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Research Paper

Critical visceral adipose tissue thresholds aassociated with type 2 diabetes mellitus in chinese population

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Abstract

Objective: To compare intervertebral location L2-L3 with L4-L5 as landmarks for measuring abdominal fat distribution and to determine critical levels of visceral adipose tissue (VAT) at those planes, exceeding which may lead to the development of type 2 diabetes. **Methods**: Abdominal fat distribution was measured using computed tomography(CT) in 29 diabetics (19 male, 10 female) and 30 non-diabetics (18 male, 12 female). CT images obtained at two intervertebral locations L2-L3 and L4-L5 were used to measure the areas of total fat, VAT and subcutaneous adipose tissue (SCAT) using slice thickness of 5mm and an attenuation range from -190 to -30 Hounsfield units (HU). Data were analyzed using logistic regression and Receiver-operating characteristic (ROC) analysis. **Results**: At L2-L3, diabetes and obesity were correctly classified at 91.53% and 83.05% respectively, while at L4-L5, the same were correctly classified at 84.75% and 88.14% respectively. VAT compared to SCAT, had significantly higher correctly classified percent values for predicting diabetes in both measurement sites. At L2-L3, VAT $\geqslant$177.29 cm^2 or VAT $\geqslant$ 51.52% of the total fat area had the highest correctly classified value for predicting diabetes in men, while VAT$\geqslant$132.27 cm^2 or VAT$\geqslant$45.7% of the total fat area had the highest correctly classified value for predicting diabetes in women. At L4-L5, VAT$\geqslant$ 130.82 cm^2 or VAT$\geqslant$45.54% of the total fat area had the highest correctly classified value for predicting diabetes in men, while VAT$\geqslant$118.56 cm^2 or VAT$\geqslant$32.24% of the total fat area had the highest correctly classified value for predicting diabetes in women. **Conclusion**: L2-L3 plane is a better landmark for measuring abdominal fat distribution for predicting diabetes, while abdominal fat distribution measured at L4-L5 has better association with obesity. Regardless of the measurement site, VAT compared to SCAT, has significantly stronger association with diabetes.

Keywords: visceral adipose tissue; type 2 diabetes; measurement; computed tomography

INTRODUCTION

Several prospective studies have documented that obesity is probably the most powerful predictor of the development of type 2 diabetes[1]. The major basis for this association of obesity with diabetes is the ability of obesity to induce and promote insulin resistance [2]. Insulin resistance is a fundamental aspect of the etiology of type 2 diabetes and is also linked to a wide array of other pathophysiologic disorders including hypertension, hyperlipidemia, atherosclerosis (i.e., the metabolic syndrome, or syndrome X), and polycystic ovarian disease [2-4]. While abdominal obesity is determined by the accumulation of both subcutaneous adipose tissue (SCAT) and visceral adipose tissue(VAT), the excess accumulation of VAT appears to play a more significant pathogenic role [3, 5-11]. Compared to SCAT, VAT is much more strongly linked to insulin resistance and type 2 diabetes [2-3, 5-8]. Abdominal SCAT is located immediately beneath the skin and on top of the abdominal musculature. VAT is located in the body cavity beneath the abdominal muscles. VAT depots are composed of the greater omentum, lesser omentum and the mesenteric fat. A lesser amount of VAT is located retroperitoneally. In general, VAT ac-

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counts for up to 20% of total fat in men and 5-8 % in women[5].

Quantifying VAT has become increasingly important and several techniques have been developed to assess VAT. Ultrasonography is a suitable technique for assessment of VAT but its reproducibility and accuracy are somewhat poor. CT has been considered the most accurate and reproducible technique for body fat measurement, particularly the VAT [12-13]. Though magnetic resonance imaging (MRI) is highly accurate for body fat measurement, MRI equipment is expensive and less available than CT. However, there is no standard protocol for the quantification of VAT using CT. No study has systematically determined an optimal site for VAT measurement. Although intervertebral location L4-L5 is the most commonly used landmark for measuring abdominal fat distribution there is reason to believe that L4-L5 is not the ideal site for quantifying abdominal fat. Recent studies reported that L1-L2 or L2-L3 was a more suitable landmark for VAT measurement than L4-L5[8, 14]. Studies have shown VAT as a strong independent predictor of insulin resistance in type 2 diabetes [3,7] but few study has been done to estimate a critical level of VAT accumulation that when achieved, may be involved in the development of diabetes, so we could not find an acurate data for the people of western countries to compare with that of our study which is fit for Chinese population. It must be emphasized that this critical VAT threshold may be unique for each individual. This may help explain the phenomena of apparently lean individuals with type 2 diabetes and those who are obese but have normal metabolic profiles. The identification of a critical VAT threshold regarding type 2 diabetes is admittedly difficult and its anatomical boundaries are not well-defined. It is encouraging that only a modest loss of 5-10 percent of body weight in obese patients is associated with preferential mobilization of VAT compared to SCAT. Such modest weight loss can prevent and reverse type 2 diabetes [5, 15-18]. Hence, quantification of a critical VAT threshold associated with diabetes may have relevance to clinical assessment, prevention and treatment of type 2 diabetes.

MATERIALS AND METHODS

Subjects

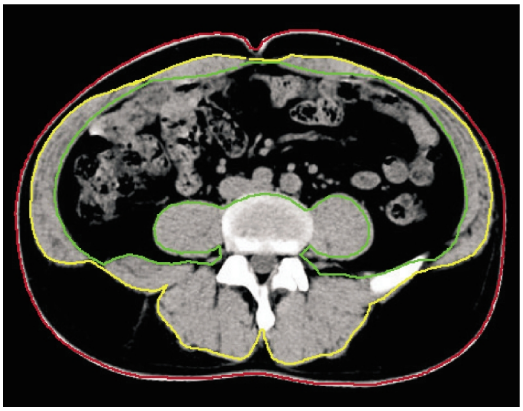
The study sample consisted of 59 Chinese subjects between 20 and 74 years of age. Among them 29 were diabetics (male:n = 19; female:n = 10), and 30 non-diabetics (male:n = 18; female:n = 12). All subjects were volunteers. The diabetic subjects were invited from the Department of Endocrinology at the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu. Inclusion criteria for diabetic subjects were age(20-75 years), type 2 diabetes and no severe chronic diabetic complications. Non diabetic subjects were selected at the same hospital, from the cohort of people who had received an abdominal CT scan for examination of lumbar spine. Those with any apparent health problem except mild lumbar spine degeneration were excluded. Height and weight were measured in all subjects before proceeding to CT scanning and the body mass indices [BMI = weight in kg/(height in m)^2] were calculated.

Measurement of abdominal adipose tissue by CT

Abdominal fat distribution was measured in all subjects by CT using a Siemens Somatom Volume Zoom CT scanner. Subjects were examined in supine position with both arms stretched above the head. An initial scan was taken from a lateral view to establish the bony landmarks on a radiograph of the skeleton as a reference. Contiguous transverse images were acquired from vertebral body L2 to vertebral body L5. The scan was performed at 120 kV and 412 mA with a 5 mm slice thickness. For each subject, an axial image obtained at midway between L2 and L3, and another one at midway between L4 and L5 were identified for measuring abdominal adipose tissue. Total fat area was estimated by demarcating the whole abdomen scan with a computerized pen and calculating the contained adipose tissue using an attenuation range of −190 to −30 HU (***Fig. 1***). Cross-sectional VAT area was calculated by applying the same attenuation range and delineating the inner margin of the abdominal musculature surrounding the abdominal cavity. SCAT area was determined by delineating the outer margin of the abdominal musculature using same method and subtracting the obtained area from the total fat area. For calculating total abdominal area, the whole abdomen scan was demarcated without attenuation limits.

Statistical Analysis

Statistical analyses were performed using STATA version 9.1. Group data were presented as means ± SD. Logistic regression analyses, adjusted for age and sex, were performed to calculate the correctly classified values for predicting diabetes and obesity



An attenuation range from -190 to -30 HU was used for measuring adipose tissue area. Area within the red line is the total fat area. Area covered by green line is the VAT area. SCAT area was calculated by subtracting the area covered by yellow line from the area covered by red line. Area within the red line measured without attenuation limits is the total cross-sectional abdominal area.

Fig. 1 Illustration of the method for determining abdominal fat distribution on a CT image scanned at L4-L5 plane

using the measurements at L2-L3 and L4-L5 as the predictor variables. Comparison between VAT and SCAT, regarding their association with diabetes, was done using logistic regression analysis adjusted for age, sex and BMI. Receiver-operating characteristic(ROC) analysis was performed to establish VAT cut-points and cut-points of VAT to total fat ratios for predicting diabetes in men and women separately. Further, men and women were categorized into two groups of normal BMI(BMI < 24.9) and higher BMI (BMI ⩾ 24.9)based on their BMI status, then VAT cut-points as well as cut-points of VAT to total fat ratios were developed for each category. Cut-points corresponding to the highest correctly classified percent values and with the largest sum of sensitivity and specificity were considered the critical threshold values for the development of diabetes.

RESULTS

The subject characteristics were listed in ***Table 1***. Mean values of BMI, total fat area, VAT area and VAT to total fat ratio were higher in men with diabetes than in diabetic women and non-diabetics. Irrespective of sex and diabetic status, mean values of total fat area, SCAT area and SCAT to total fat ratio

Table 1 **Subject characteristics of 37 men and 22 women with and without type 2 diabetes** ($\bar{x} \pm s$)

Basic variances	Diabetics		Non-diabetics	
	male	female	male	female
n	19	10	18	12
Age(years)	55.47 ± 10.1	59.000 ± 7.36	45.72 ± 14.08	50.75 ± 12.7
BMI(kg/m^2)	26.11 ± 3.83	23.877 ± 2.14	24.23 ± 2.6	23.92 ± 2.25
TF area L2-L3(cm^2)	322.82 ± 110.29	255.230 ± 58.2	233.74 ± 96.46	260.56 ± 86.8
TF area L4-L5(cm^2)	339.69 ± 126.2	300.430 ± 84.4	239.20 ± 87.34	334.37 ± 87.55
VAT area L2-L3(cm^2)	196.62 ± 58.57	125.130 ± 42.71	129.48 ± 68.35	107.38 ± 43.27
VAT area L4-L5(cm^2)	155.65 ± 62.38	105.020 ± 44.87	86.66 ± 37.39	97.19 ± 32.26
(VAT/TF)×100% L2-L3	61.66 ± 7.55	48.330 ± 8.5	52.40 ± 10.2	40.74 ± 6.32
(VAT/TF)×100% L4-L5	46.25 ± 12.49	34.500 ± 10.21	36.05 ± 7.14	28.95 ± 5.31
SCAT area L2-L3(cm^2)	113.48 ± 54.42	118.360 ± 26.96	91.56 ± 30.15	136.91 ± 47.42
SCAT area L4-L5(cm^2)	175.46 ± 82.77	182.090 ± 58.33	133.45 ± 51.17	218.62 ± 60.61
(SCAT/TF)×100% L2-L3	34.34 ± 7.3	47.080 ± 8.74	42.13 ± 10.56	52.78 ± 5.44
(SCAT/TF)×100% L4-L5	50.86 ± 10.62	60.800 ± 10.27	56.03 ± 9.8	65.39 ± 5.54

TF -Total fat

measured at L4-L5 were higher than the mean values of those measured at L2-L3. Likewise, mean values of VAT area and VAT to total fat ratio measured at L2-L3 were higher than the mean values of those measured at L4-L5.

Taking total fat, VAT, SCAT and their ratios to total fat as the predictor variables, diabetes was 91.53 % correctly classified at L2-L3 and 84.75 % correctly classified at L4-L5 with logistic regression adjusted for age, sex and BMI. Using the same predictor variables with logistic regression adjusted for age, sex and diabetic status, obesity (BMI > 24.9 kg/m^2) was 83.05 % correctly classified at L2-L3 and 88.14 % correctly classified at L4-L5. This showed that the measurements taken at L2-L3 had significantly stronger association with diabetes than those taken at L4-L5, while measurements at L4-L5 had a stronger association with obesity than those at L2-L3.

Associations of VAT and SCAT with diabetes

were shown in ***Table 2*** as correctly classified percent values computed using logistic regression with VAT and SCAT areas as predictor variables for diabetes. This analysis was adjusted for age, sex and BMI. Irrespective of the measurement site, VAT had significantly higher correctly classified value for predicting

Table 2 **Correctly classified values for diabetes with respect to VAT and SCAT areas as the predictor variables**

Predictor variable	Diabetes correctly classified
VAT(L2-L3)	77.97%(sensitivity = 82.76%; specificity = 73.33%) (Positive predictive value = 75.00%) (Negative predictive value = 81.48%)
SCAT(L2-L3)	66.10%(sensitivity = 68.97%; specificity = 63.33%) (Positive predictive value = 64.52%) (Negative predictive value = 67.86%)
VAT(L4-L5)	72.88%(sensitivity = 68.97%; specificity = 76.67%) (Positive predictive value = 74.07%) (Negative predictive value = 71.88%)
SCAT(L4-L5)	67.80%(sensitivity = 68.97%; specificity = 66.67%) (Positive predictive value = 66.67%) (Negative predictive value = 68.97%)
VAT(L2-L3),VAT(L4-L5)	76.27%(sensitivity = 75.86%; specificity = 76.67%) (Positive predictive value = 75.86%) (Negative predictive value = 76.67%)
SCAT(L2-L3), SCAT(L4-L5)	66.10%(sensitivity = 68.97%; specificity = 63.33%) (Positive predictive value = 64.52%) (Negative predictive value = 67.86%)

Logistic regression analysis was adjusted for age, sex and BMI.

diabetes than SCAT. VAT area measured at L2-L3 correctly classified diabetes at a higher percent than that measured at L4-L5. For SCAT areas, correctly classified percent values obtained at L2-L3 and L4-L5 were not significantly different.

Table 3 showed critical cut-points of VAT and VAT to total fat ratio associated with the development of diabetes. Criterion for selection of critical cut-points was the highest correctly classified percent value with the largest sum of sensitivity and specificity for diabetes. In both sex, VAT area and VAT to total fat ratio selected as the critical thresholds for development of diabetes were larger at L2-L3 than at L4-L5. ROC analyses determined few more cut-points other than mentioned in Table 3 which though had lesser sum of sensitivity and specificity, had good balance between sensitivity and specificity. At L2-L3, VAT cut-point ⩾ 171.38 cm2 and VAT cut-point ⩾ 177.29 cm^2(***Table 3***) correctly classified diabetes in men at 72.29%, the former with a higher sensitivity of 78.95% but lesser specificity of 66.67% and the latter with slightly larger sum of sensitivity and specificity. So the latter was selected as the critical VAT threshold for diabetes although the former had similar correctly classified value and a higher sensitivity.

Subjects were categorized in four groups according to their sex and BMI status. Critical VAT cut-points

Table 3 **VAT cut-points and VAT/TF cut-points selected as the critical thresholds for the development of diabetes in men and women**

Predictor variances	Male	Female
VAT cut-point (cm^2)	⩾ 177.29	⩾ 132.27
Correctly classified	72.97%	68.18%
Sensitivity	73.68%	40.00%
Specificity	72.22%	91.67%
VAT/TF cut-point	⩾ 0.5152	⩾ 0.457
Correctly classified	75.68%	81.82%
Sensitivity	100.0%	80.00%
Specificity	50.00%	83.33%
VAT cut-point (cm^2)	⩾ 130.82	⩾ 118.56
Correctly classified	78.38%	68.18%
Sensitivity	63.16%	50.00%
Specificity	94.44%	83.33%
VAT/TF cut-point	⩾ 0.4554	⩾ 0.3224
Correctly classified	70.27%	68.18%
Sensitivity	47.37%	70.00%
Specificity	94.44%	66.67%

TF-Total fat

associated with diabetes for these categories are listed in(***Table 4***). This categorization did not influence the critical VAT cut-points in men with normal BMI and women with BMI ⩾ 24.9 kg/m^2 (comparing values in Table 3 and Table 4). However, men with BMI⩾ 24.9 kg/m2 had a much larger critical VAT cut-point at both measurement sites than in overall men. At L2-L3, women with normal BMI had lesser critical VAT cut-point than in overall women (***Table 3***) or in women with BMI ⩾ 24.9 kg/m^2 (Table 4). As listed in ***Table 4***, two critical VAT cut-points(⩾ 85.15 cm^2 and ⩾ 123.81 cm^2) at L2-L3 correctly classified diabetes at 71.43% with equal sum of sensitivity and specificity in women with normal BMI. VAT ⩾ 85.15 cm^2 had 100% sensitivity and 42.86% specificity while VAT ⩾123.81 cm^2 had 42.86% sensitivity and 100% specificity. VAT cut-point selected as the critical threshold at L4-L5 was larger in women with normal BMI than in women with BMI ⩾ 24.9 kg/m^2.

Table 4 **VAT cut-points at L2-L3 and L4-L5 corresponding to the highest correctly classified value with the largest sum of sensitivity and specificity for diabetes in men and women categorized on the basis of BMI status**

Predicator variance		Male		Female	
		Normal BMI	BMI⩾24.9	Normal BMI	BMI⩾24.9
L2-L3	VAT cut-point (cm^2)	⩾177.29	⩾85.15	⩾123.81	⩾132.27
	Correctly classified	78.95%	71.43%	71.43%	75.00%
	Sensitivity	66.67%	100.00%	42.86%	66.67%
	Specificity	90.00%	42.86%	100.00%	80.00%
L4-L5	VAT cut-point (cm^2)	⩾128.37	⩾128.76		⩾118.56
	Correctly classified	78.95%	71.43%		62.50%
	Sensitivity	55.56%	42.86%		66.67%
	Specificity	100.00%	100.00%		60.00%

DISCUSSION

It is well established that VAT, being portally drained and lipolytically more active [8, 19], is a powerful independent predictor of insulin resistance in type 2 diabetes [3, 7-8, 20]. It is as well reported that the greatest deposition of omental and mesenteric fat is located in the upper abdomen within the region between L1-L2 and L3-L4[8, 19, 21]. Thus, VAT at L2-L3 level might be expected to have a stronger association with the development of diabetes than VAT at L4-L5 or SCAT at any measurement site. These observations are relevant to the findings in this study.

The results in this study showed that intervertebral location L2-L3 was a better landmark for quantification of abdominal fat distribution in terms of predicting diabetes compared to the traditional landmark L4-L5. On the other hand, abdominal fat distribution measured at intervertebral location L4-L5 had a better ability to define obesity. This could also be explained by another finding that greater deposition of VAT lorated at L2-L3 level than at L4-L5 while there was greater deposition of SCAT and total abdominal fat at L4-L5 level than at L2-L3. So for VAT L2-L3 was a more suitable landmark for measuring abdominal fat distribution regarding metabolic disorders (diabetes) whereas SCAT could be responsible for the ability of L4-L5 level to define obesity better than L2-L3.

An important finding of this study was that VAT had a stronger association with diabetes than SCAT independent of measurement site. Likewise, VAT area at L2-L3 had significantly stronger association with diabetes than VAT area at L4-L5. These findings can have important implications as it suggests that VAT at L2-L3 alone may be a better predictor of diabetes.

A novel finding in this study was the critical VAT thresholds in Chinese population, that when achieved might lead to the development of type 2 diabetes. VAT area ⩾177.29 cm^2 or VAT to total fat⩾51.52 % at L2-L3 level and VAT area ⩾130.82 cm^2 or VAT to total fat ⩾45.54 % at L4-L5 level are highly predictive of diabetes in men. In women, a VAT area ⩾132.27 cm^2 or VAT to total fat ⩾ 45.7% at L2-L3 level and a VAT area ⩾118.56 cm^2 or VAT to total fat ⩾32.24% at L4-L5 level are highly predictive of diabetes. When categorized on the basis of BMI status, the critical VAT threshold associated with diabetes didn't change in men with normal BMI and in women with increased BMI. However, men with increased BMI had larger critical VAT threshold of 240.66 cm^2 at L2-L3 level and

159.75 cm^2 at L4-L5 level. Women with normal BMI had lesser critical VAT threshold for diabetes at L2-L3 but larger at L4-L5 compared to women with increased BMI. VAT ≥85.15 cm^2 and VAT ≥123.81 cm^2 at L2-L3 in women had equal sums of sensitivity and specificity but different sensitivities and specificities. It is up to one to choose between sensitivity and specificity. If one chooses 100% sensitivity then VAT area of 85.15 cm^2 is a better critical VAT threshold and if one chooses 100% specificity then VAT area of 123.81 cm^2 is a better critical VAT threshold. In this study, VAT area of 123.81 cm^2 at L2-L3 is preferable as the critical VAT threshold for women with normal BMI. Likewise, women with normal BMI had a critical VAT threshold of 128.76 cm^2 at L4-L5 level. Thus categorization based on BMI status gives a better understanding of critical VAT threshold.

There are limitations of this study that should be noted. First, the sample size (37 men and 22 women) in this study is relatively small. In addition, there were only 3 obese subjects. The rest were either overweight or with normal BMI. A larger sample size and inclusion of more frankly obese subjects would be needed to confirm the results in this study. Fixed values of critical VAT thresholds were determined in this study. It will be better to determine a range of VAT areas as the critical threshold since the critical VAT threshold may be unique for each individual.

In summary, VAT at L2-L3 level has the strongest association with the development of diabetes. The values determined in this study may prove useful for defining "visceral obesity" and may be used as reference for critical threshold that when achieved may play a role in the development of diabetes. The findings may have relevance to clinical assessment, prevention and treatment of diabetes.

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References

[1] Tuomilehto J, Lindstrom J, Silventoinen K. Obesity and prevention of type 2 diabetes. *Obesity and Diabetes* 2004; chap 5: 79-97.

[2] Kahn BB, Flier JS. Obesity and insulin resistance. *J Clin Invest* 2000; 106:473-81.

[3] Lebovitz HE. Insulin resistance - a common link between type 2 diabetes and cardiovascular disease. *Diabetes Obes Metab* 2006; 8: 237-49.

[4] Reaven GM. Pathophysiology of insulin resistance in human disease. *Physiol Rev* 1995; 75: 473-86.

[5] Freedland ES. Role of a critical visceral adipose tissue threshold (CVATT) in metabolic syndrome: implications for controlling dietary carbohydrates. *Nutr Metab* 2004; 1:12.

[6] Waine C. Obesity and type 2 diabetes. *Nutr Bulletin* 2006; 31 111-4.

[7] Bonora E, Targher G, Alberiche M, Formentini G, Calcaterra F, Lombardi S, *et al.* Predictors of insulin sensitivity in Type 2 diabetes mellitus. *Diabetic Medicine* 2002; 19(7):535-42.

[8] Kuk JL, Church TS, Blair SN, Ross R. Does measurement site for visceral and abdominal subcutaneous adipose tissue alter associations with the metabolic syndrome?. *Diabetes Care* 2006; 29: 679-84.

[9] Nicklas BJ, Penninx BW, Ryan AS, Berman DM, Lynch NA, Dennis KE. Visceral adipose tissue cutoffs associated with metabolic risk factors for coronary heart disease in women. *Diabetes Care* 2003; 26: 1413-20.

[10] McTernan P, Kumar S. Pathogenesis of obesity-related type 2 diabetes. *Obesity and Diabetes* 2004; chap 4: 49-78.

[11] Park YW, Allison DB, Heymsfield SB, Gallagher D. Larger amounts of visceral adipose tissue in Asian Americans. *Obes Res* 2001; 9: 381-7.

[12] Ribeiro-Filho FF, Faria AN, Azjen S, Zanella MT, Ferreira SR. Methods of estimation of visceral fat: advantages of ultrasonography. *Obes Res* 2003; 11: 1488-94.

[13] Yoshizumi T, Nakamura T, Yamane M, Islam AH, Menju M, Yamasaki K *et al.* Abdominal Fat: standardized technique for measurement at CT. *Radiology* 1999; 211: 283-6.

[14] Shen W, Punyanitya M, Wang Z, Gallaqher D, St-Onqe MP, Albu J, *et al.* Visceral adipose tissue: relations between single-slice areas and total volume. *Am J Clin Nutr* 2004; 80: 271-8.

[15] Knowler WC, Barrett-Connor E, Fowler SE, Hamman RL, Lachin JM, Walker *et al.* Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; 346: 393-403.

[16] Lindstrom J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, *et al.* The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care* 2003; 26: 3230-6.

[17] Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, *et al.* Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; 344: 1343-50.

[18] Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL. Effects of weight loss on regional fat distribution and insulin sensitivity in obesity. *Diabetes* 1999; 48: 839-47.

[19] Benthem L, Kuipers F, Steffens AB, Scheurink AJ. Excessive portal venous supply of long-chain free fatty acids to the liver, leading to hypothalamus-pituitary-adrenal-axis and sympathetic activation as a key to the development of syndrome X: a proposed concept for the induction of syndrome X. *Ann NY Acad Sci* 1999; 892: 308-11.

[20] Bosello O, Zamboni M. Visceral obesity and metabolic syndrome. *Obes Rev* 2000; 1: 47-56.

[21] Abate N, Garg A, Coleman R, Grundy SM, Peshock RM. Prediction of total subcutaneous abdominal, intraperitoneal, and retroperitoneal adipose tissue masses in men by a single axial magnetic resonance imaging slice. *Am J Clin Nutr* 1997; 65: 403-8.