



# The Nonlinear Relationship Between Psoas Cross-sectional Area and BMI: A New Observation and Its Insights Into Diabetes Remission After Roux-en-Y Gastric Bypass

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## OBJECTIVE

To explore the potential relevance of muscle mass as a variable contributor to BMI in limitations on BMI-based predictions of diabetes remission (DR) after Roux-en-Y gastric bypass (RYGB).

## RESEARCH DESIGN AND METHODS

We evaluated the relationship between muscle mass and BMI in 501 patients with type 2 diabetes mellitus and overweight or obesity, of whom 186 patients who underwent RYGB were studied for determination of the role of baseline muscle mass and BMI in predicting DR. Muscle mass was assessed by estimated fat-free mass index (eFFMI) and psoas cross-sectional area (CSA).

## RESULTS

A nonlinear relationship existed between psoas CSA and BMI, whereas psoas CSA showed a highly positive correlation with eFFMI. Baseline psoas CSA and eFFMI were better than BMI for predicting 1- and 5-year DR.

## CONCLUSIONS

The nonlinear relationship between muscle mass and BMI may partially contribute to BMI limitations in predicting DR after RYGB.

BMI is widely used as a criterion to select candidates for metabolic surgery. However, no direct evidence supports the predictive ability of BMI for diabetes remission (DR) after surgery (1,2). BMI reflects both body fat mass and fat-free mass (FFM). Muscle mass, a major component of FFM (3), is crucial for glucose metabolism. Therefore, further investigation of the relationship between muscle mass and BMI might be important for understanding BMI limitations.

Cross-sectional imaging at the third lumbar (L3) vertebra level is an effective method for estimating whole-body composition (4,5), and the psoas cross-sectional area (CSA) has been suggested as a good estimate of whole-body muscle mass and has served as a prognostic biomarker (5,6). Alternatively, the estimated FFM index (eFFMI), derived from predictive equations, has also been developed (7). In this

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study, we explored the association of muscle mass assessed by psoas CSA and eFFMI with the limitations of BMI in predicting DR after Roux-en-Y gastric bypass (RYGB).

## RESEARCH DESIGN AND METHODS

### Study Participants

This study was approved by the local ethics committee. We conducted a cross-sectional study of 501 patients with type 2 diabetes mellitus (T2DM) and overweight or obesity, of whom 186 patients who underwent RYGB and had complete 1-year follow-up data were included in the longitudinal study. The primary outcome was complete DR during the 5-year follow-up period after RYGB. The population details and definitions for DR, T2DM, and obesity are presented in Supplementary Material.

### Assessment of Body Composition

Details on the magnetic resonance imaging (MRI) scan and measurement of psoas CSA, subcutaneous fat area, and visceral fat area with sliceomatic 5.0 software (TomoVision, Magog, Canada) can be found in Supplementary Material. The equation proposed by Deurenberg et al. (7) was used to calculate estimated body fat percentage (eBF[%]):  $eBF[\%] = (1.20 \times BMI) + (0.23 \times age) - (10.8 \times sex) - 5.4$ , with 1 for male and 0 for female. The eFFMI was calculated as follows:  $BMI \times (1 - (eBF[\%]/100))$ . The estimated fat mass index (eFMI) was calculated as  $BMI \times (eBF[\%]/100)$ .

### Statistical Analysis

Break point analysis was conducted with the segmented, ggplot2, Hmisc, and rms packages in RStudio v.1.3.959 (<https://www.r-project.org/>) for evaluation of the best-fit relationships of MRI-measured body composition with BMI and eFFMI or eFMI. Receiver operating characteristic (ROC) analysis was performed with MedCalc v.18.9.1 software. Kaplan-Meier curves were conducted with the survival R package. Additional statistical approaches can be found in Supplementary Material.

## RESULTS

Clinical characteristics of the participants in the cross-sectional study are presented in Supplementary Table 1. As shown in Fig. 1A and B and Supplementary Fig. 2.

There was a strong linear correlation between BMI and total fat area and subcutaneous fat area ( $r > 0.80$ ). However, the psoas CSA showed a nonlinear relationship with BMI ( $P = 0.006$  for males and  $0.005$  for females), and visceral fat area also showed similar characteristics. When BMI was divided into eFFMI and eFMI, the results were similar, except that there was a significantly positive relationship between the eFFMI and psoas CSA. The comparison between linear and segmented linear regression is presented in Supplementary Tables 2, 3, and 4.

In the longitudinal study, significantly higher psoas CSA and eFFMI were observed in the DR group at baseline and even 1 year after RYGB compared with the non-DR group (Supplementary Table 5). Logistic regression analyses revealed the psoas CSA (not sex specific) and eFFMI (for females) as new predictors of 1-year DR (Supplementary Table 6). ROC and Kaplan-Meier analyses were performed for baseline psoas CSA, eFFMI, and BMI in predicting 1- and 5-year DR (Fig. 1C–H). Comparisons of the area under the curve revealed significant differences between BMI and both psoas CSA ( $P = 0.0039$ ) and eFFMI ( $P = 0.045$ ) in females, and these differences approached statistical significance in males. Moreover, patients in the highest tertile of baseline psoas CSA and eFFMI showed the longest estimated mean remission time and greatest remission rates during the 5-year follow-up ( $P = 0.001$  and  $P = 0.020$ , respectively), while this was not the case for BMI ( $P = 0.150$ ).

## CONCLUSIONS

To our knowledge, this is the first study to report the nonlinear relationship between psoas CSA and BMI. Furthermore, baseline psoas CSA and eFFMI were better than BMI for predicting 1- and 5-year DR after RYGB. Our results demonstrate the limitations of BMI in assessing muscle mass and suggest eFFMI as an alternative muscle mass indicator for use in pre- and postoperative assessments.

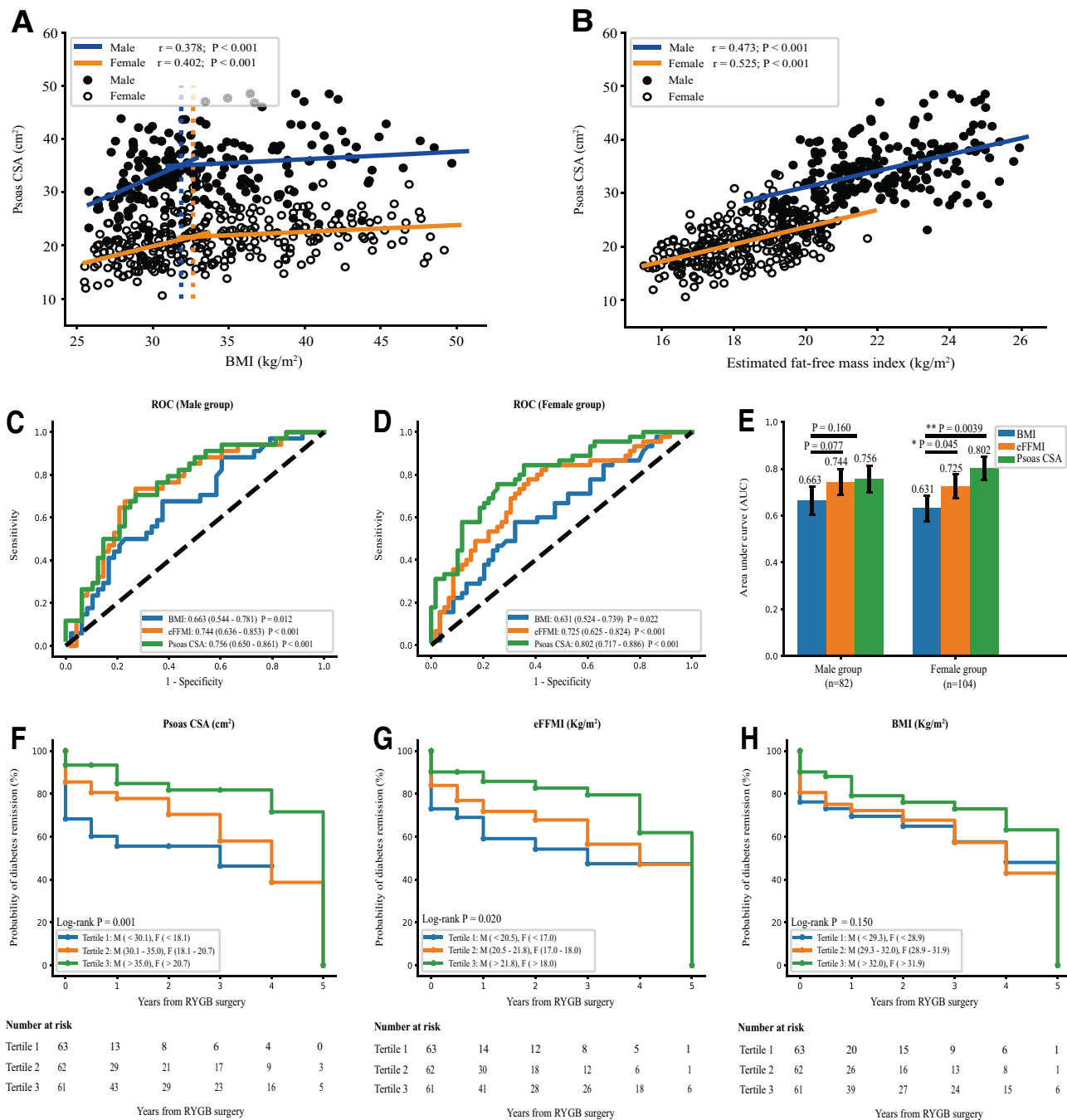
Previous studies have reported the possible positive correlation between BMI and muscle mass (8). Our findings represent new evidence that, regardless of sex, when BMI exceeds a certain threshold,

the muscle curves plateau and show almost no subsequent increment. According to Davis law (the corollary to Wolff law for bone) (9), the mechanical load and stimuli caused by weight gain may partially explain the increased muscle mass in the growth stage. However, due to the limited physiological capacity of tissue depot (10), the muscle and visceral fat showed a threshold effect. In contrast, subcutaneous fat did not show a break point due to the probable larger capacity limit. Meanwhile, the muscle lipotoxicity, inflammation, and atrophy induced by secretion of free fatty acids, chemokines, and cytokines from excessive visceral fat also inhibit the increase in muscle mass to a certain degree (11,12).

Muscle mass constitutes 40–50% of body weight and is considered the most important determinant of whole-body insulin sensitivity in normal-weight individuals (13). Individuals with high BMI almost invariably have more muscle mass; however, this does not imply an improvement in insulin sensitivity due to excessive body fat mass. Of note, a previous study revealed that the percentage change in fat mass was significantly larger than that in muscle mass at 1 year after RYGB (14). Therefore, the presence of more muscle mass before surgery means a greater possibility of a high body muscle ratio after surgery, which may contribute to DR and insulin resistance reduction following surgery.

The nonlinear relationship between muscle mass and BMI may explain why BMI is not a good predictor for DR after surgery. In the debate, the attenuated antidiabetes effect of metabolic surgery in low-BMI individuals (15) may be attributed to the significant differences in muscle mass among populations with different BMI ranges. Based on the existing guidelines, we support active surgical treatment for Asian T2DM patients with a BMI  $>32.5$  kg/m<sup>2</sup>. However, for patients with a lower BMI range, muscle mass measurement may be crucial to determine suitability for surgery. Interventions (such as strength training and adequate protein intake) to attenuate muscle atrophy during the weight loss period may be important methods to maintain excellent long-term glycemic control (3,8).

The limitations of this study include the limited generalizability due to a single ethnic group, the relatively low 5-



**Figure 1**—*A* and *B*: The best-fit relationships between psoas CSA measured by MRI and BMI and eFFMI in the cross-sectional study population (208 males and 293 females). *A*: Psoas CSA and BMI. *B*: Psoas CSA in relation to eFFMI. Each circle represents a single participant in the study. The break points showing a sharp change in slope are indicated by a dashed line with the corresponding color. Segmental linear regression is applied if the correlation is significantly better than that of linear regression ( $P < 0.05$ ). Pearson correlation coefficients and the associated  $P$  values are shown for male and female populations in the regression model. Break points of BMI (males and females, respectively): 31.88 and 32.66 kg/m<sup>2</sup> for psoas CSA. *C*–*H*: The predictive performance of baseline psoas CSA, eFFMI, and BMI for 1- and 5-year DR after RYGB surgery. The ROC curves with use of the above variables for 1-year DR are shown in the male (*C*) and female (*D*) groups. The predictive performance (ROC area under the curve) of baseline psoas CSA, eFFMI, and BMI in the male and female groups is compared using the DeLong test (*E*). Kaplan-Meier plots for long-term DR are based on sex-specific tertiles of baseline psoas CSA (*F*), eFFMI (*G*), and BMI (*H*) during the 5-year follow-up. The number at risk indicates the number of patients who achieved DR at each time point after RYGB. Estimated mean remission time among the tertiles of the variables: 2.2 years (95% CI 1.6–2.8) vs. 3.3 years (95% CI 2.7–3.9) vs. 4.1 years (95% CI 3.7–4.6) for the psoas CSA-based group; 2.8 years (95% CI 2.0–3.6) vs. 3.2 years (95% CI 2.6–3.9) vs. 4.0 years (95% CI 3.5–4.5) for the eFFMI-based group; and 3.1 years (95% CI 2.5–3.8) vs. 3.2 years (95% CI 2.5–3.8) vs. 3.8 years (95% CI 3.3–4.3) for the BMI-based group. F, female; M, male.

year follow-up rate (33.9%), and the lack of a causal effect of the association between muscle mass and DR.

In conclusion, the nonlinear relationship between muscle mass and BMI may partially contribute to the limitations of BMI in predicting DR after RYGB. Given the importance of BMI in determining the indications for metabolic surgery, this finding may be valuable for improving upon the current available scores to predict remission. Further studies are necessary to explore the potential implications in other clinical practices.

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**Author Contributions.** S.L., H.Y., J.H., and W.J. conceived and designed the study. S.L. drafted the manuscript and researched the literature. S.L., Y.T., and D.Y. collected the data. S.L. and H.Y. contributed to the statistical analysis and figure construction. P.Z., Y.X., and Y.B. supervised the study. H.Y., Y.B., J.H., and W.J. interpreted data and revised the manuscript. All authors reviewed and approved the final version of the manuscript. J.H. and W.J. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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