

Adipocyte Fatty Acid-binding Protein as a Determinant of Insulin Sensitivity in Morbid-obese Women

Inmaculada Simón¹, Xavier Escoté¹, Núria Vilarrasa², José Gómez², José M. Fernández-Real³, Ana Megía¹, Cristina Gutiérrez¹, Lluís Gallart¹, Carles Masdevall⁴ and Joan Vendrell¹

The aim of the study was to evaluate human plasma circulating levels of adipocyte fatty acid-binding protein (A-FABP) and its relationship with proinflammatory adipocytokines and insulin resistance in a severely obese cohort, before and 1 year after a surgical gastric bypass. Plasmatic levels of A-FABP were measured in 77 morbid-obese women before and 1 year after bariatric surgery. Anthropometrical parameters and body composition by bioelectrical impedance analysis were determined. Circulating levels of soluble tumor necrosis factor receptor 2 (sTNFR2), Interleukin 18 (IL-18), adiponectin, and high-sensitive C-reactive protein (hsCRP) were also analyzed. Insulin resistance by homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated. After massive weight loss, A-FABP plasmatic levels decreased significantly [7.6 (8.9) vs. 4.3 (5.1); $P < 0,001$] but no association with circulating adipokines or proinflammatory cytokines, both at the beginning and at the end of follow-up, was observed. A decrease in sTNFR2, IL-18, hsCRP, and an increase in adiponectin levels ($P < 0.001$ in all cases) were observed after the gastric bypass. HOMA-IR index improved 1 year after surgery and after multiple regression analysis remained associated with A-FABP after controlling for confounding variables ($\beta = 0.322$, $P = 0.014$; R^2 for the model 0.281). In morbid-obese women, plasma A-FABP concentrations were dramatically reduced after gastric bypass surgery. After weight loss this protein contributed to HOMA-IR index independently of proinflammatory/ant inflammatory cytokine profile. Further studies are warranted to elucidate the role of A-FABP in the pathogenesis of insulin resistance in morbid obesity.

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INTRODUCTION

Obesity is a common risk factor for dyslipidemia, insulin resistance, type 2 diabetes, hypertension, and atherosclerosis, a cluster of metabolic abnormalities included in the metabolic syndrome (MS) (1,2). The physiopathologic link between obesity and these abnormalities remains to be elucidated but several recent studies indicate a central role of adipose tissue in the development of this syndrome (3,4). Numerous evidences suggest that fat tissue is viewed as an active endocrine organ with a high metabolic activity (5). Adipocytes produce and release several bioactive substances that act as true hormones responsible for the regulation of energy intake and expenditure (6). The dysregulation in the production of these hormones called adipocytokines can contribute to the proinflammatory environment associated with obesity (7–9).

Cytoplasmic fatty acid-binding proteins (FABPs) are members of a multigenic family protein that bind with high

affinity to hydrophobic ligands such as saturated and unsaturated long-chain fatty acids and eicosanoids. The nine family members have between 20 and 70% identity in their amino acid sequence. Adipocyte fatty acid-binding protein (A-FABP or FABP4 or aP2) is a small lipid-binding protein, highly expressed in adipose tissue and also expressed in macrophages. It is one of the most abundant cytoplasmic proteins in mature adipocytes (10) and a significant proportion of this protein is also released into bloodstream (11). Its expression is transcriptionally controlled during adipocyte differentiation and is regulated by peroxisome proliferator-activated receptor- γ agonists, insulin and fatty acids (12).

Although its biological role is not yet well understood, its function has been correlated to insulin sensitivity, lipid metabolism and inflammation (13). Animal studies have shown that A-FABP deficient mice are protected for the development of obesity-induced insulin resistance, impaired glucose tolerance,

¹CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Endocrinology and Diabetes Research Department, University Hospital Joan XXIII from Tarragona, School of Medicine, Rovira i Virgili University, Pere Virgili Institute, Tarragona, Spain; ²CIBERDEM, Endocrinology and Diabetes Unit, University Hospital of Bellvitge, Barcelona, Spain; ³CIBEROBM, Endocrinology and Diabetes Unit, University Hospital Josep Trueta, Girona, Spain; ⁴Surgery Service, University Hospital of Bellvitge, Barcelona, Spain. Correspondence: I. Simón (ism@comt.org)

and atherosclerosis (14,15). Recent human clinical studies have proposed serum A-FABP levels as a plasma biomarker of MS and type 2 diabetes, both in Asian and Caucasian population (16–18). Moreover, a genetic variant at the A-FABP locus (T-87C polymorphism) has been associated with a reduced A-FABP activity and lower risk for hypertriglyceridemia, type 2 diabetes, and cardiovascular disease (19).

Morbid obesity is an extreme metabolic situation in which the imbalance of adipocytokines is amplified and in some cases they present a different regulatory pattern than the observed in nonmorbid-obese population (9). Usually many of the metabolic alterations improve after weight reduction, restoring some of the loosed regulatory mechanisms in the morbid state. We hypothesize that A-FABP should be reduced after weight loss in morbid-obese patients in parallel with inflammatory markers and after improving insulin sensitivity.

The aim of our study was to evaluate the behavior of A-FABP circulating protein levels and its relationship with proinflammatory adipocytokines in a severely obese population before and 1 year after a surgical gastric bypass.

METHODS AND PROCEDURES

Morbid-obese subjects

Seventy-seven morbid-obese women of white origin with a mean age of 45.5 ± 9.6 year were included in the study. All patients were obtained from the Endocrinology Service of the Hospital of Bellvitge (Barcelona, Spain) and had been scheduled for bariatric surgery. A gastric bypass operation was performed according to a modification of the method described by Capella and Capella (20). Pre- and postoperative anthropometric measurements were obtained and blood samples were collected at basal and 1 year after surgery. Patients were excluded if they had an acute major cardiovascular event in the previous 6 months, an acute illness, and current evidence of acute or chronic inflammatory or infective diseases, or they were taking any medication that could alter lipidic or metabolic parameters. Patients receiving medical treatment for diabetes or dyslipidemia before surgery discontinued all hypoglycemic agents and hypolipemic drugs at least 3 months before basal determinations. All subjects had signed a written consent to the study, which was approved by the research ethics board of our hospital.

Anthropometrical measurements

Height and weight were measured with the patient standing in light clothes and without shoes. BMI was calculated as body weight divided by height squared (kg/m^2). Waist–hip ratio was calculated as the ratio of waist and hip circumferences. Body composition was measured by bioelectrical impedance analysis, using a Holtain BC Analyser (Holtain, Dyfed, UK) being the precision of this test in determining body fat $\pm 3\%$. The same physician did all examinations.

Analytical methods

Blood samples were drawn from each subject before breakfast, between 8.00 and 9.00 AM, after an overnight bed rest.

Serum glucose was measured with a glucose oxidase method using an ADVIA 1200 autoanalyser (Bayer, Germany). Serum insulin was measured using specific immunoradiometric assay (Medgenix Diagnostics, Fleunes, Belgium) in which proinsulin did not crossreact. The intra- and interassay coefficients of variation were 6 and 7%, respectively. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated from fasting plasma insulin and glucose levels as $(\text{insulin} \times \text{glucose})/22.5$, where insulin concentration was reported as milliunits per liter and glucose as millimolar concentrations. HbA1c was measured by a chromatographic method (Glico Hb Quick Column Procedure, Helena Laboratories, Beaumont, TX).

Serum lipids were determined by conventional biochemical techniques. Low-density lipoprotein cholesterol was calculated through the Friedewald formula (21). Plasma high-sensitive C-reactive protein (hsCRP) was determined by a highly sensitive immunonephelometry kit (Dade Behring, Marburg, Germany).

Soluble tumor necrosis factor receptor 2 (sTNFR2) was determined by solid phase enzyme immunoassay with amplified reactivity (Bio Source Europe, Nivelles, Belgium). The limit of detection was 0.1 ng/ml and the intra- and interassay coefficients of variation were <7 and $<9\%$, respectively.

Plasma interleukine-18 (IL-18) levels were measured by human IL-18 sandwich enzyme-linked immunosorbent assay (Medical & Biological Laboratories, Japan). Assay sensitivity was 12.5 pg/ml. Intra- and interassay coefficients of variation were 10.8 and 10.7%, respectively.

Plasma adiponectin levels were measured using a standardized radioimmunoassay kit from Linco Research (Linco Research, St Charles, MO). The kit has a sensitivity of 1 ng/ml and range of 1–200 ng/ml. All samples were diluted 1/500. The intra- and interassay coefficients of variation were 8 and 12%, respectively. Plasma A-FABP levels were measured by sandwich enzyme-linked immunosorbent assay (BioVendor Laboratory Medicine, Palackeho, Czech Republic). The sensitivity was 0.2 ng/ml. The intra- and interassay coefficients of variation were 5.8 and 14.7%, respectively.

Serum free fatty acids (FFAs) were determined by a commercially available enzymatic colorimetric method (NEFA-HR(2) from Wako, Germany). The sensitivity was 0.01 mEq/l. Inter- and intrassay coefficients of variation were $<8\%$.

Statistical analysis

Descriptive data are expressed as mean value \pm s.d. or median (75th percentile) for non-normally distributed variables. Differences between groups were compared by using a Student's *t*-test, or analysis of variance of clinical or laboratory parameters. Variables that did not have a Gaussian distribution were logarithmically transformed. Correlation was analyzed by the Pearson product–moment correlation. Multiple linear regression analysis by forward stepwise regression was also used to analyze the independence of the association between quantitative variables. All statistical analyses were performed by using the SPSS/PC+ statistical package (v. 13.0 for Windows; SPSS, Chicago, IL).

RESULTS

Clinical, metabolic, and analytical characteristics of all subjects before and after gastric bypass are shown in **Table 1**. A significant weight loss after surgery was observed ($P < 0.0001$) and body composition parameters of patients, as BMI ($P < 0.0001$), fat-free mass ($P < 0.0001$), and fat mass ($P < 0.0001$), were dramatically reduced 1 year after bariatric surgery.

As expected, subjects at baseline had a significantly more adverse atherogenic profile than 1 year after gastric bypass, including total cholesterol, triglycerides, waist–hip ratio, FFA, and insulin resistance assessed by HOMA-IR (all variables at $P < 0.0001$).

In **Table 2** are summarized the changes in serum concentrations of cytokines, inflammatory markers, and A-FABP before and after bariatric surgery. Serum levels of sTNFR2, hsCRP, adiponectin, and A-FABP were logarithmically transformed for calculations. All of these circulating proteins decreased significantly 1 year after surgery ($P < 0.001$) except for adiponectin that increased after weight reduction ($P < 0.001$).

In the bivariate analysis before surgery, no correlations of A-FABP serum levels with clinical and metabolic parameters were found. Likewise no associations between A-FABP

Table 1 Clinical and analytical characteristics in morbidly obese patients before and after bariatric surgery (n = 77)

	Preoperative	12 months
Weight (kg)	123.3 ± 19	79.9 ± 14.3*
BMI (kg/m ²)	49.1 ± 7.4	31.7 ± 4.5*
WHR	0.9 ± 0.08	0.8 ± 0.06*
Fat-free mass (kg)	66.9 ± 7.2	54.1 ± 6.7 *
Fat mass (kg)	55.5 ± 14.6	23.7 ± 8.9*
Fasting glucose (mmol/l)	6.5 ± 2.6	4.7 ± 0.6*
Fasting insulin (μU/ml)	18.3 ± 14.1	5.3 ± 3.1*
HbA1c (%)	5.6 ± 1.4	4.5 ± 0.6*
HOMA-IR	5.9 ± 6.3	1.2 ± 0.8*
Cholesterol (mmol/l)	4.9 ± 1.1	4.3 ± 0.8*
HDLc (mmol/l)	1.2 ± 0.3	1.6 ± 0.4*
LDLc (mmol/l)	3.1 ± 0.9	2.4 ± 0.7*
Triglycerides (mmol/l)	1.9 ± 2.0	1.0 ± 0.5*
Free fatty acids (mmol/l)	0.9 ± 0.3	0.5 ± 0.2*

All data are presented as mean ± s.d.

HDLc, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; LDLc, low-density lipoprotein cholesterol; WHR, waist-hip ratio.

**P* < 0.0001.

Table 2 Pre- and postoperative adipokines and proinflammatory cytokines in morbidly obese women (n = 77)

	Preoperative	12 months
sTNFR2 (ng/ml)	6.3 (6.8)	4.9 (5.4)*
IL-18 (pg/ml)	275.4 (323.5)	194 (240.2)*
Adiponectin (μg/ml)	12.5 (15.2)	28.6 (28.1)*
CRP (mg/l)	12.4 (16.9)	2.2 (2.6)*
A-FABP (ng/ml)	7.6 (8.9)	4.3 (5.1)*

All data are presented as median (75th percentile). All nonparametric values were log-transformed for the statistical analysis.

A-FABP, adipocyte fatty acid-binding protein; CRP, C-reactive protein; IL-18, interleukin 18; sTNFR2, soluble tumor necrosis factor receptor 2.

**P* < 0.001.

and proinflammatory or anti-inflammatory adipokines were found ($r = -0.027$; $r = 0.19$; $r = 0.23$; $r = 0.11$; $P = \text{NS}$ for IL-18, hsPCR, sTNFR2, and adiponectin, respectively). However, after 1 year of gastric bypass a positive correlation between plasmatic levels of A-FABP and HOMA-IR ($r = 0.29$; $P = 0.01$) was observed. Among the remaining proinflammatory adipocytokines, a positive correlation was observed between sTNFR2 and age ($r = 0.35$; $P < 0.01$), fasting glucose ($r = 0.39$; $P < 0.002$), HOMA-IR ($r = 0.28$; $P < 0.03$), IL-18 ($r = 0.47$; $P < 0.001$), FFA ($r = 0.27$; $P < 0.05$), and hsCRP circulating levels ($r = 0.43$; $P = 0.001$). IL-18 circulating levels also correlated with plasmatic triglycerides ($r = 0.46$; $P < 0.0001$), hsCRP levels ($r = 0.45$; $P = 0.001$), and HOMA-IR ($r = 0.36$; $P < 0.01$). Postoperative adiponectin concentration was significantly and inversely correlated with weight ($r = -0.27$; $P < 0.05$), fat mass

Table 3 Multiple regression analysis for HOMA-IR as dependent variable in women after bariatric surgery

	β	<i>P</i>	CI 95%
BMI (kg/m ²)	0.347	0.008	0.019 to 0.119
Adiponectin (μg/ml)	-0.312	0.016	-2.05 to -0.223
A-FABP (ng/ml)	0.322	0.014	0.403 to 3.35

R: 0.530; *R*²: 0.281.

A-FABP, adipocyte fatty acid-binding protein; CI: confidence interval; HOMA-IR, homeostasis model assessment of insulin resistance.

($r = -0.28$; $P < 0.05$), fasting insulin ($r = -0.41$; $P = 0.001$), and HOMA-IR ($r = -0.31$; $P = 0.017$). A positive correlation was observed with age ($r = 0.32$; $P < 0.05$).

To evaluate the independence of the association between plasma A-FABP and HOMA-IR after bariatric surgery, a multiple linear regression analysis adjusted for age and gender was developed. BMI, adiponectin, triglycerides, FFA, and A-FABP plasmatic levels were included as independent variables and HOMA-IR as dependent variable. A-FABP remained significantly associated with HOMA-IR (Table 3).

DISCUSSION

In our study we have observed a dramatic decrease in A-FABP circulating levels 1 year after massive weight loss in morbidly obese patients, but no association with inflammatory or anti-inflammatory adipocytokines were found in this population. A positive relationship with HOMA-IR index was observed only after massive weight loss.

Evidences from animal experiments suggest that A-FABP may influence systemic inflammation. It appears to be necessary to induce a inflammatory response coordinating the lipid-mediated activation of stress kinases such as c-jun NH2-terminal kinase or inhibitor of kappa kinase (IKK) linking lipid signals to the established role of these kinases in proinflammation and anti-insulin action (13). In this sense, we expected to find a relationship between proinflammatory markers and circulating A-FABP levels. However, despite a clear improvement in these parameters after weight loss, no relationship was found at basal level or after 1 year of follow-up. Data in the literature about the relationship between inflammatory/anti-inflammatory markers and plasma A-FABP are scarce and usually related to circulating adiponectin levels, showing a negative association (11). It is difficult to give a satisfactory explanation about this absence of relationship; however, in the majority of studies the main determinant of A-FABP is the HOMA-IR index (11,16,22). In fact, in a recent work from a Chinese cohort, serum A-FABP was associated with glucose deregulation and predicted the development of type 2 diabetes with independence of cardiometabolic risk factors (17). In this sense, the independent association between A-FABP and HOMA-IR index after a multiple linear regression analysis observed in our study reinforces a predominant role of A-FABP in glucose homeostasis rather than in inflammatory pathways, at least in obese people. The mechanisms implicated in glucose homeostasis are not well

understood and may involve different pathways. The majority of data come from animal studies in mice lacking A-FABP. These mice have an altered cellular lipid transport with an increased insulin-receptor signaling, enhanced muscle AMP-activated kinase (AMP-K) activity, increased Akt phosphorylation and an increase in muscle glucose oxidation (10,23). Despite these observations may help to understand the higher insulin sensitivity in A-FABP null mice, no data about their relevance in human studies have been provided up to now. In this sense, the observed results in our obese cohort support the role of A-FABP in insulin-sensitivity pathways other than inflammatory mechanisms.

Adipose tissue expression of A-FABP has been related to circulating nonesterified fatty acid concentrations in obese subjects, trying to explain a part of the insulin resistant environment observed in obesity (24). In fact, A-FABP has been shown to physically interact with hormone-sensitive lipase and stimulate its activity, promoting adipose tissue lipolysis (25). Cytoplasmic A-FABP in adipocytes may help to prevent the toxicity of nonesterified fatty acids for the cell and its expression is reduced in adipose tissue after weight loss in morbid obesity (24). This reduction is paralleled by a fall in the bloodstream levels of this protein as has been recently demonstrated by Haider *et al.* (26) (after 6 month of bariatric surgery) and also in this work (1 year after bariatric surgery). Interestingly, no correlation between FFA serum levels and A-FABP was observed after weight loss, in accordance with a recent publication arguing that FFA circulating levels may also derive from lipolysis of plasma lipoproteins (27). Unlike the absence of correlation between HOMA-IR index and plasma levels of A-FABP described by Haider *et al.* (26) we have observed a positive relationship after weight loss. This difference may be due to the long period of follow-up included in our cohort and reinforce the role of A-FABP as a marker of components of MS (11,16–18). It is noteworthy that this association was absent before bariatric surgery, as well as with other obesity indexes like BMI or fat mass in opposite to a recent cohort of 27 morbid-obese women in whom a positive association with weight and fat mass was reported (27). Surprisingly, in the study from Engl, A-FABP showed an increase 3 months after surgery, with a progressive decrease over time, with no differences at the end of the first year of follow-up. It is difficult to explain the disagreement in A-FABP levels with our study; however, the different surgical procedures used (gastric bypass vs. adjustable gastric band) make the cohorts not fully comparable from a metabolically point of view (28). We know that the design of our study does not permit to deduce mechanistical hypothesis; however, our data suggest that there could be discordance between tissue expression and bloodstream release in the context of massive obesity. Something similar may account in obese children in whom no association between A-FABP with components of MS was found following weight reduction after 1-year obesity intervention (22). Only fat mass and leptin were related with A-FABP in that study, suggesting that this protein was not a good marker of MS in this young population.

In summary, we have observed that circulating A-FABP levels decrease after massive weight loss and are associated with HOMA-IR index after 1 year of bariatric surgery. A-FABP was not associated with inflammatory/anti-inflammatory adipocytokines in massive obese subjects. Further studies are warranted to examine the role of A-FABP in the pathogenesis of insulin resistance and to investigate the potential role of this new biomarker in the context of cardiovascular risk factors in morbid obesity.

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DISCLOSURE

The authors declared no conflict of interest.

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REFERENCES

1. Grundy SM, Brewer HB Jr, Cleeman JI *et al.* Definition of Metabolic Syndrome: report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation* 2004;109:433–438.
2. Tracy RP. Is visceral fat the “enemy within”? *Arterioscler Thromb Vasc Biol* 2001;21:881–883.
3. Moller DE, Kaufman KD. Metabolic syndrome: a clinical and molecular perspective. *Annu Rev Med* 2005;56:45–62.
4. Ferroni P, Basili S, Falco A *et al.* Inflammation, insulin resistance and obesity. *Curr Atheroscler Rep* 2004;6:424–431.
5. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab* 2004;89:2548–2556.
6. Mora S, Pressin JE. An adipocentric view of signalling and intracellular trafficking. *Diabetes Metab Res Rev* 2002;18:345–356.
7. Das UN. Is obesity an inflammatory condition? *Nutrition* 2001;7:953–966.
8. Cottam DR, Schaefer PA, Shaftan GW *et al.* Effect of surgically-induced weight loss on leukocyte indicators of chronic inflammation in morbid obesity. *Obes Surg* 2002;12:335–342.
9. Vendrell J, Broch M, Vilarrasa N *et al.* Resistin, adiponectin, ghrelin, leptin and proinflammatory cytokines: relationships in obesity. *Obes Res* 2004;12:962–971.
10. Maeda K, Cao H, Kono K *et al.* Adipocyte/macrophage fatty acid binding proteins control integrated metabolic responses in obesity and diabetes. *Cell Metab* 2005;1:107–119.
11. Xu A, Wang Y, Yu SJ *et al.* Adipocyte fatty acid-binding protein is a plasma biomarker associated with obesity and Metabolic Syndrome. *Clin Chem* 2006;52:405–413.
12. Maeda K. Role of adiponectin and adipocyte fatty acid binding protein in the metabolic syndrome. *Diabetes Res Clin Pract* 2007;77S:S17–S22.
13. Makowski L, Hotamisligil GS. Fatty acid binding-proteins—the evolutionary crossroads of inflammatory and metabolic responses. *J Nutr* 2004;134:2464S–2468S.
14. Hotamisligil GS, Johnson RJ, Distel RJ *et al.* Uncoupling of obesity from insulin resistance through a targeted mutation in aP2, the adipocyte fatty acid binding protein. *Science* 1996;274:1377–1379.
15. Boord JB, Maeda K, Makowski L *et al.* Adipocyte fatty acid binding protein, aP2, alters late atherosclerotic lesion formation in severe hypercholesterolemia. *Arterioscler Thromb Vasc Biol* 2002;22:1686–1691.
16. Xu A, Tso AW, Cheung BM *et al.* Circulating adipocyte-fatty acid binding protein levels predict the development of the metabolic syndrome: a 5 year prospective study. *Circulation* 2007;115:1537–1543.
17. Tso A, Xu AW, Sham P *et al.* Serum adipocyte fatty acid-binding protein as a new biomarker predicting the development of type 2 diabetes. *Diabetes Care* 2007;30:2667–2672.
18. Stejskal D, Karpisek M. Adipocyte fatty acid binding protein in Caucasian population: a new marker of metabolic syndrome? *Eur J Clin Invest* 2006;36:621–625.

19. Tuncman G, Erbay E, Hom X *et al*. A genetic variant at the fatty acid binding protein aP2 locus reduces the risk for hypertriglyceridemia, type 2 diabetes and cardiovascular disease. *Proc Natl Acad Sci USA* 2006;103:6970–6975.
20. Capella RF, Capella JF. Reducing early technical complications in gastric bypass surgery. *Obes Surg* 1997;7:149–156.
21. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of the low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;18:499–502.
22. Reinehr T, Stoffel-Wagner B, Roth CL. Adipocyte fatty acid-binding protein in obese children before and after weight loss. *Metabolism* 2007;56:1735–1741.
23. Baar RA, Dingfelder CS, Smith LA *et al*. Investigation of in vivo fatty acid metabolism in AFABP/aP2^{-/-} mice. *Am J Physiol Endocrinol Metab* 2005;288:E187–E193.
24. Fisher RM, Hoffstedt J, Hotamisligil GS *et al*. Effects of obesity and weight loss on the expression of proteins involved in fatty acid metabolism in human adipose tissue. *Int J Obes Relat Metab Disord* 2002;26:1379–1385.
25. Shen WJ, Liang Y, Hong R *et al*. Characterization of the functional interaction of adipocyte lipid-binding protein with hormone-sensitive lipase. *J Biol Chem* 2001;276:49443–49448.
26. Haider DG, Schindler K, Bohdjalian A *et al*. Plasma adipocyte and epidermal fatty acid-binding protein is reduced after weight loss in obesity. *Diabetes Obes Metab* 2007;9:761–763.
27. Engl J, Ciardi C, Tatarczyk T *et al*. A-FABP—a biomarker associated with the metabolic syndrome and/or an indicator of weight change? *Obesity (Silver Spring)* 2008;16:1838–42.
28. Lee H, Kim D, Lee S, Nam K, Kim E. Initial evaluation of laparoscopic Roux-en-Y gastric bypass and adjustable gastric banding in Korea: a single institution study. *Obes Surg* 2008; e-pub ahead of print 29 April 2008.