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Changes of systemic microinflammation after weight loss and regain — a five-year follow up study

Wpływ redukcji i przyrostu masy ciała na zmiany układowej przewlekłej reakcji zapalnej — 5-letnia obserwacja

Magdalena Olszanecka-Glinianowicz[1], Jerzy Chudek[2], Adam Szromek[3], Barbara Zahorska-Markiewicz[4]

[1]Health Promotion and Obesity Management Unit, Department of Pathophysiology, Medical University of Silesia, Katowice, Poland
[2]Pathophysiology Unit, Departmen t of Pathophysiology, Medical University of Silesia, Katowice, Poland
[3]The Silesian University of Technology, Faculty of Organisation and Management, Gliwice, Poland
[4]Obesity Management Clinic "WAGA" Katowice, Poland

Abstract

Introduction: The aim of this study was to evaluate the influence of body mass changes on plasma concentrations of proinflammatory cytokines in obese women after the initially obtained weight reduction in a five-year follow-up period.
Material and methods: Thirty out of 42 women with simple obesity (age 41.8 ± 11.9 years; BMI 36.5 ± 4.6 kg/m^2) who achieved a greater than 5% weight loss at the end of a three-month weight loss programme were re-examined after five years. In addition to anthropometric and body composition measurements, plasma concentrations of TNF-alpha, sTNFRs and IL-6 were determined.
Results: The mean weight loss after the three-month weight loss programme was 7.9 ± 4.4 kg. After five years, body mass was still lower than initially in 14 women, while in 16 it was higher (the so-called 'yo-yo effect'). A significant decrease of plasma TNF-α and IL-6 and increase of sTNFR1 and sTNFR2 levels obtained after weight loss therapy were maintained after five years, including in the subgroup with the yo-yo effect. During the follow-up period, the increase of body fat mass was similar in the subgroup that maintained reduced weight (+4.4 ± 10.7 kg) and in the subgroup with the yo-yo effect (+4.1 ± 7.1 kg), while a significant difference was found in changes of body free fat mass (–7.1 ± 7.1 *v.* –0.7 ± 4.5 kg, respectively).
Conclusions: The yo-yo effect has a modest influence on systemic microinflammation and seems not to abolish the benefit achieved via a weight loss programme. This may suggest that the persistence of changes in lifestyle implemented during the programme such as regular physical activity and diet composition may have a significant impact on the level of systemic microinflammation in the obese. **(Endokrynol Pol 2012; 63 (6): 432–438)**

Key words: *tumour necrosis factor, interleukin-6, body mass changes*

Streszczenie

Wstęp: Celem pracy była ocean wpływu zmian masy ciał w pięcioletniej obserwacji na stężenie w osoczu cytokin prozapalnych u otyłych kobiet po wcześniejszej redukcji masy ciała.
Materiał i metody: Trzydzieści z 42 kobiet z otyłością prostą bez chorób towarzyszących (wiek 41,8 ± 11,9 lat; BMI 36,5 ± 4,6 kg/m^2), które w czasie trzymiesięcznego programu uzyskały co najmniej 5% redukcję masy ciała, zostało zbadanych ponownie po 5 latach. Wykonano pomiary antropometryczne i składu ciała oraz oznaczono stężenie w osoczu TNF-alfa, sTNFRs i IL-6.
Wyniki: Średnia redukcja masy ciała w czasie 3 miesięcznego programu wynosiła 7,9 ± 4,4 kg. Po 5 latach u 14 kobiet masa ciała była nadal niższa niż początkowa, podczas gdy u 16 była wyższa (efekt jo-jo). Istotne obniżenie stężeń w osoczu TNF-α i IL-6 oraz wzrost stężeń sTNFR1 i sTNFR2, które zaobserwowano po redukcji masy ciała, utrzymały się po okresie 5 lat również w podgrupie, w której wystąpił efekt jo-jo. W czasie obserwacji przyrost masy tłuszczu był porównywalny w podgrupie, która utrzymała zredukowaną masę ciała (+ 4,4 ± ± 10,7 kg) i w podgrupie, w której wystąpił efekt jo-jo (+ 4,1 ± 7,1 kg). Podczas gdy w zmianach masy beztłuszczowej zaobserwowano istotne różnice (odpowiednio –7,1 ± 7,1 *v.* –0,7 ± 4,5 kg).
Wnioski: Efekt jo-jo wywiera niewielki wpływ na nasilenie układowej reakcji zapalnej i wydaje się nie powodować utraty korzyści osiągniętych w czasie programu redukcji masy ciała. Może to sugerować, że kontynuowanie zmian stylu życia realizowanych w czasie programu, takich jak regularna aktywność fizyczna i skład diety wywierają istotny wpływ na nasilenie układowej reakcji zapalnej u otyłych. **(Endokrynol Pol 2012; 63 (6): 432–438)**

Słowa kluczowe: *czynnik martwicy nowotworów, interleukina-6, zmiany masy ciała*

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Magdalena Olszanecka-Glinianowicz M.D., Ph.D., Health Promotion and Obesity Management Unit Department of Pathophysiology Medical University of Silesia, Medyków St. 18, 40–752 Katowice, Poland, tel./fax. + 48 32 252 60 91, e-mail: magols@esculap.pl

Introduction

There is no doubt that obesity, namely an excessive accumulation of visceral adipose tissue, is a cause of systemic microinflammation. Numerous studies have revealed elevated circulating TNF-α and IL-6 levels in obese subjects [1–7]. Increasing adipocytes volume during weight gain is followed by infiltration of adipose tissue with macrophages that become a source of cytokines and stimulator of their synthesis by adipocytes [8–13]. Increased release of proinflammatory cytokines in adipose tissue is followed by changes of adipokine synthesis, impaired lipids accumulation in adipocytes, and insulin resistance development [14, 15]. These disturbances are the reason for ectopic lipids accumulating in myocytes and hepatocytes, with the subsequent development of insulin resistance within these tissues [16–18]. Moreover, changes of adipokines release, especially elevated TNF-α and IL-6 as well as low adiponectin level, are factors inducing peripheral insulin resistance [19,20]. Systemic microinflammation associated with obesity is also a cause of atherosclerosis [21], hypertension [22] and nonalcoholic fatty liver disease [23, 24] development.

It has been shown that as little as a 5–10% weight loss results in significant improvements of insulin sensitivity, lipid profile and blood pressure [25–28]. Our previously published studies revealed that an approximately 10% weight loss is associated with significant decreases of circulating TNF-α and IL-6 levels [29, 30]. However, we observed no correlation between reduced levels of these proinflammatory cytokines and insulin sensitivity improvement [30, 31]. Diminished systemic microinflammation after weight loss has also been revealed by several other studies [32–35]. The results of our recently published study are particularly interesting in this regard, as they revealed that plasma TNF-α level is an early event in abdominal fat accumulation and that further fat mass gain does not enhance circulating TNF-α levels [36]. However, there is no data showing how the yo-yo effect affects the concentration of TNF-α, sTNFRs and IL-6. Therefore, the aim of this study was to evaluate the impact of body mass changes on plasma concentrations of proinflammatory cytokines after a five-year follow-up in obese women who had achieved an initial weight reduction.

Material and methods

Forty-two obese women without any concomitant diseases who had participated in a three-month group weight loss programme in 2000 and 2001 and obtained significant weight loss (i.e. 5% or more) were invited for re-examination after five years. The characteristics of the initial study groups and programme recommendations have been published previously [29]. A total of 30 women accepted the invitation for a check-up (performed in 2005 and 2006). Only the re-examined subjects were included in the statistical analysis. The study was approved by the Institutional Bioethical Committee and informed consent was obtained from each participant.

All study subjects included in the study were diagnosed as having simple obesity without concomitant diseases. The exclusion criteria included: evidence of present or recent (in the last three months) infectious disease, cigarette smoking and any medication. Medical history, physical examination, anthropometric measurements (body mass, height and waist circumference), body composition assessment by bioimpedance method using the Bodystat 1500 analyser (United Kingdom) were performed during the initial and follow-up check-up. The characteristics of the analysed group are set out in Table I.

To analyse the impact of the yo-yo effect (defined as weight regain to the baseline or higher) on changes of TNF-α, sTNFRs and IL-6 levels, the study women were divided into subgroups with and without the effect that occurred during the five-year period (Table II).

Plasma concentrations of TNF-α, sTNFRs as well as IL-6 were measured using a commercially available

Table I. *The anthropomettric parameters, the effect of weight reduction treatment and changes during 5-year period (n=30)*
Tabela I. Parametry antropometryczne, ich zmiany po kuracji odchudzającej i w 5-letnim okresie obserwacji

	Baseline	After weight loss	Δ	5-year follow-up	Δ
Body mass [kg]	95.3 ± 16.0	87.4 ± 13.6***	–7.9 ± 4.4	95.0 ± 18.0†††	7.6 ± 6.6
BMI [kg/m^2]	36.7 ± 4.8	33.8 ± 4.4 ***	–2.9 ± 1.7	36.6 ± 5.7 †††	2.8 ± 2.4
Body fat [kg]	43.2 ± 12.9	36.9 ± 9.1***	–6.3 ± 7.3	46.6 ± 14.5 †††	9.7 ± 10.5
Body fat (%)	44.6 ± 9.5	41.3 ± 7.0 *	–3.3 ± 6.9	48.2 ± 7.1 †††	6.9 ± 7.9
Fat-free mass [kg]	52.1 ± 7.2	50.5 ± 6.5	–1.6 ± 6.2	48.4 ± 6.6 †	–2.2 ± 4.4
Fat-free mass (%)	55.4 ± 9.4	58.7 ± 6.7 *	3.3 ± 6.7	51.8 ± 7.1 †††	–6.9 ± 5.3
Waist circumference [cm]	107.2 ± 11.5	99.0 ± 10.4 ***	–8.2 ± 4.1	108.4 ± 13.4 †††	9.4 ± 7.1

*p < 0.05; ***p < 0.001 *v.* baseline; †p < 0.05; †††p < 0.001 *v.* after weight loss

highly sensitive enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, Minnesota, MN, USA). The sensitivity of the TNF-α and IL-6 assays are typically less than 0.18 pg/mL. Mean intra-assay coefficient of variance was < 14.4% and 10.0% respectively and mean interassay coefficient of variance was < 18.7% and 10.0% respectively. The sensitivity of the sTNFR1 and sTNFR2 assays is typically less than 0.77 pg/mL and 0.6 pg/mL, respectively. Mean intra-assay coefficients of variances were < 3.6% and 2.6% respectively and mean interassay coefficients of variances were < 3.7% and 3.5% respectively. The kits for the TNF system at the baseline and follow-up were produced by R&D. The assessments were performed at the same analyser. The plasma specimens were stored at –80°C for up to six months.

Statistical analysis

All statistical analyses were performed using Statistica 8.0 software. Results are presented as means ± SD. The results were tested with the use of ANOVA with Newman-Keuls correction. Wilcoxon rank-sum tests (for continuous and ordered variables) and Fisher's exact tests (for discrete variables) were used to compare baseline and post-treatment and post-follow-up clinical/ /Laboratory characteristics inside the study subgroups. The Mann-Whitney *U* test was used for subgroup comparisons. The Spearman rank-order test was used to calculate the univariate correlation coefficients between changes of body mass, body composition and waist circumference and changes of plasma TNF-α, sTNFR1, sTNFR2 levels and IL-6. Multivariate stepwise analysis was performed for changes of plasma TNF-α, sTNFR1, sTNFR2 and IL-6 levels as the dependent variables, and we used age, changes of body fat and waist circumference as the independent variables.

The results were considered as statistically significant with a p value of less than 0.05.

Results

Three-month weight loss therapy resulted in mean 7.9 ± ± 4.4 kg weight loss in all study subjects. It was followed by a decrease of BMI from 36.7 ± 4.8 to 33.7 ± 4.4 kg/m^2 and some significant changes in body composition. The amount of body fat decreased much more than did fat free mass, by 6.3 ± 7.3 and 1.6 ± 6.2 kg respectively.

During the re-examination carried out five years later, a mean weight gain of 7.6 ± 6.6 kg from the values at the end of the three-month weight reduction therapy was found. The changes of body mass and body composition in the study group are presented in Table I.

During the five-year follow-up, 14 study subjects maintained lower body mass than initially, while the

Table II. *Changes of anthropometric parameters in obese women who maintained weight reduction (without yo-yo effect) and with yo-yo effect in 5-year follow-up*

Tabela II. *Zmiany parametrów antropometrycznych u otyłych kobiet, które utrzymały zredukowaną masę ciała (bez efektu jo-jo) oraz z przyrostem masy ciała (efekt jo-jo) w 5-letniej obserwacji*

	Without yo-yo effect (n = 14)				With yo-yo effect (n = 16)			
	Baseline	After weight loss	Δ	5-year follow-up	Baseline	After weight loss	Δ	5-year follow-up	Δ
Body mass [kg]	91.0±14.8	82.3±12.9***	–8.6±3.7	86.0±15.0^{***+}	–5.0±4.5‡	98.8±16.6	91.5±13.2***	–7.3±4.9	102.2±17.6$^{***\,\dagger\dagger\dagger\$\$}$	3.4±2.4$^{‡‡‡\$\$\$}$
BMI [kg/m^2]	35.3±4.9	31.8±4.4***	–3.5±1.3	33.5±5.4**†	–1.8±1.6‡	37.8±4.7	35.2±3.7$^{***\$}$	–2.6±1.9	39.0±4.8$^{***\,\dagger\dagger\dagger\,\$\$}$	1.2±1.0$^{‡‡‡\,\$\$\$}$
Body fat [kg]	35.4±9.7	32.3±7.9	–3.1±6.6	39.8±11.5††	4.4±10.7‡‡	47.5±12.8$^{\$\$\$}$	39.5±9.1$^{***\$}$	–8.6±7.1	51.6±15.1$^{\dagger\dagger\,\$}$	4.1±7.7‡‡
Body fat (%)	40.6±7.7	40.2±6.1	–0.4±7.4	45.7±7.1††	5.1±7.8‡‡	47.6±6.0$^{\$}$	42.9±5.1**	–4.7±5.0	49.7±6.7††	2.1 ±5.3‡‡
FFM [kg]	55.6±7.3	50.1±6.3	–5.5±6.6	46.2±6.8**††	–7.1±7.1‡‡	51.3±6.8	52.0±6.5	0.7±4.4	50.6±5.7	–0.7±4.5$^{‡\,\$\$}$
FFM (%)	59.4±8.4	59.8±6.1	0.5±7.5	54.3±7.1††	–5.0±8.5‡‡	52.4±4.9$^{\$}$	57.1±4.7**	4.7±5.0	50.3±6.7$^{*\,\dagger\dagger}$	–2.2±4.8‡‡
WC [cm]	105.7±13.5	96.9±12.4***	–8.8±3.5	102.2±13.9††	–3.6±5.0‡‡	108.7±9.5	100.9±8.0***	–7.8±4.5	113.8±10.7$^{***\,\dagger\dagger\dagger\,\$}$	5.1±3.1$^{‡‡‡\$\$\$}$

**p<0.01; ***p<0.001 *v.* baseline; †p<0.05; ††p<0.01; †††p<0.001 *v.* after weight loss; ‡p<0.05; ‡‡p<0.01; ‡‡‡p<0.001 *v.* changes between baseline and after weight loss; $^{\$}$p<0.05; $^{\$\$}$p<0.01; $^{\$\$\$}$p<0.001 *v.* without effect yo-yo

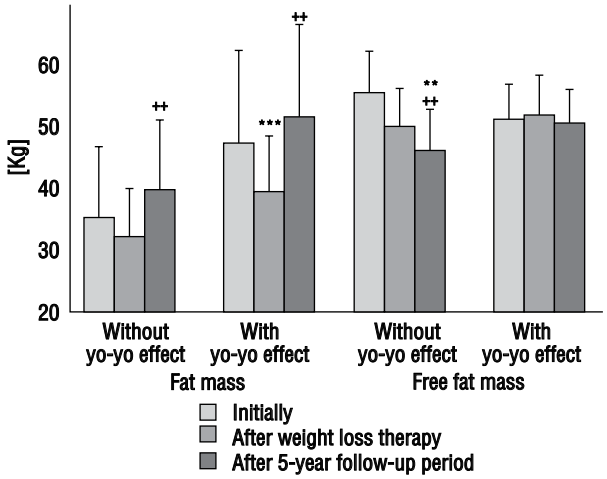

Figure 1. *Changes of body composition in study subgroups. **p < 0.01; ***p < 0.001 v. baseline, ++p < 0.01 v. after weight loss*

Rycina 1. *Zmiany składu ciała w badanych podgrupach. **p<0,01; ***p<0,001 v. przed kuracją; ++p<0,01 v. po redukcji masy ciała*

yo-yo effect occurred in 16 women (Table II). The weight loss and waist circumference decrease were similar in both subgroups after the three-month weight loss therapy. However, the changes of body composition during therapy differed significantly. In the subgroup without a later yo-yo effect, weight reduction was mainly due to the loss of free fat mass, while in the subgroup with later yo-yo effect it was mainly due to the loss of fat mass (Table II and Fig. 1). During the five-year follow-up period, weight regain was observed in both subgroups. As predefined, in the subgroup without the yo-yo effect body mass, BMI and subsequently waist circumference were lower, while in the subgroup with the yo-yo effect they were higher than initially. Regardless of weight changes, the increase of body fat mass was similar. The free fat mass decreased significantly only in the subgroup without the yo-yo effect (Table II and Fig. 1).

Markers of systemic microinflammation

Serum concentrations of TNF-α and IL-6 decreased significantly after weight loss therapy (Table III). However, we did not observe changes of these parameters after weight regain during re-examination after the five-year follow-up period, while serum concentrations of sTNFR1 and sTNFR2 increased significantly after weight loss, and remained significantly increased after the five-year follow-up period (Table III).

In the subgroup analysis, a greater and significant decrease of serum TNF-α level after weight loss therapy was observed in the subgroup with the yo-yo effect, while the changes of sTNFRs and IL-6 concentrations were not significant in either subgroup (Table IV). In the five-year re-examination, concentrations of TNF-α, sTNFR2 and IL-6 levels were not significantly different than previously, while sTNFR1 level was increased in the subgroup without the yo-yo effect. In the subgroup with the yo-yo effect, plasma TNF-α level was significantly lower than initially and similar to the after weight loss therapy measurements; sTNFR1 concentration was significantly higher than at baseline. The levels of sTNFR2 and IL-6 did not change significantly (Table IV).

Correlation between anthropometric parameters and study cytokines

There was no correlation between changes of body mass, BMI, body fat and weight circumference and changes of serum concentrations of TNF-α and sTNFR2 after both weight loss and the following weight regain in the whole study group.

After the three-month weight loss therapy, a positive correlation between the decrease of body mass, BMI or waist circumference and increase in sTNFR1 levels ($R = 0.48$, $p < 0.01$; $R = 0.41$, $p = 0.02$ and $R = 0.44$, $p = 0.02$, respectively) was found. However, we observed no correlation between changes of these parameters after the five-year follow-up period. There was a negative correlation between changes of IL-6 in the five-year re-examination (from baseline) and corresponding changes of weight, body fat mass and waist circumference ($R = –0.44$, $p = 0.02$; $R = –0.41$, $p = 0.02$ and $R = –0.42$, $p = 0.02$, respectively). We found also a negative correlation between five-year changes (from baseline) of BMI and IL-6 values ($R = –0.48$, $p < 0.01$).

In the subgroup without the yo-yo effect, a strong positive correlation between changes of sTNFR1 levels induced by the three-month weight loss therapy and

Table III. *Changes of serum concentrations of proinflammatory cytokines in all study subjects (n=30)*
Tabela III. Zmiany stężeń w surowicy cytokin prozapalnych w całej grupie badanej (n = 30)

	Baseline	After weight loss	Δ	5-year follow-up	Δ
TNF-α [pg/mL]	7.1 ± 2.3	5.5 ± 1.7 **	–1.6 ± 1.9	5.7 ± 2.1*	0.2 ± 2.3
sTNFR1 [pg/mL]	1257 ± 234	1425 ± 323**	168 ± 270	2061 ± 508***	636 ± 600
sTNFR2 [pg/mL]	1729 ± 421	2066 ± 339**	337 ± 397	2120 ± 418***	54 ± 538
IL-6 [pg/mL]	10.9 ± 4.6	8.8 ± 2.3**	–2.1 ± 4.5	7.9 ± 3.5**	–0.9 ± 4.1

*p < 0.05; **p<0.01; ***p < 0.001 *v.* baseline

Table IV. Changes of proinflammatory cytokines in obese women who maintained weight reduction (without yo-yo effect) and with yo-yo effect in 5-year follow-up

Tabela IV. Zmiany stężeń w surowicy cytokin prozapalnych u otyłych kobiet, które utrzymały zredukowaną masę ciała (bez efektu jo-jo) oraz z przyrostem masy ciała (efekt jo-jo) w 5-letniej obserwacji

	Without yo-yo effect (n = 14)				With yo-yo effect (n = 16)			
	Baseline	After weight loss	Δ	5-year follow-up	Δ	Baseline	After weight loss	Δ	5-year follow-up	Δ
TNF-α [pg/mL]	6.8 ± 1.9	5.8 ± 1.6	–1.0 ± 1.7	6.1 ± 2.4	–0.7 ± 2.6	7.4 ± 2.5	5.2 ± 1.8**	–2.3 ± 1.9	5.4 ± 1.7*	–2.0 ± 3.0
sTNFR1 [pg/mL]	1326 ± 285	1487 ± 344	161 ± 325	2195 ± 366**	868 ± 503‡‡	1196 ± 164	1383 ± 302	187 ± 230	1900 ± 549*	704 ± 560‡‡
sTNFR2 [pg/mL]	1725 ± 446	2132 ± 400	407 ± 389	2073 ± 422	348 ± 657‡	1759 ± 391	1981 ± 241	222 ± 310	2208 ± 493	449 ± 637‡
IL-6 [pg/mL]	10.7 ± 6.0	8.5 ± 2.2	–2.2 ± 6.0	7.9 ± 3.4	–2.8 ± 7.7	10.7 ± 3.5	8.7 ± 2.5	–2.0 ± 2.9	8.6 ± 4.5	–2.1 ± 6.0

*p<0.05; **p<0.01 *v.* baseline; ‡p<0.05; ‡‡p<0.01 *v.* changes between baseline and after weight loss therapy

percentage of free fat mass (R = 0.70, p = 0.01) but negative with percentage of body fat (R = –0.67, p = 0.02) and body fat mass (R = –0.64, p = 0.02) was found. Moreover, there was a positive correlation between initial and after five-year changes of sTNFR1 and initial and after weight loss changes of BMI (R = 0.59, p = 0.03).

In the subgroup with the yo-yo effect, there was a positive correlation between changes of sTNFR1 levels induced by the three-month weight loss therapy and corresponding changes of body mass, BMI, free fat mass as well as waist circumference (R = 0.66, p = 0.01; R = 0.52, p = 0.04; R = 0.52, p = 0.04 and R = 0.58, p = 0.02, respectively). Moreover, we observed a positive correlation between changes of IL-6 induced by the three-month weight loss therapy and corresponding changes of free fat mass (R = 0.52, p = 0.04). Furthermore, there was a positive correlation between induced by three-month weight loss therapy changes of free fat mass and five-year changes of IL-6 (from baseline) (R = 0.57, p = 0.02), but negative between changes of BMI, percentage of body fat, body fat mass and waist circumference and of those of IL-6 (R = –0.76, p = 0.001; R = –0.56, p = 0.03; R = –0.53, p = 0.04 and R = –0,59, p = 0.02, respectively). Additionally, a positive correlation between five-year changes of waist circumference and corresponding changes of IL-6 (R = 0.51, p = 0.04) was shown.

Multivariate stepwise analysis did not reveal any significant data.

Discussion

The results of our study support previously published data showing a significant decrease of circulating TNF-α and IL-6 levels, and an increase of sTNFRs, after short term weight loss [29, 30, 32–37]. The novelty of the presented results is the lack of rebound of TNF-α system activity in subjects with the yo-yo effect in the five-year follow-up. The explanation of this finding is not related to body fat mass, as this increased both in obese women who maintained decreased body mass and in those with the yo-yo effect. Therefore we should assign the changes observed in the five-year follow-up to some lifestyle changes such as physical activity and diet composition. It has been recently reported that regular aerobic exercise training (walking and jogging) up to 65% of maximal heart rate, three times a week for 24 weeks and omega-3 polyunsaturated fatty acids (N-3 PUFAs) supplementation results in significantly decreased TNF-α level [38]. Additionally, it has been shown that reduced fat intake from 36% to 27% of daily energy consumption with high amount of fish-derived N-3 PUFAs decreases production of IL-1β and TNF-α by peripheral blood mononuclear cells [39]. Moreover,

some authors have observed that physical activity alone may decrease systemic microinflammation [40]. On the other hand, another study has revealed that the decrease in TNF-α, sTNFRs and IL-6 is only the effect of weight loss with significant total and intra-abdominal adipose tissue reduction and that exercise did not alter the response [41].

As described above in both study groups, we observed a significant increase in sTNFRs and decrease in IL-6 level. It should be emphasised that only the increase of sTNFR1 was proportional to body mass, BMI or waist circumference changes. There was no association between changes of anthropometric parameters and sTNFR2 as well as IL-6 levels. However, when study subjects were divided into subgroups, the numbers of study subjects in the analysis declined, and only a tendency to increase sTNFRs and decrease IL-6 after weight loss therapy persisted. The results of studies assessing the effect of weight loss on sTNFRs levels are inconsistent. It has been reported that weight loss is followed by increased sTNFRs levels [29, 31], decreased only sTNFR2 level and not changed sTNFR1 [32], and decreased both sTNFR1 and sTNFR2 levels [40]. Similarly conflicting results have been reported from studies evaluating the effect of exercise on their concentrations [42, 43]. The differences may be due to age and obesity grade differences between study subjects.

It is worth noting that changes of nutritional status during the five-year follow-up did not alter the decreased TNF-α and IL-6 and increased sTNFRs after weight loss. In the subgroup with the yo-yo effect, a lower than initially TNF-α level was maintained, while plasma sTNFR1 level was significantly higher in both study subgroups. This aligns with our recently published results which revealed that plasma TNF-α level is an early event in abdominal fat accumulation and that further fat mass gain does not enhance circulating TNF-α levels [36].

To the best of our knowledge, this is the first report assessing the effect of weight loss and following weight changes on plasma TNF-α, sTNFRs and IL-6 levels. More detailed explanation of the observed differences is difficult and requires further studies involving a larger group, homogeneous in terms of age, and controlled for physical activity and diet composition.

Despite the fact that multivariate stepwise analysis evaluating the association between changes of study cytokines and changes of anthropometric parameters did not reveal any significant data, it cannot be excluded that the observed differences between study subgroups were partially caused by varying profiles of body composition after weight loss and subsequent weight regain. In this aspect, our study revealed some interesting results. Firstly, regardless of the completion of the same educational programme and receiving similar recommendations, some of the study women achieved weight loss mainly due to loss of fat free mass, while in the remainder it was due to body fat reduction. It should be emphasised that in both these subgroups the waist circumference significantly decreased. Secondly, we observed the yo-yo effect in the group without free fat mass loss during weight therapy; this contradicts the results of studies which have revealed that a lack of free fat mass loss during weight reduction therapy is a predictor of successful long-term weight maintenance [44, 45]. Surprisingly, the body fat gain was similar during the five-year follow-up in both subgroups, although the percentage increase in relation to body fat mass after weight loss was higher in the subgroup with the yo-yo effect. An explanation for this finding is difficult. Perhaps women in the subgroup with the yo-yo effect maintained increased physical activity during the weight loss programme but returned to their previous eating habits, while subjects in the subgroup without the yo-yo effect maintained a sedentary lifestyle but changed their eating habits. This hypothesis is indirectly supported by the revealed changes of free fat mass in our study, as training prevents any loss of free fat mass during weight reduction therapy [46, 47]. Moreover, it has been shown that low-fat intake prevents weight regain [48, 49]. In the subgroup without the yo-yo effect, decreased free fat mass was found after 3-month weight loss therapy and further deteriorated during the five-year follow-up, while in the subgroup with the yo-yo effect free fat mass was constant during this time. Contrary to our findings, a recently published study revealed that weight loss therapy decreases fat mass and protects fat free mass regardless of the intervention applied (i.e. diet only, diet and aerobic training, diet and resistance training) in young overweight women [41]. The main limitation of our study is the size of the study group. Thus, larger longitudinal studies are necessary to clarify the effect of body mass cycling on systemic microinflammation. The lack of diet composition and physical activity assessment during both the weight loss period and the five-year follow-up is another weak point of our study. Moreover, the distribution of body fat and its visceral deposits were not directly assessed using DEXA or a CT scanner.

Conclusions

The yo-yo effect has a modest influence on systemic microinflammation and seems not to abolish the benefit achieved with a weight loss programme. This may suggest that the persistence of changes in lifestyle implemented during the programme such as regular physical activity and diet composition may have a significant

impact on the level of systemic microinflammation in the obese.

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