m^2, range from 26.0–45.0 kg/m^2; 55.9% females) in the above population who underwent RYGB and had complete 1-year follow-up data. Patient outcomes were also assessed at 0.5, 2, 3, 4, and 5 years post-RYGB. The 5-year follow-up endpoint data were available for 33.9% of the 186 patients: 154 patients (57.8% females) completed the 2-year follow-up, 136 patients (58.1% females) completed the 3-year follow-up, 109 patients (56.9% females) completed the 4-year follow-up, and 63 patients (52.4% females) completed the 5-year follow-up. Time to follow-up was 1–5 years (mean [SD] follow-up, 3.48 [1.4] years; median [IQR] follow-up, 4.0 [2.0, 5.0] years). Patients were evaluated at inpatient or outpatient control visits, and all prespecified data were recorded thoroughly. Follow-up visits were scheduled at least once a year after surgery. Patients lost to follow-up due to various factors (e.g., busy work, geographical distance, changes in telephone number, etc.) were contacted multiple times by telephone. Supplementary Figure S1 shows the flow of patients through the study.

The RYGB surgery was performed by the same experienced surgeons according to a previously reported standardized laparoscopic protocol (1). This included creation of a 25-mL gastric pouch with a length of 100–120 cm from the distal remnant and biliopancreatic and alimentary limbs. Data on anthropometric characteristics and serum biochemical parameters were collected and input into a follow-up study database. More details about the diabetes mellitus status, including disease duration, medication use, fasting plasma glucose (FPG) concentration, fasting C-peptide concentration, and HbA1c levels, were collected in addition to routine investigations.

T2DM was determined in accordance with the 1999 World Health Organization criteria: fasting plasma glucose concentration of 7.0 mmol/L or greater and/or 2-hour plasma glucose concentration of 11.1 mmol/L or greater. Overweight (BMI ≥24.0 to BMI <28.0 kg/m^2) and obesity (BMI ≥28.0 kg/m^2) were determined in accordance with the standard definitions proposed by the Working Group on Obesity in China (2). Complete DR was considered if the patient showed HbA1c <42 mmol/mol (6.0%) and fasting glucose <100 mg/dL (5.6 mmol/L) without active pharmacologic therapy or ongoing procedures for 1 year or more, while long-term diabetes remission was defined as complete DR that lasted for at least 5 years after surgery (3). The primary outcome was complete DR during the five-year follow-up period after RYGB.

Measurement of Body Composition

Abdominal MRI examination was performed using a Philips Achieva 3.0-T magnetic resonance imaging system (Philips Medical Systems, Eindhoven, The Netherlands). Breath-hold fast imaging with a 40-ms repetition time, 2-ms echo time, 50-cm field of view, and 256 × 256 matrix was used to acquire the cross-sectional MR images. One 10-mm slice positioned at the L3 level with a clear outline was selected for analysis using SliceOmatic 5.0 software (TomoVision, Magog, Canada) by a medically trained technician. The psoas CSA, SFA, and VFA were measured using the following steps: regional threshold procedures were first applied using the "Region Growing" mode, after which manual delineation was used to draw borders among different tissues in the "edit mode" when necessary (4). The software calculated different colored areas and expressed the measurements in cm^2. The TFA was calculated as the sum of SFA and VFA.

Additional Statistical Approaches

All data were tested for normality using the Shapiro-Wilk test. Categorical variables were presented as numbers (percentages). Continuous variables with normal and non-normal distributions were presented as mean (standard deviation, SD) and medians (interquartile range, IQR), respectively. Differences between the two groups were assessed using the Chi-squared or Fisher's exact test for categorical variables and the independent-sample t-test or the Mann-Whitney U test for continuous factors. Follow-up comparisons were performed using the paired t-test and Wilcoxon signed-rank test.

The breakpoint identified by the best-fit analysis is one that minimized the sum residual square error of the two linear segments, above and below this point. Binary logistic regression analyses were performed to identify the baseline factors independently related to 1-year DR after RYGB surgery. All associated variables in the univariate analyses ($P < 0.20$) and those known or likely to be associated with remission (based on previous literature) were considered for inclusion in the multivariate model. Psoas CSA and eFFMI were entered in the multivariable model separately because of the co-linearity. The tertiles of baseline psoas CSA, eFFMI, and BMI used for Kaplan–Meier analysis was stratified by sex to avoid the potential influence of significant differences in body composition. Missing data were handled by listwise deletion. A *P*-value < 0.05 (two-tailed tests) was considered statistically significant. All analyses were performed using SPSS version 25.0 (SPSS, Chicago, IL, USA).

Reference

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2. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. Biomed Environ Sci 2002; 15: 245-252
3. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? Diabetes Care 2009; 32: 2133-2135
4. Shen W, Punyanitya M, Wang Z, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol (1985) 2004; 97: 2333-2338

Supplementary Table S1. Characteristics of cross-sectional study participants stratified by sex

Variable	Total (n=501)	Male (n=208)	Female (n=293)	*P* value
Age (years)	41.5 ± 12.8	40.6 ± 12.1	42.2 ± 13.2	0.163
Diabetes duration (years)	5.0 ± 5.0	5.2 ± 4.9	4.9 ± 5.1	0.483
BMI (kg/m^2)	34.0 ± 5.4	33.6 ± 5.1	34.2 ± 5.5	0.168
Waist circumference (cm)	110.2 ± 12.8	111.4 ± 13.6	109.4 ± 12.2	0.089
Waist-to-hip ratio	0.99 ± 0.06	1.01 ± 0.06	0.97 ± 0.06	**<0.001**
SBP (mmHg)	133.2 ± 15.7	133.6 ± 14.9	132.9 ± 16.2	0.614
DBP (mmHg)	85.0 ± 11.3	85.6 ± 11.7	84.5 ± 11.0	0.294
Total cholesterol (mmol/L)	5.1 ± 1.2	4.9 ± 1.1	5.2 ± 1.3	**0.002**
Triglycerides (mmol/L)	2.7 ± 2.7	3.0 ± 2.8	2.5 ± 2.6	**0.019**
HDL cholesterol (mmol/L)	1.0 ± 0.2	0.9 ± 0.2	1.1 ± 0.2	**<0.001**
LDL cholesterol (mmol/L)	3.0 ± 0.9	2.8 ± 0.9	3.1 ± 0.9	**<0.001**
FPG (mmol/L)	8.7 ± 3.1	8.7 ± 3.0	8.8 ± 3.1	0.749
2-h plasma glucose (mmol/L)	13.2 ± 4.4	13.3 ± 4.2	13.1 ± 4.6	0.610
Fasting C-peptide (ng/mL)	3.4 ± 1.9	3.6 ± 2.0	3.3 ± 1.7	0.151
HbA1c (%)	8.5 ± 3.4	8.5 ± 3.9	8.5 ± 3.1	0.883
HbA1c (mmol/mol)	69.0 ± 14.0	69.0 ± 19.0	69.0 ± 10.0	0.883
HOMA-IR	7.7 (4.6, 13.0)	7.9 (3.4, 12.3)	7.5 (3.4, 11.7)	0.463
HOMA-B	102.3(49.3,189.8)	108.4(34.6,182.1)	101.5(33.5,169.6)	0.462
ALT (U/L)	47.2 ± 45.5	52.0 ± 44.4	43.8 ± 46.0	**0.049**
AST (U/L)	31.8 ± 25.6	32.0 ± 23.2	31.6 ± 27.3	0.875
Serum creatinine (μmol/L)	59.5 ± 19.0	71.2 ± 16.5	51.1 ± 16.0	**<0.001**
Body Composition (L_3)				
Visceral fat area (cm^2)	169.7 ± 58.1	180.2 ± 65.3	162.3 ± 51.3	**0.001**
Subcutaneous fat area (cm^2)	367.5 ± 155.0	334.9 ± 156.2	390.6 ± 150.1	**<0.001**
Total fat area (cm^2)	537.2 ± 179.8	515.1 ± 188.9	552.8 ± 171.2	**0.021**
Psoas CSA (cm^2)	26.4 ± 8.0	34.1 ± 5.8	21.0 ± 4.1	**<0.001**
Estimated Body Composition				
Body fat percentage (%)	40.4 ± 8.5	33.4 ± 5.8	45.3 ± 6.4	**<0.001**
Fat-free mass index (kg/m^2)	19.9 ± 2.4	22.1 ± 1.7	18.4 ± 1.4	**<0.001**
Fat mass index (kg/m^2)	14.0 ± 4.9	11.5 ± 3.8	15.8 ± 4.8	**<0.001**
Anti-diabetes agent (%)				
Oral anti-diabetes drugs	310 (61.9%)	130 (62.5%)	180 (61.4%)	0.809
Insulin	168 (33.5%)	77 (37.0%)	91 (31.1%)	0.164
Antihypertension agent (%)				
Calcium-channel blockers	86 (17.2%)	38 (18.3%)	48 (16.4%)	0.581
RAAS inhibitors	98 (19.6%)	50 (24.0%)	48 (16.4%)	**0.033**
β-Blockers	26 (5.2%)	10 (4.8%)	16 (5.5%)	0.745
Lipid-lowering agents (%)				
Statins	32 (6.4%)	15 (7.2%)	17 (5.8%)	0.525
Fibrates	24 (4.8%)	12 (5.8%)	12 (4.1%)	0.387

Data are presented as mean ± SD, median (interquartile range, IQR), or n (%). SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-B, HOMA of β-cell function; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Psoas CSA, psoas cross-sectional area.

Supplementary Table S2. Comparison of linear regression with segmented linear regression used for the best-fit relationship between body composition measured by MRI and BMI in males and females

	Linear regression		**Segmented linear regression**			**comparison**	
	Slope	**R^2**	**Slope1**	**Slope2**	**R^2**	**Breakpoint**	***P***
Male (n = 208)							
Psoas CSA	0.380	0.108	1.211	0.136	0.143	(**31.88, 35.09**)	**0.006**
Visceral fat area	7.099	0.307	10.82	4.915	0.314	(33.71, 193.6)	0.124
Subcutaneous fat area	24.84	0.746	23.95	33.27	0.745		0.423
Total fat area	33.98	0.848	32.88	38.25	0.847		0.548
Female (n = 293)							
Psoas CSA	0.280	0.136	0.684	0.123	0.162	(**32.66, 21.66**)	**0.005**
Visceral fat area	4.097	0.194	7.323	2.193	0.210	(**33.91, 173.0**)	**0.022**
Subcutaneous fat area	24.55	0.787	25.83	18.47	0.788		0.176
Total fat area	28.50	0.823	11.55	28.85	0.823		0.519

R^2, coefficient of determination; Slope1, the slope before breakpoint; Slope2, the slope after breakpoint; *P*, Log likelihood ratio test P-value (linear regression model vs. segmented linear regression model).

Supplementary Table S3. Comparison of linear regression with segmented linear regression used for the best-fit relationship between MRI-measured body composition and FFMI estimated from the Deurenberg formula in males and females

	Linear regression		Segmented linear regression			comparison	
	Slope	**R^2**	**Slope1**	**Slope2**	**R^2**	**Breakpoint**	***P***
Male (n = 208)							
Psoas CSA	1.528	0.220	4.334	1.278	0.228		0.133
Female (n = 293)							
Psoas CSA	1.608	0.273	1.935	0.983	0.274		0.336

R^2, coefficient of determination; Slope1, the slope before breakpoint; Slope2, the slope after breakpoint; *P*, Log likelihood ratio test P-value (linear regression model vs. segmented linear regression model).

Supplementary Table S4. Comparison of linear regression with segmented linear regression used for the best-fit relationship between MRI-measured body composition and FMI estimated from the Deurenberg formula in males and females

	Linear regression		Segmented linear regression			comparison	
	Slope	**R^2**	**Slope1**	**Slope2**	**R^2**	**Breakpoint**	***P***
Male (n = 208)							
Visceral fat area	10.22	0.353	12.56	0.803	0.368	(**16.87, 251.3**)	**0.029**
Subcutaneous fat area	33.82	0.667	18.63	35.53	0.667		0.346
Total fat area	44.12	0.777	46.41	32.57	0.778		0.232
Female (n = 293)							
Visceral fat area	5.243	0.239	9.681	2.046	0.270	(**16.55, 182.6**)	**0.001**
Subcutaneous fat area	27.66	0.714	29.57	20.17	0.716		0.151
Total fat area	33.50	0.782	35.46	24.24	0.784		0.117

R^2, coefficient of determination; Slope1, the slope before breakpoint; Slope2, the slope after breakpoint; *P*, Log likelihood ratio test P-value (linear regression model vs. segmented linear regression model).

Supplementary Table S5. Characteristics of the diabetes remission and non-remission groups before and one year after RYGB surgery

	Male (n=82)				Female (n=104)			
	DR (n=34)		Non-DR (n=48)		DR (n=45)		Non-DR (n=59)	
Variable	**Baseline**	**1 Year**	**Baseline**	**1 Year**	**Baseline**	**1 Year**	**Baseline**	**1 Year**
Age (years)	41.4 ± 9.9		49.7 ± 10.9 †		43.4 ± 11.8		51.8 ± 11.6 †	
Diabetes duration (years)	4.0 ± 3.4		9.2 ±4.7 ‡		4.4 ± 3.8		8.9 ± 4.8 ‡	
BMI (kg/m^2)	32.2 ± 3.2	24.5 ± 2.6 ¶	30.7 ± 3.6	24.7 ± 3.3 ¶	31.5 ± 3.2	23.1 ± 2.5 ¶	30.1 ± 3.0 *	23.5 ± 2.5 ¶
Waistline (cm)	109.4 ± 10.6	87.1 ± 8.2 ¶	105.4 ± 10.2	88.3 ± 10.1 ¶	103.5 ± 10.4	84.7 ± 10.2 ¶	101.2 ± 7.6	84.7 ± 8.7 ¶
FPG (mmol/L)	9.1 ± 3.0	4.8 ± 0.44 ¶	8.7 ± 2.8	6.5 ± 1.1 ¶‡	8.3 ± 2.6	4.9 ± 0.41¶	8.7 ± 2.7	6.2 ± 1.3 ¶‡
2hPG (mmol/L)	14.0 ± 4.8	5.9 ± 2.4 ¶	14.0 ± 4.0	10.1 ± 3.3 ¶‡	12.8 ± 3.9	5.3 ± 1.2 ¶	13.4 ± 3.9	7.7 ± 3.1 ¶‡
FCP (ng/mL)	3.1 ± 1.3	1.9 ± 0.55 ¶	2.5 ± 1.5	1.9 ± 0.69 ¶	2.9 ± 1.1	1.8 ± 0.43 ¶	2.4 ± 1.0 *	1.9 ± 0.67 ¶
HbA1c (%)	8.7 ± 2.4	5.3 ± 0.31 ¶	8.4 ± 1.6	6.4 ± 0.90 ¶‡	8.1 ± 1.9	5.5 ± 0.32 ¶	8.7 ± 1.8	6.5 ± 0.74 ¶‡
HbA1c (mmol/mol)	72.0 ± 26.3	34.0 ± 3.40 ¶	68.0 ± 17.5	46.0 ± 9.80 ¶‡	65.0 ± 20.8	37.0 ± 3.50 ¶	72 ± 19.7	48.0 ± 8.09 ¶‡
HOMA-IR	7.2 (5.6, 14.6)	1.3 (0.9, 1.8) ¶	7.7 (3.4, 12.0)	1.6 (1.1, 2.6) ¶*	6.0 (4.2, 10.0)	1.2 (1.0, 1.7) ¶	7.3 (3.8, 22.3)	1.6 (1.0, 2.6) ¶*
eBF (%)	32.0 ± 4.4	23.1 ± 3.9 ¶	32.1 ± 4.2	24.9 ± 3.9 ¶*	42.5 ± 4.4	33.3 ± 4.0 ¶	42.7 ± 4.3	35.0 ± 3.6 ¶*
eFFMI (kg/m^2)	21.8 ± 1.2	18.8 ±1.3 ¶	20.7 ± 1.4 ‡	18.4 ± 1.7 ¶	18.0 ± 1.1	15.6 ± 1.3 ¶	17.2 ± 1.0 ‡	15.2 ± 1.1 ¶

eFMI (kg/m^2)	10.4 ± 2.5	5.7 ± 1.6 ¶	10.0 ± 2.5	6.3 ± 1.8 ¶	13.5 ± 2.7	7.9 ± 1.7 ¶	13.0 ± 2.5	8.3 ± 1.7 ¶
Psoas CSA (cm^2)	35.5 ± 4.8	31.5 ± 4.2 ¶	30.4 ± 5.6 ‡	27.9 ± 5.0 ¶ †	21.5 ± 3.3	17.3 ± 2.5 ¶	17.6 ± 3.2 ‡	14.7 ± 2.5 ¶ ‡
VFA (cm^2)	169.7 ± 57.7	50.1 ± 36.7 ¶	157.3 ± 55.6	59.5 ± 40.4 ¶	151.1 ± 51.5	57.3 ± 22.6 ¶	148.3 ± 41.8	56.8 ± 23.7 ¶
SFA (cm^2)	294.2 ± 111.3	154.6 ± 67.4 ¶	245.8 ± 105.8 *	152.9 ± 100.0 ¶	298.7 ± 98.6	170.6 ± 75.6 ¶	278.4 ± 93.6	155.8 ± 49.1 ¶
TFA (cm^2)	463.9 ±124.5	204.6 ± 89.1 ¶	403.2 ± 136.3 *	212.5 ± 133.2¶	449.8 ± 118.1	228.0 ± 86.0 ¶	426.7 ± 116.7	215.2 ± 63.6 ¶
OHA (%)	21 (61.8%)	0 (0%) ¶	28 (58.3%)	5 (10.4%) ¶	28 (62.2%)	0 (0%) ¶	41 (69.5%)	10 (16.9%) ¶ †
Insulin therapy (%)	13 (38.2%)	0 (0%) ¶	30 (62.5%) *	3 (6.3%) ¶	14 (31.1%)	0 (0%) ¶	30 (50.8%) *	2 (3.4%) ¶

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

FPG, fasting plasma glucose; 2hPG, 2-h plasma glucose; FCP, Fasting C-peptide; eBF%, estimated body fat percentage; eFFMI, estimated fat-free mass index; eFMI, estimated fat mass index; OHA, oral hypoglycemic agents.

*$P < 0.050$ between same-gender subgroups; †$P < 0.010$ between same-gender subgroups; ‡$P < 0.001$ between same-gender subgroups.

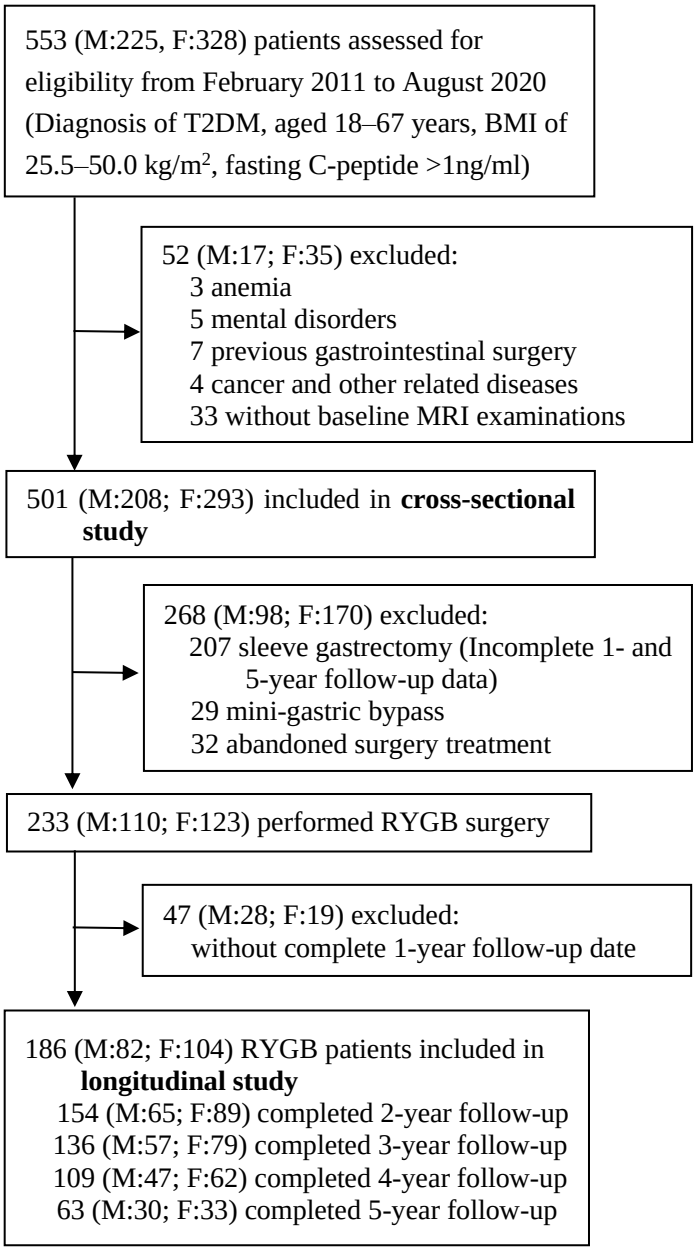
§$P < 0.050$ within the same-gender subgroup vs. baseline; ‖$P < 0.010$ within the same-gender subgroup vs. baseline; ¶$P < 0.001$ within the same-gender subgroup vs. baseline.

Supplementary Table S6. Univariate and multivariate logistic regression analysis for baseline predictors of diabetes remission 1 year after RYGB surgery

Model 1: Male group (n=82)						
	Univariate analysis		**Multivariate analysis A**		**Multivariate analysis B**	
Variable	**Standardized β**	***P* value**	**Standardized β**	***P* value**	**Standardized β**	***P* value**
Age	0.841	**0.001**	NS		NS	
Diabetes duration	1.530	**<0.001**	1.528	**<0.001**	1.530	**<0.001**
Fasting C-peptide	-0.437	0.074	NS		NS	
HOMA-IR	0.243	0.457	NS		NS	
HbA1c	-0.134	0.552	NS		NS	
BMI	-0.444	0.065	NS		NS	
Insulin use	0.388	0.094	NS		NS	
Psoas CSA	-1.135	**<0.001**	-1.257	**0.003**	NI	
eFFMI	-0.876	**0.001**	NI		NS	
eBF	0.054	0.882	NI		NI	
eFMI	-0.174	0.440	NI		NI	
SFA	-0.454	0.057	NS		NS	
VFA	-0.221	0.329	NI		NI	
TFA	-0.471	**0.049**	NS		NS	
Model 2: Female group (n=104)						
	Univariate analysis		**Multivariate analysis A**		**Multivariate analysis B**	
Variable	**Standardized β**	***P* value**	**Standardized β**	***P* value**	**Standardized β**	***P* value**
Age	0.724	**0.001**	NS		NS	
Diabetes duration	1.262	**<0.001**	1.018	**0.003**	1.091	**0.001**
Fasting C-peptide	-0.449	**0.034**	NS		NS	
HOMA-IR	1.072	**0.019**	2.085	**0.011**	1.744	**0.012**
HbA1c	0.327	0.125	NS		NS	
BMI	-0.471	**0.025**	NS		NS	
Insulin use	0.392	0.059	NS		NS	
Psoas CSA	-1.535	**<0.001**	-1.620	**<0.001**	NI	
eFFMI	-0.861	**<0.001**	NI		-0.606	**0.032**
eBF	0.079	0.800	NI		NI	
eFMI	-0.212	0.289	NI		NI	
SFA	-0.214	0.286	NI		NI	
VFA	-0.062	0.753	NI		NI	
TFA	-0.199	0.319	NI		NI	

Standardized β, Standardized regression coefficients; NI, not included; NS, not significant. Boldface indicates significance at $P < 0.050$.

Supplementary Figure S1. Patient flow chart. MRI, magnetic resonance imaging; RYGB, Roux-en-Y gastric bypass; M, male; F, female.



Supplementary Figure S2. The best-fit relationship of fat area measured by MRI with BMI (*A, C, E*) and estimated fat mass index (*B, D, F*) in the cross-sectional study population (208 males and 293 females). *A*: Total fat area and BMI. *B*: Total fat area in relation to estimated fat mass index. *C*: Visceral fat area and BMI. *D*: Visceral fat area in relation to estimated fat mass index. *E*: Subcutaneous fat area and BMI. *F*: Subcutaneous fat area in relation to estimated fat mass index. Each circle represents a single participant in the study. The point showing a sharp change in slope is indicated by a dashed line with the corresponding color. Segmental linear regression is applied if the correlation is significantly better than linear regression ($P < 0.05$). Pearson correlation coefficients and the associated *P*-values are shown for male and female populations in the regression model. Breakpoints of visceral fat (male and female): 33.71 and 33.91 kg/m^2 for BMI, and 16.87 and 16.55 kg/m^2 for estimated fat mass index.