

Original Article

A retrospective cohort study of the effect of weight loss on chronic inflammation and sleep quality

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Received March 24, 2021; Accepted May 11, 2022; Epub June 15, 2022; Published June 30, 2022

Abstract: While obesity and other diseases have been linked to chronic inflammation of the body, the underlying mechanisms of the relationship between obesity and chronic inflammation remain unclear. Neutrophil-to-lymphocyte ratio (NLR) is an effective indicator of chronic inflammation. Thus, we aimed to explore the relationship between obesity and inflammation by tracking weight changes and NLR. This study included 425 participants who received health examinations at our hospital for two consecutive years, and whose body mass index (BMI) was greater than 28 at the time of their first consultation. Participants were divided into three groups based on BMI changes (less than one unit, greater than one but less than three units, and greater than three units). BMI and NLR changes were examined over two years to assess the relationship between them, compared to baseline data while using linear regression to do correlation analysis, and to observe changes of BMI in improving sleep quality. NLR decreased significantly among participants with a BMI change greater than three units. There were no significant changes in people with BMI changes of less than three units. Linear regression between BMI and NLR showed a significant linear relationship. Sleep quality was also significantly reduced in people with a BMI change greater than three units. The present study indicated that chronic inflammation might be ameliorated by a decrease in BMI. Further, a decline in BMI plays an important role in improving sleep quality.

Keywords: Neutrophil-to-lymphocyte ratio, obesity, chronic inflammation, sleep quality

Introduction

Obesity is a worldwide health concern that may increase the prevalence of some chronic diseases, such as hypertension, diabetes, and coronary heart disease [1, 2]. Some studies suggest that obesity-associated chronic systemic inflammation may be the basis of obesity's relationship with other diseases [3]. The exact etiology of obesity-associated systemic inflammation remains unclear. Adipose tissue inflammation is considered to play a key role, causing major events of immune response, such as the early participation of neutrophils and lymphocytes, as well as the polarization of macrophage and mast cells [4]. However, there is no direct evidence linking obesity and chronic inflammation.

Recently, neutrophil-to-lymphocyte ratio (NLR) in peripheral blood has been found to be a valuable predictor of systemic inflammation, showing superiority in terms of stability, as well

as some clinical advantages, such as rapid application, wide availability, and low cost [5]. Some studies have found a negative correlation between NLR and body mass index (BMI), with obese individuals exhibiting a lower NLR value. However, NLR is associated with many diseases, which is why the aforementioned correlation needs to be validated [6]. Therefore, the current study assessed the correlation between body weight and chronic inflammation by observing changes in NLR during weight loss. We also observed whether sleep quality improved among this study's participants. Since sleep, obesity, and chronic inflammation are suspected to be linked, this study attempts to confirm this relationship.

Materials and methods

Patient enrollment

We retrospectively analyzed the records of patients who underwent health examinations at

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Chongqing University Cancer Hospital for two consecutive years (from January 2018 to December 2019). Patients diagnosed as being obese (BMI>28) at their initial consultation were included. This study's design was approved by the independent Ethical Committees of Chongqing University Cancer Hospital. For this type of study formal consent is not required but the participants gave written informed consent for publication.

The physical examination items included health and sleep psychology clinics. Obese patients received advice on diet and exercise, aimed at achieving weight loss, and they participated in periodic telephonic follow-up consultations. Patients exhibiting the following conditions were excluded: uncontrolled diabetes mellitus (fasting blood glucose greater than 10 mmol/L), suspected acute infectious diseases (white blood cell count $>10 \times 10^9/L$), unstable heart disease, acute attack of pulmonary disease, and pregnancy. Participants' basic characteristics (including gender, age, smoking status, height, and weight) were recorded. BMI was computed by dividing weight (kg) by height squared (m^2). Participants were divided into three groups, based on their reduction in BMI at the second year (compared with the first year): a change of less than 1 unit; between 1 and 3; and more than 3 units.

Evaluation of NLR

During patients' follow-up visits, a 10 mL blood sample was drawn from the antecubital vein by applying minimal tourniquet pressure in the early morning. Complete blood count (CBC) was measured within 1 h after venipuncture using the Sysmex-XE 2000i automated blood cell analyzer (Sysmex, Kobe, Japan). This procedure is standard for the participating laboratory, as it helps prevent EDTA-induced swelling. NLR was recorded at each time. The time point of the first examination was set to T1 and the second to T2.

Evaluation of sleep quality

Sleep quality was evaluated routinely using the Pittsburgh Sleep Quality Index (PSQI) at every examination as a measure of psychological health. Sleep quality was calculated as the sum score of the 18 items in the PSQI with a

total of 21 points and 18 items to make up seven components. Each component was scored according to the 0-3 level. A PSQI score of ≤ 5.0 indicated good sleep quality, whereas higher scores indicated poorer sleep quality. The time point of the first examination was set to T1, the second to T2.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows v20.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean (standard deviation [SD]) or median (interquartile range), according to distribution state. Categorical variables were expressed as numbers and percentages. Age, systolic blood pressure, smoking condition and NLR, were performed using Student's t-test if the standard of normally distributed data was met, and the Mann-Whitney test if not. Linear regression was used to analyze the relationship between BMI and NLR. *P*-value of <0.05 was regarded as statistically significant.

Results

The groups were comparable with respect to age, BMI, smoking status, and blood pressure (as shown in **Table 1**). Five patients were excluded from the study due to signs of acute infection during physical examinations. From 425 eligible participants, 307 had a BMI decrease of less than one unit in two years, including those who exhibited increases in BMI. Seventy-six participants showed a BMI decrease between one and three units in two years, whereas 42 others showed a BMI decrease of more than three units. **Figure 1** shows that NLR values significantly decreased among participants with a BMI change greater than three (2.91 ± 1.33 vs. 2.34 ± 1.28 , $P < 0.05$). As shown in **Figure 2**, PSQI scores significantly decreased among participants with a BMI change greater than three (4.20 ± 1.77 vs. 3.02 ± 1.21 , $P < 0.0001$). No significant effects were observed among participants with a BMI change of less than three units. Linear regression between BMI and NLR showed a significant linear relationship ($P < 0.0001$, $F = 187.2$) and equation was "Y = $0.1333 \times X - 1.308$ " (Y: NLR, X: BMI) (**Figure 3**).

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Table 1. Participants' characteristics

	Male	Female
n	152	273
age	45.6+7.6	47.1+8.2
systolic blood pressure	136+26.4	141+32.9
smoking (Y/N)	114/38	36/237*
T1		
30>BMI>28	114	208
35≥BMI≥30	35	54
BMI>35	3	11
T2		
ΔBMI<1	107	200
3≥ΔBMI≥1	27	49
ΔBMI>3	18	24

*Statistical significance when compared with male.

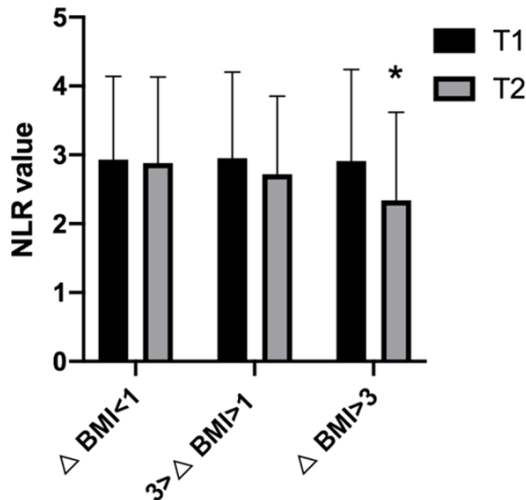


Figure 1. NLR values corresponding to different BMI changes in the two physical examinations. * Statistical significance when compared with T1.

Discussion

The results of this retrospective study confirm that obesity is directly related to chronic inflammation and that weight loss can reduce the degree of chronic inflammation in the body, which could improve sleep quality. Chronic inflammation is believed to be closely related to a variety of cardiovascular and chronic diseases, such as chronic obstructive pulmonary disease, coronary artery disease, and cardiac arrhythmias [7]. Other studies have shown a relationship between obesity and chronic inflammation [8]. Obesity is thought to be associated

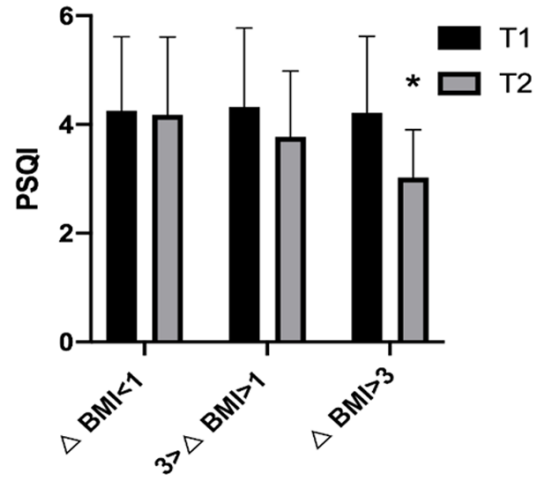


Figure 2. PSQI values corresponding to different BMI changes in the two physical examinations. * Statistical significance when compared with T1.

with a pro-inflammatory environment, including increased secretion of interleukin 6, tumor necrosis factor alpha, and other cytokines; however, this result comes from different individuals, and there are likely more factors involved [9, 10].

For the physical examination population, test results like interleukin cells or cytokines are not routine items. Therefore, we measured NLR levels to assess chronic inflammation. NLR represents the ratio of two different complementary immune pathways, responsible for active nonspecific inflammation and lymphopenia. Being an integrated reflection of two important and opposite immune pathways, NLR is more predictive than using either parameter separately [11]. Our findings confirm that weight loss causes NLR values to decrease, indicating a direct relationship between obesity and inflammation. Meanwhile we found a clear linear relationship between NLR and BMI by performing linear regression analysis.

Obesity and sleep are also considered to be inextricably linked. One longitudinal meta-analysis found that insufficient sleep in adults increased their odds of obesity by 45% [12]. Another experimental study indicated that a decrease in either the time or quality of sleep increased the risk of obesity [13]. Physiological, hormonal, and food behavioral changes were observed in studies implementing experimental sleep restriction; sleep deprivation pro-

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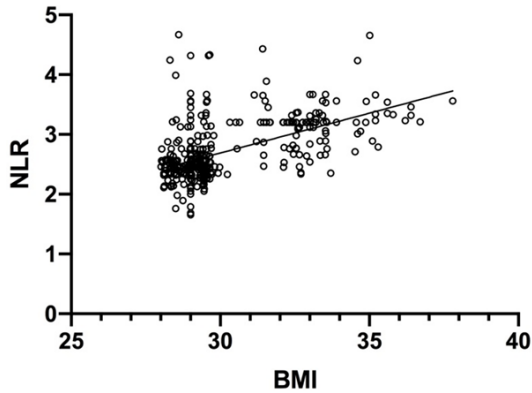


Figure 3. Linear regression between BMI and NLR.

notes a compensatory increase in food intake and a positive energy balance, as well as a decrease in physical activity, and an increase in weight [14]. Meanwhile, obstructive sleep apnea (OSA) is the most prevalent type of obesity-related sleep disorder linked to an increased risk for multiple chronic health conditions [15]. In one study, an increase of six BMI units resulted in a fourfold risk of developing OSA, leading to sleep disorders and short sleep duration [16]. Besides, increased visceral adipose tissue may be responsible for the secretion of inflammatory cytokines, which could produce alterations in the sleep-wake rhythm [17].

There is no definite evidence to suggest that a decline in sleep quality caused by obesity leads to chronic inflammation. However, our findings suggest that weight loss has a significant effect on sleep quality. The mechanisms between sleep disturbance and inflammation remain relatively unexplored. Nevertheless, previous research shows that sleep could influence two primary effector systems, namely, the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system. Both of these systems shift the basal gene expression profile toward increased proinflammatory skewing [18]. Future studies should further explore this topic to confirm the exact relationship between sleep and chronic inflammation.

Limitations

Some limitations need to be considered in the interpretations of our results. Our physical examination population included over 400 individuals, whereas the number of people who

actually lost weight in accordance with the study guidelines was very small, resulting in a small sample size. Further, chronic inflammation is related to various factors, and even though we attempted to rule out acute-stage diseases, there may be additional unknown interfering factors at play.

Acknowledgements

This work was supported by the Laboratory Open Fund of Chongqing University Cancer Hospital (2021); High-Level Medical Personnel Training Project of Chongqing (2019GDRC017); Shapingba District of Chongqing Decision-making Consultation and Management Innovation Guiding Plan (Jcd202112); HY.Z.: guarantor of integrity of the entire study. HY.Z. and JQ.L.: study concepts. HY.Z. and L.L.: study design. L.L. and JJ.J.: definition of intellectual content. JJ.J. and L.L.: experimental studies. JQ.L. and JY.T.: data analysis. JJ.J. and L.L.: statistical analysis. JQ.L. and L.L.: manuscript preparation. JQ.L. and L.L.: manuscript editing. HY.Z.: manuscript review.

For this type of study formal consent is not required but the participants gave written informed consent for publication.

Disclosure of conflict of interest

None.

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References

- [1] Vecchié A, Dallegrì F, Carbone F, Bonaventura A, Liberale L, Portincasa P, Frühbeck G and Montecucco F. Obesity phenotypes and their paradoxical association with cardiovascular diseases. *Eur J Intern Med* 2018; 48: 6-17.
- [2] Pagidipati NJ, Zheng Y, Green JB, McGuire DK, Mentz RJ, Shah S, Aschner P, Delibasi T, Rodbard HW, Westerhout CM, Holman RR and Peterson ED; TECOS Study Group. Association of obesity with cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease: insights from TECOS. *Am Heart J* 2020; 219: 47-57.

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- [3] Ying W, Fu W, Lee YS and Olefsky JM. The role of macrophages in obesity-associated islet inflammation and β -cell abnormalities. *Nat Rev Endocrinol* 2020; 16: 81-90.
- [4] Tanaka M. Molecular mechanism of obesity-induced adipose tissue inflammation; the role of Mincle in adipose tissue fibrosis and ectopic lipid accumulation. *Endocr J* 2020; 67: 107-111.
- [5] Barker T, Fulde G, Moulton B, Nadauld LD and Rhodes T. An elevated neutrophil-to-lymphocyte ratio associates with weight loss and cachexia in cancer. *Sci Rep* 2020; 10: 7535.
- [6] Suárez-Cuenca JA, Ruíz-Hernández AS, Mendoza-Castañeda AA, Domínguez-Pérez GA, Hernández-Patricio A, Vera-Gómez E, De la Peña-Sosa G, Banderas-Lares DZ, Montoya-Ramírez J, Blas-Azotla R, Ortíz-Fernández M, Salamanca-García M, Melchor-López A, Mondragón-Terán P, Contreras-Ramos A and Alcaráz-Estrada SL. Neutrophil-to-lymphocyte ratio and its relation with pro-inflammatory mediators, visceral adiposity and carotid intima-media thickness in population with obesity. *Eur J Clin Invest* 2019; 49: e13085.
- [7] Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, Ferrucci L, Gilroy DW, Fasano A, Miller GW, Miller AH, Mantovani A, Weyand CM, Barzilai N, Goronzy JJ, Rando TA, Effros RB, Lucia A, Kleinstreuer N and Slavich GM. Chronic inflammation in the etiology of disease across the life span. *Nat Med* 2019; 25: 1822-1832.
- [8] Furuncuoğlu Y, Tulgar S, Dogan AN, Cakar S, Tulgar YK and Cakiroglu B. How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. *Eur Rev Med Pharmacol Sci* 2016; 20: 1300-6.
- [9] Villarroja F, Cereijo R, Gavaldà-Navarro A, Villarroja J and Giralt M. Inflammation of brown/beige adipose tissues in obesity and metabolic disease. *J Intern Med* 2018; 284: 492-504.
- [10] Koca TT. Does obesity cause chronic inflammation? The association between complete blood parameters with body mass index and fasting glucose. *Pak J Med Sci* 2017; 33: 65-69.
- [11] Faria SS, Fernandes PC Jr, Silva MJ, Lima VC, Fontes W, Freitas-Junior R, Eterovic AK and Forget P. The neutrophil-to-lymphocyte ratio: a narrative review. *Ecancermedicallscience* 2016; 10: 702.
- [12] Fatima Y, Doi SA and Mamun AA. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obes Rev* 2015; 16: 137-49.
- [13] Ahern T, O'Malley E, Dunlevy C, Khattak A, O'Brien H, Hassan T, Cusack T, McNicholas WT and O'Shea D. Sleep duration and physical function in people with severe obesity: a prospective cross-sectional study. *Ir J Med Sci* 2020; 189: 517-523.
- [14] St-Onge MP, Wolfe S, Sy M, Shechter A and Hirsch J. Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *Int J Obes (Lond)* 2014; 38: 411-6.
- [15] Jordan AS, McSharry DG and Malhotra A. Adult obstructive sleep apnoea. *Lancet* 2014; 383: 736-47.
- [16] Quintas-Neves M, Preto J and Drummond M. Assessment of bariatric surgery efficacy on Obstructive Sleep Apnea (OSA). *Rev Port Pneumol* 2016; 22: 331-336.
- [17] Patinkin ZW, Feinn R and Santos M. Metabolic consequences of obstructive sleep apnea in adolescents with obesity: a systematic literature review and meta-analysis. *Child Obes* 2017; 13: 102-110.
- [18] Irwin MR and Opp MR. Sleep health: reciprocal regulation of sleep and innate immunity. *Neuropsychopharmacology* 2017; 42: 129-155.