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Impact of the HALP Score on Long-Term Mortality among Patients Undergoing EVAR

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ABSTRACT

Introduction: Endovascular aortic repair (EVAR) is commonly used for abdominal aortic aneurysms, but its mortality rate remains high. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score, which measures hemoglobin, albumin, lymphocyte, and platelet levels, provides prognostic value by reflecting the nutritional status and systemic inflammation. This study aimed to explore the relationship between the HALP score upon admission and long-term mortality in patients with EVAR.

Methods: Consecutive patients with EVAR at our tertiary center from October 2010 to August 2021 were retrospectively analyzed. HALP scores were calculated using the following formula: hemoglobin (g/L) × albumin (g/L) × lymphocyte count (/L)/platelet count (/L). In-hospital and long-term mortality data were extracted. Receiver operating characteristic curve analysis identified predictors of in-hospital mortality. Multivariate Cox regression analysis was performed to examine determinants of long-term mortality.

Results: Among the 162 participants (mean age: 69.4±8.2 years, 90.1% male), the HALP score was the most significant predictor of in-hospital mortality (area under the curve: 0.752, 95% confidence interval: 0.674-0.830; p<0.001). Multivariate Cox regression analysis revealed HALP (p=0.001) and C-reactive protein (p=0.004) as independent determinants of long-term mortality.

Conclusion: This study is the first to investigate the association between the HALP score and in-hospital and long-term mortality in EVAR patients. The HALP score is a robust prognostic tool compared with its components and other parameters in this patient population.

Keywords: Endovascular aortic repair, HALP score, long-term mortality

Introduction

Abdominal aortic aneurysm (AAA) manifests as the enlargement of the abdominal aorta, which is the primary artery in the abdomen. Often asymptomatic, it is typically incidentally diagnosed during imaging examinations. Risk factors associated with AAA include advanced age, male sex, tobacco use, familial predisposition, and atherosclerosis (1-3). AAA, often linked with elevated morbidity and mortality rates if rupture occurs, presents considerable health hazards that necessitate timely detection and suitable intervention. Initially reliant on open surgery, endovascular aneurysm repair (EVAR) emerged in 1986 (4), and it has gained wide acceptance as a safe AAA treatment since Parodi et al.'s (5) report in 1991 (6). Although initially used for elderly or unsuitable surgical candidates, EVAR has become the gold standard for anatomically suitable patients today (7).

The hemoglobin, albumin, lymphocyte, and platelet (HALP) score, a novel indicator reflecting both nutritional status and systemic inflammation, has demonstrated prognostic significance for diverse cancer types (8). Looking at the components that make up HALP; Anemia and hypoalbuminemia signify malnutrition, lymphocytes modulate inflammation, and platelets contribute to thromboembolism and atherosclerosis (9).

Considering advanced age and potential malnutrition in AAA patients undergoing EVAR, alongside atherosclerosis risk factors, we investigated the HALP score's association with long-term mortality in this cohort, recognizing the dearth of similar studies in the literature.

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Methods

Study Population

This observational, retrospective study was conducted at a solitary center. We included 162 consecutive patients who underwent successful EVAR between October 2010 and August 2021. All participants were monitored for an average duration of 40±27 months. Patients with AAA rupture, neoplastic diseases, receiving chemotherapy, evidence of acute or chronic inflammatory diseases, glucocorticoid therapy in the last 3 months, immunosuppressive drug use, major trauma or surgery within the last 6 months, severe liver or kidney dysfunction, and those with missing demographic data were excluded. All clinical and demographic data were extracted from the hospital's electronic database. Thirty-nine patients (24.1%) were symptomatic, and the majority (75.9%) were asymptomatic, with AAA diagnosed incidentally through imaging modalities. All procedures were performed in the catheterization laboratory under sterile conditions with anesthesia administered by two experienced invasive cardiologists. Procedural success was determined by the absence of intraoperative fatalities, no need for conversion to open procedures, the absence of type 1-3 endoleaks, peripheral arterial circulation issues, and no stenosis in the renal and hypogastric arteries. After the procedure, all patients underwent postoperative monitoring in the coronary intensive care unit. Blood samples were collected from all patients via the antecubital vein following a 12 h fast prior to the endovascular procedure. Complete blood counts and biochemical analyses were conducted using an automated analyzer (Roche Diagnostic Modular Systems, Tokyo, Japan) at our institution. All patients were monitored for an average duration of 40±27 months. The study's endpoint was long-term all-cause mortality. The study protocol was approved by the University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital's Ethics and Research Committee and adhered to the principles of the Helsinki Declaration (approval number: 2024.01-11, date: 27.02.2024). Written informed consent was obtained from all participants.

Definition

The HALP score was calculated using the following formula: hemoglobin level (g/L) × albumin level (g/L) × lymphocyte count (/L)/platelet count (/L). The score was determined for each patient. Coronary artery disease included a history of angina pectoris, myocardial infarction, or coronary revascularization. Chronic obstructive pulmonary disease (COPD) includes chronic bronchitis or emphysema. Chronic kidney failure was defined as an estimated glomerular filtration rate ≤60 mL/min. Cerebrovascular accident involving a history of stroke or transient ischemic attack. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive medication. Diabetes mellitus was defined as a fasting blood glucose level ≥126 mg/dL, hemoglobin A1C ≥6.5%, or prescribed antidiabetic medication. High cholesterol was defined as a lipid-lowering drug use or LDL-C level ≥140 mg/dL. Heart failure was characterized by a preoperative ejection fraction <50%. Peripheral artery disease included arterial disease identified by Doppler ultrasonography and evidenced by lower extremity claudication.

Follow-up and Outcome

To monitor aortic health, contrast-enhanced computed tomography angiography was performed on all patients at intervals of 1, 6, and 12 months postoperatively, followed by annual evaluations. The study's primary endpoint was all-cause mortality, and patients were monitored from the day of EVAR until death. The reasons and time of mortality were obtained from hospital records and national death registries.

Statistical Analysis

The normality of variables was evaluated utilizing Kolmogorov-Smirnov tests, histograms, and probability plots. Numeric variables are reported as mean ± standard deviation (e.g., age, AAA diameter, etc.) or median (interquartile range) (e.g., HALP score, triglycerides, etc.) depending on their distribution. Categorical variables like gender, smoking status, etc., are expressed as percentages (%). Numerical variables between the two groups were compared using either unpaired Student's t-test or Mann-Whitney U test, while categorical variables were compared using the chi-square or Fisher's exact test. Kaplan-Meier modeling was utilized to depict the duration until the cessation of service events, serving as a proxy for mortality following aneurysm surgery. The analysis was conducted using SPSS 26.0 software (SPSS, Chicago, IL). Statistical comparisons of the time-to-event data for various interventions and controls were performed using log-rank tests and reported as median survival rates [years ± 95% confidence interval (CI)]. Additionally, in patients undergoing EVAR, a single-variable Cox proportional hazards model was utilized to compute hazard ratios and corresponding 95% CIs for long-term mortality. Multivariable Cox proportional hazards regression models were used to assess potential independent predictors of survival. The significance level was set at $p<0.050$.

Results

The study comprised 162 participants, with a mean age of 69.4±8.2 years, predominantly consisting of males (146 participants, 90.1%). Throughout the follow-up period, 50 out of 162 participants experienced mortality. Participants were stratified into two cohorts: survivors and non-survivors. The basic demographic, laboratory, and procedural data of the study group are summarized in Table 1. While demographic characteristics were similar between the two groups, non-survivors exhibited higher rates of congestive heart failure ($p=0.013$), COPD ($p=0.021$), and ES replacement requirement ($p<0.001$), whereas survivors demonstrated higher left ventricular ejection fraction (LVEF), % ($p<0.001$).

Regarding laboratory parameters, higher hemoglobin ($p<0.001$), albumin ($p<0.001$), lymphocyte count ($p<0.001$), and HALP score ($p<0.001$) were observed in the survivor group, whereas C-reactive protein (CRP) ($p=0.004$) and glucose ($p=0.023$) values were elevated in the non-survivor group. Other laboratory parameters did not differ significantly between the two groups. No significant differences were found in procedural data between the groups.

Univariate Cox regression analyses were performed to identify determinants of long-term mortality, revealing parameters significantly associated with mortality, such as COPD, LVEF, HALP, Glucose, and CRP (Table 2). In the multivariate Cox regression analysis, HALP ($p=0.001$)

Table 1. Characteristics of all-cause mortality and survivors among patients undergoing EVAR

	All patients (n=162)	Survivors (n=112)	Non-survivors (n=50)	p-value
Age, years	69.4±8.2	69±8.2	70.3±8.3	0.346
Sex (male), n (%)	146 (90.1)	100 (89.3)	46 (92)	0.593
BMI, kg/m^2	26.1±3.4	25.7±3.1	26.9±3.9	0.052
Smoking frequency, n (%)	50 (30.9)	35 (31.3)	15 (30)	0.874
Comorbidities				
Diabetes mellitus, n (%)	42 (25.9)	27 (24.1)	15 (30)	0.429
Hypertension, n (%)	98 (60.5)	67 (59.8)	31 (62)	0.793
CAD, n (%)	78 (48.1)	54 (48.2)	24 (48)	0.980
CHF, n (%)	25 (15.4)	12 (10.7)	13 (26)	**0.013**
Hyperlipidemia, n (%)	49 (30.2)	33 (29.5)	16 (32)	0.746
History of cancer, n (%)	14 (8.6)	12 (10.7)	2 (4)	0.160
Cerebrovascular disease, n (%)	7 (4.3)	6 (5.4)	1 (2)	0.332
Atrial fibrillation, n (%)	17 (10.5)	13 (11.6)	4 (8)	0.489
PAD, n (%)	12 (7.4)	7 (6.3)	5 (10)	0.400
COPD, n (%)	26 (16)	13 (11.6)	13 (26)	**0.021**
CKD, n (%)	22 (13.6)	15 (13.4)	7 (14)	0.917
LVEF, (%)	55.3±9.3	57.2±7.8	51±10.9	**<0.001**
Laboratory data				
Hemoglobin, g/dL	12.6±1.9	13±1.8	11.8±2	<0.001
WBC, 10^6/L	7.9±2.4	8.1±2.2	7.7±2.7	0.313
Platelet, 10^3/mL	226.7±77.2	226.8±80.9	226.4±68.7	0.972
Neutrophil, 10^3/mL	4.8±1.9	4.7±1.6	5±2.5	0.315
Lymphocyte, 10^3/mL	2.1±0.8	2.2±0.8	1.7±0.6	**<0.001**
Albumin, g/dL	3.9±0.5	4±0.4	3.7±0.5	**<0.001**
Glucose, mg/dL	106.4±27.7	103.1±25.6	113.9±31.1	**0.023**
Creatinine, mg/dL	1.1±0.4	1.1±0.5	1.1±0.4	0.221
C-reactive protein level, mg/dL	9 (4-18)	7 (3-13.8)	13 (7-33.5)	**0.004**
LDL-C, mg/dL	108.6±37.4	104.6±37.6	117.7±35.7	0.059
HDL-C, mg/dL	42.8±11.5	45.5±12	41.3±10.3	0.290
Triglyceride, mg/dL	122 (88-169)	118 (88.5-160)	124 (84-185.8)	0.490
Total cholesterol level, mg/dL	178±36.7	174.7±36.6	185.5±36.1	0.084
HALP score	0.45 (0.31-0.64)	0.52(0.38-0.70)	0.32(0.24-0.45)	**<0.001**
AAA diameter, mm	65.9±11.6	64.9±11.3	68.1±12	0.102
ES replasmanı, n (%)	61 (37.7)	30 (26.8)	31 (62)	**<0.001**
Symptomatic, n (%)	39 (24.1)	30 (26.8)	9 (18)	0.227
Procedure-related data				
The type of endograft				0.311
Medtronic endurant, n (%)	124 (76.5)	89 (79.5)	35 (70)	
Triventricular ovation, n (%)	15 (9.3)	7 (6.3)	8 (16)	
Cook zenith, n (%)	9 (5.6)	7 (6.3)	2 (4)	
Medtronic talent, n (%)	9 (5.6)	5 (4.5)	4 (8)	
Vascutec anaconda, n (%)	3 (1.9)	2 (1.8)	1 (2)	
Gore exluder, n (%)	2 (1.2)	2 (1.8)	0 (0)	
Operation time (min)	147.8±54.2	142.8±60.6	158.9±34.1	0.080
Scopy time (min)	31±16.5	29.5±17.4	34.5±13.7	0.070
Fallow time, months	40±27	42.4±27.2	34.7±26.1	0.094

Data are presented as percentage, mean standard deviation, or median (interquartile range). AAA: Abdominal aortic aneurysm, BMI: Body mass index, CAD: Coronary artery bypass disease, CHF: Congestive heart failure, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, HALB: Hemoglobin, albumin, lymphocyte, and platelet, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, LVEF: Left ventricular ejection fraction, PAD: Peripheral artery disease, WBC: White blood cells, min.: Minimum

Table 2. Univariate and multivariate Cox regression analyses to identify long-term predictors of mortality

	Univariate analyses			Multivariate analyses		
Variables	**HR**	**95% CI (lower-upper)**	**p-value**	**HR**	**95% CI (lower-upper)**	**p-value**
COPD	2.234	1.182-4.220	**0.013**	1.461	0.584-3.652	0.417
LVEF	0.965	0.942-0.988	**0.003**	0.974	0.942-1.007	0.118
HALP	0.223	0.108-0.459	**<0.001**	0.229	0.093-0.565	**0.001**
Glukoz	1.009	1.001-1.018	**0.034**	1.009	0.999-1.018	0.075
CRP	1.015	1.008-1.022	**<0.001**	1.012	1.004-1.020	**0.004**

HR: Hazard ratio, CI: Confidence interval, COPD: Chronic obstructive pulmonary disease, LVEF: Left ventricular ejection fraction, HALB: Hemoglobin, albumin, lymphocyte, and platelet, CRP: C-reactive protein

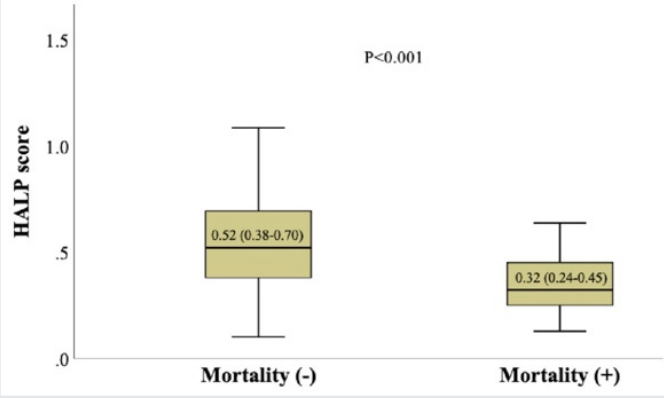
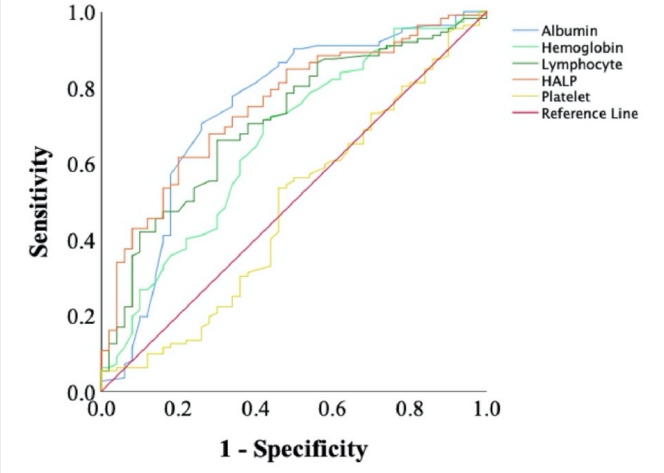


Figure 1. Box plots comparing HALP scores between patients with and without mortality
HALB: Hemoglobin, albumin, lymphocyte, and platelet



	AUC	95%CI Lower-Upper	P value
Albumin	742	0.652-0.833	**<0.001**
Hemoglobin	660	0.567-0.752	**0.001**
Lymphocyte	710	0.625-0.794	**<0.001**
HALP	752	0.674-0.830	**<0.001**
Platelet	480	0.380-0.580	0.679

Figure 2. ROC curve analysis including albumin, hemoglobin, lenfosit, HALP, and platelet values was performed to determine the most suitable parameter for predicting long-term mortality
ROC: Receiver operating characteristic

and CRP (p=0.004) emerged as independent determinants of long-term mortality.

To identify the most suitable parameter indicating in-hospital mortality, a receiver operating characteristic curve analysis was conducted using albumin, hemoglobin, lymphocyte, platelet, and the combined HALP score. The HALP score exhibited the highest predictive power, with an area under the curve of 0.752 (95% CI: 0.674-0.830; p<0.001). A cut-off value of 0.46 for the HALP score was used to detect long-term mortality development with a sensitivity of 61.6% and specificity of 80%.

Kaplan-Meier survival analysis illustrated that patients with higher HALP scores experienced significantly increased long-term mortality rates (log-rank: p<0.001).

Discussion

Our study, to our knowledge, represents the first investigation into the use of the HALP score in evaluating prognosis in this patient cohort. The primary findings of our study are as follows:

1. The HALP score is an independent predictor of long-term mortality among patients undergoing EVAR.

2. The HALP score is the strongest parameter indicating in-hospital mortality compared with its components, including hemoglobin, albumin, lymphocytes, and platelets.

3. Patients' survival time is prolonged as the HALP score increases.

As life expectancy increases, the risk of AAA also rises (1), and with the assistance of advancing technology, AAA can be detected early and treated. The advent of cutting-edge percutaneous suture-mediated vascular closure devices and the development of lower-profile endograft devices have revolutionized the aortic repair landscape. These advancements have rendered complete percutaneous endovascular access not only a viable but also an unequivocally preferable option for patients undergoing aortic repair procedures (10). With the increasing number of patients undergoing EVAR in this field and their impact on in-hospital and long-term mortalities in the postoperative period, it has become a matter of curiosity whether the HALP score, which has been previously proven to affect prognosis in cancer and stroke patients, would provide any benefit in this patient group (8,11).

In a study by Diehm et al. (12), the relationship between hemoglobin, one of the parameters constituting the HALP score, AAA diameter, and long-term survival in patients undergoing EVAR was investigated, and

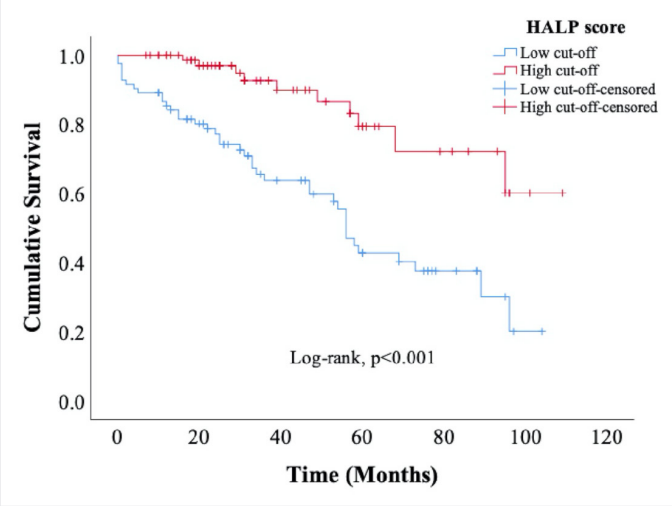


Figure 3. Kaplan-Meier survival curves of the HALP score in long-term mortality
HALP: Hemoglobin, albumin, lymphocyte, and platelet

during long-term follow-up, survival was significantly lower in patients with anemia than in those without anemia. Moreover, in a separate investigation by Nishibe et al. (13), the association between albumin, another component of the HALP score, and long-term mortality among patients undergoing EVAR was explored. Their findings revealed that albumin was an independent risk factor for long-term mortality in this patient population undergoing EVAR. Additionally, the relationship between the Geriatric Nutritional Risk Index, which is used as a marker of malnutrition, and long-term mortality in patients undergoing EVAR has been demonstrated in other studies (13,14). The difference between these studies and ours lies in the evaluation of albumin and body mass index. However, systemic inflammation plays an undeniable role in the formation of AAA and the post-EVAR treatment process.

The relationship between AAA and inflammatory processes is an undisputed fact. CRP is recognized as an acute-phase protein that is typically elevated in patients with AAA. In a study conducted by Shangwei et al. (15), it was determined that elevated serum high-sensitivity C-reactive protein (hsCRP) levels constituted an independent risk factor for AAA after adjusting for confounding variables through adjustment. In a separate investigation conducted by Wang et al. (16), the correlation between hsCRP levels and the presence of AAA was examined. Their findings suggested that hsCRP levels could serve as a diagnostic biomarker in AAA patients with medium or small aortic diameters, but not in those with large aortic diameters (16). In this study, we observed that preoperative CRP levels independently contributed to long-term mortality after EVAR, together with the HALP score.

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are recognized as biomarkers of systemic inflammation and atherosclerosis stemming from distinct immune pathways (17-19). In a study by King et al. (20), an increase in preoperative NLR was associated with increased mortality after EVAR. Octeau et al. (21) showed in another study that a high NLR was significantly associated with post-EVAR mortality and reintervention, even after adjusting for variables such as age, AAA diameter, and NLR-related clinical comorbidities. Furthermore, the indirect relationship between NLR and PLR and aneurysm sac shrinkage, which is considered an indicator of postoperative improvement, appears to be connected to inflammation (21). Patients with lower preoperative inflammatory status are more likely to have aneurysm sac regression after EVAR, leading to higher medium- and long-term survival rates (22). As demonstrated in these studies, systemic inflammation clearly affects long-term mortality. In this study, we evaluated the relationship between the HALP score and long-term mortality among patients undergoing EVAR, reflecting both nutritional status and systemic inflammation. In this regard, our study appears to be more comprehensive and complementary than other studies.

The HALP score is a simple index that can be easily calculated from routine complete blood counts at hospital admission without any additional cost or additional work. The ease of calculating the HALP score at bedside is advantageous compared with other indices. This risk stratification approach could empower clinicians to identify patients at elevated risk and tailor their treatment, incorporating intensive medical therapy and implementing vigilant monitoring protocols for such individuals. However, further prospective studies involving long-term follow-up in a larger multicenter patient population are needed to elucidate the effectiveness of the HALP score in predicting in-hospital and out-of-hospital morbidity and mortality in treated patients with EVAR.

Study Limitations

The study's single-center and retrospective nature can impact the generalizability of the findings. Future multicenter, prospective studies may provide more comprehensive insights. The relatively small sample size in this study is a significant limitation. Larger prospective cohort studies are essential to validate and extend the current findings. Second, patients with AAA who were medically observed and surgically repaired were not included in the study, which may have caused this score to not be generalizable to other patient groups. Incorporating this aspect into future studies may provide a more holistic understanding of patients' conditions. Finally, the HALP score was not compared with other risk scoring systems linked to mortality in patients undergoing EVAR.

Conclusion

In our study, we used the HALP score, which has not been previously evaluated in this patient group, and found that the HALP score is an independent predictor of long-term mortality in patients undergoing EVAR. This result provides us with a new perspective that the HALP score, which can be easily calculated and applied in practice, can be used as a guide in the follow-up and treatment of EVAR patients.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital's Ethics and Research Committee and adhered to the principles of the Helsinki Declaration (approval number: 2024.01-11, date: 27.02.2024).

Informed Consent: Written informed consent was obtained from all participants.

Authorship Contributions: Surgical and Medical Practices - M.A., Ö.Ç., Concept - M.A., A.A.Ş., Design - M.A., M.K., N.U., A.A.Ş., Data Collection or Processing - M.A., T.A., O.E., S.A., Analysis or Interpretation - M.A., A.E., Y.D., Literature Search - M.A., A.E., Y.D., Writing - M.A., A.E.,

Conflict of Interest: No conflict of interest was declared by the authors.

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