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The Association Between Weight Loss and Platelet Markers in Morbidly Obese Patients

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Abstract

Objective: To examine the association of weight loss achieved through obesity treatment with platelet number and markers (mean platelet volume, MPV; plateletcrit, PCT; platelet/lymphocyte ratio, PLR; and platelet distribution width, PDW) in morbidly obese patients.

Methods: A total of 300 patients diagnosed with morbid obesity between 2017 and 2019 were included in this retrospective study. Weight at baseline and 6 months, body mass index (BMI), complete blood count (platelet, lymphocyte, plateletcrit, platelet/lymphocyte ratio, and platelet distribution width), and demographic data were evaluated.

Results: A total of 300 morbidly obese patients with a BMI ≥ 40 kg/m2 were included. A weight loss of ≥ 10% was considered "significant", and a weight loss of < 10% was considered insignificant. A significant decrease in platelet number was found in association with weight loss ($p < 0.05$), as were the changes in PCT and PLR. These findings suggest that platelet markers PCT and PLR may be associated with the degree of weight loss.

Conclusion: Our results suggest that platelet markers simply obtained through a complete blood count may be utilized in the treatment and follow-up of obesity, which may lead to a number of different conditions such as coronary artery disease, cerebrovascular events, and myocardial infarction through predisposition to thrombosis.

Keywords: morbid obesity, plateletcrit, mean platelet volume, body mass index

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Morbid Obez Hastalarda Kilo Kaybı ile Platelet Belirteçleri Arasındaki İlişki

Öz

Amaç: Morbid obez hastalarda, obezite tedavisi ile sağlanan kilo kaybının, platelet sayısı ve belirteçleri [ortalama platelet hacmi (MPV), platekrit (PCT), platelet/lenfosit oranı (PLR) ve platelet dağılım genişliği (PDW)] arasındaki ilişkiyi araştırmak.

Yöntemler:Bu retrospektif çalışmaya, 2017- 2019 yılları arasında morbid obezite tanısı almış 300 hasta dahil edildi. Başlangıç ve 6.aydaki kilo, beden kitle indeksi (BKİ), tam kan sayımları (platelet, lenfosit, platekrit, platelet/lenfosit oranı ve platelet dağılım genişliği) ile demografik verileri incelendi.

Bulgular: Bu çalışmada BKİ 40 ve üzeri olan toplam 300 morbid obez hasta kaydedildi. Çalışmaya alınan morbid obez hastalardan, kilosunun %10 ve daha fazlasını kaybedenler "anlamlı", %10'dan azını kaybedenler ise "anlamsız" grub olarak adlandırıldı. İstatistiksel analizde platelet sayılarında kilo kaybıyla kaydedilen düşme istatiksel olarak anlamlı ($p<0.05$) saptanırken; PCT sayısı ve PLR'deki değişim de istatiksel açıdan anlamlı saptandı. Bu da platelet göstergelerinden olan PCT ve PLR'nin kilo kaybının derecesi ile ilişkili olabileceğini gösterdi.

Sonuç: Bu çalışma, basit bir test olan hemogramdaki platelet belirteçlerinin; tromboza yatkınlık oluşturarak koroner arter hastalığı, serebrovasküler olay, miyokard enfarktüsü gibi pek çok hastalığa neden olan obezitenin takip ve tedavisinde kullanılabileceğini göstermiştir.

Anahtar kelimeler: morbid obezite, platekrit, ortalama platelet hacmi, beden kitle indeksi.

INTRODUCTION

Globally, we have witnessed an increased prevalence of obesity in the past 50 years[1]. Obesity is a chronic and complex metabolic disorder that affects multiple organ systems and that is associated with various complications such as cardiovascular disease and atherosclerosis[2]. Body Mass Index (BMI), the most commonly utilized measurement for obesity, was originally described and graded by the World Health Organization in 1995. Based on a BMI formula of weight (kg)/square meter of height (m2), a BMI ≥ 30 kg/m2 is considered "obesity" and a BMI of ≥ 40 kg/m2 is considered morbid obesity in adults[3]. Individuals with a BMI of > 27 kg/m2 have been shown to have a three-fold increased risk of hypertension[4]. The foremost function of platelets is to contribute to the process of homeostasis as a component of blood. Recent developments in the field of clinical laboratory techniques have paved the way to for identifying new roles for platelets in thrombosis, immunity, inflammation, and angiogenesis[5]. As a result, platelet markers have been utilized to monitor the disease course and response to treatment in a variety of conditions. While the mean platelet volume (MPV) indicates the functional change and activation of platelets[6], platelet distribution width (PDW) can be used as a volume index for platelets. MPV, PDW, and other platelet-related parameters can be readily obtained and assessed through the use of hematologic analyzers. Several cardiovascular disorders, peripheral arterial disease, and cerebrovascular disorders are associated with increased MPV [6]. Thus, platelet activation is considered to represent a therapeutic target in obesity, atherothrombosis, hypertension, and diabetes. In this study, we aimed to examine the association of weight loss achieved through obesity treatment with platelet number and markers in morbidly obese patients.

METHODS

The Study Design

A total of 300 patients diagnosed with morbid obesity at Obesity and Diabetes Center, Medical Faculty of Zonguldak Bulent Ecevit University between 1st May 2017 and 1st May 2019 were

included in this retrospective study. The study protocol was approved by the Institutional Ethics Committee (date:12th June 2019; protocol number 2019/09). Demographic characteristics (age, gender), physical examination and measurement findings (height, weight, body mass index, waist circumference), and complete blood count results were recorded. Patients losing ≥ 10% of their bodyweight were compared with those who had a weight loss of < 10% were compared after obesity treatment consisting of diet, exercise, and medical treatment. Those who lost ≥ 10% of their weight compared to baseline were considered "responders".

Statistical Analyses

Data were analyzed with SPSS 19.0 software. Descriptive statistics for qualitative variables were expressed as frequency and percentage, while quantitative variables were expressed as arithmetic means, standard deviation, median, minimum, and maximum. Normal distribution of continuous variables was examined with Shapiro Wilk test. Variables without normal distribution were compared using Mann Whitney U test between the groups, and Wilcoxon test was used for within-group comparisons. Yates chi-square test was utilized for comparing qualitative variables between groups. For all statistical analyses, a p value of less than 0.05 was considered significant.

RESULTS

Data from 300 patients undergoing treatment for morbid obesity between 2017 and 2019 were analyzed. Of these 300 patients, 267 (89%) were female and 33 (11%) were male. Overall, the mean age was 48.91 ± 11.68 years, and BMI was 46.53 ± 5.15 kg/m2(Table 1). Demographic data and BMI indices were compared with baseline in patients losing weight as a result of diet, exercise, lifestyle change, and anti-obesity drug use (orlistat) (Table 2). The weight difference between baseline and at 6 months was calculated as kilograms, while the percent weight loss (%) was calculated using the following formula: 100 x [(weight at 6 months – weight at baseline)/weight at baseline]. Accordingly, the overall average weight had declined from 117.4 kg to 106 kg, and BMI had declined from 46.53 to 41.75 kg/m2 at 6 months as compared to baseline. Average weight loss and reduction in BMI were found to be significant in the overall group (Table 2), with a percent weight loss of 8.34% compared to baseline. The objective of our study was to examine associations between total weight loss at 6 months and platelet number and markers. Thus, while weight loss was associated with significant reductions in platelet number and platelet lymphocyte ratio (PLR), no significant changes occurred in plateletcrit (PCT), PDWFF and MPV ($p > 0.05$, for all) (Table 3). All 300 patients included in the study experienced some degree of weight loss as compared to baseline. Patients were re-grouped to better understand the association of the degree of weight loss with alterations in platelet indices. Therefore, patients were categorized as those with significant weight loss (≥ 10% weight loss at 6 months) and insignificant weight loss (< 10% weight loss at 6 months) and were compared in terms of platelet markers. The former group included 89 patients (29.7%) and the latter included 211 patients (70.3%) (Figure 1) As compared to the group with insignificant weight loss, those who lost significant weight had significantly more reduction in platelet number, PLR, and PCT ($p < 0.05$), while there were no differences in terms of PDW and MPV ($p > 0.05$) (Table 4).

Table I: Demographic data for morbid obese patients at baseline

	Minimum	Maximum	Mean	SS
Age (years)	19	75	48.91	11.6
Height (cm)	139	181	158	7.4
Weight (kg)	86	178.8	117.4	15.3
BMI (kg/m²)	40.0	66.4	46.5	5.15

(SD: standard deviation, BMI: body mass index)

Table II: Demographic characteristics at baseline and after weight loss at 6 months

	BASELINE			AFTER WEIGHT LOSS (6 MO)			6-0 AY
	n	Mean ± SD	Median (min-max)	n	Mean ± SD	Median (min-max)	P
Body weight (kg)	300	117.4±15.3	115.0 (86.0-178)	300	107.6±70.0	106.0 (76-160)	0.000*
BMI (kg/m² ± SD)	300	46.53±5.15	45.40 (40.0-66.4)	300	42.65±4.98	41.75 (31.6-61.1)	0.000*

(Min: Minimum; Max: maximum; SD: standard deviation; BMI: body mass index).

Table III: Changes in platelet markers at 6 months from baseline in the overall group

	BASELINE (MO 0)			AFTER WEIGHT LOSS (MO 6)			6-0 MO
THR PRMT	n	Mean ± SD	Median (min-max)	n	Mean ± SD	Median (min-max)	P
PLT	300	282.0±69.9	276.5 (139-554)	300	274.4±70.0	266.0 (120-638)	0.000*
PCT	300	0.248±0.05	0.243(0.12-0.43)	300	0.245±0.05	0.239(0.12-0.45)	0.086
PDW	300	25.14±34.2	16.80 (15.7-171)	300	16.76±0.44	16.80 (15.6-18.2)	0.058
MPV	300	13.29±17.9	8.900 (6.60-101)	300	9.048±0.93	9.000 (6.80-11.9)	0.71
PLR	300	180.9±341	121.8 (7.14-3850)	300	139.2±129	118.7 (45.9-1760)	0.002*

(THR PRMT: platelet parameters, Min: Minimum; Max: maximum; SD: standard deviation, PLT: platelet number, PCT: plateletcrit; PDW: platelet distribution width; MPV: mean platelet volume; PLR: platelet/lymphocyte ratio)

Table IV: The change in platelet number and other platelet indices according to the degree of weight loss

	SIGNIFICIANT			INSIGNIFICANT			
	n	Mean ± SD	Median (min-max)	n	Mean ± SD	Median (min-max)	p
PLTPC	89	-0.051±0.13	-0.0495 (-0.32-0.45)	211	-0.003±0.14	-0.127 (-0.52-0.56)	0.007*
PDWPC	89	-0.049±0.20	0.0000 (-90-0.05)	211	-0.049±0.20	0.000 (-0.90-0.06)	0.149
MPVPC	89	-0.031±0.22	0.0115 (-0.90-0.16)	211	-0.038±0.21	0.0110 (-0.91-0.17)	0.396
PCTPC	89	-0.034±0.11	-0.0312 (-0.36-0.24)	211	0.0093±0.13	-0.0033 (-0.51-0.49)	0.017*
PLRPC	89	0.478±2.63	-0.0839 (-0.96-18.6)	211	0.5841±2.51	0.0047 (-0.90-19.8)	0.008*

(Min: Minimum; Max: Maximum; SD: standard deviation; PLTPC: platelet percent change; (Min: Minimum; Max: maximum SD: standard deviation, PLTPC: Platelet percent change: PCTPC: plateletcrit percent change; PDWPC: platelet distribution width percent change; MPVPC: mean platelet volume percent change; PLRPC: platelet/lymphocyte ratio percent change)

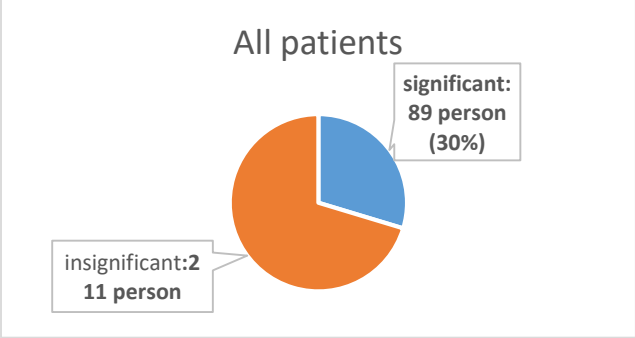

Figure 1: Patients According to the Degree of Weight Loss

DISCUSSION

Obesity is a metabolic disorder with multi-organ involvement that is associated with a number of complications such as hypertension, cardiovascular diseases, and atherosclerosis[2]. Clinical and epidemiological evidence have consistently suggested a close link between obesity and cardiovascular disorders, insulin resistance, and type 2 diabetes mellitus[8]. Abdominal obesity is particularly associated with cardiovascular mortality[9], and also represents a significant risk factor for arterial and venous thromboembolic events[10]. In recent years, platelet number and platelet indices have been explored and utilized in terms of their role in the diagnosis and monitoring of patients with myocardial infarction, atheroma plaques, cerebrovascular events, malignancy, and rheumatoid arthritis. Platelets are anuclear cellular fragments that are released into the circulation following the programmed fragmentation of the megakaryocytes of the bone marrow. Studies showed gender

differences in platelet numbers in healthy individuals. In a 2006 study by Anna M. et al[11]. women have been found to have higher platelet numbers than men, which might be due to the higher percent fat in women. In a large-scale study in 2007 involving 6319 obese and morbidly obese patients, obese patients have also been found to have elevated platelet numbers in comparison with normal weight individuals. During the process of megakaryopoiesis, interleukins originating from fat tissue such as interleukin-6 (IL 6) and growth factors act synergistically with thrombopoietin to increase the number platelets. In vivo administration of IL 6 has been reported to increase platelet number in both human and monkey studies[12]. The elevated platelet counts observed in obese patients have been purported to be secondary to the chronic inflammation and hypoxia associated with obesity [13]. In the current study, the platelet count at baseline (i.e.282.000 ± 69.000) was found to be significantly reduced following 6 months of obesity treatment. MPV is a marker of activated platelets and has been associated with proclivity toward thrombosis and a number of different inflammatory conditions. In a review study by Gasparyan et al[7] it has been suggested that MPV may be utilized as a prognostic and therapeutic marker in conditions involving thrombosis and inflammation. Cardiovascular risk factors including smoking, hypertension, obesity, dyslipidemia, and diabetes have an impact on MPV through inflammation. Elevated MPV is related to cardiologic and cerebrovascular events as well as arterio-venous thrombotic events[7]. Also, MPV is an indicator of platelet activation[14]. In a 2005 study by Çoban et al[15] from our country, obese patients have been found to have significant elevation of MPV as compared to controls. In a 2014 study by Furman-Niedziejko et al[16] a positive correlation between MPV and waist circumference in those with metabolic syndrome and abdominal obesity, and patients with these abnormalities had significantly higher MPV than those without them. Similar to previous reports, the mean MPV among our 300 morbidly obese patients was 13.2 fL at baseline, which was above the normal MPV range. Toplak et al[17] reported a decrease in MPV in patients undergoing a 8-week obesity intervention. In our study, we also observed a decline in MPV following weight loss at 6 months. However, although there was a positive association between weight loss and decrease in MPV in our study similar to previous reports, this was not statistically significant ($p>0.05$). PDW may be utilized in conjunction with MPV in the assessment of platelet functions[18]. Many previous studies showed an association of low PDW and MPF with mild cognitive disorders, Alzheimer's disease, vascular dementia, and osteoporosis[19]. On the other hand, elevated PDW and MPV are related to acute myocardial infarction and vascular complications of diabetes[20]. In the current study, although there was a reduction in PDW with weight loss, this did not reach statistical significance. PCT is defined as the percent volume of platelets in the blood[21]. Previously, a positive and significant association between BMI and PCT was observed by Furuncuoğlu et al[22]. Similarly in a more comprehensive study including 3327 patients, statistically significant correlations between BMI, abdominal obesity, platelet number, and PCT[22]. In 2019, Erdal et al[23] found statistically significantly higher PCT in 45 morbidly obese patients than in normal weight controls. PCT may serve as a useful marker for thrombotic predisposition and for determination of the inflammatory response. We observed significantly more marked reduction in PCT in those with a weight loss of ≥ 10% as compared to those who lost only < 10% of their bodyweight ($p < 0.05$). PLR is calculated by dividing the platelet number to lymphocytes[24]. In their study, Erdal et al[23] observed statistically higher PLR among obese patients than in non-obese subjects. In a 2018 study by Nemli et al[25]

obese patients undergoing bariatric surgery and losing significant weight had significant lowering in PLR at 3 and 6 months after the intervention. A similar reduction was observed among our study subjects ($p<0.05$), in parallel with previous reports. The limitations of our study include exclusion of patients with cardiovascular diseases, DM, thrombosis etc., in an effort to minimize the effect of these conditions on platelet markers. The clinical significance of platelet indices is inherently limited, due to lack of standardization. Therefore, standardization measures should be taken in terms of the delay between blood sampling and assays, type of anticoagulant used in sampling tubes, as well as the type of analyzer to be used for platelet volume quantification.

In conclusion, treatment and monitoring of obesity and related comorbidities are associated with significant healthcare cost. Platelet indices that can be readily derived from a practical and inexpensive test such as complete blood counts may provide information on obesity and a number of related conditions. Our study suggests that significant improvement in platelet numbers and indices may be achieved with BMI values approaching to normal range in patients with morbid obesity. Therefore, we believe that PLR and PCT may serve as useful and cost-effective markers of increased thrombotic predisposition and inflammatory process in patients with morbid obesity. However, our observations should be corroborated by further studies.

Ethics Committee Approval: A total of 300 patients diagnosed with morbid obesity at Obesity and Diabetes Center, Medical Faculty of Zonguldak Bulent Ecevit University between 1st May 2017 and 1st May 2019 were included in this retrospective study. The study protocol was approved by the Institutional Ethics Committee (date:12th June 2019; protocol number 2019/09).

Declaration of Conflicting Interests: The authors declare that they have no conflict of interest.

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REFERENCES

1. Leitner DR, Frühbeck G, Yumuk V, et al. Obesity and type 2 diabetes:Two diseases with a need for combined treatment strategies-EASO can lead the way. Obes Facts. 2017; 10: 483-92.

2. Rueda- Clausen CF, Ogunleye AA, Sharma AM. Health benefits of long-term weight-loss maintenance. Annu Rev Nutr. 2015; 35: 475-516

3. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA. 2002; 288: 1723-7.

4. Samur G, Yıldız E. Obezite ve kardiyovasküler hastaliklar/hipertansiyon Sağlık Bakanlığı Yayın 2008.

5. Nording H, Langer HF. Complement links platelets to innate immunity. Seminars in immunology. 2018; 37: 43-52.

6. Mutlu H, Artış TA, Erden A, et al. Alteration in mean platelet volume and platicrit values in patients with cancer that developed thrombosis. Clinical and Applied Thrombosis/Hemostasis. 2013; 19: 331-3.

7. Gasparyan YA, Ayvazyan L, Mikhailidis DP, et al. Mean platelet volume:a link between thrombosis and inflammation. Current Pharmaceutical Design. 2011; 17: 47-58.

8. Morange PE, Alessi MC. Thrombosis in central obesity and metabolic syndrome: mechanisms and epidemiology. Thromb Haemost. 2013; 110: 669-80.

9. Coutinho T, Goel K, Corrêa de Sá D, et al. Central obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. J Am Coll Cardiol. 2011; 57: 1877-86.

10. Borch KH, Nyegaard C, Hansen JB, et al. Joint effects of obesity and body height on the risk of venous thromboembolism: The Tromsø Study. Arteriosclerosis, Thrombosis and Vascular Biology. 2011; 31: 1439–44.

11. Butkiewicz AM, Kemona H, Dymicka-Piekarska V, et al.Platelet count, mean platelet volume and thrombocytopoietic indices in healthy women and men. Thrombosis Research. 2006; 118: 199-204.

12. Samocha-Bonet D, Justo D, Rogowski O, et al. Platelet counts and platelet activation markers in obese subjects. Mediators of inflammation 2008.

13. Lebedeva EV,Yushkov BG, Chereshnev VA. Megakaryocytopoiesis under hypoxic conditions. Bulletin of Experimental Biology and Medicine. 2003; 136: 554-6.

14. Greisenegger S, Endler G, Hsieh K, et al. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events. Stroke. 2004; 35: 1688–91.

15. Çoban E, Özdoğan M, Yazıcıoğlu G, et al. The mean platelet volume in patients with obesity. Int J Clin Pract. 2005; 59: 981-2.

16. Furman-Niedziejko A, Rostoff P, Rychlak R, et al. Relationship between abdominal obesity, platelet blood count and mean platelet volume in patients with metabolic syndrome. Folia Med Cracov. 2014; 54: 55-64.

17. Toplak H, Sagmeister E, Wascher TC. Cardiovascular risk factors in obesity. The effect of weight reduction on platelet size in overweight patients. International Journal of Obesity and Related Metabolic Disorders:Journal of the International Association for the Study of Obesity. 1994; 18: 355-6.

18. Vagdatli E, Gounari E, Lazaridou E, et al. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010; 14: 28–32.

19. Wang R-t, Jin D, Li Y, et al. Decreased mean platelet volume and platelet distribution width are associated with mild cognitive impairment and Alzheimer's disease. Journal of Psychiatric Research. 2013; 47: 644-9.

20. Gupta S, Saxena SK, Lalchandani A, et al. Significance of platelet volume indices in patients of coronary artery diseases (CAD) and acute myocardial infarction (mi): a new predictor for Ihd. Indian Journal of Cardiology. 2012; 15; 22-5.

21. Akpinar I, Sayın MR, Gursoy YC, et al. Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. Journal of Cardiology. 2014; 63: 112-8.

22. Furuncuoğlu Y, Tulgar S, Dogan AN, et al. How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. European Review for Medical and Pharmacological Sciences. 2016; 20: 1300-6.

23. Erdal E, İnanir M. Platelet-to-lymphocyte ratio (PLR) and Plateletcrit (PCT) in young patients with morbid obesity. Rev. Assoc. Med. Bras. 2019; 65: 1182-7.

24. Gunaldi M, Göksu S, Erdem D, et al. Prognostic impact of platelet/lymphocyte and neutrophil/lymphocyte ratios in patients with gastric cancer: a multicenter study. Int J Clin Exp Med. 2015; 8: 5937–42.

25. Nemli H, Kısakol G, Küçüksaraç Kıyıcı SD, Güçlü M, Koca N. Effect of surgical weight loss on the inflammatory hematological parameters in short term. In 20th European Congress of Endocrinology. BioScientifica. 2018.