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Contribution of skeletal muscle mass on sex differences in 2-hour plasma glucose levels after oral glucose load in Thai subjects with normal glucose tolerance

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Abstract

Women have higher 2-hour plasma glucose levels after oral glucose challenge than men. The smaller skeletal muscle mass in women may contribute to the higher postload glucose levels. The objective of this study was to test the hypothesis that the different amount of skeletal muscle mass between men and women contributed to sex difference in postload plasma glucose levels in subjects with normal glucose tolerance. Forty-seven Thai subjects with normal glucose tolerance, 23 women and 24 age- and body mass index–matched men, were studied. Body fat, abdominal fat, and appendages lean mass were measured by dual-energy x-ray absorptiometry. Skeletal muscle insulin sensitivity was determined by euglycemic-hyperinsulinemic clamp. First-phase insulin secretion and hepatic insulin sensitivity were determined from oral glucose tolerance data. β-Cell function was estimated from the homeostasis model assessment of %B by the homeostasis model assessment 2 model. Correlation and linear regression analysis were performed to identify factors contributing to variances of postload 2-hour plasma glucose levels. This study showed that women had significantly higher 2-hour plasma glucose levels and smaller skeletal muscle mass than men. Measures of insulin secretion and insulin sensitivity were not different between men and women. Male sex ($r = -0.360$, $P = .013$) and appendages lean mass ($r = -0.411$, $P = .004$) were negatively correlated with 2-hour plasma glucose, whereas log 2-hour insulin ($r = 0.571$, $P < .0001$), total body fat ($r = 0.348$, $P = .016$), and log abdominal fat ($r = 0.298$, $P = .042$) were positively correlated with 2-hour plasma glucose. The correlation of 2-hour plasma glucose and sex disappeared after adjustment for appendages lean mass. By multivariate linear regression analysis, log 2-hour insulin ($\beta = 18.9$, $P < .0001$), log 30-minute insulin ($\beta = -36.3$, $P = .001$), appendages lean mass ($\beta = -1.0 \times 10^{-3}$, $P = .018$), and hepatic insulin sensitivity index ($\beta = -17.3$, $P = .041$) explained 54.2% of the variance of 2-hour plasma glucose. In conclusion, the higher postload 2-hour plasma glucose levels in women was not sex specific but was in part a result of the smaller skeletal muscle mass. The early insulin secretion, hepatic insulin sensitivity, and skeletal muscle mass were the significant factors negatively predicting 2-hour postload plasma glucose levels in Thai subjects with normal glucose tolerance.

1. Introduction

Several epidemiologic studies indicate that women appear to have higher 2-hour glucose levels after oral glucose tolerance test (OGTT) than men. The studies regarding the prevalence of impaired glucose regulation in several populations demonstrated that the prevalence of isolated post–glucose load hyperglycemia, particularly isolated impaired glucose tolerance (IGT), is more common in women than in men, whereas the prevalence of isolated fasting hyperglycemia is more common in men than in women [1-4]. Data from 13 European cohorts in the DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study indicated that IGT was more prevalent in women than in men in all age groups particularly those younger than 70 years [1]. The community-based survey in Mauritius showed that the prevalence of isolated IGT was higher in women and among nondiabetic subjects; 2-hour plasma glucose (PG) levels after OGTT was also higher in women than in men [2]. The study by Pomerleau et al [3] in mixed population of European, South Asian, and Afro-Caribbean subjects also confirmed those findings. The mechanism by which 2-hour PG levels after OGTT are higher in women is unknown. Basu

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et al [5] studied the differences in postprandial glucose metabolism in healthy men and women and reported that the ability of insulin to stimulate glucose disposal measured by oral glucose minimal model was lower in young women than in young men despite lower visceral adiposity in the former. Whole-body insulin sensitivity was not significantly different. This study demonstrated that insulin secretion and postprandial hepatic glucose production did not significantly contribute to the sex difference in postprandial glucose levels after mixed meal in healthy nondiabetic subjects. Because peripheral glucose uptake is responsible for most total glucose disposal particularly 60 minutes post–oral glucose load and skeletal muscle is the major organ of peripheral glucose disposal [6], it is possible that the smaller skeletal muscle mass in women may have an effect on peripheral glucose disposal and contributes to the higher postload glucose levels. Nevertheless, the role of skeletal muscle mass in postprandial glucose regulation has rarely been studied. The objective of this study was to test the hypothesis that the different amount of skeletal muscle mass between men and women is responsible for the sex difference in 2-hour postload PG levels in Thai subjects with normal glucose tolerance (NGT).

2. Subjects and methods

Forty-seven Thai subjects with NGT, 23 women and 24 men, with mean age of 33.2 ± 8.8 (SD) years and mean body mass index (BMI) of 22.9 ± 3.9 kg/m^2 were studied. All had no known chronic or acute medical illnesses. None of the women was in postmenopause period. *Normal glucose tolerance* was defined by 2-hour PG levels after standard OGTT of less than 140 mg/dL and fasting glucose levels of less than 100 mg/dL. None of the subjects in the study had history of habitual exercise. All were advised to not have strenuous exercise and to stop smoking and alcohol drinking for at least 24 hours before the study.

Subjects gave written informed consent before the beginning of the study. The study protocol was approved by Prince of Songkhla University Ethical Committee.

2.1. OGTT and body composition measurements

The standard 75-g OGTT was performed in the morning after overnight fast. Body composition was measured after OGTT. Blood was collected via retained intravenous catheter before and at 0.5, 1, and 2 hours after glucose ingestion for measurement of glucose and insulin. Total body fat, abdominal fat, and appendages lean mass (the sum of lean soft tissue mass in both right and left arms and legs) were measured by dual-energy x-ray absorptiometry (DEXA version 4.7; DPX-MD Lunar, Madison, WI) software. Total body fat and appendages lean mass were calculated by standard software, whereas abdominal fat was measured by manually defining the area of measurement from the top of L1 to the bottom of L4 as previously described [7]. Appendages lean mass measured by DEXA has been shown to be highly correlated with total skeletal muscle mass (R^2 = 0.96) by multislice magnetic resonance imaging or multislice computerized tomography in healthy adults [8,9].

2.2. Insulin sensitivity and insulin secretion measurements

Skeletal muscle insulin sensitivity was measured by euglycemic-hyperinsulinemic clamp on the next morning after OGTT as previously described [7]. Briefly, a prime continuous intravascular infusion of regular insulin (Actrapid HM; Novo Nordisk, Copenhagen, Denmark) was given at a rate of 50 mU/m^2 body surface area per minute from 0 to 120 minutes together with 20% dextrose solution to maintain glucose at 90 mg/dL (5.0 mmol/L) throughout the clamp period. Blood was obtained every 5 minutes from the dorsal hand vein kept in a thermoregulated box at 55°C to 60°C for determination of arterialized glucose. Insulin sensitivity was determined from glucose infusion rate (GIR) during the last 40 minutes of the clamp and expressed as milligram of glucose per lean kilogram per minute.

Hepatic insulin sensitivity index (ISI) is calculated from the inverse of the product of total area under the curve (AUC) for glucose and insulin concentrations during the first 30 minutes of the OGTT multiplied by 1000, where 1000 represents a constant that allows one to obtain the numbers ranging from 0 to 10. The product of AUC for glucose and insulin concentrations of the first 30 minutes of the OGTT has been shown to be significantly correlated (r = 0.64) with the standard hepatic insulin resistance measured by the product of basal endogenous hepatic glucose production and fasting plasma insulin concentrations in subjects with NGT [10]. β-Cell function was estimated from the homeostasis model assessment (HOMA) of %B by the HOMA-2 model (available at http://www.dtu.ox.ac.uk/homa). First-phase insulin secretion was determined from OGTT data by the ratio of the incremental insulin and glucose concentrations above basal at 30 minutes (iIns/iGlu$_{0\text{-}30\ min}$). To determine insulin secretion adjusted for degree of peripheral insulin sensitivity, disposition index of first-phase (DI$_{0\text{-}30\ min}$) insulin secretion was calculated by multiplying iIns/iGlu$_{0\text{-}30\ min}$ with GIR.

2.3. Biochemical analysis

Blood for plasma insulin was collected and frozen at −80°C until analysis, all within 1 month after collection. Plasma insulin was measured by double-antibody radioimmunoassay (Diagnostic Products, Los Angeles, CA) with intraassay coefficient of variation of 0.9% to 4.7%. Glucose was measured by glucose oxidase method (Synchron CX-3 Delta; Beckman Coulter, Fullerton, CA) with interassay coefficient of variation of 0.9% to 2.3%.

2.4. Statistical analysis

The unpaired Student t test was used for mean comparison. Data that were not normally distributed were

log-transformed before analysis. Correlation coefficients were determined by Pearson product moment. Multiple linear regression analysis was performed to identify independent factors contributing to variances of 2-hour PG levels. All statistical analyses were performed using SPSS for Windows (version 11.5; SPSS, Chicago, IL). Area under the curve was calculated by trapezoidal rule. $P < .05$ was considered statistically significant.

3. Results

Clinical characteristics, glucose and insulin responses to OGTT, as well as parameters of insulin secretion and insulin sensitivity are shown in Table 1. With similar age and BMI, women had significantly higher total body fat, lower waist-hip ratio (WHR), and smaller appendages lean mass than men. Although there was no difference in fasting PG levels between men and women, after challenging with 75-g oral glucose, levels of 2-hour PG were significantly higher in women than in men. No difference in fasting and postload insulin responses between men and women was observed. Skeletal muscle insulin sensitivity, hepatic ISI, first-phase insulin secretion, as well as its disposition index were also not different.

Male sex ($r = -0.360$, $P = .013$) and appendages lean mass ($r = -0.411$, $P = .004$) (Fig. 1) were negatively correlated with 2-hour PG, whereas log 2-hour insulin ($r = 0.571$, $P < .0001$), total body fat ($r = 0.348$, $P = .016$), and log abdominal fat ($r = 0.298$, $P = .042$) were positively correlated with 2-hour PG. The partial correlation of 2-hour PG and sex disappeared (partial $r = -0.044$, P = not significant) after adjustment for appendages lean mass. Age, BMI, waist, WHR, fasting PG, 30-minute PG, 1-hour PG, log fasting insulin, log 30-minute insulin, log 1-hour insulin, GIR, hepatic ISI, HOMA %B, log iIns/iGlu$_{0\text{-}30\ min}$, and log DI$_{0\text{-}30\ min}$ were not significantly correlated with 2-hour PG.

By multivariate linear regression analysis using 2-hour PG as a dependent variable and sex, appendages lean mass, log 2-hour insulin, and total body fat as independent variables, only log 2-hour insulin ($\beta = 15.1$, $P < .0001$) and appendages lean

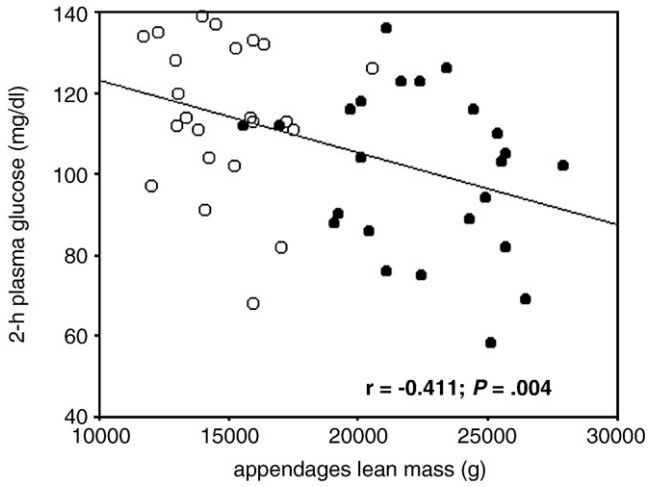

Fig. 1. Correlation of appendages lean mass and 2-hour PG levels after oral glucose challenges in women (○) and men (●) with NGT. To convert glucose to millimoles per liter, multiply by 0.056.

Table 1
Clinical characteristics, PG, and insulin responses to OGTT and measures of insulin secretion and insulin sensitivity of subjects in the study

	NGT		*P*
	Women (n = 23)	Men (n = 24)	
Age (y)	34.2 ± 8.9	32.3 ± 8.8	NS
Weight (kg)	55.1 ± 10.8	62.7 ± 9.7	.015
Height (m)	1.55 ± 0.05	1.66 ± 0.06	<.0001
BMI (kg/m^2)	23.0 ± 4.4	22.8 ± 3.5	NS
Waist circumference (cm)	73.7 ± 9.7	77.4 ± 11.6	NS
WHR	0.79 ± 0.05	0.86 ± 0.09	.005
Total body fat (kg)	19.0 ± 7.6	11.6 ± 7.2	.001
Abdominal fat[a] (kg)	1.9 ± 1.1	1.5 ± 1.1	NS
Appendages lean mass (kg)	14.9 ± 2.1	22.5 ± 3.2	<.0001
Glucose (mg/dL): fasting	83.1 ± 9.0	83.5 ± 6.9	NS
30 min	148.4 ± 26.0	153.8 ± 22.1	NS
1 h	147.1 ± 32.7	140.6 ± 32.7	NS
2 h	115.1 ± 18.5	100.5 ± 19.9	.013
Insulin (μU/mL)[a]: fasting	7.96 ± 3.78	9.88 ± 5.32	NS
30 min	62.69 ± 27.68	67.55 ± 37.49	NS
1 h	83.56 ± 82.44	67.75 ± 45.12	NS
2 h	53.58 ± 28.35	45.90 ± 29.69	NS
iIns/iGlu$_{0\text{-}30\ min}$[a]	0.90 ± 0.46	0.84 ± 0.42	NS
DI$_{0\text{-}30\ min}$[a]	8.34 ± 4.94	6.88 ± 2.99	NS
Hepatic ISI	1.20 ± 0.66	1.12 ± 0.54	NS
GIR (mg/[lean kg min])	9.22 ± 3.2	8.84 ± 2.94	NS
HOMA %B	117.6 ± 36.9	125.0 ± 37.5	NS

Data are expressed as mean ± SD. To convert glucose to millimoles per liter, multiply by 0.056. To convert insulin to picomoles per liter, multiply by 7.175. NS indicates not significant.

[a] Log-transformed before analysis.

Table 2
Predictors of 2-hour PG levels after 75-g OGTT in subjects with NGT by multivariate linear regression analysis

Model	Adjusted R^2	Coefficient (β)	Standard error	*P*
Model 1	0.377			<.0001
Predictors:				
log 2-h insulin		15.1	3.6	<.0001
Appendages lean mass		-1.0×10^{-3}	1.0×10^{-3}	.021
Model 2	0.505			<.0001
Predictors:				
log 2-h insulin		18.6	3.4	<.0001
Appendages lean mass		-1.0×10^{-3}	$<1.0 \times 10^{-3}$	.034
log 30-min insulin		−16.4	4.7	.001
Model 3	0.542			<.0001
Predictors:				
log 2-h insulin		18.9	3.2	<.0001
Appendages lean mass		-1.0×10^{-3}	$<1.0 \times 10^{-3}$	.018
log 30-min insulin		−36.3	10.4	.001
Hepatic ISI		−17.3	8.2	.041

mass ($\beta = -1.0 \times 10^{-3}$, $P = .021$) were the significant independent parameters predicting 2-hour PG (model adjusted $R^2 = 0.377$, $P < .0001$). Entering log abdominal fat or 1-hour PG into the model did not change model outcome. As shown in Table 2, inclusion of log 30-minute insulin (model 2) and hepatic ISI (model 3) into baseline model (model 1) increased the adjusted R^2 of the model. The final model (model 3) that consisted of log 2-hour insulin, log 30-minute insulin, appendages lean mass, and hepatic ISI explained 54.2% of the variance of 2-hour PG.

4. Discussion

This study demonstrated that, with similar age and BMI, nonobese women with NGT had smaller appendages lean mass and greater 2-hour PG levels after OGTT than men. Appendages lean mass, 30-minute insulin levels, and hepatic ISI are the independent factors negatively predicting 2-hour PG levels, whereas 2-hour PG levels positively predict 2-hour insulin levels in this study. Because 30-minute and 2-hour insulin levels and hepatic ISI are not different between men and women and appendages lean mass measured by DEXA has been shown to be strongly correlated with total skeletal muscle mass measured by computerized tomography or magnetic resonance imaging [8,9,11], it is likely that the sex difference in 2-hour PG levels after glucose load is not sex specific but is largely the result of the smaller skeletal muscle mass in women.

The study that examines the relationship of skeletal muscle mass and postprandial PG levels in human is quite rare. To our knowledge, this study is the first that demonstrates the effect of skeletal muscle mass on PG levels after glucose challenges in subjects with NGT. The result of this study is in contrast with the recent findings by Kuk et al [12] where the relationship of skeletal muscle mass and 2-hour PG levels after OGTT could not be demonstrated in men and women with NGT. However, the differences in subject characteristics and study design may explain this discrepancy. Although subjects in the study of Kuk et al had NGT, they were much more obese (BMI >30 kg/m^2) than ours; and women were younger and heavier than men in that study. Furthermore, the relationship of skeletal muscle mass and 2-hour PG levels was separately studied in men and women. Given the small difference in skeletal muscle mass in the same sex, it is possible that such relationship could not be observed. Although the negative relationship of appendages lean mass and postload 2-hour PG levels in our study does not prove causality, it is theoretically not unreasonable. Skeletal muscle is the major organ of glucose disposal particularly at postprandial state; therefore, in subjects with equivalent degrees of insulin sensitivity and β-cell function, those who have smaller skeletal muscle mass would have lower capacity to accommodate glucose disposal than those who have larger skeletal muscle mass. This would result in higher circulating glucose levels in the former. Brochu et al [13] studied the contribution of lean body mass to insulin resistance in obese (BMI ~30-34 kg/m^2), nondiabetic, postmenopausal women and reported that subjects with high lean BMI (lean body mass measured by DEXA divided by height) had greater postload PG levels than those with lower lean BMI. The positive correlation of 2-hour PG and lean BMI was observed in that study. Those findings contradict our hypothesis. However, we found that, even if we used lean BMI in our analysis, the results of the study would not change (data not shown). Because subjects in the study of Brochu et al were in menopause state, were centrally obese, and had severe insulin resistance, it is possible that the negative relationship of skeletal muscle mass and 2-hour PG levels is obliterated by the severe degree of insulin resistance. Our findings may partly explain why the prevalence of isolated IGT is higher in women than in men [1-4]. Whether the effect of skeletal muscle mass could have contributed to a higher prevalence of isolated IGT in Asians than in whites is intriguing [14]. Because our study revealed the strong association of height and lean body mass ($r = 0.808$, $P < .0001$), it is possible that the negative association of height and 2-hour PG responses to OGTT in the AusDiab study may be explained by the difference in skeletal muscle mass [15].

Our study supports other previous studies in that indexes of insulin secretion and measures of insulin sensitivity that include skeletal muscle and hepatic insulin sensitivities assessed by clamp method are not different between age-matched men and women with NGT [5,16,17]. Although our study used OGTT-derived hepatic insulin resistance index as a means to measure hepatic insulin sensitivity, this parameter has been shown to have a significant correlation with that measured by the standard radiolabeled glucose tracer technique [10]. Our study suggests that the lower initial insulin secretion and the lower hepatic insulin sensitivity are the important and independent factors determining the higher 2-hour PG levels after oral glucose load in subjects with NGT. Our findings in subjects with NGT are in line with the findings by Mitrakou et al [18] in subjects with IGT. Our study adds skeletal muscle mass as one of those negative predictors.

The strength of this study is that the techniques of the measurements used in the study are well standardized or have been well validated with the reference standards. Age and BMI of men and women in the study were well matched. Nevertheless, this study has several limitations. Firstly, systemic oral glucose appearance after oral glucose load, which has been reported to be higher in women in some studies, was not determined in this study [5,19]. Whether this factor has an effect on a higher 2-hour PG levels in women of this study is uncertain. Secondly, the sample size of the study is relatively small. However, despite the small sample size, the strong negative effect of skeletal muscle mass on postload PG levels can still be demonstrated. Thirdly, because our study did not measure physical activity levels, it is possible that the higher 2-hour PG levels observed in

women are due to their lesser physical activity [20]. However, we speculate that this factor may not play an important role given the history of sedentary lifestyle in all participating subjects and similar skeletal muscle insulin sensitivity between groups. The result of this study is specific for lean subjects with NGT. Whether this is true in obese subjects with NGT or in subjects with abnormal glucose tolerance is unknown. Whether the difference in skeletal muscle mass could have an effect on 2-hour PG levels after mixed meal is also unknown. However, the pattern of postprandial glucose metabolism after glucose or mixed-meal ingestion has been reported to be not different [21]. Furthermore, whether there is a difference in skeletal muscle mass properties between men and women that could have contributed to sex difference in postload 2-hour PG levels is also unknown. Based on the results of our study, it implies that using fixed amount of 75-g glucose testing protocol for OGTT may be inadequate to accurately compare postload glucose homeostasis between men and women and that it can give misleading results. The amount of glucose load should be individualized based on the amount of actual lean body mass.

In conclusion, the higher postload 2-hour PG level after OGTT in women is not sex specific but is in part a result of the smaller skeletal muscle mass. The early insulin secretion, hepatic insulin sensitivity, and skeletal muscle mass were the significant factors negatively predicting 2-hour postload PG levels in Thai subjects with NGT. More studies are required to elucidate the effect of skeletal muscle mass on postprandial glucose homeostasis in subjects with abnormal glucose tolerance.

References

[1] The DECODE Study Group. Age- and sex-specific prevalences of diabetes and impaired glucose regulation in 13 European cohorts. Diabetes Care 2003;26:61-9.
[2] Williams JW, Zimmet PZ, Shaw JE, et al. Gender differences in the prevalence of impaired fasting glycaemia and impaired glucose tolerance in Mauritius. Does sex matter? Diabet Med 2003;20:915-20.
[3] Pomerleau J, McKeigue PM, Chaturvedi N. Relationships of fasting and postload glucose levels to sex and alcohol consumption. Diabetes Care 1999;22:430-3.
[4] Novoa FJ, Boronat M, Saavedra P, et al. Differences in cardiovascular risk factors, insulin resistance, and insulin secretion in individuals with normal glucose tolerance and in subjects with impaired glucose regulation. Diabetes Care 2005;28:2388-93.
[5] Basu R, Man CD, Campioni M, et al. Effects of age and sex on postprandial glucose metabolism. Differences in glucose turnover, insulin secretion, insulin action and hepatic insulin extraction. Diabetes 2006;55:2001-14.
[6] Ferrannini E, Bjorkman O, Reichard GA, et al. The disposal of an oral glucose load in healthy subjects. Diabetes 1985;34:580-8.
[7] Rattarasarn C, Leelawattana R, Soonthornpun S, et al. Relationships of body fat distribution, insulin sensitivity and cardiovascular risk factors in lean, healthy non-diabetic Thai men and women. Diabetes Res Clin Pract 2003;60:87-94.
[8] Kim J, Wang ZM, Heymsfield SB, Baumgartner RN, Gallagher D. Total-body skeletal muscle mass: estimation by a new dual-energy x-ray absorptiometry method. Am J Clin Nutr 2002;76:378-83.
[9] Levine JA, Abboud L, Barry M, Reed JE, Sheedy PF, Jensen MD. Measuring leg muscle and fat mass in humans: comparison of CT and dual-energy x-ray absorptiometry. J Appl Physiol 2000;88:452-6.
[10] Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA. Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 2007;30:89-94.
[11] Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85:115-22.
[12] Kuk JL, Kilpatrick K, Davidson LE, Hudson R, Ross R. Whole-body skeletal muscle mass is not related to glucose tolerance or insulin sensitivity in overweight and obese men and women. Appl Physiol Nutr Metab 2008;33:769-74.
[13] Brochu M, Mathieu M-E, Karelis AD, Lavoie M-E, Garrel D, Rabasa-Lhoret R. Contribution of the lean body mass to insulin resistance in postmenopausal women with visceral obesity: a Monet study. Obesity 2008;16:1085-93.
[14] Qiao Q, Nakagami T, Tuomilehto J, et al. Comparison of the fasting and the 2-h glucose criteria for diabetes in different Asian cohorts. Diabetologia 2000;43:1470-5.
[15] Sicree RA, Zimmet PZ, Dunstan DW, Cameron AJ, Welborn TA, Shaw JE. Differences in height explain gender differences in the response to the oral glucose tolerance test—the AusDiab study. Diabet Med 2008;25:296-302.
[16] Soeters MR, Sauerwein HP, Groener JE, et al. Gender-related differences in the metabolic response to fasting. J Clin Endocrinol Metab 2007;92:3646-52.
[17] Perseghin G, Scifo P, Pagliato E, et al. Gender factors affect fatty acids–induced insulin resistance in nonobese humans: effects of oral steroidal contraception. J Clin Endocrinol Metab 2001;86:3188-96.
[18] Mitrakou A, Kelly D, Mokan M, et al. Role of reduced suppression of glucose production and diminished early insulin release in impaired glucose tolerance. N Eng J Med 1992;326:22-9.
[19] Robertson MD, Livesey G, Mathers JC. Quantitative kinetics of glucose appearance and disposal following a ^{13}C-labelled starch-rich meal: comparison of male and female subjects. Br J Nutr 2002;87:569-77.
[20] Healy GN, Dunstan DW, Shaw JE, Zimmet PZ, Owen N. Beneficial associations of physical activity with 2-h but not fasting blood glucose in Australian adults. Diabetes Care 2006;29:2598-604.
[21] McMahon M, Marsh H, Rizza R. Comparison of the pattern of postprandial carbohydrate metabolism after ingestion of a glucose drink or a mixed meal. J Clin Endocrinol Metab 1989;68:647-53.