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General Surgery

The relationship between preoperative hemoglobin, albumin, lymphocyte, and platelet (HALP) score and right colon cancer surgery outcomes: a retrospective cohort study

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ABSTRACT

Objectives: This study aims to investigate the association between the preoperative Hemoglobin Albumin Lymphocyte Platelet (HALP) score and surgical outcomes in right colon cancer patients.

Methods: This retrospective cohort study included patients undergoing elective right colon adenocarcinoma surgery from January 2017 to June 2023 at Bursa Yuksek Ihtisas Training and Research Hospital. The HALP score, calculated from hemoglobin, albumin, lymphocyte, and platelet levels, aimed to predict perioperative morbidity through receiver operating characteristic (ROC) curve analysis.

Results: The study involved 67 patients, mostly male with an average age of 68.28 years, undergoing 46 open and 21 laparoscopic surgeries. Although the HALP score's cutoff value was established, it did not significantly predict perioperative morbidity (P>0.05). However, lower platelet counts (<318×103/L) and open surgery type correlated significantly with higher morbidity (P<0.05).

Conclusions: This study reveals that the HALP score may not effectively predict perioperative morbidity in right colon cancer surgeries, highlighting platelet counts as a more promising marker. Our findings also confirm the increased morbidity associated with open surgeries, challenging existing assumptions and guiding clinical practice.

Keywords: Colon cancer, surgery, morbidity, nutrition

olon cancer is the second leading cause of mortality from cancer globally and is categorized based on its anatomical site [1-3]. The differentiation of right and left colon cancer is crucial to optimize approaches to therapy, considering their distinct

molecular and immunological pathological characteristics [4-6].

While there is growing interest in exploring alternative treatment approaches for colon cancer, it is widely acknowledged that surgery remains the most

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efficacious treatment modality. Consequently, accurately predicting and proactively preventing perioperative complications is of crucial significance to ensure optimal outcomes [1, 7].

Malnutrition is a common occurrence among individuals diagnosed with cancer, and it has been linked to the development of various perioperative complications [8, 9]. The Hemoglobin Albumin Lymphocyte Platelet (HALP) score, a metric thought to indicate the immune nutritional status of individuals diagnosed with cancer, has been extensively investigated across various cancer types, including colorectal cancer [10]. The HALP score is determined by the formula: (hemoglobin concentration in grams per liter multiplied by albumin concentration in grams per liter multiplied by lymphocyte count per liter divided by platelet count per liter). These four markers are important factors that should be considered when assessing the immune and nutritional status of cancer patients [11].

The purpose of this study is to investigate the relationship between surgical outcomes in patients diagnosed with right colon cancer and the HALP score, a metric that assesses immune-nutrition status.

METHODS

A retrospective study was conducted on patients who underwent elective surgery for right colon adenocarcinoma at our clinic from January 2017 to June 2023 at Bursa Yuksek Ihtisas Training and Research Hospital. This study was approved by clinical research ethics committee of the Bursa Yuksek Ihtisas Training and Research Hospital (Decision number: 2011-KAEK-25 2023/10-03, Date: 18.10.2023). At our clinic, patients diagnosed with right colon cancer following a colonoscopic examination undergo a comprehensive evaluation by a multidisciplinary tumor council. Subsequently, surgical procedures according to the principles of total mesocolic excision are performed either laparoscopically or by open surgery.

As previously indicated, our study focused specif-

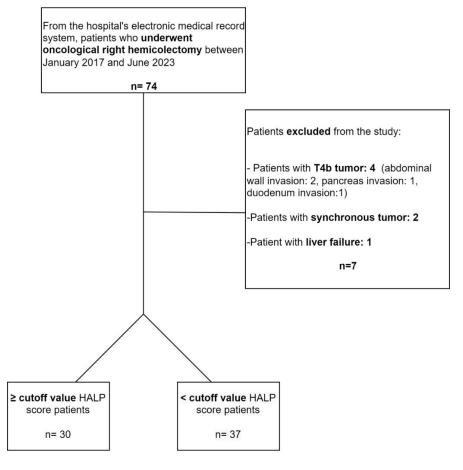


Fig. 1. Flowchart for patient selection and evaluation.

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ically on patients with right colon cancer rather than including all individuals with colorectal tumors, due to the notable pathological and clinical distinctions between these subgroups. The hypothesis proposes that patients who exhibit a favorable immunonutrition status, specifically those with elevated HALP scores, are likely to experience improved surgical outcomes. The present study aimed to assess the superiority of surgical outcomes through analyzing the incidence of morbidity during the perioperative period of 30 days. Our assessment for complication was based on the Clavien-Dindo Classification system.

Patiences eligible for this study were adults over the age of 18 who were diagnosed with adenocarcinoma through colonoscopic examination and underwent total mesocolic excision. The study excluded patients presenting with T4b stage adenocarcinoma involving adjacent organs, those with synchronous or metachronous tumors, and those suffering from severe organ failures, such as in the heart or liver (Fig. 1).

Statistical Analysis

Categorical variables were presented as numbers and percentages. Continuous variables were expressed as mean \pm standard deviation (SD), with minimum and maximum values. For categorical variables, Chisquare or Fisher's exact tests were utilized. The optimal cutoff point for the HALP score in relation to morbidity was defined as the point closest to 0% false positive and 100% true positive on the ROC (Receiver Operating Characteristic) curve. For comparing parameters with normal distribution across HALP groups, Student's t-test was employed, while the Mann-Whitney U test was used for parameters not showing a normal distribution in HALP groups. In the research, initial analyses of age, gender, certain clinical features, and laboratory results on morbidity were conducted using Univariate Logistic Regression (LR). Subsequently, variables found to be significant were analyzed using Stepwise Multivariate LR (Enter method). Quantitative variables were included in the logistic regression model based on their median values as cutoff points. A P-value of <0.05 was considered statistically significant. Clinical data were analyzed using IBM SPSS (IBM Corporation, Armonk, New York, United States) version 25.

Table 1. Sociodemographic and clinical characteristics of the cases (n=67)

Parameters	Data
Gender, n (%)	
Male	35 (52.2)
Female	32 (47.8)
Age (years)	68.28±12.14 (38-89)
BMI (kg/m ²)	28.38±3.73 (20-37.1)
ASA score, n (%)	,
1	3 (4.6)
2	32 (47.7)
3	32 (47.7)
Operation type, n (%)	
Open procedure	46 (68.6)
Laparoskopic procedure	21 (31.4)
Length of stay (days)	
Open procedure	9±4.1 (5-25)
Laparoskopic procedure	7±1.8 (4-13)
Overall	9.04±3.67 (4-25)
Surgery duration (min)	
Open procedure	183.10±55.19 (100-300)
Laparoskopic procedure	204.57±50.25 (120-320)
Overall	197.94±52.37 (100-320)
Number of lynph nodes dissected	
Open procedure	21±10.7
Laparoskopic procedure	23±7.7
Tumor size (cm)	5.7±2.5 (2-15) cm
Tumor localization, n (%)	
Cecum	23 (34.3)
Cecum (ileocecal valve)	3 (4.4)
Ascending colon	16 (23.8)
Hepatic flexure	19 (28.3)
Transverse colon proximal	6 (8.9)
T stage, n (%)	
T	2 (2.9)
T2	3 (4.4)
T3	40 (59.7)
T4	22 (32.8)

Table 1 contunied.

TNM stage, n (%)					
1	5 (7.4)				
2A	19 (28.3)				
2B	10 (14.9)				
3A	4 (5.9)				
3B	20 (29.8)				
3C	9 (13.4)				
Lymphovascular invasion, n (%)					
Yes	27 (40.3)				
No	40 (59.7)				
Hemoglobin (g/dL)	96.85±35.88 (8-147)				
Albumin (g/L)	37.46±42,76 (2-371)				
Platelets (×10 ³ /L)	322.49±97.74 (105-622)				
Lymphocyte(×10 ³ /L)	1.75±0,68 (0.27-3.6)				
HAALP score	22.28±14.92 (1-76)				
Readmission, n (%)					
Yes	7 (10.6)				
No	59 (89.3)				
Morbidity, n (%)					
Yes-open procedure	22/46 (47,8)				
Yes-laparoscopic	5/21 (23,8)				
Clavian-Dindo morbidity score, n (%)					
<3	16 (59.3)				
≥3	11 (40.7)				
Mortality, n (%)					
Yes	1 (1.5)				
No	66 (98.5)				

Qualitative variables are presented as n (%), and quantitative variables are presented as mean±standard deviation (min-max). BMI=Body Mass Index, ASA= American Society of Anaesthesiologists, T=Tumor, TNM=Tumor, Imph node, metastasis, BMI=Body Mass Index, ASA=American Society of Anaesthesiologists

RESULTS

The demographic, clinical, and pathological features of 67 patients who underwent surgery are listed in

Table 1. The study sample comprised 35 (52.2%) male and 32 (47.8%) female patients. The average age of the cases was 68.28±12.14 years (range: 38-89). The mean BMI was 28.38±3.73 (range: 20-37.1). The average values and standard deviations for HALP score, tumor size, number of lymph nodes, operation and hospitalization durations, were calculated 22.28±14.92, 5.7±2.5 cm, 23.18±9.78, 197.94±52.37 minutes, 9.04±3.67 days, respectively. Among the cases, 32 (47.7%) had an ASA score of 2, 46 (68.6%) underwent open surgery, and 23 (34.3%) had tumors located in the cecum. Forty patients (59.7%) were in stage T3, twenty (29.8%) in pathological stage 3B, and lymphovascular invasion was observed in 27 (40.3%) cases. Clinically, 7 patients (10.6%) were readmitted, morbidity was observed in 27 (40.3%), and there was 1 case (1.5%) of mortality.

In this study, a ROC (Receiver Operating Characteristic) curve was drawn using the HALP parameter to assess morbidity in cases (Fig. 2). Upon conducting ROC analysis, it was determined that the cutoff point for the HALP value, which could predict patients with morbidity, was values less than 21.5. It was found that the HALP index's ability to distinguish patients with morbidity was not statistically significant (P=0.498). According to this cutoff point, the area under the ROC curve (AUC) was calculated to be 0.549, with a Sensitivity of 55.6% and a Specificity of 62.5% (Table 2). The clinicopathological characteristics of patients in high and low HALP groups were compared in Table 3. Thirty-seven patients were classified into the low HALP group, while thirty were assigned to the high HALP group. Upon examining the results, it was observed that there were no statistically significant differences in the demographic, surgical, pathological parameters of the cases. Naturally, in laboratory results, Hemoglobin (HB), Platelet (PLT), and Lymphocyte (LYM) values were found to be associated with HALP (P<0.05).

The distribution of surgical characteristics among cases in high and low HALP groups was compared in Table 4. Upon examination of the results, it was found that the distribution of surgical characteristics, other than morbidity, had no association with HALP (P>0.05).

After conducting a Univariate Logistic Regression

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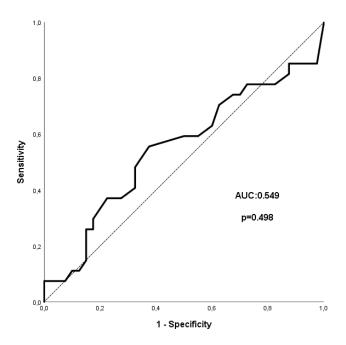


Fig. 2. Receiver operational characteristic (ROC) curve of HALP score to predict morbidity in cases.

(LR) analysis, it was observed that the type of operation, incidence of readmission, and platelet (PLT) variables were statistically significant risk factors for morbidity in Table 5 (P<0.05). It was determined that cases with open surgery had a 3.443 times higher risk of morbidity compared to those with laparoscopic surgery (1.090-10.879) (P=0.035). Similarly, cases with readmission had a 6.158 times higher risk of morbidity compared to others (1.134-33.427) (P=0.035). Additionally, cases with PLT values below 318 000/L had a 4.177 times higher risk of morbidity than those with PLT values above 318 (1.452-11.673) (P=0.008). It was found that the HALP score, based on the determined cutoff value, did not have a significant relationship with perioperative morbidity. Factors found to be significant were included in the Multivariate LR (Multivariate Logistic Regression) model using the Enter method. Upon examination of the results, it was established that the significance of PLT values continued in the Multivariate LR model.

DISCUSSION

Based on the statistical analysis findings obtained from our dataset, it is not possible to establish a significant association between the HALP score and perioperative morbidity in patients with right colon cancer. Based on our findings, it is interesting to consider the higher prevalence of morbidity among patients with platelet values below 318×103/L, as indicated in the existing literature [12].

Chaouch et al. [13] 's analysis of the demographic information of the patients included in the study suggests that, in comparison to the literature on right colon cancer surgery series, our patient profile is more geriatric (mean age=68.28 years). Our preponderance of male patients (52%) is consistent with the published data, and it is possible to conclude that our patients are more obese (mean BMI=28.38 kg/m²) than the patients described in the literature [14-20]. With an ASA score of 3 for 47% of our patients, we are able to claim

Table 2. ROC analysis of the Halp scores of the cases on morbidity

Parameter	Cut-off	AUROC	95 % CI	Sensitivity (%)	Specificity (%)	P
HALP	≤21.5	0.549	0.403-0.696	55.6	62.5	0.498

AUROC: Area Under the ROC, CI: Coenfidence Interval

Table 3. Comparison of distributions of patient characteristics according to HALP score cut-off point

point			
	HALP <21.5	HALP >21.5	P value
	(n=37)	(n=30)	
Gender, n (%)			
Male	23 (62.2)	12 (40)	0.071*
Female	14 (37.8)	18 (60)	
Age (years)	69.57±12.21 (39-88)	67.5±11.5 (38-89)	0.482‡
BMI (kg/m²)	28.52±3.76 (22-37.1)	28.39±3.71 (20-32.8)	0.887‡
Tumor size (cm)	6±2.4 (2-13)	5.4±2.7 (2.5-15)	0.293‡
Number of lmph nodes dissected	22.27±9.78 (4-52)	24.03±9.92 (7-52)	0.468‡
Hemoglobin (g/dL)	89.84±38.71 (8-134)	105.5±30.47 (10-147)	0.044 †
Albumin (g/L)	32.19±10.19 (3-46)	43.97±62.88 (2-371)	0.582†
Platelets (×10 ³ /L)	357.19±95.81 (184-622)	279.7±83.16 (105-461)	0.001‡
Lymphocyte(×10³/L)	1.48±0.51 (0.27-2.5)	2.08±0.72 (0.68-3.6)	0.001‡
ASA Score, n (%)			
1	2 (5.4)	1 (3.3)	0.199*
2	14 (37.8)	18 (60)	
3	21 (56.8)	11 (36.7)	
Type of operation, n (%)			
Open procedure	27 (73)	19 (63.3)	0.395*
Laparoskopic procedure	10 (27)	11 (36.7)	
Tumor lacalization, n (%)			
Cecum	12 (32.4)	11 (36.7)	0.671*
Cecum (ileocecal valve)	2 (5.4)	1 (3.3)	
Ascending colon	9 (24.3)	7 (23.3)	
Hepatic flexure	9 (24.3)	10 (33.3)	
Transverse colon proximal	5 (13.5)	1 (3.3)	
T stage, n (%9			
T1	1 (2.7)	1 (3.3)	0.956*
T2	2 (5.4)	1 (3.3)	
Т3	21 (56.8)	19 (63.3)	
T4	13 (35.1)	9 (30)	
TNM stage, n (%)			
1	3 (8.1)	2 (6.7)	0.857*
2A	12 (32.4)	7 (23.3)	
2B	5 (13.5)	5 (16.7)	
3A	2 (5.4)	2 (6.7)	
3B	9 (24.3)	11 (36.7)	
3C	6 (16.2)	3 (10)	
Lymphovascular invasion, n (%)(%)	()	()	
None (70)(70)	21 (58.3)	18 (60)	0.861*
Exist	15 (41.7)	12 (40)	

Qualitative variables are presented as n (%), and quantitative variables are presented as mean±standard deviation (min-max). BMI=Body Mass Index, ASA= American Society of Anaesthesiologists, T=Tumor, TNM=Tumor, Imph node, metastasis, *P value was obtained from Chi-square test, †P value was obtained from Mann Whitney U test, ‡P value was obtained from Student's t test.

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Table 4. Comparison of the distribution of surgical characteristics of the cases according to the HALP score cut-off point

	HALP <21.5	HALP <21.5 HALP >21.5		
	(n=37)	(n=30)	P value	
Surgery duration (min)				
Open procedure	197.04±51.84 (120-315)	209.21±41.51 (140-300)	0.400†	
Laparoscopic procedure	179.50±44.75 (120-255)	186.36±65.31 (100-300)	0.784†	
Length of stay (day)	8.62±50.04 (5-20)	9.60±4.48 (4-25)	0.510†	
Tumor size (cm)	6.01±2.42 (2-13)	5.35±2.67 (2.5-15)	0.114†	
Number of lymph nodes dissected	22.27±9.78 (4-52)	24.03±9.92 (7-52)	0.384†	
Readmission, n (%)				
Exist	4 (10.8)	3 (10.3)	0.921*	
None	33 (89.1)	26 (89.7)		
Mortality, n (%)				
Exist	0 (0)	1 (3.3)	0.448*	
None	37 (100)	29 (96.7)		

Qualitative variables are presented as n (%), and quantitative variables are presented as mean \pm standard deviation (min-max). *P value was obtained from Chi-square test, †P value was obtained from Mann Whitney U test

Table 5. Univariate and multivariate logistic regression analysis of clinical and surgical characteristics of the cases based on morbidity

	Univariate LR		Multivariate LR	
	OR (95% CI)	P value	OR (95% CI)	P value
Gender (ref: male)	1.190 (0.449-3.150)	0.726		
Age>70 (ref≤70)	2.273 (0.843-6.126)	0.105		
BMI >30 (ref≤30)	0.277 (0.031-2.513)	0.254		
ASA score 3 (ref≤2)	2.273 (0.843-6.126)	0.105		
Type of procedure - Open(ref: Lap)	3.443 (1.090-10.879)	0.035		
Tumor size >5 (ref≤5 cm)	0.971 (0.362-2.606)	0.953		
Number of dissecten lymph node >22 (ref≤22)	0.884 (0.335-2.338)	0.804		
T stage >2 (ref≤2)	12.125 (0.015-45.151)	0.999		
TNM stage=3 (ref≤2)	1.636 (0.425-6.301)	0.474		
Lymphovascular invasion	1.724 (0.637-4.669)	0.284		
Operation duration >190 (ref≤190)	0.691 (0.260-1.834)	0.458		
Readmission	6.158 (1.134-33.427)	0.035		
Hemoglonin>106 (ref≤106)	0.691 (0.260-1.834)	0.458		
Albumin>35 (ref≤35)	0.639 (0.233-1.755)	0.385		
Platelets≤318 (ref>318)	4.117 (1.452-11.673)	0.008	4.501 (1.077-18.801)	0.04
Lymphocyte>1.7 (ref≤1.7)	0.567 (0.212-1.511)	0.256		
HALP <21.5	2.083 (0.772-5.623)	0.147		

LR=Logistic regression, CI=Confidence interval, Lap=Laparoscopic

that they are more comorbid than those reported in the literature, with the exception of the series by Chen et al. [21].

Our operation times for laparoscopic right hemicolectomy are consistent with current surgical standards, averaging 204.57 minutes, which is consistent with the 201.31 minutes reported by Zedan et al. [22]. However, our open surgeries averaged 183.10 minutes, exceeding the durations reported by Zedan et al. [22] at 152.04 minutes, Chen et al. [21] at 123/118.5 minutes, and Han et al. [17] at 110/133 minutes. These extended times in open procedures could reflect the complexities involved in managing a geriatric and comorbid patient cohort. At this point, our oncological laparoscopic right hemicolectomy performance is comparable to that of the literature; however, our oncological open right hemicolectomy operation time lags behind that of the literature.

In terms of hospital stays, our study shows shorter durations, ranging from 7.18 to 9.41 days, compared to the values reported by Zedan et al. [22] (9.13 to 13.04 days), Chen et al. [21] (9.2 to 15.2 days), and Li et al. [23] (18.5 to 17 days). The reduced length of hospital stays, particularly in open surgeries, may highlight the efficiency of our postoperative care protocols and indicate areas for potential improvement in patient management and discharge processes.

The number of lymph nodes retrieved in our surgeries, ranging from 21 to 23, meets the recommended threshold for accurate staging, which is above the 12-node minimum noted in the literature [22]. This node count is consistent with findings from Sheng et al. [20] who reported 19.2 to 19.9 nodes but is lower than the counts in studies by Zedan et al. [22] at 32.65 to 39.8 and Chen et al. [21] at 24.8 to 22.4. Our approach to lymph node dissection remains robust and ensures comprehensive staging essential for guiding treatment decisions.

Our perioperative morbidity rates for open oncological right hemicolectomy are 22/46 (47.8%) and for laparoscopic oncological right hemicolectomy to be 5/21 (23.8%), respectively, in comparison to the literature rates of 36.3% to 23.2% [14], 21.3% to 18.3% [19], and 27.2% to 14.7% [22]. While there is no clear advantage of laparoscopic or open surgery over the other in terms of perioperative morbidity [13], our morbidity rates, particularly in open surgery, are higher than those reported in the literature. The anas-

tomotic leak was categorized according to the Clavien-Dindo classification system as grade 3b. The occurrence rate of this complication was observed to be 2 out of 46 (%4,3) cases in open surgery and 1 out of 21 cases (4.7%) in laparoscopic surgery. One patient required a second surgical intervention as a result of evisceration, while another patient necessitated reoperation due to post-operative bleeding. The cause of our mortality was caused by sepsis that occurred because of anastomotic leakage.

The current research explores the association between HALP score and colorectal cancer, primarily focusing on overall survival and disease-free survival outcomes [10, 24, 25]. Research studies have demonstrated that when the HALP score above a specific threshold, there is a correlation with improved survival outcomes [24-26]. In our study, we endeavored to examine the correlation between the HALP score and perioperative morbidity in the context of right colon surgery. In the colorectal surgery study conducted by Yalav et al. [25], it was observed that there was no significant association between perioperative morbidity and the HALP score.

The composition of the tumor microenvironment depends on by the presence of inflammatory cells and host cells, and it has been suggested that it has a critical role in determining the clinical outcome [27]. Currently, there existed studies indicating that the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, albumin, and hemoglobin, when examined in peripheral blood, demonstrate association with the prognosis of colon cancer, similar to various other types of cancer [12, 28, 29]. Nevertheless, these factors do not provide conclusive evidence regarding the prognosis [27]. The primary focus of these research focuses around an indicator of overall survival, with no specific threshold established for platelet levels. Furthermore, based on the findings of these studies, there exists a mathematical correlation between elevated platelet levels and a poor outcome in relation to overall survival. Hence, it is obvious that no comparable findings exist in the current pool of literature regarding the association between perioperative morbidity and the additional outcome of our study, specifically the presence of 318,000 platelets.

Limitations

There are certain limitations inherent in our study

that need to be acknowledged. Firstly, the retrospective nature of our study raises concerns regarding the generalizability of our findings. Additionally, the limited number of patients included in our study further restricts the applicability of our results, particularly within a relatively specific group. Enhanced outcomes can be achieved for this subject matter through the utilization of larger sample sizes. In essence, while our study contributes valuable insights into the realm of right colon cancer surgery, it also highlights the need for continual, expansive research to unravel the intricate interplay of various factors influencing patient outcomes.

CONCLUSION

Our study highlights demographic features such as a geriatric population and higher BMI, which may influence morbidity outcomes in right colon cancer surgeries. Despite longer operation times and hospital stays compared to existing reports, our lymph node dissection adhered to standard protocols for accurate staging. Significantly, we found no correlation between the HALP score and perioperative morbidity, challenging previous assertions of its predictive value for survival outcomes in colorectal cancer. Contrary to earlier studies, our data also suggest that elevated platelet levels do not correlate with a better prognosis, calling for a reevaluation of their prognostic significance.

Authors' Contribution

Study Conception: OFA; Study Design: OFA; Supervision: MFE; Funding: N/A; Materials: MFA, SA; Data Collection and/or Processing: OFA, MK; Statistical Analysis and/or Data Interpretation: MK; Literature Review: OFA; Manuscript Preparation: OFA and Critical Review: MFE, SA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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