Serum vaspin level as a predictive indicator in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after laparoscopic vertical banded gastroplasty

Yong Wang, MD, Zong-Fan Yu, MM, Yun-Sheng Cheng, MM, Ben-Li Jia, MM, Gang Yu, MM, Xiao-Qiang Yin, MB, Yang Wang, MD

Abstract
Background: This study is all about predicting the value of serum vaspin level in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after laparoscopic vertical banded gastroplasty (LVBG).

Methods: A total of 164 patients (from January 2012 to May 2015) with severe obesity were chosen and performed LVBG. Enzyme-linked immunosorbent assay was performed to detect the serum vaspin level. The patients were given a biochemical automatic analyzer to measure the biochemical indicators. Homeostasis model assessment (HOMA) helps in the calculation of fasting insulin level (FINS) and insulin resistance (IR). The changes in fatty liver were examined by computed tomography (CT). Receiver operating characteristic curve is used to increase the predictive value of serum vaspin level in the amelioration of liver function and disturbances in the metabolism.

Results: Weight, BMI, waist circumference, serum vaspin level, and triglyceride (TG) decreased, but CT value of liver increased at 4th, 7th, and 12th month after surgery. After the 7th and 12th month period of surgery, the alanine aminotransferase, aspartate aminotransferase, FINS, and HOMA-IR reduced in the patients (P<.005). The area under ROC curve (AUC) is about 0.871 ± 0.031 with 95%CI of 0.810–0.931 (P<.001). The sensitivity, specificity, and accuracy of serum vaspin level ≤0.9 were 87.80%, 78.05%, and 83.28%, respectively. BMI, FINS, and serum vaspin level ≤0.9 were the influencing factors of the amelioration of fatty liver and metabolic disturbance.

Conclusion: This study proves that the serum vaspin level serves as a predictive indicator in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after LVBG.

Keywords: vaspin, fatty liver, metabolic disturbance, predictive value, serum vaspin level, severe obese patients

1. Introduction
Obesity is now one of the most increasingly serious threat to global health, which affects more than 300 million adults worldwide.1,2 The more important alarming fact is the incidence of severe obesity body mass index (BMI) ≥35 kg/m².3,4 Severe obesity is highly associated with some chronic diseases like cardiovascular disease, diabetes, and carcinoma, leading to high mortality and morbidity.5-7 It is also proved that severe obesity contributes to fatty liver and metabolic disturbances; several factors, including insulin sensitivity, blood pressure, as well as plasma lipid profile, are associated with excessive accumulation of fat in visceral adipose tissue (VAT), resulting in dyslipidemia, damaged glucose tolerance, and hypertension.8,9 According to the study, it is reported that adipocytokines secreted from VAT have regulatory effects on insulin sensitivity, energy homeostasis, inflammation, vascular functions as well as lipid metabolism.10,11 Presently, bariatric surgeries have been generally considered as the most effective treatment for sustained and durable weight loss in patients with severe obesity due to its preventability and therapeutic effect.11,12

Vaspin (VAT-derived serine proteinase inhibitor), is a significant and relatively novel adipocytokine with regulation functions in lipid and glucose metabolisms, has been found to be exclusively
present in the VAT with obesity of Otsuka Long-Evans Tokushima Fatty rats. Then later all the researches have proved that vaspin is present in human tissues, such as skin, stomach, pancreas, liver, and adipose tissue. It has been proved that serum vaspin levels are positively correlated to metabolic syndrome parameters. As a beneficiary adipocytokine, vaspin acts on obesity-related metabolic dysfunction through genetic manipulation and exerts insulin-sensitizing effects and anti-inflammatory properties to improve insulin sensitivity and alleviate endoplasmic reticulum stress in liver.

Proved that serum vaspin levels are independent predictive value for liver fibrosis with nonalcoholic fatty liver diseases in patients. However, the patients with severe obesity with serum vaspin levels who had surgery are not yet fully explored. This study proves about the predictive value of serum vaspin level for the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after treating with laparoscopic vertical banded gastroplasty (LVBG).

2. Materials and methods

2.1. Ethical statement

This study was approved by the Ethical Committee of The Second Hospital of Anhui Medical University and Jiangsu Province Hospital. All the patients included in this study signed the informed consents to be involved in this research.

2.2. Study subjects

From January 2012 to May 2015, 164 patients with severe obesity were recruited in this study from The Second Hospital of Anhui Medical University and Jiangsu Province Hospital (91 males and 73 females, mean age: 28.12 ± 6.46 years, Quetelet index (BMI) ≥35 kg/m²). BMI of patients ranged from 37.03 to 52.69 kg/m². The number of daily steps of patients in a year were recorded by Yamax pedometer (sw-701), and mean steps/day was measured. According to the standard of physical activity (PA)23,24, 49 case of ≥10,000 steps/day and 115 cases of <10,000 steps/day. Clinical evaluation was performed on patients like physical examination (weight, height, and waist circumference for the calculation of BMI) and relevant biochemical detection by professional doctors to rule out the secondary obesity, followed by other evaluation tests and they are prepared for the operation by the surgeons. In the mornings the day before the surgery, the fasting venous blood of all subjects was obtained, and the serum was separated after centrifugation and stored for further uses. The exclusion criteria includes: the patients with severe heart, liver, or renal dysfunction; the patients with diseases related to abnormalities of glucose and lipid metabolisms, such as diabetic ketoacidosis (DKA), pituitary damage, adrenal gland injury, thyroid damage, and secondary pancreatic injury; the patients with transient hyperglycemia caused by acute infection, trauma, or other stress.

2.3. Diagnostic criteria for severe obesity

Quetelet’s index (BMI) is a type of measure of fatness performed on adults whose physical developments were relatively stable. BMI = weight (kg)/height (m)². Generally, a man with BMI ≥25 kg/m², and a woman with BMI ≥24 kg/m² are known as overweight persons. According to research results in Shanghai, 15- to 19-year-old adolescents with BMI between 18 and 22 kg/m² were considered as normal weight, with BMI ≥22 kg/m² were considered as overweight, and with BMI ≥24 kg/m² were considered as obese patients. Adults more than 20 years old with BMI between 20 and 24 kg/m² were considered as normal weight, with BMI ≥24 kg/m² were considered as overweight, and with BMI ≥26 kg/m² were considered as obese patients. According to the World Health Organization, the BMI classification in 2014 confirms that, BMI between 25 and 30 kg/m² is consider as overweight. The obese patients are subclassified into 3 types: pre-obese or class I obesity (BMI 30, 35 kg/m²), severe or class II obesity (BMI 35–40 kg/m²), and extreme or class III obesity (BMI ≥40 kg/m²). The value of BMI for the diagnostic criteria for severe obesity in this research is ≥40 kg/m².

2.4. Operation method

After general anesthesia is given, the patient is placed on the table in a supine or lithotomy position. After the pneumoperitoneum was established, 4–5 holes were opened, where it includes the peephole in the upper middle abdomen, the auxiliary operating hole at 5 cm under the xiphoid process, and 2 main operating holes on the left and right midclavicular lines in the upper abdomen. Another auxiliary operating hole (10 mm) could be opened on the anterior axillary line in the left mid-abdomen if necessary. The ultrasonic knife is used to dissociate the lesser curvature below the cardiac and gastric fundus. Then, fenestration of the left and right sides of the lesser curvature of the stomach was conducted at 6–7 cm below the curvula (near the lesser curvature) using a 21-mm circular stapler. The insula of the upper lesser curvature from the gastro window directing to the left side of the lesser curvature of the liver is done by using the 60-mm endovascular anastomosis (Endo GIA) stapler. The band of gastric pouch was formed at the gastric window using a mesh the tube drainage was set in the operating area for fasting the venous blood of all patients and obtained at 1st, 4th, 7th, and 12th month after surgery, and then the serum was separated after centrifugation and stored at −20°C for future use.

2.5. Diagnosis and evaluation of fatty liver

For this research before the surgery was started, 164 patients were diagnosed as fatty liver by B-mode ultrasonography. The diagnostic evidences were as follows: the near-field of liver is diffusely hypechoic with higher echo intensity than spleen; the far-field spot is in low density accompanied by echo attenuation; and the liver is mildly or moderately enlarged with blunted leading edges. The patients were chosen on the basis of no drinking history or weekly based alcohol consumption about less than 40g was found; negative markers of vertical transmission of hepatitis B virus (HBV) infection were detected, which were consistent with the diagnostic criteria for nonalcoholic fatty liver. Computed tomography (CT) examination of the liver was performed by the specialists using a CT scanner (Picker PQ5000, Marconi Medical Systems, Cleveland, OH). CT values of 4 lobes of liver were examined and the mean CT value of the entire liver was used for comparison. The CT diagnostic criteria of fatty liver were as follows: hepatic density decreased and CT value of the liver was lower than that of spleen (liver/spleen CT value ratio ≤1).

2.6. Enzyme-linked immunosorbent assay

The venous blood of all patients with limosis was collected at the 1st, 4th, 7th, and 12th month after examination on admission and surgery. The collected blood specimens from the patients
were placed in a refrigerator for about an hour at 4°C with an angle of 45°–60°. Serum specimens were obtained by low-speed centrifugation at 3000 rpm/min for 5 min and stored at −20°C. The vaspin level was detected using an enzyme-linked immunosorbent assay (ELISA) kit (Bender Medsystems Gmbh, Vienna, Austria) according to the manufacturer’s instruction, and the optical density value was then measured at 450 nm using a microplate reader. This experiment was repeated 3 times to obtain the mean value.

2.7. Detection of biochemical indicators

During the detection of biochemical indicators, the fasting venous blood was obtained from the patients during the time of admission and also at 1st, 4th, 7th, and 12th month after surgery. A HITACH 17170A biochemical automatic analyzer (Hitachi Co. Ltd, Tokyo, Japan) was applied to detect the levels of fasting blood glucose (FBG), fasting blood lipid (FPL, including total cholesterol [TC], triglyceride [TG], high-density lipoprotein [HDL], and low-density lipoprotein [LDL]), liver enzyme levels (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and γ-glutamyl transpeptidase [γ-GT]), and serum uric acid (SUA). The operation was repeated 3 times to obtain the mean value.

2.8. Homeostasis model assessment of insulin resistance (HOMA-IR) and β-cell function (HOMA-β)

This is a different type of processes where the insulin resistance and pancreatic β-cell function were assessed by the homeostasis model assessment (HOMA). The β-cell function in response to glucose loading was assessed using the modified β-cell function index (MBCI). HOMA-insulin resistance (IR) = [INS × FBG/22.5], HOMA-β-cell function (HOMA-β) = [FBG × (2 × PG + 1 × PG) – 2 × PG], where INS is fasting insulin level, FBG is fasting blood glucose; 1 hour PG is 1-hour plasma glucose during oral glucose tolerance test (OGTT); and 2 hour PG is 2-hour plasma glucose during OGTT.

2.9. Statistical analysis

The data collected in this research were analyzed by SPSS version 21.0 (SPSS Inc., Chicago, IL) and the measurement data were expressed as mean ± standard deviation (SD). Comparisons between preoperative and postoperative data in normal distribution were analyzed using paired t-test. Receiver operating characteristic (ROC) curve was drawn to evaluate the predictive value of serum vaspin level in amelioration of liver function and metabolic disturbance. Logistic regression analysis was exhibited for factors that influence the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after surgery. P < 0.05 indicates the statistical significance of serum vaspin level.

3. Results

3.1. Weight, BMI, and waist circumference of patients before and after surgery

Compared with the preoperative data, no significant changes were found in the weight, BMI, and waist circumference of patients at first month after surgery (P > 0.05), but decreases in the weight, BMI, and waist circumference were observed at fourth month later (P < 0.05). At 12th month after surgery, the weight, BMI, and waist circumference of patients reduced by 31.26 ± 14.72 kg, 10.96 ± 5.34 kg/m², and 20.24 ± 3.36 cm on average, respectively (Table 1).

3.2. Decreases in serum vaspin level at 4th, 7th, and 12th month after surgery

The serum vaspin levels of the patients were detected by ELISA before surgery and at 1st, 4th, 7th, and 12th month after surgery. And the serum vaspin level was gradually decreased at 4th, 7th, and 12th month after LVBG (P < 0.05) (Fig. 1).

3.3. Reduction of serum TG level at 4th, 7th, and 12th month after surgery

The details compared with data after and before surgery there are no obvious differences were presented in serum TC, LDL, HDL, and SUA levels (P > 0.05), but the serum TG level was gradually reduced at 4th, 7th, and 12th month after surgery (P < 0.05) (Table 2).

3.4. The amelioration of fatty liver at 4th, 7th, and 12th month after surgery

Among the 164 patients, 145 patients were found to suffer from at least 1 liver enzyme abnormality that was 2 times lower than...
the upper limit of normal value. No significant difference was exhibited in serum γ-GT level before and after surgery (P > 0.05). Serum ALT and AST levels had no obvious change at 1st and 4th month after surgery, but decreased significantly at 7th and 12th month (P < 0.05). The mean CT value of liver at 4th, 7th, and 12th month after surgery were remarkably higher than that before surgery (P < 0.05) (Table 3).

3.5. Decreases in FINS and HOMA-IR at 7th and 12th month after surgery

At the fourth month after surgery, FINS and HOMA IR decreased in patients with severe obesity, and significantly decreased at the seventh month (P < 0.05) (Table 4).

3.6. ROC curve analysis

In the ROC curve analysis according to the criteria of obesity (BMI ≥ 35 kg/m²) and diagnostic criteria of CT value for fatty liver, patients with BMI ≥35 kg/m² and liver/spleen ratio of CT value ≥1 after surgery were considered to be unimproved in fatty liver and metabolic disturbances, and patients with BMI < 35 kg/m² and liver/spleen ratio of CT value >1 after surgery were considered as improved. Then an ROC curve was drawn to analyze the predictive value of serum vaspin level in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after LVBG (Fig. 2). Area under the curve (AUC) was 0.871 (95% confidence interval [CI] = 0.810–0.931, P < 0.001), which demonstrated that the serum vaspin level has a predictive value for the amelioration of fatty liver and metabolic disturbances in metabolism after the surgery is done. And the sensitivities of serum vaspin level ≤0.6, 0.7, 0.8 and 0.9 in predicting the amelioration of fatty liver and metabolic disturbance were 93.90%, 92.68%, 92.68%, and 87.80%, respectively, with the specificities of 28.05%, 35.37%, 51.22%, and 78.05%, respectively, and the accuracies of 63.38%.

Figure 2. ROC curve of the predictive value of serum vaspin level in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after LVBG. LVBG = laparoscopic vertical banded gastroplasty, ROC = receiver operating characteristic.
Physical activity/C0

ALT/C0

AST/C0

the serum vaspin level decreased gradually. This may reveal

condition of metabolic disturbance improved and eventually

metabolic disturbance. level acts as a predictive indicator of improved fatty liver and

liver and metabolic disturbance after LVBG, and serum vaspin

LVBG. Our

fi

serum vaspin level in predicting the amelioration of fatty liver and

metabolic disturbance in patients with severe obesity after

obesity,

Logistic regression analysis for factors that in

amelioration of fatty liver and metabolic disturbance in patients with severe

obesity.

Factors

B

SE

Wald

OR

P

95%CI

BMI

1.621

0.699

5.378

5.056

.02

1.285–19.693

Blood glucose

–0.751

0.603

1.549

0.472

.213

0.145–1.54

Fasting insulin level

0.473

0.206

5.254

1.604

.022

1.071–2.404

Serum vaspin level <0.9

–5.913

2.476

5.703

0.003

.017

<0.001–0.346

ALT

–0.219

0.129

2.892

0.803

.089

0.624–1.034

AST

–0.062

0.081

0.58

0.94

.446

0.802–1.102

γ-GT

0.017

0.05

0.121

1.018

.727

0.922

physical activity

–2.711

1.769

2.349

0.066

.125

0.002–2.129

ALT=alanine aminotransferase, AST=aspartate aminotransferase, B=regression coefficient, BMI=body mass index, CI=confidence interval, γ-GT=γ-glutamyl transpeptidase, OR=odds ratio, SE=standard error.

66.12%, 73.47%, and 83.28%, respectively. According to the research in the clinical and epidemiological studies the serum vaspin level <0.9 is the most common diagnostic criteria for the prevalence of peripheral arterial disease (PAD). Therefore, the serum vaspin level could be used as the cut-off value to predict the amelioration of fatty liver and metabolic disturbance in patients with severe obesity after surgery, among which had high specificity, good sensitivity, and high accuracy for getting good results relatively.

3.7. Logistic regression analysis

Logistics regression is defined as a regression model where the

dependent variable (DV) is categorical, and the analysis

conducted by this regression is called logistics regression analysis,

and it was performed with physical activity, BMI, blood glucose

level, FINS, serum vaspin level <0.9, and liver enzyme levels such

ALT, AST, and γ-GT as independent variables, there are also

dependent variables likewise amelioration of fatty liver and

metabolic disturbance in the patients with severe obesity after

LVGB. The results are shown in Table 5. BMI, FINS, and serum

vaspin level <0.9 were factors that influenced the amelioration

of fatty liver and metabolic disturbance in patients with severe

obesity. Their odds ratios (OR) were 3.294 (95%CI =

1.602–6.775, P = .001), 1.413 (95%CI = 1.138–1.755, P = .002), and

0.009 (95%CI = 0.000–0.272, P = .007), respectively. And the partial regression coefficients were 1.192, 0.346, and –4.743, respectively. Additionally, physical activity, blood glucose, ALT, AST, and γ-GT were excluded from predictive factors in the amelioration of fatty liver and metabolic disturbance in patients with severe obesity (P > .05).

4. Discussion

In the discussion, the most important thing should be discussed is

the Vaspin, which is one of the adipokines and associated with

obesity,[26] and LVBG is one of the most frequent and effective

treatments for morbid obesity.[27] We investigated the role of

serum vaspin level in predicting the amelioration of fatty liver and

metabolic disturbance in patients with severe obesity following

LVGB. Our findings indicate that patients have improved fatty

liver and metabolic disturbance after LVBG, and serum vaspin

level acts as a predictive indicator of improved fatty liver and

metabolic disturbance.

The main thing about this study was found that the condition of metabolic disturbance improved and eventually the serum vaspin level decreased gradually. This may reveal

that vaspin could act as a harmful molecule in the development of metabolic disturbances after LVBG. By performing the potential treatment for metabolic disturbance, the excessive amount of VAT is decreased. In the deep cases, it is also proved that there is a positive association between serum vaspin levels and metabolic disturbance in the humans.[19] Dysregulation of adipokines production with anti-inflammatory properties may contribute to metabolic disturbance related to obesity.[28] The vaspin demonstrated by the Phalitakul et al.[29] is considered as a novel adipokine, which plays an anti-inflammatory role in vascular smooth muscle cells. Therefore, it is reasonable that vaspin may cause metabolic disturbance with its anti-inflammatory action, especially in abnormal higher level. The at most important thing is serum vaspin has anti-inflammatory property through antioxidative mechanism; this mechanism protects the effects on metabolic diseases.[30] Although further studies are needed, these results suggest that vaspin might be involved in the development of metabolic disturbance. And we suggest an underlying mechanism that low level of vaspin may improve metabolic disturbance by inhibiting its anti-inflammatory property through suppression of antioxidative effect.

Meanwhile, it has also been found that fatty liver increased while serum vaspin level decreased, which revealed a correlation between low level of human serum vaspin and amelioration of fatty liver following LVBG. Orlik et al.[31] demonstrated that insulin resistance plays a critical role in the pathogenesis of nonalcoholic fatty liver. Besides, serum vaspin level is closely associated with insulin resistance because fatty liver increased while serum vaspin level decreased.[32] Weight loss affects serum vaspin level in obese people by the regulation of insulin resistance.[33] The findings in this study support our assumption, that there seems to be a strong association between low-expressed vaspin and also fatty liver through the mechanism of insulin resistance, this is the most important thing. And it completely proved that through the signaling pathways, the substrate flux are leading the pathogenesis of insulin resistance.[34] And adipokines regulate various insulin resistance-related pathways through 3 mechanisms: endocrine, paracrine, or autocrine.[35] Thus, it is reasonable to hypothesize that vaspin plays a role in modulating insulin resistance-related signaling pathways of via secretion. Changes in serum vaspin level related to meal might be modulated by insulin rather than by nutrient intake.[36] In contrast, Oberbach et al.[37] proved that exercise associated improvement in insulin sensitivity does not help in the reduction of serum vaspin level but oxidative stress is not included. Differences in the results might attribute to diverse period of

Table 5

Logic regression analysis for factors that influence the amelioration of fatty liver and metabolic disturbance in patients with severe obesity.

| Factors                  | B     | SE    | Wald   | OR    | P      | 95%CI          |
|-------------------------|-------|-------|--------|-------|--------|----------------|
| BMI                     | 1.621 | 0.699 | 5.378  | 5.056 | .02    | 1.285–19.693  |
| Blood glucose           | –0.751| 0.603 | 1.549  | 0.472 | .213   | 0.145–1.54    |
| Fasting insulin level   | 0.473 | 0.206 | 5.254  | 1.604 | .022   | 1.071–2.404   |
| Serum vaspin level <0.9 | –5.913| 2.476 | 5.703  | 0.003 | .017   | <0.001–0.346  |
| ALT                     | –0.219| 0.129 | 2.892  | 0.803 | .089   | 0.624–1.034   |
| AST                     | –0.062| 0.081 | 0.58   | 0.94  | .446   | 0.802–1.102   |
| γ-GT                    | 0.017 | 0.05  | 0.121  | 1.018 | .727   | 0.922          |
| physical activity       | –2.711| 1.769 | 2.349  | 0.066 | .125   | 0.002–2.129   |

ALT=alanine aminotransferase, AST=aspartate aminotransferase, B=regression coefficient, BMI=body mass index, CI=confidence interval, γ-GT=γ-glutamyl transpeptidase, OR=odds ratio, SE=standard error.
measurement. Further study with large sample sizes and follow-up should be investigated to warrant our findings.

From the above discussed study, it is clearly proved that the serum vaspin level could be used for predicting the efficacy of LVBG surgery in the severe obesity patients. Furthermore, low serum vaspin levels indicate the amelioration of severe obesity due to weight loss. Few similar changes have been reported not only for amelioration of surgery also for other surgery too. Laparoscopic restrictive bariatric surgery reduced the serum vaspin levels by decreasing dietary intake in a short term. However, elevated serum vaspin level was observed in women with polycystic ovary syndrome in response to weight loss, because a small weight reduction cannot affect serum vaspin levels significantly. Thus, it’s proved that the serum vaspin level can be reduced by the patients having large weight reduction. Moreover, in a long term, insulin resistance may not be the reason which caused the change in serum vaspin level after LVBG.

In conclusion, our study provides evidence that serum vaspin level could be regarded as the predictor for improvement of fatty liver and metabolic disturbance after LVBG surgery in patients with severe obesity. However, the exact correlation between changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period. The underlying mechanism needs more strong changes in serum vaspin level and insulin sensitivity is not clear at early period.

Acknowledgment

The authors thank the reviewers for critical comments.

References

[1] Wang YC, McPherson K, Marsh T, et al. Health and economic burden of the projected obesity trends in the USA and the UK. Lancet 2011;378:815–25.
[2] Rurik I, Torzsa P, Szodor J, et al. A public health threat in Hungary: obesity, 2013. BMC Public Health 2014;14:798.
[3] Magi R, Manning S, Youssef A, et al. Contribution of 32 GWAS-identified common variants to severe obesity in European adults referred for bariatric surgery. PLoS One 2013;8:e70735.
[4] Finkelstein EA, Khayou OA, Thompson H, et al. Obesity and severe obesity forecasts through 2030. Am J Prev Med 2012;42:563–70.
[5] Seetho IW, Wilding JP. How to approach endocrine assessment in severe obesity? Clin Endocrinol (Oxf) 2013;79:163–7.
[6] Wehr E, Pilé S, Boehm BO, et al. The lipid accumulation product is associated with increased mortality in normal weight postmenopausal women. Obesity (Silver Spring) 2011;19:873–80.
[7] Robbins JM, Malyia G, Polansky M, et al. Prevalence, disparities, and trends in obesity and severe obesity among students in the Philadelphia, Pennsylvania, school district, 2006–2010. Prev Chronic Dis 2012;9:E145.
[8] O’Connell JJ, Lynch L, Lawood TJ, et al. The relationship of omental and subcutaneous adipose size to metabolic disease in severe obesity. PLoS One 2010;5:e9997.
[9] Guenard F, Bouchard L, Tchernev A, et al. DUSP1 gene polymorphisms are associated with obesity-related metabolic complications among severely obese patients and impact on gene methylation and expression. Int J Genomics 2013;2013:690748.
[10] Inoue J, Wada J, Teshigawara S, et al. The serum vaspin levels are reduced in Japanese chronic hemodialysis patients. BMC Nephrol 2012;13:163.
[11] Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. JAMA 2013;310:2416–25.
[12] Kral JG, Kova RA, Catalano PM, et al. Severe obesity: the neglected epidemic. Obes Facts 2012;5:234–69.
[36] Kovacs P, Miehle K, Sandner B, et al. Insulin administration acutely decreases vaspin serum concentrations in humans. Obes Facts 2013;6:86–8.
[37] Oberbach A, Kirsch K, Lehmann S, et al. Serum vaspin concentrations are decreased after exercise-induced oxidative stress. Obes Facts 2010;3:328–31.
[38] Golpaie A, Tajik N, Masoudkabir F, et al. Short-term effect of weight loss through restrictive bariatric surgery on serum levels of vaspin in morbidly obese subjects. Eur Cytokine Netw 2011;22:181–6.
[39] Koiou E, Tziomalos K, Dinas K, et al. The effect of weight loss and treatment with metformin on serum vaspin levels in women with polycystic ovary syndrome. Endocr J 2011;58:237–46.