OPEN

Insights into the clinical impact of complete blood cell inflammatory markers on body composition variations and fatty liver grading in Iranian adults undergoing bariatric surgery: a retrospective longitudinal study

Hanieh Radkhah^a, Ali Alirezaei^b, Peyvand Parhizkar^c, Razieh Khalooeifard^{d,*}, Batoul Khoundabi⁹, Khosrow Najjari^e, Mohammad Talebpour^e, Reza Hajabi^f

Background: In bariatric surgery, inflammatory biomarkers predict outcomes. Limited research on complete blood cell (CBC) markers stresses the need for correlation study. This research explores links between CBC inflammatory markers, body changes, and fatty liver grades in Iranian bariatric patients.

Materials and methods: This retrospective longitudinal study examined 237 bariatric surgery patients who satisfied the inclusion criteria and were deemed eligible for participation. These criteria encompassed patients who had undergone sleeve or mini-bypass surgery and were aged between 18 and 65 years. The study gathered demographic data, pre and post-surgery changes in CBC inflammatory biomarkers [neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), mean platelet volume (MPV), MPV-to-platelet count ratio (MPV/PC), and red cell distribution width (RDW)] and fatty liver grades. Additionally, it recorded pre and post-surgery changes in body composition, such as weight, muscle mass (MM), fat mass (FM), and fat-free mass (FFM).

Results: The pre-surgery RDW marker significantly associated with FM changes, highlighting its predictive nature. While no significant association was found between changes in patients' fatty liver grade and baseline marker values, it's worth noting that individuals with higher MM at 3 months achieved a fatty liver grade of zero. Also, at 6 months, higher FFM and MM were also associated with reaching a fatty liver grade of zero.

Conclusions: While the retrospective design of this study limits its findings to existing clinical data, future prospective research should collect additional samples, extend the observation time, and examine the long-term predictive value of these markers.

Keywords: bariatric surgery, body composition, inflammatory biomarkers, fatty liver

Introduction

Obesity has emerged as a substantial contemporary societal challenge. Its prevalence has increased significantly over the past decades, making it a paramount global public health issue^[1]. Extensive research underscores the variability in obesity prevalence, ranging from 5% in certain African regions to nearly 80% in Eastern Europe^[2], accompanied by diverse health

consequences^[3]. Although numerous molecular pathways connect obesity to its related disorders, inflammation is a prevalent characteristic that has been associated with the underlying mechanisms of various complications. There have been significant endeavors to elucidate the impact of obesity on overall physiology, with particular emphasis on significant inflammatory signaling molecules^[4]. While the complications of obesity may vary in different patients, oxidative stress and inflammation are

^aSina Hospital, Department of Internal Medicine, ^bSchool of Nutritional Sciences and Dietetics, ^cTehran University of Medical Sciences, ^dDepartment of Clinical Nutrition School of Nutritional Sciences and Dietetics, ^eDepartment of General Surgery, ^fDepartment of General Surgery, School of Medicine, Sina Hospital, Tehran University of Medical Sciences and ^gIran Helal Institute of Applied-Science and Technology, Red Crescent Society of Iran, Research Center for Health Management in Mass Gathering, Red Crescent Society of the Islamic Republic of Iran, Tehran, Iran

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran 1416753955, Iran. Tel.: +21 888 966 96; fax: +21 888 985 32. E-mail: shkhalooei1367@gmail.com (R. Khalooeifard).

Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Medicine & Surgery (2024) 86:4990-4998

Received 24 January 2024; Accepted 27 May 2024

Published online 18 July 2024

http://dx.doi.org/10.1097/MS9.000000000002257

common in all of them. The presence of oxidative stress in obesity can lead to the development of pathological alterations^[5]. Obesity triggers cellular death and inflammation in adipose tissue, which in turn contributes to metabolic syndromes associated with inflammation. The mechanisms of cellular death and nuclear factor κ B (NF- κ B) mediated inflammation play a role in regulating energy balance and insulin sensitivity. The interaction between adipocytes and macrophages in adipose tissue results in widespread metabolic inflammation in obese individuals^[6,7].

Bariatric surgery is widely recognized as the most efficacious intervention for obesity and has demonstrated positive outcomes in various obesity-related complications in addition to its effectiveness in weight reduction and enhancement of quality of life. Average weight loss is 32% of preoperative weight within two years after surgery. This weight loss does not only include the reduction of fat mass, but also the loss of muscle mass. Studies have shown that a large proportion of weight loss in the first three months after surgery, about 30-33%, is related to fat-free mass (FFM), indicating that excessive loss of FFM occurs mainly in the short period after surgery. Also, there is a significant decrease in lean body mass (LBM) and FFM in 12 months after surgery, most of which decreases during 3 months after surgery and continuously until 6 months. In fact, more than 50% of the total loss of LBM and FFM occurs within 3-6 months after surgery. This amount of changes is affected by various factors^[8,9]. Therefore, it is imperative to identify individuals who would derive the greatest benefits from this procedure^[10-12]. Researchers are still in the process of finding the best predictive procedures for post-bariatric results^[13,14]. The complete blood count (CBC) is an affordable and readily available laboratory test. In recent times, there has been research interest in exploring the utility of leukocyte and platelet counts, as well as ratios such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyteto-lymphocyte ratio (MLR), as indicators of inflammation in different chronic subclinical conditions. These indicators, which can be derived from routine CBC, offer a dependable and convenient measure of the intensity of immune responses^[15-17]. Recent studies have shown the role of NLR and PLR in different inflammatory and thrombotic conditions like their role in predicting and prognosis of thromboembolism in COVID-19 patients^[18], predicting long covid symptoms^[19] or different cancer prognoses^[20]. In metabolic surgery studies have found NLR various roles in predicting post-bariatric surgery compli-cations like leak^[21], or its correlation to post-metabolic surgery weight loss^[22]. MPV has also a promising role in differentiating between non-alcoholic fatty liver disease (NAFLD) or non-NAFLD patients in a recent systematic review^[23]. The positive correlation of MPV with fibrosis stage in biopsy of NAFLD patients besides its role in the prediction of NAFLD development has also been revealed^[24].

CBC inflammatory markers such as NLR, mean platelet volume (MPV), PLR are novel and accessible markers. They can easily check and monitor over time, in routine laboratory tests. On the other hand, many studies have shown their promising role in predicting prognosis in a wide variety of infectious, inflammatory and malignant diseases. However, there are few studies with controversies that assess their significance in obesity and metabolic syndrome and their role in monitoring of those patients. The lack of comprehensive investigations into the CBC inflammatory markers in patients undergoing bariatric surgery highlights the need to explore these predictors and their

HIGHLIGHTS

- In bariatric surgery, inflammatory biomarkers serve as crucial predictors of postoperative outcomes, prompting the need for further exploration of complete blood count (CBC) inflammatory markers and their correlation with body composition changes and fatty liver grades.
- The pre-surgery red cell distribution width (RDW) marker demonstrated a significant association with changes in fat mass (FM), emphasizing its predictive nature.
- While no significant association was found between changes in patients' fatty liver grade and baseline marker values, higher muscle mass (MM) and fat-free mass (FFM) were associated with reaching a fatty liver grade of zero, suggesting their potential impact on hepatic improvements.

correlation with the prognosis of this procedure. This exploration is crucial for making informed clinical decisions and predicting surgery's success. Therefore, the aim of this study is to reveal the association between inflammatory biomarkers obtained from CBC and changes in body composition and fatty liver status among patients undergoing bariatric surgery.

Material and methods

Study design and participants

This longitudinal retrospective study was conducted on patients registered in the obesity surgery database from February to October 2023 who met the inclusion criteria and were eligible for participation. The inclusion criteria included patients who underwent bariatric surgery, specifically sleeve or mini-bypass, age between 18 and 65 years and the exclusion criteria encompassed individuals suffering from inflammatory diseases, patients taking anti-inflammatory drugs, individuals with a history of cancer and hematologic diseases, and those diagnosed with iron deficiency anemia or thalassemia. This study was carried out following the guidelines outlined in the Strengthening the Reporting of cohort, cross-sectional, and case-control studies in Surgery (STROCSS) criteria^[25].

Data collection and outcome measures

Demographic data of eligible patients were retrieved from the Hospital database. Routine CBC assessments on the first day of hospitalization, as well as at 3 and 6 months post-surgery, were compiled. Various hematological parameters, including NLR, PLR, MLR, MPV, MPV-to-platelet count ratio (MPV/PC), and red cell distribution width (RDW), were recorded. Assessment of fatty liver grade was conducted at baseline and subsequently at 1, 3, and 6 months post-surgery using Sonography techniques. The study's outcomes included monitoring changes in body composition, comprising the rate of weight change, presented as a percentage of excess weight, alterations in muscle mass (MM), adjustments in fat mass (FM), and modifications in FFM. By using the bio impedance analysis (BIA) device (In body 270) in fasting conditions, not drinking much water, not doing physical activity and vigorous exercise before performing the test and after defecation, by using 8 electrodes (two under the right foot and two (right and left hand) weight, body fat and muscles were measured. These measures were evaluated at baseline, 10 days, 1, 3, and 6 months post-surgery, alongside assessments of changes in fatty liver grade. In order to eliminate the confounding effect of food intake and physical activity, only the information of patients who had the same diet and exercise plan under the supervision of a nutritionist and sports medicine specialist and were registered in the database were included in the study.

Statistical analysis

The recorded data were analyzed using IBM software version 26. The normality of quantitative variables was assessed using the Kolmogorov–Smirnov test. Descriptive statistics, including mean and standard deviation (Mean \pm SD) for normally distributed quantitative variables and median and interquartile range [Median [interquartile range (IQR)]] for non-normally distributed quantitative variables, were used to summarize the data. To examine changes in quantitative variables over time, repeated measures models or Generalized Estimating Equations (GEE) were employed. Spearman's correlation coefficients and generalized linear models were used to investigate the relationships and influences of hematological indicators on the study outcomes. All statistical tests were conducted at a significance level of 5%.

Results

Demographic and basic information of patients

Table 1 encompassed a detailed summary of the demographic and fundamental information pertaining to the patients participating in the study, offering key insights into the characteristics of the study.

Item	n (%)/ Mean + SD/median [10]
Sev (male)	64 (24 5)
	41.4 ± 11.0
Fatty liver grade before	41.4 ± 11.0
Grade1	69 (26 4)
Grade2	117 (1/1 8)
Grade3	32 (12.3)
No fatty liver	26 (10.0)
Fatty liver grade month 3	20 (10.0)
Grade1	50 (19.2)
Grade2	35 (13.4)
Grade3	8 (3.0)
No fatty liver	45 (17.2)
Fatty liver grade month 6	
Grade1	29 (11.2)
Grade2	14 (5.4)
No fatty liver	43 (16.5)
Type of WLS	
One anastomosis gastric bypass	81 (31.0)
SASI	1 (0.4)
Sleeve gastrectomy	155 (59.4)
Baseline weight	117.1 [105–129.5]
Baseline BMI	43 [40–47]
Baseline FM	52.45 [45.82-61.8]
Baseline FFM	61.05 [55.9–71.55]
Baseline MM	57.8 [52.87-68.05]

Table 2	
Repeated m	easurement analysis results for indicators

Indicators	Baseline	3 months	6 months	P
WBC	7.97 ± 1.81	6.27 ± 1.58	6.52 ± 1.52	< 0.001*
Neutrophil	53.92 ± 7.20	53.64 <u>+</u> 8.76	53.84 ± 7.13	0.016*
Monocyte	10.09 ± 7.40	8.35 ± 6.69	10.23 ± 5.94	0.960
lymphocyte	32.29 ± 8.96	35.16 ± 8.05	35.29 ± 8.18	0.189
RDW	14.05 ± 1.33	15.00 <u>+</u> 1.78	14.92 ± 3.07	0.105
Plt	293.00 ± 75.75	258.25 ± 73.32	259.71 <u>+</u> 61.56	< 0.001*
MPV	10.00 <u>+</u> 0.68	10.68 ± 0.80	10.47 <u>+</u> 0.81	0.004*
NLR	1.98 ± 0.67	1.73 ± 1.04	1.74 ± 1.05	0.302
LMR	3.28 ± 0.81	4.15 ± 0.90	3.95 ± 1.40	0.112
				0.024**
PLR	10.49 ± 3.72	8.67 ± 3.31	9.13 ± 5.64	0.235
MPV/PC	0.0344 ± 0.012	0.0405 ± 0.0129	0.0396 ± 0.0113	0.004*
Alb	4.36 ± 0.34	4.41 ± 0.38	4.34 ± 0.33	0.895
Urea	27.06 ± 8.87	22.55 ± 7.82	23.39 <u>+</u> 8.87	0.012*
Feritin	42.14 ± 27.03	53.65 ± 33.14	36.00 ± 26.83	0.480

Alb, albumin; LMR, lymphocyte-monocyte ratio; MPV, mean platelet volume; NLR, neutrophil-tolymphocyte ratio; PC, platelet count; PLR, platelet-to-lymphocyte ratio; Plt, platelet; RDW, red cell distribution width.

*Significant at 0.05 level for linear pattern.

**Significant at 0.05 level for quadratic pattern.

Comparison of indicator changes over time

The findings presented in Table 2 reveal that changes in white blood cell (WBC), MPV, PC, MPV, Platelet, Neutrophil, and Urea markers are statistically significant at a 5% level, underscored by the observed alterations in these indicators over time.

Impact of baseline markers on body composition components

Table 3 meticulously examines the influence of baseline markers on various components of body composition, with a dedicated pvalue column for markers and time inserted separately for each body composition component. The results unequivocally demonstrate significant changes in all components over time, as illustrated in Figure 1. Notably, the effect of the RDW marker before surgery is found to be specifically impactful on FM, indicating a noteworthy association between the pre-surgery RDW value and subsequent FM changes.

Correlation between pre-surgery RDW and FM changes

The correlation coefficient values presented in Table 4 unveil the substantial influence of the RDW value before surgery on FM changes at different time intervals. Notably, the correlation value of – 0.298 between RDW before surgery and FM changes during the 3–6 months interval elucidates the predictive nature of RDW concerning FM alterations, signifying that higher RDW values before surgery correlate with reduced FM changes during this period (Table 4). Furthermore, a scatter plot in Figure 2 visually represents the linear relationship between FM changes from 3 to 6 months and RDW before surgery.

Fatty liver grade changes

The transition in fatty liver grade between the baseline and 3 months demonstrated that:46 patients (17.6%) experienced no change in grade. Thirty-eight cases (14.6%) were downgraded by one grade (from 1 to 0, from 2 to 1, from 3 to 2, or from 4 to 3).

Table 3 Repeated measureme	Table 3 Repeated measurement analysis results of baseline markers effect on body composition items										
						Р					
Body composition items	Baseline	10 days	1 month	3 months	6 months	Time	NLR	PLR	RDW	MPV	MPV/PC
Weight	122.1 ± 19.4	114.9 ± 16.3	108.6 ± 16.4	94.9 ± 18.1	85.0 ± 15.4	< 0.001	0.123	0.542	0.061	0.803	0.466
BMI	44.5 ± 4.6	41.7 ± 3.7	39.5 ± 3.4	34.5 ± 5.6	30.7 ± 5.1	< 0.001	0.383	0.359	0.447	0.486	0.586
MM	63.2 ± 13.7	58.7 ± 12.6	57.6±11.9	55.0 ± 13.7	52.7 ± 13.6	< 0.001	0.196	0.878	0.449	0.144	0.254
FM	57.1 ± 11.6	54.1 ± 9.6	49.0 ± 8.5	37.3 ± 9.2	29.2 ± 8.5	< 0.001	0.385	0.840	0.017*	0.267	0.742
FFM	66.2 ± 14.3	61.6 ± 12.9	60.4 ± 12.2	57.9 ± 13.5	55.7 ± 12.7	< 0.001	0.108	0.619	0.325	0.174	0.365

FFM, fat-free mass; FM, fat mass; MM, muscle mass; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PC, platelet count; PLR, platelet-to-lymphocyte ratio; RDW, red cell distribution width.

Twenty-six cases (10%) were downgraded by two grades (from 2 to 0, from 3 to 1, or from 4 to 2). Additionally, 5 cases (1.9%) were downgraded to grade 0 from grade 3, and 1 case (0.4%) moved to grade 3 from grade 0. Moreover, from the 3 to 6-month interval: 39 patients (14.9%) exhibited no change in grade. 17

patients (6.5%) experienced a one-grade reduction, while 5 patients (1.9%) were downgraded by two grades. Additionally, 8 patients (3.1%) faced an increase of 1 grade (Table 5). Although statistical tests such as ANOVA and Kruskal–Wallis revealed no significant association between the change in patients' grade and





Table 4				
Correlation of	coefficients RDW	at baseline and FM	changes during	time

FM changes during time	10 days-Baseline	1 month-10 days	3 months-1 month	6 months–3 months
Correlation coefficient	-0.133	-0.134	0.066	-0.298
P value	0.110	0.118	0.493	0.034*

FM, fat mass; RDW, red cell distribution width

*Significant at 5%.

baseline marker values, the results underscored that the grade of fatty liver changes over time alongside alterations in body composition (Table 6). Notably, as indicated in Table 7, patients with higher MM achieved a fatty liver grade of zero. Subsequently, in the 6-month period, as illustrated in Table 8, patients with higher FFM and MM achieved a fatty liver grade of zero.

Discussion

Obesity as an increasing source of morbidity and mortality worldwide, is contributed to a state of chronic low-grade inflammation^[26]. While weight loss has been shown to decrease inflammation, further research is needed to demonstrate the specific alterations in inflammatory markers following significant weight loss besides the impacts of these biomarkers in predicting bariatric surgery results. Thus, in this study, we focused on investigating the relationship between various inflammatory indicators, including NLR, MLR, PLR, RDW, MPV, and MPV/ PC, and changes in body composition and fatty liver grade following bariatric surgery. The statistical significance of the RDW marker before surgery, particularly in relation to the FM component has been found by our study. This study highlights that the RDW value before surgery significantly influences the average change in fat mass, with higher preoperative RDW values correlating with a lesser reduction in fat mass between 3 and 6 months post-surgery. Also, the relationship between fatty liver grade and changes in body composition over time, specifically within 3- and 6-month periods have been mentioned by this study.

Biochemical and hematological markers, such as WBC count and its subtypes, can be used to identify systemic inflammation in the absence of infection^[27]. Similarly, in the present study, repeated measures tests of inflammatory markers were utilized to evaluate the changes of biomarkers over time. A significant alteration was observed in various markers, specifically WBC, MPV/PC, MPV, platelets, neutrophil, and urea. These significant changes in the mentioned markers indicate that there are notable alterations in the CBC inflammatory profile following bariatric surgery. The effects of these indicators on inflammation status besides thrombosis, and atherogenesis has also been documented by other studies. Previous studies have shown that cardiovascular diseases and their inflammation-related complications are associated with increased platelet counts. MPV has also been found to increase during acute myocardial infarction as a biomarker of platelet activity. PLR has been known to act as an inflammation biomarker and has been shown to have prognostic significance. Decreased lymphocyte levels and increased platelet value in acute coronary syndrome have been linked to poor prognosis, while PLR has been correlated with adverse results accompanied by cardiac pathologies independent of platelet or lymphocyte levels. The results also indicated that PCT levels were notably higher in obese patients, and PLR was also





Table 5 Fatty liver grade changes

Table 6

I	Baseline	with 3 m	onths after	surgery		
		Co	ount			
			Fatty_liver	_grade_3M		
		0	1	2	3	Total
Fatty_liver_before	0	6	4	2	1	13
	1	13	17	5	1	36
	2	18	20	22	4	64
	3	5	8	5	1	19
Total	42	49	34	7	132	
P value			0.431			
	3 month	s with 6 r	nonths after s	surgery		
		Сс	ount	0,		
		Fat	ty_liver_grad	e_6M		
		0	1	2	Total	
Fatty liver grade 3M	0	23	5	0	28	
)	1	9	11	3	23	
	2	4	5	5	14	
	3	0	1	3	4	
Total		36	22	11	69	
P value		<	0.001*			

significantly higher in individuals with morbid obesity. These findings suggest that in patients who are morbidly obese, PLR or PCT may function as indicators of an elevated thrombotic status and inflammatory response^[28].

The NLR, a newer marker of inflammation, indicates the balance between innate and adaptive immune responses. Elevated NLR levels are linked to higher levels of proinflammatory

Body composition by fatty liver grade at baseline

	Fatty liver month 3	Mean	Std. deviation	р
Weight_3M	0	95.80	13.83	0.188
-	1	92.28	15.10	
	2	99.43	14.34	
	3	98.17	22.13	
	Total	95.49	15.04	
BMI_3M	0	34.30	3.98	0.338
	1	34.54	3.64	
	2	35.45	3.27	
	3	35.71	3.99	
	Total	34.75	3.68	
FM_3M	0	36.00	10.18	0.231
	1	36.63	9.10	
	2	39.50	7.76	
	3	39.79	8.78	
	Total	37.30	9.17	
FFM_3M	0	60.05	11.28	0.074
	1	56.20	10.72	
	2	60.26	11.21	
	3	58.31	14.83	
	Total	58.53	11.28	
MM_3M	0	57.82	10.35	0.035*
	1	53.61	10.37	
	2	57.66	10.71	
	3	55.37	14.16	
	Total	56.03	10.72	

*p-value less than 0.05 was considered as statistically significant.

FFM, fat-free mass; FM, fat mass; MM, muscle mass.

Table 8

Table 7

cytokines, which can potentially lead to DNA damage. Rodríguez-Rodríguez *et al.*^[27] have demonstrated a positive correlation between abdominal obesity, as measured by waist-to-

Baseline	Fatty liver baseline	Mean	Std. deviation	р
Weight_B	0	116.33	17.71	0.193
	1	117.64	14.92	
	2	119.99	19.80	
	3	126.57	21.56	
	Total	119.82	18.72	
BMI_B	0	42.04	4.28	0.413
	1	43.71	4.16	
	2	43.58	4.29	
	3	44.35	4.66	
	Total	43.56	4.31	
FM_B	0	51.28	10.19	0.669
	1	55.14	10.27	
	2	54.08	11.66	
	3	54.69	12.37	
	Total	54.16	11.21	
FFM_B	0	65.03	12.01	0.095
	1	63.01	10.62	
	2	65.37	14.04	
	3	71.79	15.46	
	Total	65.48	13.32	
MM_B	0	61.79	11.50	0.087
	1	59.81	10.25	
	2	62.07	13.51	
	3	68.40	14.86	
	Total	62.21	12.84	

Body composition by fatty liver grade at month 6 items Fatty liver month 6 Std. deviation Mean р Weight_6M 0 87.37 11.44 0.210 1 83.78 12.80 2 89.96 11.97 Total 86.55 12.08 BMI_6M 0 30.47 3.60 0.120 31.08 3.40 1 2 32.77 2.71 Total 31.10 3.45 FM_6M 0 27.62 7.91 0.234 31.35 1 12.12 2 32.03 7.88 Total 29.74 9.70 0.016* FFM_6M 0 58.78 11.04 10.47 54.46 1 2 57.95 8.18 57.09 10.44 Total MM_6M 0 56.47 11.00 0.022* 1 51.72 10.05 2 55.06 7.87 Total 54.53 10.27 *p-value less than 0.05 was considered as statistically significant.

FFM, fat-free mass; FM, fat mass; MM, muscle mass.

*p-value less than 0.05 was considered as statistically significant. FFM, fat-free mass; FM, fat mass; MM, muscle mass. height ratio (WHtR), and the inflammatory state, as determined by NLR. In Sapele, Southern Nigeria, obese individuals exhibited significantly elevated values of BMI, NLR, and monocyte count compared to healthy controls^[29]. Increased leukocyte and NLR levels in children, especially boys, who are overweight or obese may serve as biomarkers of insulin resistance and are useful for predicting and preventing potential complications^[30]. It has been shown that obese children and adolescents have lower NLR values than adults, indicating a lower level of systemic inflammation regardless of the disease severity. It has been concluded that while obesity is known to cause chronic low-grade systemic inflammation, this condition has less effects in childhood, as the NLR did not distinguish between subgroups^[31]. In other investigation, it was found that obese individuals have higher leukocyte counts and levels of leukocyte subtypes compared to healthy individuals. However, the NLR ratio was significantly elevated only in cases of obesity accompanied by insulin resistance, which may show a link between NLR, insulin resistance, and inflammation^[32]. Laparoscopic sleeve gastrectomy (LSG) has been observed to have anti-inflammatory impacts by reducing NLR. However, improvements in hepatosteatosis following LSG were not found to be related to the average decrease in NLR^[33]. Another study also revealed that the severity of inflammation can be indicated by an elevated NLR ratio, which is linked to the initial stages of atherosclerosis^[21].

Understanding the complications of bariatric surgery and predicting its results is crucial. Alongside the clinical variables currently utilized for postoperative evaluation, Makal and colleagues proposed that CAR3 is the most diagnostic marker and can aid in determining the point of care. PLR3 values in addition to CAR1, CRP3, and CRP1, followed in terms of diagnostic significance. They also demonstrated that the preoperative NLR value may assist in identifying patients who are more likely to experience complications^[13]. Also, the preoperative NLR has been shown to have the capacity to serve as a prognostic marker for weight loss and diabetes remission in individuals undergoing sleeve gastrectomy (SG). When used in conjunction with other existing scores, it can provide valuable data prior to SG. Although PLR did not appear to be related to metabolic parameters in this population^[34]. However, our study did not demonstrate the significant association between NLR and postoperative measured results. In the study by Zhou and colleagues, it has been mentioned that the initial baseline RDW level before surgery can serve as an initial predictor of the outcomes of various metabolic surgeries in patients with obesity and diabetes. However, the baseline MPV value before surgery did not appear to have a significant predictive effect on the outcomes of Roux-en-Y gastric bypass (RYGB) surgery in patients with obesity and diabetes. Although it showed some predictive value for weight loss in the three months following SG surgery^[35]. The findings of a study at the 12-month follow-up after weight loss surgery demonstrated that there was a significant reduction in platelet count, but the decrease in MPV was not statistically significant. Furthermore, the study found that SG resulted in a more significant decrease in platelet count compared to RYGB. However, there was no significant difference in the changes in MPV between the two surgical intervention groups^[36]. It has been mentioned that MPV has the potential to serve as an indicator of inflammation in obesity and diabetes and considering cost-effective and easy-to-assess characteristic, periodic screening of MPV besides HbA1c and other measures, can help monitoring the inflammatory status associated with these disorders.^[37]. But some contradictory findings exist. A study by Sen and colleagues showed a significant reduction in platelets and WBC levels after one year of LSG, while MPV showed unchanged values. No correlation was mentioned between the decreased platelets levels and weight reduction. More research is required to better understand the role of hematologic markers in the pathogenesis of prothrombotic cardiac diseases in obese patients and those who have had bariatric surgery^[38]. The results of a study indicated that the preoperative RDW level can predict the amount of weight loss that the patient will lose and the effectiveness of the operation after SG. Furthermore, the findings suggested that RDW is an indicator of excess BMI loss at one year following laparoscopic RYGB, which could serve as a novel biomarker offering prognostic data that is clinically significant. The study highlighted the need for larger research for more extensive investigation into how inflammatory indicators affect weight reduction outcomes after bariatric surgery^[39].

The association between inflammatory markers and fatty liver diseases has also been investigated so far. The findings of an investigation revealed a non-linear connection between NLR and PLR with NAFLD considering potential confounding variables. The outcomes indicate that a PLR value of greater than or equal to 42.29 may act as a protective factor against non-alcoholic fatty liver disease (NAFLD), whereas an NLR value below 1.23 may pose a risk for the development of NAFLD^[40]. In other study by Duan and colleagues no links has been found between NLR, PLR, LMR, PDW, and MPV and NAFLD in obese children. Despite previous suggestions of the enhanced predictive power of novel inflammatory ratios, including NLR, PLR, and MPV, over traditional cytokines, their results did not support their effectiveness in predicting NAFLD. PDW and MPV, commonly used as platelet biomarkers, were also inadequate for NAFLD prediction in this demographic. Limited participants and the multifaceted nature of these markers may contribute to the lack of significance. Notably, inflammatory cytokines remained more predictive than other potential biomarkers in this study^[41]. On the other hand, Elevated MPV and RDW levels in NAFLD patients, showed a significant correlation with liver damage and these markers suggested to be valuable for assessing NAFLD onset and progression^[42]. In our study, no significant association was observed between the change in fatty liver grade and the baseline values of the markers. Also in our study, there is a correlation between the progression of fatty liver grade and alterations in body composition, specifically within the 3- and 6-month intervals. Notably, individuals exhibiting higher MM display a fatty liver grade of zero, while patients characterized by elevated levels of both FFM and MM concurrently exhibit a fatty liver grade of zero. Following a 6-month duration subsequent to the surgical procedure, a complete absence of patients classified as grade 3 was observed. Similarly the results of a meta-analysis have confirmed that the majority of patients experience improvement or complete resolution of steatosis, steatohepatitis, and fibrosis following weight loss induced by bariatric surgery^[43].

The primary limitation of our study lies in its nature as a singlecenter retrospective observational study, making it susceptible to selection bias. To validate the efficacy of MPV and RDW, further confirmation is needed through multicenter designed studies. Additionally, crucial factors like lifestyle, economy, and environment influencing obesity and fatty liver progression were not accounted for due to the absence of participant data. Also, the absence of liver biopsy confirmation, the gold standard for diagnosing NAFLD, are noteworthy limitations. Instead, NAFLD diagnosis relied on ultrasonography, which lacks sensitivity for detecting mild steatosis.

Conclusion

In conclusion, our study results revealed that the cost-effective and easy-to-assess nature of blood tests, particularly those assessing inflammatory markers particularly RDW can aid in predicting weight loss and surgical success following bariatric surgery. On the other hand, no patients classified as grade 3 of fatty liver after a 6-month postoperative period, despite the absence of a significant association between the change in fatty liver grade and the baseline values of the markers. While the retrospective design of this study limits its findings to existing clinical data, future prospective research should collect additional samples, extend the observation time, and examine the long-term predictive value of these markers. Ultimately, identifying simple and effective indicators that accurately predict surgical outcomes could aid in making optimal choices for metabolic surgeries.

Ethical approval

The study was conducted with the approval of the institutional review board of Tehran University of Medical Sciences (IR. TUMS.SINAHOSPITAL.REC.1402.033).

Consent

For this type of study formal consent is not required.

Source of funding

This study received no funding or financial support.

Author contribution

Conceptualization: H.R., R.K., K.N. Data curation: A.A., H.R. Formal analysis: B.K. Investigation: P.P., A.A., R.H. Methodology: M.T., R.K. Project administration: R.K., K.N. Resources: B.K., M.T. Software: B.K. Supervision: R.K. Validation: R.K., M.T. Visualization: H.R., R.K. Writing original draft: H.R., P.P., R.H. Writing—review and editing: R.K.

Conflicts of interest disclosure

The authors declare that they have no conflict of interest.

Research registration unique identifying number (UIN)

This longitudinal retrospective study was conducted on patients registered in the obesity surgery database of Sina Hospital (https://sinaobesity.ir).

Guarantor

Razieh Khalooeifard.

Data availability statement

Data sharing is not applicable to this article.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

The authors thank the Research Development Center Of Sina Hospital for their technical assistance.

References

- [1] Elder KA, Wolfe BM. Bariatric surgery: a review of procedures and outcomes. Gastroenterology 2007;132:2253-71.
- [2] Vreeken D, Seidel F, Custers EM, et al. Factors associated with cognitive improvement after bariatric surgery among patients with severe obesity in the Netherlands. JAMA Netw Open 2023;6:e2315936.
- [3] Kinlen D, Cody D, O'Shea D. Complications of obesity. QJM 2018;111: 437–43.
- [4] Ferrante AW Jr. Obesity-induced inflammation: a metabolic dialogue in the language of inflammation. J Intern Med Suppl 2007;262:408–14.
- [5] Naomi R, Teoh SH, Embong H, et al. The role of oxidative stress and inflammation in obesity and its impact on cognitive impairments—a narrative review. Antioxidants 2023;12:1071.
- [6] Hildebrandt X, Ibrahim M, Peltzer N. Cell death and inflammation during obesity: "Know my methods, WAT(son)". Cell Death Differ 2023; 30:279–92.
- [7] Keshavjee SH, Schwenger KJP, Yadav J, *et al.* Factors affecting metabolic outcomes post bariatric surgery: role of adipose tissue. J Clin Med 2021; 10:714.
- [8] Nuijten MA, Eijsvogels TM, Monpellier VM, et al. The magnitude and progress of lean body mass, fat-free mass, and skeletal muscle mass loss following bariatric surgery: a systematic review and meta-analysis. 232022:e13370.
- [9] Sjöström LJJoim. Review of the key results from the Swedish Obese Subjects (SOS) trial-a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273:219–34.
- [10] Abdul Wahab R, le Roux CW. A review on the beneficial effects of bariatric surgery in the management of obesity. Expert Rev Endocrinol Metab 2022;17:435–46.
- [11] Alabduljabbar K, le Roux CW. Pharmacotherapy before and after bariatric surgery. Metabolism 2023;148:155692.
- [12] Khalooeifard R, Adebayo O, Rahmani J, *et al.* Health effect of bariatric surgery on patients with asthma: a systematic review and meta-analysis. Bariatr Surg Pract Patient Care 2021;16:2–9.
- [13] Bora Makal G, Yıldırım O. Are the C-reactive protein/albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (NLR) novel inflammatory biomarkers in the early diagnosis of postoperative complications after laparoscopic sleeve gastrectomy? Obes Res Clin Pract 2020;14:467–72.
- [14] Lasselin J, Magne E, Beau C, *et al.* Adipose inflammation in obesity: relationship with circulating levels of inflammatory markers and association with surgery-induced weight loss. J Clin Endocrinol Metab 2014; 99:E53–61.
- [15] Rodríguez-Rodríguez E, Salas-González MD, Ortega RM, et al. Leukocytes and neutrophil–lymphocyte ratio as indicators of insulin resistance in overweight/obese school-children. Front Nutr 2022;8: 811081.
- [16] Zheng C-F, Liu W-Y, Zeng F-F, et al. Prognostic value of platelet-tolymphocyte ratios among critically ill patients with acute kidney injury. Crit Care 2017;21:238.
- [17] Oh GH, Chung SP, Park YS, *et al.* Mean platelet volume to platelet count ratio as a promising predictor of early mortality in severe sepsis. Shock 2017;47:323–30.
- [18] Radkhah H, Mansouri ES, Rahimipour Anaraki S, *et al.* Predictive value of hematological indices on incidence and severity of pulmonary embolism in COVID-19 patients. Immun Inflamm Dis 2023;11:e1012.

- [20] Grassadonia A, Graziano V, Iezzi L, et al. Prognostic relevance of neutrophil to lymphocyte ratio (NLR) in luminal breast cancer: a retrospective analysis in the neoadjuvant setting. Cells 2021;10:1685.
- [21] Aydin M, Yilmaz A, Donma MM, et al. Neutrophil/lymphocyte ratio in obese adolescents. North Clin Istanb 2015;2:87–91.
- [22] Chi P-J, Wu K-T, Chen P-J, et al. The serial changes of neutrophilelymphocyte ratio and correlation to weight loss after laparoscopic sleeve gastrectomy. Front Surg 2022;9:939857.
- [23] Madan SA, John F, Pitchumoni CS. Nonalcoholic fatty liver disease and mean platelet volume. J Clin Gastroenterol 2016;50:69–74.
- [24] Karaoğullarindan Ü, Üsküdar O, Odabaş E, et al. Is mean platelet volume a simple marker of non-alcoholic fatty liver disease? Indian J Gastroenterol 2023;42:219–25.
- [25] Mathew G, Agha R, Albrecht J, *et al.* STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. Int J Surg 2021;96:106165.
- [26] Schmatz R, Bitencourt MR, Patias LD, et al. Evaluation of the biochemical, inflammatory and oxidative profile of obese patients given clinical treatment and bariatric surgery. Clin Chim Acta 2017;465: 72–9.
- [27] Rodríguez-Rodríguez E, López-Sobaler AM, Ortega RM, et al. Association between neutrophil-to-lymphocyte ratio with abdominal obesity and healthy eating index in a representative older spanish population. Nutrients 2020;12:855.
- [28] Erdal E, İnanir M. Platelet-to-lymphocyte ratio (PLR) and plateletcrit (PCT) in young patients with morbid obesity. Revista Associação Médica Brasileira 2019;65:1182–7.
- [29] ETIM EA, Amaihunwa K, Jeremiah Z, et al. Evaluation of neutrophillymphocyte ratio and monocyte count among adult obese subjects in Sapele, Southern Nigeria. J Med Res Health Sci 2021;4:1324–8.
- [30] Rodríguez-Rodríguez E, Salas-González MD, Ortega RM, et al. Leukocytes and neutrophil-lymphocyte ratio as indicators of insulin resistance in overweight/obese school-children. Front Nutr 2022;8:11081.
- [31] Marra A, Bondesan A, Caroli D, et al. The neutrophil to lymphocyte ratio (NLR) positively correlates with the presence and severity of metabolic

syndrome in obese adults, but not in obese children/adolescents. BMC Endocr Disord 2023;23:121.

- [32] Karakaya S, Altay M, Efe FK, *et al.* The neutrophil-lymphocyte ratio and its relationship with insulin resistance in obesity. Turkish J Med Sci 2019; 49:245–8.
- [33] Yildirim K, Karabicak İ, Ulu EK, et al. Does neutrophil-lymphocyte ratio correlate with the improvement of hepatosteatosis after laparoscopic sleeve gastrectomy? Obes Facts 2022;15:711–6.
- [34] Zubiaga L, Ruiz-Tovar J. Correlation of preoperative neutrophil-tolymphocyte ratio and platelet-to-lymphocyte ratio with metabolic parameters in patients undergoing sleeve gastrectomy. Surg Obes Relat Dis 2020;16:999–1004.
- [35] Zhou L, Lin S, Zhang F, et al. The correlation between RDW, MPV and weight indices after metabolic surgery in patients with obesity and DM/IGR: Follow-up observation at 12 months. Diabetes Ther 2020;11:2269–81.
- [36] Raoux L, Moszkowicz D, Vychnevskaia K, et al. Effect of bariatric surgery-induced weight loss on platelet count and mean platelet volume: a 12-month follow-up study. Obes Surg 2017;27:387–93.
- [37] Aktas G, Kocak MZ, Taslamacioglu Duman T, *et al.* Mean Platelet Volume (MPV) as an inflammatory marker in type 2 diabetes mellitus and obesity. Bali Med J 2018;7.
- [38] Sen O, Oray S, Çalikoglu I, et al. Effect of laparoscopic sleeve gastrectomy on platelet count and mean platelet volume. J Minim Access Surg 2023; 19:482–92.
- [39] Wise ES, Hocking KM, Weltz A, et al. Red cell distribution width is a novel biomarker that predicts excess body-mass index loss 1 year after laparoscopic Roux-en-Y gastric bypass. Surg Endosc 2016;30:4607–12.
- [40] Zhou Y, Tian N, Li P, et al. The correlation between neutrophil-tolymphocyte ratio and platelet-to-lymphocyte ratio with nonalcoholic fatty liver disease: a cross-sectional study. Eur J Gastroenterol Hepatol 2022;34:1158–64.
- [41] Duan Y, Luo J, Pan X, et al. Association between inflammatory markers and non-alcoholic fatty liver disease in obese children. Front Public Health 2022;10:991393.
- [42] Verma S, Verma M, Khari S. Association of hematological parameters (mean platelet volume and red cell distribution width) with nonalcoholic fatty liver disease. APIK J Intern Med 2023;11:37–44.
- [43] Mummadi RR, Kasturi KS, Chennareddygari S, et al. Effect of bariatric surgery on nonalcoholic fatty liver disease: systematic review and metaanalysis. Clin Gastroenterol Hepatol 2008;6:1396–402.