Obesity-related low-grade chronic inflammation: implementation of the dietary inflammatory index in clinical practice is the milestone?

Debljinom uzrokovana kronična upala niskog intenziteta: uvođenje DII-a (*dietary inflammatory index*) u kliničku praksu je prekretnica?

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Abstract. Diet is a main modifiable determinant involved in the development of obesity-related visceral adipose tissue low-grade chronic inflammation (LGCI). Pro-inflammatory and anti-inflammatory properties of majority of whole foods and dietary constituents have been determined and presented as dietary inflammatory index (DII). The DII is a scoring algorithm based on extensive review of literature linking 45 food parameters with six biomarkers of inflammation. Overall DII score can take on values ranging from 7.98 (maximal pro-inflammatory dietary pattern) to -8.87 (maximal anti-inflammatory dietary pattern). Integrative anti-inflammatory approach to nutrition seems to be the milestone for tackling overweight/obesity, LGCI, and inflammation-related chronic diseases.

Key words: diet; inflammation; nutrition assessment; obesity

Sažetak. Prehrana je najvažniji promjenjivi čimbenik uključen u razvojni proces kronične upale niskog intenziteta na razini visceralnog masnog tkiva. Proupalni/protuupalni potencijali glavnine namirnica i nutritivnih komponenti određeni su, vrednovani te prikazani kao DII (eng. *dietary inflammatory index*). DII je nutricionistički alat dizajniran na temelju opsežnog pregleda literature o učincima konzumacije pojedinih prehrambenih parametara na biomarkere upalnog procesa. Obrascu prehrane pridružen ukupni DII može se nalaziti u rasponu od 7.98 (maksimalni proupalni) do -8,87 (maksimalni protuupalni). Integrativni protuupalni pristup potencijalna je prekretnica u suočavanju s preuhranjenosti/debljinom, kroničnom upalom niskog intenziteta i njoj pridruženim kroničnim bolestima.

Ključne riječi: debljina; nutritivna procjena; prehrana; upala

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OBESITY AND LOW-GRADE CHRONIC INFLAMMATION

Obesity, which refers to body mass index (BMI) ≥30 kg/m^2 accompanied by detrimental excessive fat accumulation, has nowadays become a serious worldwide health problem due to its rapidly growing prevalence and interconnection with a wide spectrum of metabolic and non-metabolic diseases. The main function of the adipose tissue is to store energy reserves in the form of tryglycerides, however adipose tissue is also very important as an endocrine organ, since the adipocytes secrete a variety of hormones, inflammatory mediators and immune system effectors into the systemic circulation[1]. Obesity and its comorbidities are closely related to the inflammatory environment created by expanded dysregulated adipose tissue[2]. Under lean conditions, adipose tissue is predominantly populated with regulatory cells (eosinophils, type 2 innate lymphocytes), which maintain homeostasis by excreting type 2 interleukins (IL-4, IL-5 and IL-13). Latter excretion preserves adipose tissue macrophages (ATMs) in M2-like (anti-inflammatory) state. Lean ATMs produce anti-inflammatory cytokines such as IL-1 receptor antagonist, IL-4, IL-10 and TGF(transforming growth factor)-β1, and express arginase-1, which inhibits inducible nitric oxide synthase. Induction of obesity-related visceral adipose tissue low-grade chronic inflammation (LGCI) is associated with ATMs hypertrophy and hyperplasia, loss of tissue homeostasis (shift in adipokine production from adiponectin to leptin/MCP(monocyte chemotactic protein)-1), development of type 1 inflammatory response characterized by IFN(interferon)-γ, and consequential shift in ATMs polarization from M2 (anti-inflammatory) to M1-like (pro-inflammatory) state. M1 ATMs secrete high levels of pro-inflammatory cytokines such as IL-1β, IL-6, IL-12, TNF (tumor necrosis factor)-α and MCP-1, generate inducible nitric oxide synthase, and maintain LGCI[3,4]. Inflammation is generally considered to be a protective mechanism, however in case of obesity, LGCI plays a pivotal role in development of complications such as type 2 diabetes, cardiovascular diseases (CVD), dyslipidemia, arterial hypertension, non-alcoholic fatty liver disease, osteoarthritis, cancer etc.[5] Moreover, it is being hypothesised that increased levels of pro-inflammatory cytokines are orexigenic, thereby increasing energy intake, promoting further fat accumulation and consequently initiating/maintaining obesity-LGCI vicious circle[6].

Alterations in food consumption have strong and significant effect on overall health throughout life. Various dietary factors seem to modulate key pro-inflammatory pathways, such as nuclear factor kappa B (NF-κB) pathway. Furthermore, not only dietary pattern as a whole, but various food-groups separately, have effect on inflammatory biomarkers.

INTERCONNECTION BETWEEN DIETARY FACTORS AND INFLAMMATORY PROCESS

Multiple factors, including individual characteristics, smoking, usage of certain medications, physical activity and diet, contribute to chronic inflammatory process[7]. Diet is a main modifiable determinant involved in the development of LGCI and inflammation-related chronic diseases. Alterations in food consumption have strong and significant effect on overall health throughout life[1,8]. Various dietary factors, including oxidative stress from excess calories and hormones derived from arachidonic acid, seem to modulate key pathways, such as nuclear factor kappa B (NF-κB), that promote inflammation[9-13]. Furthermore, not only dietary pattern as a whole, but various food-groups separately, have effect on biomarkers of inflammation. Certain diet components, such as red meat, sweetened soft drinks, processed and fried food, are considered to be pro-inflammatory stimulants[7,14,15]. On contrary, higher intake of fruits, vegetables, extra-virgin olive oil, nuts, and legumes has been associated with lower serum concentrations of C-reactive protein (CRP), IL-6 and/or TNF-α[7,16-21]. Therefore, pro-inflammatory and anti-inflammatory properties of majority of whole foods and dietary constituents have been determined, scored and presented as dietary inflammatory index (DII). The design and development of the DII have been comprehensively described by Shivappa et al.[22]

Table 1. Forty-five food parameters included in the dietary inflammatory index and their overall food parameter-specific inflammatory effect scores, global daily mean intakes and global standard deviations (SD). Modified according to reference 22

Food parameter	Weighted number of articles	Raw inflammatory effect score	Overall inflammatory effect score	Global daily mean intake (units/d)	Global standard deviation (SD)
Alcohol (g)	417	-0.278	-0.278	13.98	3.72
Vitamin B12 (µg)	122	0.205	0.106	5.15	2.70
Vitamin B6 (mg)	227	-0.379	-0.365	1.47	0.74
β-Carotene (µg)	401	-0.584	-0.584	3718	1720
Caffeine (g)	209	-0.124	-0.110	8.05	6.67
Carbohydrate (g)	211	0.109	0.097	272.2	40.0
Cholesterol (mg)	75	0.347	0.110	279.4	51.2
Energy (kcal)	245	0.180	0.180	2056	338
Eugenol (mg)	38	-0.868	-0.140	0.01	0.08
Total fat (g)	443	0.298	0.298	71.4	19.4
Fibre (g)	261	-0.663	-0.663	18.8	4.9
Folic acid (µg)	217	-0.207	-0.190	273.0	70.7
Garlic (g)	277	-0.412	-0.412	4.35	2.90
Ginger (g)	182	-0.588	-0.453	59.0	63.2
Fe (mg)	619	0.032	0.032	13.35	3.71
Mg (mg)	351	-0.484	-0.484	310.1	139.4
MUFA (g)	106	-0.019	-0.009	27.0	6.1
Niacin (mg)	58	-1.000	-0.246	25.90	11.77
n-3 Fatty acids (g)	2588	-0.436	-0.436	1.06	1.06
n-6 Fatty acids (g)	924	-0.159	-0.159	10.80	7.50
Onion (g)	145	-0.490	-0.301	35.9	18.4
Protein (g)	102	0.049	0.021	79.4	13.9
PUFA (g)	4002	-0.337	-0.337	13.88	3.76
Riboflavin (mg)	22	-0.727	-0.068	1.70	0.79
Saffron (g)	33	-1.000	-0.140	0.37	1.78
Saturated fat (g)	205	0.429	0.373	28.6	8.0
Se (µg)	372	-0.191	-0.191	67.0	25.1
Thiamin (mg)	65	-0.354	-0.098	1.70	0.66
Trans fat (g)	125	0.432	0.229	3.15	3.75
Turmeric (mg)	814	-0.785	-0.785	533.6	754.3
Vitamin A (RE)	663	-0.401	-0.401	983.9	518.6
Vitamin C (mg)	733	-0.424	-0.424	118.2	43.46
Vitamin D (µg)	996	-0.446	-0.446	6.26	2.21
Vitamin E (mg)	1495	-0.419	-0.419	8.73	1.49
Zn (mg)	1036	-0.313	-0.313	9.84	2.19
Green black tea (g)	735	-0.536	-0.536	1.69	1.53
Flavan-3-ol (mg)	521	-0.415	-0.415	95.8	85.9
Flavones (mg)	318	-0.616	-0.616	1.55	0.07
Flavonols (mg)	887	-0.467	-0.467	17.70	6.79
Flavonones (mg)	65	-0.908	-0.250	11.70	3.82
Anthocyanidins (mg)	69	-0.449	-0.131	18.05	21.14
Isoflavones (mg)	484	-0.593	-0.593	1.20	0.20
Pepper (g)	78	-0.397	-0.131	10.00	7.07
Thyme/oregano (mg)	24	-1.000	-0.102	0.33	0.99
Rosemary (mg)	9	-0.333	-0.013	1.00	15.00

DIETARY INFLAMMATORY INDEX OVERVIEW

The DII is a scoring algorithm based on an extensive review of literature, 1943 peer-reviewed articles published in English from 1950 to 2010, linking 45 food parameters with inflammatory biomarkers. Based on the effect of the food parameter on inflammation, values were assigned as follows: '+1' if the effect was pro-inflammatory (significantly increased IL-1β, IL-6, TNF-α and/or CRP, and/or significantly decreased IL-4 and/or IL-10), '-1' if the effect was anti-inflammatory (significantly decreased IL-1β, IL-6, TNF-α and/or CRP, and/or significantly increased IL-4 and/or IL-10), or '0' in case if the food parameter did not have significant effect on inflammatory biomarkers. Moreover, articles were first weighted by study caharacteristics (presented by Shivappa et al. in Figure 2). Weighted values were used for calculating the pro-inflammatory and anti-inflammatory fractions for each food parameter. Food parameter-specific overall inflammatory effect score was calculated by dividing the weighted pro-inflammatory and anti-inflammatory articles by the total weighted number of articles and substracting the anti-inflammatory fraction from the pro-inflammatory fraction. The full value of the calculated score was assigned to food parameters with a weighted number of articles ≥236. However, food parameter-specific overall inflammatory effect score for those parameters with weighted number of articles <236 was adjusted by dividing the number of weighted articles by 236, and multiplying the latter fraction by the food parameter-specific raw inflammatory effect score (Table 1). Furthermore, individual's z-score and centred percentiles should be calculated separately for each food parameter based on respective daily intake. Z-score can be obtained by substracting the individual's food parameter daily mean intake from the global daily mean intake and dividing the latter result by the global standard deviation (collected from the regionally representative world database). Z-score is then converted to a percentile score (to minimize the effect of 'right skewing'), which is then doubled and substracted by 1 in order to achieve a symmetrical distribution (ranging from '-1'-maximally anti-inflammatory to '1'-maximally pro-inflammatory, and centred on '0'). The next step is the calculation of the food parameter-specific DII score, which is based on multiplication of the latter centred percentile value by its respective overall food parameter-specific inflammatory effect score. Finally, individual's overall DII score is obtained by summarizing all of the food parameter-specific DII scores[22]. Construct validity of the DII indicated its utility as a tool for assessing diet quality based on inflammatory potential[23]. Overall positive DII scores represent a pro-inflammatory dietary pattern, whereas negative DII scores are associated with an anti-inflammatory diet. Overall DII score can take on values ranging from 7.98 (maximal pro-inflammatory dietary pattern) to -8.87 (maximal anti-inflammatory dietary pattern)[22]. For comparison, DII scores for the macrobiotic and Mediterranean diet have strong anti-inflammatory potentials (-5.54 and -3.98, respectively), whereas the fast food diet produce strong pro-inflammatory DII score (4.07)[24].

Overall positive dietary inflammatory index (DII) scores represent a pro-inflammatory dietary pattern, whereas negative DII scores are associated with an anti-inflammatory diet. Integrative anti-inflammatory approach to nutrition is focused on eating mindfully and in energy balance, which results in reduction of the silent inflammation.

ASSOCIATION OF DIETARY INFLAMMATORY INDEX WITH OBESITY AND ITS COMORBIDITIES

Ramallal et al. assessed the association of inflammatory potential of a diet with average yearly weight changes and overweight/obesity incidence in their prospective 10-year cohort study. Participants with the highest DII score had a +57.3 g higher yearly weight change, and what is more, a higher risk of experiencing a relevant (>3 kg and >5 kg) weight gain within the first 2 years of follow-up (OR=1.29 and OR=1.43) in comparison to the participants in the most anti-inflammatory quartile. In addition, authors also reported a significant 32% higher relative risk of

developing new-onset overweight/obesity in the pro-inflammatory group[25]. Ruiz Canela et al. reported progressive increase in waist circumference and waist-hip ratio across quintiles of the DII compared to the lowest (most anti-inflammatory) quintile, both in men and women. BMI increased progressively across quintiles only among women[26]. The role of DII in CVD, metabolic syndrome and mortality has been extensively presented in a narrative review by Ruiz Canela et al.[7] Furthermore, a systematic review and meta-analysis of Namazi et al. indicated a trend toward the positive DII and the risk for CVD (RR=1.35, 95% CI: 1.13-1.60), all-cause mortality (HR=1.21, 95% CI: 1.09-1.35), CVD mortality (HR=1.30, 95% CI: 1.07-1.57) and cancer mortality (HR=1.28, 95% CI: 1.07-1.53). However, the consumption of the most pro-inflammatory versus the most anti-inflammatory diet showed no significant difference in overall risk for metabolic syndrome (RR=1.01, 95% CI: 0.82-1.24), most probably due to limited studies (Egger's regression confirmed the publication bias for metabolic syndrome)[8].

CONCLUSION

Integrative anti-inflammatory approach to nutrition is focused on eating mindfully and in energy balance, which results in silent inflammation reduction. The DII has been shown to be an effective tool for assessing diet quality based on inflammatory potential, hence its implementation in clinical practice seems to be the milestone for tackling overweight/obesity, low-grade chronic inflammation and inflammation-related chronic diseases in general.

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