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Decrease of Circulating SAA is Correlated with Reduction of Abdominal SAA Secretion During Weight Loss

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Abstract

Objective—The study goal was to determine the effect of weight loss (WL) alone and with aerobic exercise (WL+AEX) on SAA levels and adipose SAA secretion from gluteal and abdominal depots.

Design and Methods—Ninety-six overweight or obese postmenopausal women undertook a 6 month WL alone (n=47) or with aerobic exercise training (n=49) (6 months WL and WL+AEX are considered WL when groups were combined). Their serum SAA levels, body weight and adipose SAA secretion *ex vivo* from gluteal and abdominal depot were measured before and after WL interventions.

Results—The participants lost an average of 8% body weight with a 10% decrease of serum SAA. Serum SAA levels remained significantly correlated with body weight before and after WL. However, the changes of serum SAA level did not correlate with changes of body weight. The gluteal adipose tissue secreted ~50% more SAA than the abdominal tissue, but the changes of abdominal, but not gluteal, SAA secretion correlated ($R^2 = 0.19$, $p < 0.01$) with those of serum SAA levels during WL.

Conclusion—We find no linear correlation between the decrease in systemic SAA and WL. There is a depot-dependent difference in adipose SAA secretion and abdominal SAA secretion which may partially account for the systemic SAA reduction during WL.

Introduction

Obesity is characterized by an elevation of local adipose (1, 2) as well as systemic low-grade systemic inflammation (3, 4), which contributes to its associated comorbidities such as insulin resistance, type 2 diabetes and cardiovascular diseases (CDV) (5, 6). Whether and

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how these two inflammatory processes relate in humans is not well understood. Acute-phase protein serum amyloid A (SAA) is selectively expressed in adipose tissue and its tissue expression and circulating levels increase in obese subjects (7–9), suggesting that SAA may serve as a molecular link between adipose tissue and systemic inflammation. Several studies show that SAA plays an active role in regulating the inflammation process (7–9), and suggest that SAA is a pro-inflammatory cytokine that may be responsible for macrophage infiltration in the adipose tissue (10). A recent study shows that elevations in systemic SAA by transgenic overexpression increases circulating serum IL-6 and TNFα and significantly promotes atherosclerosis in mice (11), thus providing direct evidence that SAA is a causative factor for systemic inflammation and CVD in animals.

Weight loss (WL) via life-style change with or without aerobic exercise (AEX) is an effective regimens for prevention and treatment for obesity and its associated metabolic disturbances by lowering circulating SAA levels (12, 13) and adipose SAA expression (13, 14). However, few studies have examined the effects of WL+AEX on adipose SAA secretion; thus, the relationship between changes in adipose SAA secretion and systemic SAA levels during WL remains unknown.

Adipose tissues of different depots have distinctive molecular, cellular and metabolic properties (15–17) with discrete systemic metabolic and endocrine consequences (18). Indeed, the gene expression of fatty acid amide hydrolase (FAAH), an enzyme participating in endocannabinoid synthesis and implicated in adipocyte dysfunction (19), is higher in the abdominal than gluteal adipose tissue and that WL by hypocaloric feeding decreases the gene expression of gluteal, but not abdominal, cannabinoid receptor 1 and FAAH. These observations suggest that abdominal and gluteal adipose tissue respond to metabolic and nutritional challenges differently; this study examines whether there are differences in SAA secretion between abdominal and gluteal subcutaneous fat depots to WL with and without AEX.

Considering that SAA plays a pivotal role in mediating inflammation and that the reduction of circulating SAA may be responsible for the reduced systemic inflammation in lifestyle change-induced WL, it will be valuable to understand the effects of WL on systemic and adipose SAA levels. As the adipose tissue is a prominent organ that expresses and releases SAA, the goal of this study was to determine 1) whether there is a relationship between changes of systemic SAA levels and body weight/fat mass, and 2) whether there are differences in SAA secretion between gluteal and abdominal depots and if these changes are related to circulating SAA during WL.

Research Design and Methods

Human subjects

The Institutional Review Board of the University of Maryland approved all human studies, and each volunteer provided written informed consent to participate. All subjects were relatively healthy, non-diabetic by fasting glucose (<126mg/dl), but overweight or obese [body mass index (BMI) > 25 kg/m^2, range of 25–48 kg/m^2] women between the ages of 49 and 76 years. The women were postmenopausal and had not menstruated for ≥1 yr. Details

about this WL program have been described elsewhere (20). In brief, all women in WL and WL+AEX attended weekly WL classes led by a registered dietitian. Women were instructed to reduce their caloric intake by 300–500 kcal/day. For the WL+AEX intervention, women exercised three times per week for six months using treadmills and elliptical trainers as described (20). Fat mass was determined by dual-energy X-ray absorptiometry (Prodigy; Lunar Radiation Corp., Madison, WI). Blood samples were obtained from an antecubital vein after a 12-hour overnight fast, 36–48 hours after the last bout of exercise in WL+AEX, and stored at −80 °C until analysis. Fasting serum levels of SAA were measured before and after the intervention in all participants.

Adipose tissue culture and SAA measurement

Some of the participants underwent adipose tissue biopsy before and after the WL regimen. Biopsies were performed 36–48 hours after the last bout of exercise in the WL+AEX group. Abdominal and gluteal adipose tissue samples were obtained from overnight fasted subjects by aspiration with a 3 mm cannula under local anesthesia with lidocaine as previously described (21). Adipose tissue fragments were incubated for 3 hours in M199-1% BSA (~100 mg/ml) and the media was collected and stored at −80°C as previously described (22), until SAA assay.

Serum SAA levels were measured with an enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions (BioSource, Camarillo, CA, USA). For high sensitive measurement of SAA levels in a small volume of conditional media of the acute human adipose culture, a Meso Scale Discovery (MSD) multiplex electrochemiluminescence (ECL) assay (Meso Scale Discovery, Gaithersburg, MD, USA) was employed. The SAA detection sensitivities by ELISA and MSD were 5 ng/ml and 8 pg/ml, respectively. For ELISA, the intra- and inter-assay coefficients of variation (CV) were 5% and 8%, respectively, whereas for MSD, the intra-assay CV was 4%. The inter-assay CV was not determined since all samples were assayed in one time. The correlation co-efficient between the two assays was 0.87. All samples were assayed in duplicate and the mean was used for data analysis.

Statistical analysis

Data are expressed as mean ± SEM unless otherwise specified. Variables that were not normally distributed were logarithm transformed for analysis. The Student's unpaired or paired *t* test was performed when appropriate. Significance of correlations between two variables was determined by the Spearman rank correlation coefficient. Graphpad Prism 5 (La Jolla, CA, USA) was used for statistical analysis and differences were considered to be significant at $p < 0.05$.

Results

Effects of WL on body weight and serum SAA

A total of 96 postmenopausal women, aged 60 years ± 0.79 (mean ± SE) with an average body weight of 85.9 ± 2.4 kg, participated in the study. Of them, 47 subjects were enrolled into the WL program and 49 subjects into the WL+AEX program. Fig. 1 shows that at the

basal level, serum SAA was well correlated with BMI and body fat mass (R = 0.46 and 0.44, respectively, $p < 0.0001$ for both). After six months of the WL programs, the participants lost an average of 7.9 % body weight with a reduction of 10.4% serum SAA. The WL group lost about 7.7 % body weight from 87.4 ± 2.4 to 80.7 ± 2.4 kg, whereas SAA decreased by 11.4 % from 42.5 ± 4.8 to 35.1 ± 4.5 μg/ml. The WL+AEX group lost 8.1% body weight from 84.4 ± 1.9 to 77.6 ± 1.8 kg, whereas SAA decreased by 10.6 % from 32.5 ± 4.1 to 27.5 ± 3.9 μg/ml ($p < 0.01$ for all comparisons of pre- vs. post-WL). No statistical difference was observed in the extent of changes of body weight and SAA between the WL and WL +AEX groups during WL. Thus, both groups were combined for the regression analyses. The relationships between serum SAA and BMI (R = 0.46, $p < 0.0001$) and fat mass (R = 0.44, $p < 0.0001$) remained strong post-WL (Fig. 1c).

Relationships between the changes of serum SAA and body weight during WL

The significant correlations between serum SAA levels and fat mass at baseline were maintained after WL (Figs. 1a and 1c). This suggests a possible relationship between the changes of the systemic SAA vs. fat mass. However, despite the fact that the extent of overall reduction of serum SAA and BMI was comparable to the degree of WL (~ 10%, Fig. 1b) in the whole cohort, the inter-individual changes in serum SAA levels varied dramatically, ranging from −84 to 248% compared to the relatively narrow changes of WL between −2.1 and −24.0 %. There was no correlation between the changes of serum SAA and the changes in body weight expressed in absolute or relative terms with respect to either percentage (Fig. 2) or log-transformed percentage (not shown) in participants pooled or separated by group.

Effects of WL on SAA secretion

Reduced serum SAA levels post-WL could be a result of normal SAA secretion from reduced fat mass and/or reduced secretion from the adipose or other tissues. To investigate these possibilities, 42 subjects underwent abdominal and gluteal adipose tissue biopsy before and after WL and the adipose SAA secretion was measured *ex vivo*. Since there was no significant difference in the effect of WL vs. WL+AEX on adipose SAA secretion (data not shown), SAA secretion data were pooled from both groups for subsequent statistical analyses. As a result (Fig. 3), gluteal adipose tissue secreted ~50% more SAA than the abdominal ($p < 0.01$, Fig. 3a). The amount of SAA secreted from the gluteal region was well correlated with that from the abdominal depot before (R = 0.54, $p < 0.001$) and after (R = 0.74, $p < 0.001$) WL (Fig. 3b). Notably, there was a larger variation of up to 100-fold difference in SAA secretion before and after WL. Thus, although the overall adipose SAA secretion decreased by 30% ($p = 0.09$) and 22% ($p = 0.6$) in abdominal and gluteal depots, respectively, after WL, the reduction after WL did not reach statistical significance.

Effects of WL on relationships between changes of adipose SAA secretion and serum SAA levels

We examined the relationship between changes in systemic SAA levels and adipose secretion from abdominal and gluteal regions after WL. Spearman analysis revealed a

moderate correlation of the changes of serum SAA levels with changes in SAA secretion in abdominal ($R = 0.43$, $p < 0.01$), but not in gluteal, adipose tissues (Fig. 4).

Discussion

Numerous studies demonstrate that SAA is an adipokine that is elevated in the circulation in obesity and considered to be a mediator between obesity and associated insulin resistance, low-grade inflammation and risk for CVD (23–25). To better understand the relationship between adipose and systemic SAA levels, we conducted this study and examined the changes of adipose SAA secretion *ex vivo* in relationship to its circulating level in a cohort of well-characterized postmenopausal women who went through WL via WL or WL+AEX (20). Our results show that serum SAA levels correlate with BMI and fat mass in overweight or obese subjects before WL. An average loss of 8% body weight resulted in a comparable reduction of systemic SAA after the six-month WL program alone or with AEX. Moreover, the relationship of systemic SAA and body fat mass remained after WL. These observations further support that BMI/fat mass is a determinant of circulating SAA levels. However, no correlation was detected between the changes of BMI vs. changes in serum SAA at the individual level (Fig. 2). This is a somewhat unexpected finding, considering that serum SAA levels are well correlated with BMI before and after WL (Fig. 1c). A possible explanation is that a marked variation of serum SAA relative to the narrow changes of body weight during the WL period significantly reduced the statistical power to detect such a correlation. Another explanation is that fat mass accounts for ~19 and 26 % of systemic SAA variation in pre- and post-WL states (Fig. 1), and fat mass-independent mechanisms (e.g., the rate of adipose SAA secretion and non-adipose SAA secretion) have a greater effect to determine systemic SAA levels.

Since there are regional differences in gene expression and regulation in the subcutaneous fat depot (26–28), we examined the changes of SAA release *ex vivo* of adipose samples from abdominal and gluteal regions. Results show that adipose tissue in the gluteal depot secretes ~50 % more SAA than that of the abdominal, both before and after WL. A strong correlation is observed in the amount of SAA secretion between the two depots, suggesting a similar regulatory mechanism for adipose SAA production between the depots. Remarkably, a large individual variation in SAA secretion was observed during WL, indicating that the rate of SAA secretion is highly variable among individuals before and after WL. As a result, the dramatic ~25% reduction in SAA secretion after WL did not reach statistical significance.

This study finds a moderate correlation between the reduction of serum SAA levels and that of abdominal SAA secretion ($R = 0.43$, Fig. 4), suggesting that the decrease in abdominal SAA secretion could contribute to the lower SAA in circulation after WL. It is intriguing to note that although gluteal adipose tissue releases more SAA than abdominal adipose tissue, only abdominal adipose tissue SAA secretion is significantly related to circulating SAA levels. One possible explanation is that the local abdominal condition facilitates the release of SAA at the whole body level. This is supported by the finding that the blood flow rate in abdominal depot is three times that in the gluteal depot (29). Moreover, the abdominal skin temperature is 1°C higher than the gluteal (33.3 vs. 32.2 °C), which may enhance SAA release from abdominal depot into the circulation. Another possibility is via an indirect

mechanism, wherein abdominal adipose tissue releases more pro-inflammatory fatty acids systemically (29). The local SAA reduction would lower lipolysis and the output of fatty acids and inflammatory cytokines into the circulation, resulting in a systemic reduction in inflammatory status and SAA production from non-adipose tissue, such as the liver.

Collectively, our data further support the fact that BMI and fat mass are a determinant of systemic SAA levels. However, the post-WL systemic SAA reduction appears not to be the direct consequence of the reduction in BMI or fat mass alone and may be attributable to other chronic diseases like stress, hypertension and osteoarthritis (30–32). Such a large variation might have obscured or overwhelmed the contribution of fat mass changes to systemic SAA levels during WL. Reasons for the greater individual pre- vs. post-WL variation in *ex vivo* SAA secretion from adipose tissue are unclear. Possible explanations include that SAA is a highly and rapidly regulated protein; hence, the large SAA variation in the acute explant study may reflect the actual state of rapid dynamics of SAA production and secretion as well as newly synthesized SAA at the time of fat biopsy. Further, the finding that in the same individual, the gluteal and abdominal SAA secretion correlate well pre- and post-WL (Fig. 3), suggests similar regulatory mechanisms may exist within the two fat regions in response to the loss of body weight.

In summary, these findings show that BMI and fat mass are determinants of the circulating SAA levels. The overall extent of serum SAA decrease is comparable to that of weight loss with and without exercise in the cohort, but only collectively do the changes in SAA directly relate to the reduction of fat mass. We also find that the gluteal adipose tissue secretes ~50% SAA more than the abdominal adipose tissue, and that adipose SAA secretion tends to decrease after weight loss; however, only the reduction of abdominal SAA secretion correlated with that of systemic SAA. Thus, both reduced fat mass and decreased abdominal adipose SAA secretion, along with other yet unidentified factors, contribute to the reduction in systemic SAA levels after weight loss.

Acknowledgments

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References

1. Chen A, Mumick S, Zhang C, Lamb J, Dai H, Weingarth D, Mudgett J, Chen H, MacNeil DJ, Reitman ML, et al. Diet induction of monocyte chemoattractant protein-1 and its impact on obesity. Obes Res. 2005; 13:1311–1320. [PubMed: 16129712]
2. Xu H, Barnes GT, Yang Q, Tan G, Yang D, Chou CJ, Sole J, Nichols A, Ross JS, Tartaglia LA, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest. 2003; 112:1821–1830. [PubMed: 14679177]
3. Solinas G. Molecular pathways linking metabolic inflammation and thermogenesis. Obes Rev. 2012; 13(Suppl 2):69–82. [PubMed: 23107261]
4. Hummasti S, Hotamisligil GS. Endoplasmic reticulum stress and inflammation in obesity and diabetes. Circ Res. 2010; 107:579–591. [PubMed: 20814028]

5. Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. Nat Rev Immunol. 2011; 11:85–97. [PubMed: 21252989]
6. Schmidt AM. Insulin resistance and metabolic syndrome: mechanisms and consequences. Arterioscler Thromb Vasc Biol. 2012; 32:1753. [PubMed: 22815339]
7. Whitehead AS, de Beer MC, Steel DM, Rits M, Lelias JM, Lane WS, de Beer FC. Identification of novel members of the serum amyloid A protein superfamily as constitutive apolipoproteins of high density lipoprotein. J Biol Chem. 1992; 267:3862–3867. [PubMed: 1740433]
8. Hatanaka E, Furlaneto CJ, Ribeiro FP, Souza GM, Campa A. Serum amyloid A-induced mRNA expression and release of tumor necrosis factor-alpha (TNF-alpha) in human neutrophils. Immunol Lett. 2004; 91:33–37. [PubMed: 14757367]
9. Furlaneto CJ, Campa A. A novel function of serum amyloid A: a potent stimulus for the release of tumor necrosis factor-alpha, interleukin-1beta, and interleukin-8 by human blood neutrophil. Biochem Biophys Res Commun. 2000; 268:405–408. [PubMed: 10679217]
10. Han CY, Subramanian S, Chan CK, Omer M, Chiba T, Wight TN, Chait A. Adipocyte-derived serum amyloid A3 and hyaluronan play a role in monocyte recruitment and adhesion. Diabetes. 2007; 56:2260–2273. [PubMed: 17563062]
11. Dong Z, Wu T, Qin W, An C, Wang Z, Zhang M, Zhang Y, Zhang C, An F. Serum amyloid A directly accelerates the progression of atherosclerosis in apolipoprotein E-deficient mice. Mol Med. 2011; 17:1357–1364. [PubMed: 21953420]
12. Imayama I, Ulrich CM, Alfano CM, Wang C, Xiao L, Wener MH, Campbell KL, Duggan C, Foster-Schubert KE, Kong A, et al. Effects of a caloric restriction weight loss diet and exercise on inflammatory biomarkers in overweight/obese postmenopausal women: a randomized controlled trial. Cancer Res. 2012; 72:2314–2326. [PubMed: 22549948]
13. O'Brien KD, Brehm BJ, Seeley RJ, Bean J, Wener MH, Daniels S, D'Alessio DA. Diet-induced weight loss is associated with decreases in plasma serum amyloid A and C-reactive protein independent of dietary macronutrient composition in obese subjects. J Clin Endocrinol Metab. 2005
14. Lappalainen T, Kolehmainen M, Schwab U, Pulkkinen L, Laaksonen DE, Rauramaa R, Uusitupa M, Gylling H. Serum concentrations and expressions of serum amyloid A and leptin in adipose tissue are interrelated: the Genobin Study. Eur J Endocrinol. 2008; 158:333–341. [PubMed: 18299466]
15. Min JL, Nicholson G, Halgrimsdottir I, Almstrup K, Petri A, Barrett A, Travers M, Rayner NW, Magi R, Pettersson FH, et al. Coexpression network analysis in abdominal and gluteal adipose tissue reveals regulatory genetic loci for metabolic syndrome and related phenotypes. PLoS Genet. 2012; 8:e1002505. [PubMed: 22383892]
16. Berman DM, Nicklas BJ, Rogus EM, Dennis KE, Goldberg AP. Regional differences in adrenoceptor binding and fat cell lipolysis in obese, postmenopausal women. Metabolism. 1998; 47:467–473. [PubMed: 9550547]
17. Tchoukalova YD, Koutsari C, Karpyak MV, Votruba SB, Wendland E, Jensen MD. Subcutaneous adipocyte size and body fat distribution. Am J Clin Nutr. 2008; 87:56–63. [PubMed: 18175737]
18. Manolopoulos KN, Karpe F, Frayn KN. Gluteofemoral body fat as a determinant of metabolic health. Int J Obes (Lond). 2010; 34:949–959. [PubMed: 20065965]
19. Engeli S, Bohnke J, Feldpausch M, Gorzelniak K, Janke J, Batkai S, Pacher P, Harvey-White J, Luft FC, Sharma AM, et al. Activation of the peripheral endocannabinoid system in human obesity. Diabetes. 2005; 54:2838–2843. [PubMed: 16186383]
20. Ryan AS, Ortmeyer HK, Sorkin JD. Exercise with calorie restriction improves insulin sensitivity and glycogen synthase activity in obese postmenopausal women with impaired glucose tolerance. Am J Physiol Endocrinol Metab. 2012; 302:E145–152. [PubMed: 22008454]
21. Dowling HJ, Fried SK, Pi-Sunyer FX. Insulin resistance in adipocytes of obese women: effects of body fat distribution and race. Metabolism. 1995; 44:987–995. [PubMed: 7637656]
22. Russell CD, Petersen RN, Rao SP, Ricci MR, Prasad A, Zhang Y, Brolin RE, Fried SK. Leptin expression in adipose tissue from obese humans: depot-specific regulation by insulin and dexamethasone. Am J Physiol. 1998; 275:E507–515. [PubMed: 9725819]

23. Yang RZ, Lee MJ, Hu H, Pollin TI, Ryan AS, Nicklas BJ, Snitker S, Horenstein RB, Hull K, Goldberg NH, et al. Acute-Phase Serum Amyloid A: An Inflammatory Adipokine and Potential Link between Obesity and Its Metabolic Complications. PLoS Med. 2006; 3:e287. [PubMed: 16737350]
24. Sjoholm K, Palming J, Olofsson LE, Gummesson A, Svensson PA, Lystig TC, Jennische E, Brandberg J, Torgerson JS, Carlsson B, et al. A microarray search for genes predominantly expressed in human omental adipocytes: adipose tissue as a major production site of serum amyloid A. J Clin Endocrinol Metab. 2005; 90:2233–2239. [PubMed: 15623807]
25. Poitou C, Coussieu C, Rouault C, Coupaye M, Cancello R, Bedel JF, Gouillon M, Bouillot JL, Oppert JM, Basdevant A, et al. Serum amyloid A: a marker of adiposity-induced low-grade inflammation but not of metabolic status. Obesity (Silver Spring). 2006; 14:309–318. [PubMed: 16571858]
26. You T, Disanzo BL, Wang X, Yang R, Gong D. Adipose tissue endocannabinoid system gene expression: depot differences and effects of diet and exercise. Lipids Health Dis. 2011; 10:194. [PubMed: 22035053]
27. Karastergiou K, Fried SK, Xie H, Lee MJ, Divoux A, Rosencrantz MA, Chang RJ, Smith SR. Distinct developmental signatures of human abdominal and gluteal subcutaneous adipose tissue depots. J Clin Endocrinol Metab. 2013; 98:362–371. [PubMed: 23150689]
28. Rantalainen M, Herrera BM, Nicholson G, Bowden R, Wills QF, Min JL, Neville MJ, Barrett A, Allen M, Rayner NW, et al. MicroRNA expression in abdominal and gluteal adipose tissue is associated with mRNA expression levels and partly genetically driven. PLoS One. 2011; 6:e27338. [PubMed: 22102887]
29. Tan GD, Goossens GH, Humphreys SM, Vidal H, Karpe F. Upper and lower body adipose tissue function: a direct comparison of fat mobilization in humans. Obes Res. 2004; 12:114–118. [PubMed: 14742849]
30. Uhlar CM, Whitehead AS. Serum amyloid A, the major vertebrate acute-phase reactant. Eur J Biochem. 1999; 265:501–523. [PubMed: 10504381]
31. Yamada T. Serum amyloid A (SAA): a concise review of biology, assay methods and clinical usefulness. Clin Chem Lab Med. 1999; 37:381–388. [PubMed: 10369107]
32. Urieli-Shoval S, Linke RP, Matzner Y. Expression and function of serum amyloid A, a major acute-phase protein, in normal and disease states. Curr Opin Hematol. 2000; 7:64–69. [PubMed: 10608507]

What is already known about this subject?

- SAA is an adipokine and considered to be a link between obesity and its associated diseases.
- Circulating SAA is correlated with fat mass/BMI.
- Weight loss decreases adipose SAA gene expression and secretion in small scale studies.

What does this study add?

- Largest sample size study of weight loss on adipose SAA secretion in humans.
- The finding of adipose depot-dependent difference in SAA secretion: that the gluteal adipose tissue/per tissue weight secretes 50% more SAA than the abdominal.
- The changes of abdominal, but not gluteal, fat SAA secretion correlate with those of serum SAA during WL and account for ~19% variation of the systemic SAA reduction during WL. This suggests that abdominal SAA secretion may partially account for the systemic SAA reduction during WL and that the mechanisms for WL-induced systemic reductions in cytokines are complex, and not simply related to changes in fat mass.

Fig 1a.

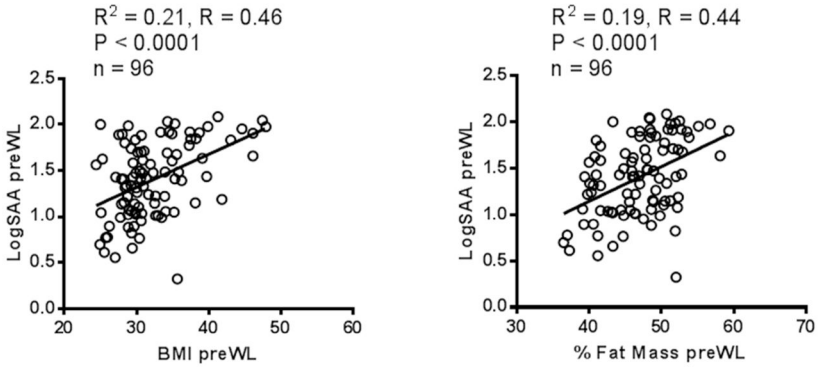

Fig.1b

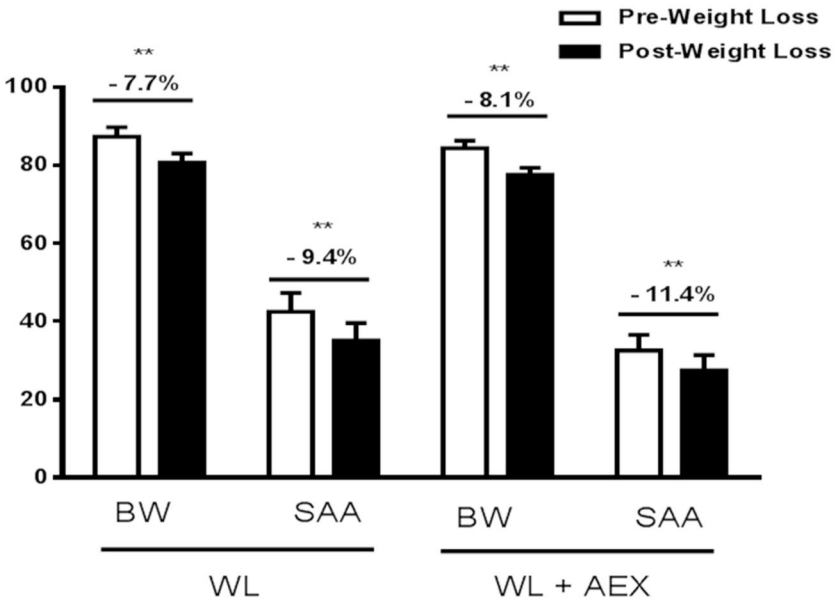

Fig 1c.

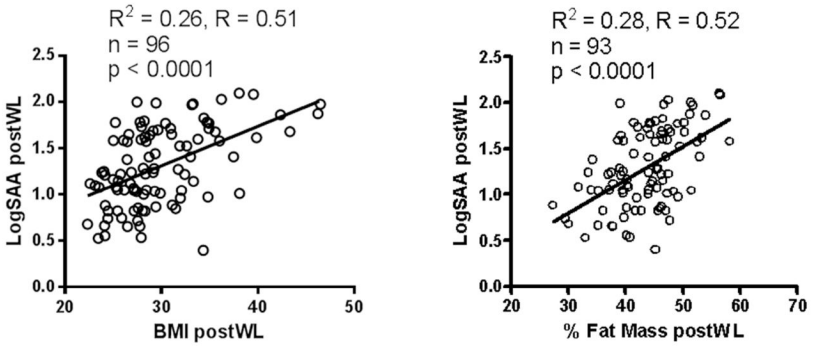

Figure 1. Change of serum SAA levels and its relationship with BMI/fat mass before and after WL

A. Relationship between BMI and % Fat Mass and Serum SAA pre-WL. Linear correlation analysis of serum SAA levels (μg/ml, log-transformed and presented) with BMI and percentage of fat mass (% of fat mass) pre-WL in 96 overweight or obese postmenopausal women. **B.** Changes in Body Weight (BW) and SAA after WL and WL+AEX. 47 subjects underwent a WL program and 49 subjects received WL +AEX. SAA levels (μg/ml) and body weight (kg) changes were compared before and after WL (**: $p < 0.01$, paired t-test) with the mean % reduction of SAA and body weight shown. No difference was detected between WL vs. WL +AEX treatment by two-way ANOVA. **C.** Relationship between BMI and % Fat Mass and Serum SAA post-WL. Linear and regression analysis of serum SAA levels (log-transformed) with BMI and percentage of fat mass post-WL in the 96 participants.

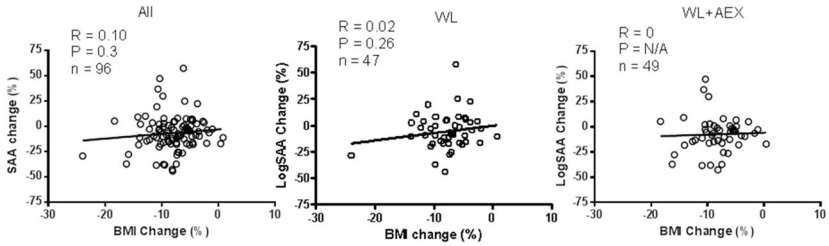

Figure 2.
Relationship between changes in BMI and changes in serum SAA.

Fig. 3a

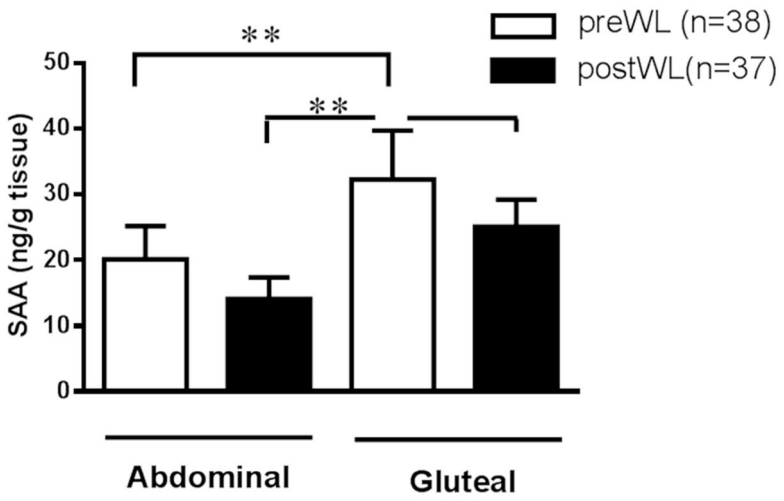

Fig. 3b

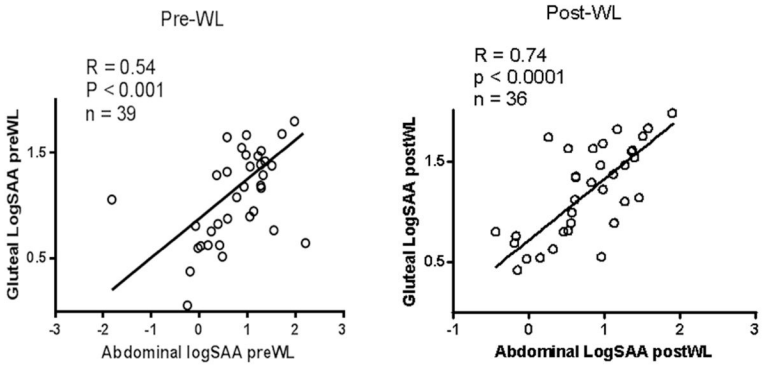

Figure 3. Adipose SAA secretion from subcutaneous abdominal and gluteal depots before and after WL

A. Adipose SAA secretion before and after weight loss. Data were expressed as mean ± SE. **: $p < 0.01$ between the two depots in pre- or post-WL state. **B.** Correlation between Abdominal and Gluteal Adipose SAA Secretion. A total of forty-four subjects had fat biopsies at abdominal and gluteal depots before and after WL. SAA secreted *ex vivo* from the acute adipose tissue culture (ng SAA/g fat tissue/3 hours) were measured in conditioned media. Data were log-transformed for analyses.

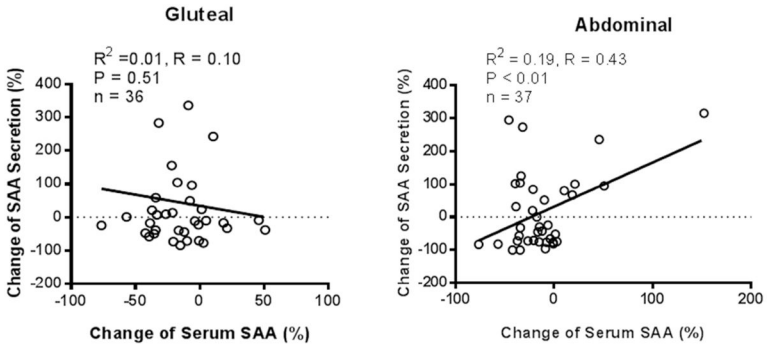

Figure 4.

Correlation of the change in systemic SAA with the change in adipose SAA secretion from abdominal, but not gluteal, adipose depot during WL.