Social Medicine and Health Management (2025)
Clausius Scientific Press, Canada

DOI: 10.23977/socmhm.2025.060117
ISSN 2616-2210 Vol. 6 Num. 1

Correlation of Coronary Heart Disease Mortality with HALP Score: A Cross-Sectional Study Based on NHANES

Ji Ouyang[1,a], Mengjiao Li[2,b], Jiayuan Song[3,c], Zhixi Hu[1,d,*]

[1]College of Traditional Chinese Medicine, Hunan University of Traditional Chinese Medicine, Changsha, China
[2]The Second of Clinical Medicine, Zhejiang University of Traditional Chinese Medicine, Hangzhou, 310053, Zhejiang, China
[3]College of Integrative Medicine, Changchun University of Chinese Medicine, 130117, Changchun, China
[a]428299050@qq.com, [b]310709454@qq.com, [c]13894754778@163.com, [d]003405@hnucm.edu.cn
[*]Corresponding author

Keywords: *Coronary Heart Disease; HALP; All-Cause Mortality; NHANES*

Abstract: This study investigates the association between HALP score (hemoglobin, albumin, lymphocytes, platelets) and all-cause mortality in coronary heart disease (CHD) patients using NHANES data (1998-2018). Eligible CHD patients were grouped into Q1-Q4 by HALP quartiles. Analyses included weighted Cox models, restricted cubic spline (RCS) regression, Kaplan-Meier (K-M) curves, and subgroup analyses. Results showed 937 all-cause deaths. After covariate adjustment, Q2-Q4 had lower mortality risk (HR=0.74, 0.68, 0.70; 95% CIs respectively). A significant J-shaped nonlinear relationship was found (nonlinear $P<0.001$) with a turning point at 78.02: each 1-unit increase in HALP ≤78.02 reduced death risk by 1.3% (HR=0.987), while the protective effect plateaued above this. K-M curves showed higher HALP correlated with higher survival, and subgroup analyses confirmed robustness. The HAL*P* score exhibits a J-shaped relationship with all-cause mortality in patients with coronary heart disease (CHD) and has potential prognostic value.

1. Introduction

Coronary heart disease (CHD) is the most common form of cardiovascular disease (CVD), a group of clinical syndromes caused by atherosclerotic lesions in the coronary arteries, resulting in

narrowing or occlusion of the vascular lumen, causing myocardial ischemia, hypoxia, and even necrosis, and it belongs to the major types of ischemic heart disease [1].In 2022, CHD was the leading cause of death due to cardiovascular disease worldwide, accounting for 39.5%, posing a great challenge to global public health [2]. Therefore finding convenient and effective metrics to predict the risk of death in patients with CHD is essential to improve prognostic management.

In recent years, the hemoglobin, albumin, lymphocyte, and platelet (HALP) score has been shown to be valuable as a new biomarker tool in the prognostic assessment of a variety of diseases, including cancer and cardiovascular disease [3], and to provide a comprehensive picture of a patient's nutritional status and systemic inflammatory state [4]. Whereas anemia and hypoalbuminemia are indirect indicators of malnutrition, lymphocytes and platelets play an important role in inflammation, and lymphopenia is strongly associated with reduced survival in patients with heart failure [5, 6]. In addition, platelet counts likewise increase the risk of thromboembolism and atherosclerotic lesions [7]. In the field of cardiovascular disease, the HALP score has been shown to be a powerful prognostic indicator [8].The HALP score can be used as an important marker for predicting the absence of reflow phenomenon and short-term mortality in patients with ST-segment elevation myocardial infarction (STEMI) [9]. Also, HALP score has shown significant discriminatory ability in predicting short-term mortality in patients with acute heart failure [10].

These studies suggest that the HALP score may be a reliable tool for identifying high-risk populations among CHD patients, thereby improving patient management and reducing mortality. Therefore, the aim of this study was to investigate the relationship between HALP score and all-cause mortality in patients with CHD and to assess the potential predictive value of HALP score in CHD prognosis for the identification of high-risk populations for poor CHD prognosis.

2. Manuscript Preparation

2.1 Research design and purpose

Data from the National Health and Nutrition Examination Survey (NHANES) were used, and patients with CHD from 1999-2018 were selected for the study.NHANES was conducted by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS)) are responsible for it. It uses a complex, multistage stratified probability sample based on selected counties, neighborhoods, households, and persons within households to assess the nutritional and health status of the U.S. deinstitutionalized population. Participants are interviewed in their homes by NCHS-trained professionals and undergo an extensive physical examination, including blood and urine collection, at a Mobile Examination Center (MEC). Detailed information on study implementation is available online at https://www.cdc.gov/nchs/nhanes/index.htm.

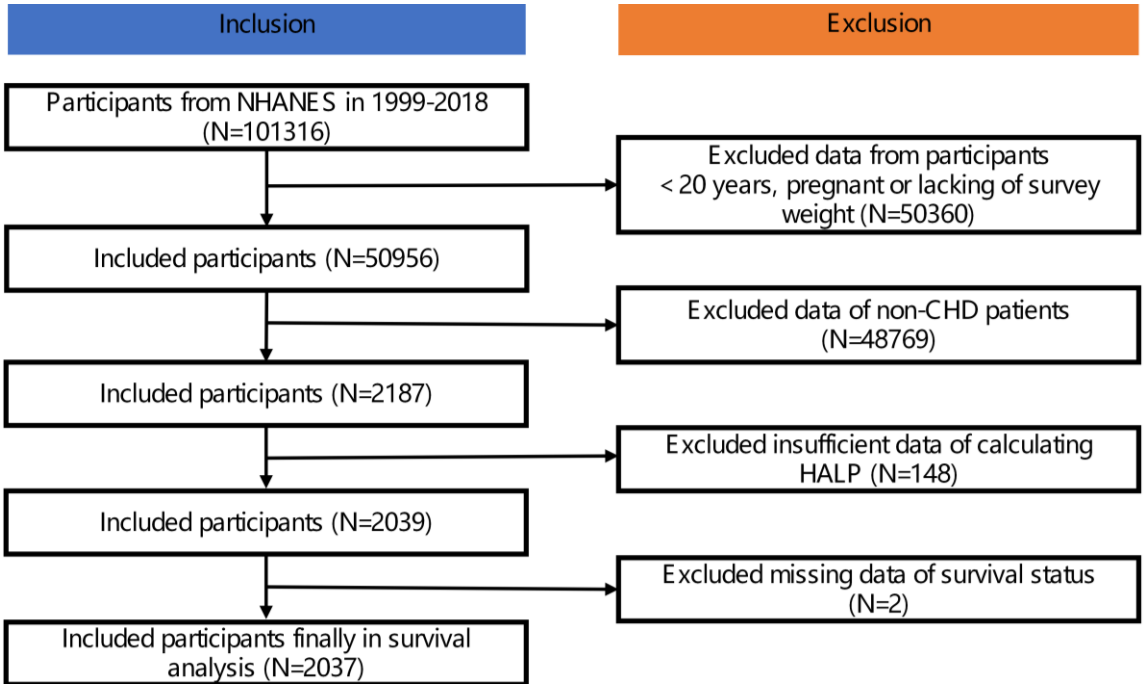

Figure 1 Flow chart for inclusion and exclusion of study populations

A total of 101,316 NHANES participants were initially enrolled. Exclusion criteria:(1) 50,360 participants younger than 20 years of age, pregnant, or lacking survey weighting (2) 48,769 non-CHD patients (3) 148 with insufficient HALP data (4) 2 with missing survival status, and finally 2,037 were eligible, as shown in Figure 1.

2.2 Diagnosis of coronary heart disease

Diagnosis of CHD: Participants who answered “yes” to the question “Has a doctor or other health professional ever told you that you have CHD?” in the NHANES Multiple Choice Questionnaire (MCQ160C) were categorized as having CHD [11].

2.3 Definition of HALP score

In NHANES, blood samples were obtained by examination at the MEC and further analyzed in the laboratory for HALP score related markers including HB, ALB, lymphocyte, and platelet levels. The HALP score was calculated according to the following formula: HB (g/l) x ALB (g/l) x lymphocytes (109/l)/platelets (109/l). Because the ALB unit in the database is “g/dl”. We categorized the study population into four levels [5, 12], Q1-Q4 (<37.31, 37.31-51.15, 51.15-69.68, and >69.68) based on their quartiles of HALP scores.

2.4 Covariates

Potential covariates were identified in terms of sociodemographic, lifestyle behavioral variables, and chronic disease. Sociodemographic characteristics included sex (female or male), age subgroups (<60 and ≥60 years), race (non-Hispanic white, non-Hispanic black, and other races,

including multiracial mix), and educational attainment (less than high school, high school graduate/General Equivalency Diploma (GED) or equivalent, and high school or higher). Poverty-to-income ratio (PIR) is used to measure income in relation to the federal poverty level, which takes into account factors such as economic inflation and family size. Marital status is categorized into three groups: those who are married or living with a partner, those who are widowed, divorced, or separated, and those who have never been married. Lifestyle behavior variables include body mass index (BMI), smoking status, and drinking status.BMI is calculated using the formula BMI = weight (kg) / height (m) ². Smoking status was categorized into two groups: current non-smokers and smokers, and drinking status was categorized into two groups: non-drinkers and drinkers [13]. Chronic diseases were categorized as diabetes mellitus and hypertension, and results were obtained from self-reporting in the questionnaire. Total cholesterol (TC), uric acid (UA) and serum creatinine (SCr) results were obtained by laboratory tests.

2.5 Outcomes and Follow-up

The study finalized and recorded all-cause mortality of patients through International Classification of Diseases, Ninth Revision (ICD-9 and ICD-10) codes. Death information was obtained through the National Death Index (NDI) link at https: //www. cdc. gov/nchs/data-linkage/mortality.html. Follow-up ended after the subject's death or as of December 31, 2019.

2.6 Statistical analysis

All statistical analyses were conducted using R software (4.4.1). Two-tailed *P* values < 0.05 were considered statistically significant. Part of the analysis in this study took into account appropriate weights[14]. We first divided the participants into four groups based on quartiles of HALP. Continuous variables were expressed as weighted means ± standard deviations (SD) or weighted median or (25th, 75th) and categorical variables were presented as unweighted frequencies and weighted percentages. Weighted t-test or Kruskal-Wallis test was conducted for continuous variables, while weighted chi-square tests were used to compare categorical variables [15]. Multiple imputation achieved by “MICE” package was applied to accurately deal with missing covariates [16]. To investigate the relationship between HALP and all-cause mortality in CHD patients, we conducted weighted Cox proportional hazards models for estimation of hazard ratios (HRs) and their 95% confidence intervals (CI)[17]. We established three models: Model 1, without adjusting for any covariates; Model 2, only adjusting for demographic variables; Model 3: adjusting for all covariates. Then, considering potential nonlinear relationships, we employed restricted cubic splines (RCS) regression with 3 knots[18]. If there is a significant nonlinear correlation, two-piecewise linear regression based on threshold analysis was employed[19]. Kaplan-Meier (K-M) curve was utilized to explore the differences of survival possibility in quartiles of HALP group[17]. Subgroup analysis was to check if there was an interaction effect between HALP and covariates including age, gender, race, BMI, drinking status, smoking status, diabetes and

hypertension.

3. Results

3.1 Baseline Characteristics of Study Participants

A total of 2,037 participants with CHD were included in this study, with a median follow-up period of 78 months. Participants were stratified into four groups based on HALP quartiles: Q1 (<36), Q2 (36–49.84), Q3 (49.84–66.41), and Q4 (>66.41). Significant differences were observed across HALP groups in terms of follow-up time, age distribution, gender, marital status, smoking status, and survival status (all $P < 0.05$). Other demographic and clinical variables, such as race, BMI, diabetes, and hypertension, were balanced among groups (Table 1).

Table 1 Baseline Characteristics of participants grouped by quartiles of HALP from NHANES 1999-2018.

Variables	Total	Quartiles of HALP				*P*
		Q1(< 36)	Q2 (36, 49.84]	Q3 (49.84, 66.41]	Q4 (> 66.41)	
Follow-up time, months, median (25th, 75th)	78.00 (39.00, 135.00)	66.00 (30.49, 130.00)	86.00 (40.00, 142.00)	91.27 (42.00, 141.00)	77.00 (40.00, 125.09)	0.016
n	2037	510	509	509	509	
Age, n (%)						0.012
<60	366 (24.8)	67 (18.3)	81 (21.8)	99 (27.1)	119 (31)	
≥60	1671 (75.2)	443 (81.7)	428 (78.2)	410 (72.9)	390 (69)	
Gender, n (%)						< 0.001
Male	1379 (65.1)	307 (54.3)	323 (59.4)	354 (68.2)	395 (77.4)	
Female	658 (34.9)	203 (45.7)	186 (40.6)	155 (31.8)	114 (22.6)	
Race, n (%)						0.086
Non-Hispanic White	1314 (82)	335 (83.2)	339 (83.9)	321 (79.3)	319 (81.6)	
Non-Hispanic Black	256 (5.8)	73 (7.1)	62 (5.4)	59 (5.5)	62 (5.4)	
Other Race	467 (12.2)	102 (9.7)	108 (10.7)	129 (15.2)	128 (13)	
Education, n (%)						0.563
Less than high school	687 (25.1)	159 (23.8)	181 (24.6)	172 (26.5)	175 (25.4)	
High school grad/GED or equivalent	472 (25.6)	122 (25.1)	127 (29.1)	107 (22.1)	116 (26)	
Higher than high school	878 (49.3)	229 (51.1)	201 (46.4)	230 (51.4)	218 (48.6)	
PIR, n (%)						0.702
≤1.3	648 (21.9)	151 (22.7)	170 (22.1)	148 (19.2)	179 (23.7)	
1.3-3.5	843 (40.9)	238 (43.7)	189 (39.7)	222 (42.1)	194 (38.5)	
>3.5	546 (37.1)	121 (33.7)	150 (38.2)	139 (38.7)	136 (37.8)	
Marital status, n (%)						0.012
Married/living with partner	1260 (65.3)	293 (60.3)	309 (61.7)	316 (66.7)	342 (71.8)	
Widowed/divorced/separated	682 (29.9)	193 (35.8)	178 (34.1)	169 (27.1)	142 (23.4)	
Never married	95 (4.8)	24 (3.9)	22 (4.1)	24 (6.2)	25 (4.7)	
BMI, n (%)						0.075
<25 kg/m^2	460 (21)	144 (26.7)	114 (19.8)	106 (21.2)	96 (17)	
25-30 kg/m^2	726 (34.7)	168 (31.5)	188 (34.9)	176 (32.6)	194 (39.5)	
≥30 kg/m^2	851 (44.3)	198 (41.8)	207 (45.3)	227 (46.2)	219 (43.6)	

Smoking status, n (%)						< 0.001
Non smokers	1704 (82.2)	452 (86.7)	444 (87.3)	415 (80.2)	393 (75.3)	
Smokers	333 (17.8)	58 (13.3)	65 (12.7)	94 (19.8)	116 (24.7)	
Drinking status, n (%)						0.067
Non drinkers	1020 (44.9)	275 (50.3)	261 (46.9)	231 (40)	253 (42.9)	
Drinkers	1017 (55.1)	235 (49.7)	248 (53.1)	278 (60)	256 (57.1)	
Diabetes, n (%)						0.54
Yes	680 (31.6)	188 (34.1)	158 (33.1)	164 (28.7)	170 (30.6)	
No	1357 (68.4)	322 (65.9)	351 (66.9)	345 (71.3)	339 (69.4)	
Hypertension, n (%)						0.222
Yes	1501 (71.8)	371 (71.1)	382 (76.6)	370 (69.9)	378 (69.7)	
No	536 (28.2)	139 (28.9)	127 (23.4)	139 (30.1)	131 (30.3)	
TC, mg/dL, mean (SD)	179.05 (45.58)	179.28 (51.69)	177.54 (42.95)	179.66 (41.96)	179.69 (45.61)	0.867
UA, mg/dL, mean (SD)	6.06 (1.59)	6.06 (1.67)	5.93 (1.71)	6.11 (1.49)	6.13 (1.49)	0.45
Scr, mg/dL, mean (SD)	1.09 (0.59)	1.18 (0.80)	1.06 (0.58)	1.07 (0.51)	1.04 (0.44)	0.016
Survival status, n (%)						< 0.001
Alive	1100 (60.1)	214 (49.4)	260 (57)	301 (63.6)	325 (69.5)	
Dead	937 (39.9)	296 (50.6)	249 (43)	208 (36.4)	184 (30.5)	

3.2 The associations between HALP and all-cause mortality in CHD patients

Table 2 presented the associations between HALP and all-cause mortality in CHD patients. In the unadjusted Model 1, higher HALP levels were significantly associated with reduced all-cause mortality risk. Compared to Q1, the HRs for Q2–Q4 were 0.71 (95% CI: 0.56–0.89), 0.59 (0.46–0.76), and 0.57 (0.44–0.72). After adjusting for demographic (Model 2) and full covariates (Model 3: age, gender, race, BMI, smoking, etc.), the inverse association remained robust. In Model 3, the HRs for Q2–Q4 were 0.74 (0.59–0.94), 0.68 (0.53–0.86), and 0.70 (0.55–0.88) (all $P < 0.05$).

Table 2 The associations between HALP and all-cause mortality in Cox regression models.

	Model 1		Model 2		Model 3	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Q1	Reference		Reference		Reference	
Q2	0.71 (0.56, 0.89)	0.003	0.73 (0.58, 0.92)	0.007	0.74 (0.59, 0.94)	0.012
Q3	0.59 (0.46, 0.76)	< 0.001	0.61 (0.48, 0.78)	< 0.001	0.68 (0.53, 0.86)	0.001
Q4	0.57 (0.44, 0.72)	< 0.001	0.67 (0.53, 0.84)	0.001	0.70 (0.55, 0.88)	0.002

Model 1 was not adjusted for any covariate.

Model 2 was adjusted for age, gender, race, education, PIR and marital status.

Model 3 was adjusted for age, gender, race, education, PIR, marital status, BMI, smoking status, drinking status, diabetes, hypertension, TC, UA and Scr.

The results of the RCS regression model indicate a J-shaped association between HALP and all-cause mortality, with a turning point of 78.02 (*P* for non-linear < 0.001). Before the turning

point, HALP was negatively correlated with all-cause mortality, and after the turning point, HALP was positively correlated with all-cause mortality (Figure 2).

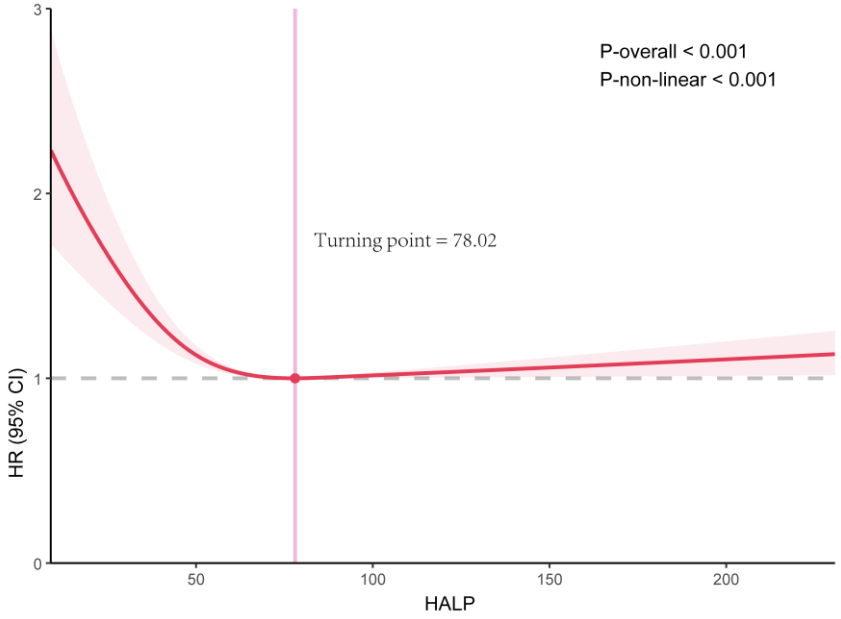

Figure 2 The association between HALP and all-cause mortality in RCS regression model. The model was adjusted for age, race, education, PIR, marital status, BMI, smoking status, drinking status, diabetes, hypertension, TC, UA and Scr.

Based on this discovery, we established threshold analysis to verify the existence of nonlinear relationships (Table 3). A nonlinear relationship was identified between HALP and mortality risk. The log-likelihood ratio test confirmed a significant threshold at HALP=78.02 ($P < 0.001$). Below this threshold, each unit increase in HALP was associated with a 1.3% reduction in mortality risk (HR: 0.987, 95% CI: 0.987–0.994). Above 78.02, the protective effect plateaued (HR: 1.001, 95% CI: 1.000–1.002).

Table 3 Two-piecewise Cox regression models of HALP and all-cause mortality.

HALP	HR (95%CI)	*P*
≤78.02	0.99(0.987, 0.994)	< 0.001
>78.02	1.001(1.000, 1.002)	0.023
Log likelihood ratio test		< 0.001

The model was adjusted for age, race, education, PIR, marital status, BMI, smoking status, drinking status, diabetes, hypertension, TC, UA and Scr.

3.3 K-M curve and subgroup analysis

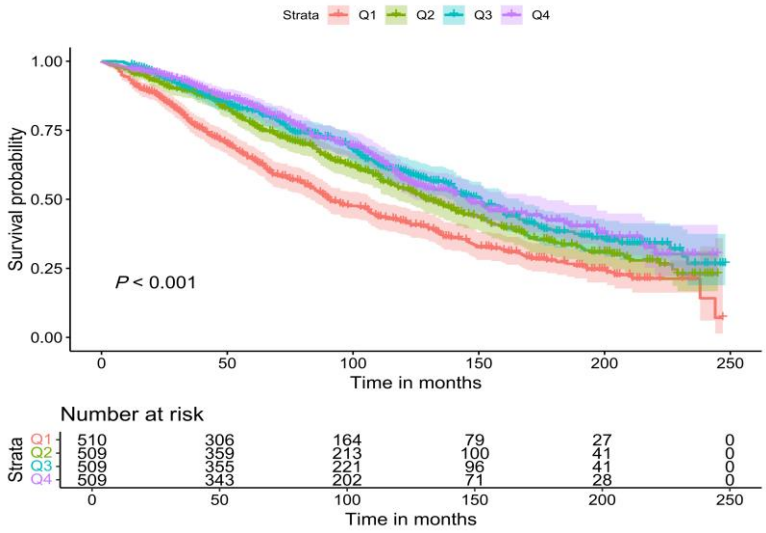

Figure 3 K-M Curve of different quartiles of HALP groups.

As shown in Figure 3, K-M curve showed a significant decrease in the survival rate in the higher HALP group compared to the lowest HALP group. Then, we employed subgroup analysis to check if there was an interaction effect between HALP and some covariates(Table 4). We did not find any interaction between HALP and any covariates on all-cause mortality in CHD patients, indicating that their association is robust across all subgroups.

Table 4 Subgroup analyses.

Variable	Levels	HR (95% CI)	*P for interaction*
Age			0.897
<60	Q1	Reference	
	Q2	0.84 (0.34, 2.09)	
	Q3	0.74 (0.29, 1.93)	
	Q4	0.59 (0.24, 1.45)	
≥60	Q1	Reference	
	Q2	0.73 (0.57, 0.92)	
	Q3	0.63 (0.49, 0.82)	
	Q4	0.72 (0.57, 0.90)	
Gender			0.348
Male	Q1	Reference	
	Q2	0.85 (0.64, 1.11)	
	Q3	0.72 (0.53, 0.97)	
	Q4	0.64 (0.49, 0.86)	
Female	Q1	Reference	
	Q2	0.62 (0.44, 0.88)	

	Q3	0.6 (0.38, 0.95)	
	Q4	0.83 (0.57, 1.20)	
Race			0.679
Non-Hispanic White	Q1	Reference	
	Q2	0.79 (0.61, 1.03)	
	Q3	0.72 (0.55, 0.95)	
	Q4	0.72 (0.56, 0.93)	
Non-Hispanic Black	Q1	Reference	
	Q2	0.6 (0.34, 1.06)	
	Q3	0.38 (0.19, 0.74)	
	Q4	0.31 (0.14, 0.67)	
Other Race	Q1	Reference	
	Q2	0.52 (0.26, 1.04)	
	Q3	0.52 (0.29, 0.95)	
	Q4	0.65 (0.35, 1.18)	
BMI			0.744
<25 kg/m^2	Q1	Reference	
	Q2	0.63 (0.42, 0.95)	
	Q3	0.81 (0.54, 1.23)	
	Q4	0.79 (0.53, 1.17)	
25-30 kg/m^2	Q1	Reference	
	Q2	0.77 (0.55, 1.09)	
	Q3	0.56 (0.38, 0.84)	
	Q4	0.57 (0.38, 0.84)	
≥30 kg/m^2	Q1	Reference	
	Q2	0.82 (0.58, 1.15)	
	Q3	0.71 (0.47, 1.07)	
	Q4	0.85 (0.61, 1.19)	
Smoking			0.393
Yes	Q1	Reference	
	Q2	0.71 (0.55, 0.91)	
	Q3	0.59 (0.46, 0.76)	
	Q4	0.68 (0.53, 0.87)	
No	Q1	Reference	
	Q2	0.93 (0.46, 1.91)	
	Q3	1.15 (0.59, 2.23)	
	Q4	0.68 (0.35, 1.31)	
Drinking			0.423
Yes	Q1	Reference	

	Q2	0.65 (0.49, 0.85)	
	Q3	0.71 (0.52, 0.98)	
	Q4	0.78 (0.58, 1.03)	
No	Q1	Reference	
	Q2	0.97 (0.69, 1.35)	
	Q3	0.70 (0.50, 0.99)	
	Q4	0.62 (0.44, 0.89)	
Diabetes			0.91
Yes	Q1	Reference	
	Q2	0.93 (0.66, 1.31)	
	Q3	0.77 (0.53, 1.11)	
	Q4	0.70 (0.49, 1.00)	
No	Q1	Reference	
	Q2	0.64 (0.47, 0.88)	
	Q3	0.61 (0.45, 0.83)	
	Q4	0.69 (0.53, 0.91)	
Hypertension			0.657
Yes	Q1	Reference	
	Q2	0.71 (0.54, 0.94)	
	Q3	0.72 (0.54, 0.96)	
	Q4	0.69 (0.53, 0.91)	
No	Q1	Reference	
	Q2	0.97 (0.61, 1.52)	
	Q3	0.62 (0.38, 1.00)	
	Q4	0.70 (0.43, 1.14)	

The models were adjusted for age, race, education, PIR, marital status, BMI, smoking status, drinking status, diabetes, hypertension, TC, UA and Scr.

4. Discussions

In this study, we explored the relationship between HALP score and all-cause mortality in patients with CHD, there was a J-type nonlinear relationship with a significant negative correlation within a certain threshold, and patients with CHD with lower HALP scores appeared to have a higher risk of all-cause mortality, and we also evaluated the effect of HALP score on the prognosis of CHD, which suggests that the HALP score has a potential predictive value.The HALP score integrates HB, ALB, lymphocyte count and platelet count, combining the advantages of the triple dimensions of nutrition, immunity and inflammation[20]; HB levels reflect the body's oxygen transport capacity, while ALB reflects liver function and overall nutritional status, lymphocyte count directly reflects the body's immune function, and platelet activation and aggregation promotes the release of inflammatory factors, which further exacerbates the inflammatory response[21-24].

The association between cardiovascular disease and HALP scores has received increasing attention in epidemiological studies.Akbulut et al. found a correlation between lower HALP scores and in-hospital mortality in patients requiring hospitalization for acute heart failure (AHF)[8].Liu et al. demonstrated that HALP scores independently predicted in patients with STEMI undergoing PCI development of no-reflow and long-term mortality[25].Evsen et al. demonstrated that the HALP score is a strong predictor of prognosis in peripheral arterial disease (PAD), with lower scores correlating with reduced life expectancy due to disease[26].Tunca et al. found that the HALP score can be used as a valid predictor for the diagnosis of the severity of lower extremity peripheral arterial disease (LEAD), a and a practical tool for clinical risk assessment[27]. All these studies showed that CVD is not only a global health problem, but also closely related to HALP score.

The pathological basis of CHD is coronary atherosclerosis, which is a slow and complex pathologic process involving multiple factors such as endothelial damage, lipid deposition, platelet aggregation, inflammatory cell infiltration, oxidative stress, and smooth muscle proliferation and migration[28]. A retrospective study of plasma proteins and CVD mortality in patients with chronic CHD[29] showed that myocardial strain-dysfunction-hypertrophy-fibrosis, cardiomyocyte death and apoptosis, renal injury, hemodynamic stress, renin-angiotensin system (RAS) activation, oxidative stress and inflammation, as well as angiogenesis and hemangioblastogenesis (HGF) were the Important mechanisms. In CHD patients, high or low BMI is associated with cardiac metabolism and function, suggesting that nutrition also plays a major role in cardiovascular function[30]. Meanwhile, each parameter in the HALP score is closely related to the pathogenesis of coronary heart disease (CHD), in which HB and ALB reflect the body's nutritional reserve, and a low level of reserve is associated with impaired myocardial energy metabolism and decreased vascular endothelial repair [31]; a lower lymphocyte count suggests a weakened immune function, which increases the risk of infectious complications, and affects the prognosis of patients with CHD[32]; and an elevated platelet count is closely associated with inflammatory response, prothrombotic state and plaque instability, which together drive CHD progression and poor prognosis[33]. Previous studies have demonstrated the prognostic value of the HALP score in the areas of acute ischemic stroke and post-stroke cognitive impairment[34], which, like the results of the present study, further confirms the validity of the HALP score as a comprehensive biomarker tool for assessing the prognosis and mortality of cardiovascular disease.

The J-curve results revealed by RCS regression may stem from the body's adaptive regulatory effects on nutritional and inflammatory states. before the turning point of the J-curve, improved nutritional status and reduced inflammation levels reflected by elevated HALP scores may reduce the risk of death by optimizing the body's metabolic and immune functions, whereas beyond the turning point, excessively high HALP scores are associated with an increased all-cause mortality rate suggesting that excessive inflammatory response or underlying pathology may counteract nutritional and immune advantages[35]. At low HALP scores, malnutrition and chronic inflammation (e.g., elevated IL-6, TNF-α) synergistically promote atherosclerotic plaque progression, myocardial remodeling, and deterioration of cardiac function, which directly increase the risk of death[36], whereas excessively high HALP scores (>78.02) may reflect excessive

inflammatory activation (e.g., platelet over-activation leading to thrombosis) or metabolic disturbances (e.g., hypercoagulable states triggering (e.g., microcirculatory disturbances due to hypercoagulability), creating a "pro-inflammatory-pro-embolic" vicious cycle[37]. A moderate inflammatory response may help clear pathogens and repair tissues, but an excessive inflammatory response may lead to tissue damage and disease progression [38]. This threshold effect suggests that we need to avoid blindly pursuing excessive HALP scores in clinical practice, and instead pay attention to the dynamic balance of each component, such as monitoring platelet activity while boosting nutritional support to prevent excessive intervention from triggering negative effects. It is worth mentioning that no interaction was found between HALP and any covariates in the subgroup analyses, suggesting that the association between the two was robust in all subgroups; however, different results may occur in some cardiovascular diseases, which is worth further exploration.

This study suggests that the HALP score can be used as a convenient tool for comprehensive prognostic assessment of CHD patients, especially for identifying people at high risk of malnutrition or inflammation. In clinical practice, it is recommended that HALP scores be included in routine blood tests, and individualized intervention strategies be developed in conjunction with the tipping point thresholds: strengthening nutritional support and controlling chronic inflammation in patients with low HALP scores, and being vigilant about thrombotic risk and avoiding excessive activation of platelet function in patients with high HALP scores. The strength of this study lies in the use of the large-scale NHANES database, which has a large sample size and high data quality, and can provide reliable results for statistical analysis. In addition, this study used multiple statistical methods, including Cox regression modeling, RCS regression, and K-M curve analysis, to comprehensively assess the relationship between HALP score and all-cause mortality. However, there are some limitations in this study: (1) the NHANES database is a cross-sectional study, which cannot completely exclude the reverse inference of causality; (2) the calculation of HALP score relies on the measurement of blood parameters, which may have some measurement errors. In the future, prospective cohort studies are needed to validate the predictive value of dynamic changes in the HALP score for CHD prognosis and to explore the potential of its combined application with other cardiovascular risk scores (e.g., ASCVD risk score).

In conclusion, the HALP score, as a comprehensive biomarker tool, has an important potential value in predicting all-cause mortality in patients with CHD.The J-shaped relationship between the HALP score and all-cause mortality suggests that we need to consider the nutritional, inflammatory, and immune status of patients comprehensively in our clinical practice in order to formulate a more precise treatment strategy. Follow-up studies will further investigate the value of HALP score in different cardiovascular diseases and validate its predictive efficacy in prospective cohort studies.

Data Sharing Statement

The Laboratory data from our study is publicly accessible online at https: //wwwn. cdc. gov/nchs/nhanes/Default. aspx for global data users and researchers.

Ethical approval

Ethics approval and consent to participate were obtained. The study was approved by the ethics review board of the National Center for Health Statistics, and all participants provided written informed consent. The experimental protocol adhered to the ethical guidelines of the Declaration of Helsinki.

Acknowledgments

We are grateful to the National Health and Nutrition Examination Survey (NHANES) staff and participants for their valuable contributions, particularly for providing data licenses. We extend special thanks to Zhixi Hu Professor for his invaluable contributions to the research ideas and funding support for this paper. This work was supported by the National Natural Science Foundation of China (Grant No. 82274412).

Author Contributions

Ji Ouyang contributed to hypothesis development and manuscript preparation. Zhixi Hu contributed to the study design and funding acquisition. Ji Ouyang and Mengjiao Li undertook data analyses. Jiayuan Song, Mengjiao Li drafted and revised the manuscript. All authors approved the final draft of the manuscript for publication. All authors have approved the final version of the manuscript for publication and have agreed to be responsible for the research presented.

Disclosure

The authors report no conflicts of interest in this work.

References

[1] Li M, Song S, Rong Y, Wu D, Yin Y. Zhishi Xiebai Guizhi Decoction for coronary heart disease: A systematic review and meta-analysis. Medicine (Baltimore). 2024. 103(3): e36588.

[2] TSAO C W, ADAY A W, ALMARZOOQ Z I, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association[J]. Circulation, 2023, 147(8):e93-e621.

[3] XU H, ZHENG X, AI J, et al. Hemoglobin, albumin, lymphocyte, and platelet (HALP) score and cancer prognosis: A systematic review and meta-analysis of 13,110 patients[J]. Int Immunopharmacol, 2023,114:109496.

[4] LIU Q, XIE H, CHENG W, et al. The preoperative hemoglobin, albumin, lymphocyte, and platelet score (HALP) as a prognostic indicator in patients with non-small cell lung cancer[J]. Front Nutr, 2024,11:1428950.

[5] XU M, CHEN L, HU Y, et al. The HALP (hemoglobin, albumin, lymphocyte, and platelet) score is associated with early-onset post-stroke cognitive impairment[J]. Neurol Sci, 2023,44(1):237-245.

[6] HU X, CHENG S, DU H, et al. Association of platelet-to-lymphocyte ratio with 1-year all-cause mortality in ICU patients with heart failure[J]. Sci Rep, 2024,14(1):32016.

[7] Von Hundelshausen P, Schmitt MM. Platelets and their chemokines in atherosclerosis-clinical applications. Front Physiol. 2014. 5: 294.

[8] MUGE A, CENAN I, NIL O, et al. A Potential Relationship Between HALP Score and In-Hospital Mortality in Acute Heart Failure [J]. Clin Cardiol, 2025,48(3):e70108.

[9] ILIS D, ARSLAN A, ARTAC I, et al. Prognostic value of HALP score in predicting in-hospital mortality in patients

with NSTEMI[J]. Biomark Med, 2025,19(5):139-147.
[10] YILMAZ R, TOPRAK K, YILMAZ M, et al. Investigation of the Usefulness of HALP Score in Predicting Short-Term Mortality in Patients with Acute Decompensated Heart Failure in a Coronary Care Unit[J]. Medicina (Kaunas), 2024,60(9):1385.
[11] KOTSAKIS G A, THAI A, IOANNOU A L, et al. Association between low-dose aspirin and periodontal disease: results from the continuous national health and nutrition examination survey (NHANES) 2011-2012[J]. J Clin Periodontol, 2015,42(4):333-341.
[12] TIAN M, LI Y, WANG X, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Is Associated With Poor Outcome of Acute Ischemic Stroke[J]. Front Neurol, 2020,11:610318.
[13] ALHARTHI S, NATTO Z S, MIDLE J B, et al. Association between time since quitting smoking and periodontitis in former smokers in the National Health and Nutrition Examination Surveys (NHANES) 2009 to 2012[J]. J Periodontol, 2019,90(1):16-25.
[14] WANG X, YANG S, HE G, et al. The association between weight-adjusted-waist index and total bone mineral density in adolescents: NHANES 2011-2018[J]. Front Endocrinol (Lausanne), 2023,14:1191501.
[15] PEI H, LI S, SU X, et al. Association between triglyceride glucose index and sleep disorders: results from the NHANES 2005-2008[J]. BMC Psychiatry, 2023,23(1):156.
[16] WHITE I R, ROYSTON P, WOOD A M. Multiple imputation using chained equations: Issues and guidance for practice[J]. Stat Med, 2011,30(4):377-399.
[17] HOU X Z, LV Y F, LI Y S, et al. Association between different insulin resistance surrogates and all-cause mortality in patients with coronary heart disease and hypertension: NHANES longitudinal cohort study[J]. Cardiovasc Diabetol, 2024,23(1):86.
[18] DING L, ZHANG H, DAI C, et al. The prognostic value of the stress hyperglycemia ratio for all-cause and cardiovascular mortality in patients with diabetes or prediabetes: insights from NHANES 2005-2018[J]. Cardiovasc Diabetol, 2024,23(1):84.
[19] YAN Y, ZHOU L, LA R, et al. The association between triglyceride glucose index and arthritis: a population-based study[J]. Lipids Health Dis, 2023,22(1):132.
[20] FARAG C M, ANTAR R, AKOSMAN S, et al. What is hemoglobin, albumin, lymphocyte, platelet (HALP) score? A comprehensive literature review of HALP's prognostic ability in different cancer types[J]. Oncotarget, 2023, 14: 153-172.
[21] Otto JM, Montgomery HE, Richards T. Haemoglobin concentration and mass as determinants of exercise performance and of surgical outcome. Extrem Physiol Med. 2013. 2(1): 33.
[22] Sun L, Ke X, Wang D, et al. Prognostic Value of the Albumin-to-γ-glutamyltransferase Ratio for Gallbladder Cancer Patients and Establishing a Nomogram for Overall Survival. J Cancer. 2021. 12(14): 4172-4182.
[23] Tang G, Yuan X, Luo Y, et al. Establishing immune scoring model based on combination of the number, function, and phenotype of lymphocytes. Aging (Albany NY). 2020. 12(10): 9328-9343.
[24] Gomes RN, Bozza FA, Amâncio RT, et al. Exogenous platelet-activating factor acetylhydrolase reduces mortality in mice with systemic inflammatory response syndrome and sepsis. Shock. 2006. 26(1): 41-49.
[25] Liu Huiliang, Zhang Feifei, Li Yingxiao, Liu Litian, Song Xuelian, Wang Jiaqi, Dang Yi, Qi Xiaoyong. The HALP score predicts no-reflow phenomenon and long-term prognosis in patients with ST-segment elevation myocardial infarction after primary percutaneous coronary intervention. Coron Artery Dis, 2024 .
[26] Evsen Ali, Aktan Adem, Kılıç Raif, Yalçın Abdulaziz, Özbek Mehmet. Assessing the prognostic value of HALP score in peripheral artery disease: Correlation with lesion severity and long-term mortality. Vascular, 2025: 17085381251327000.
[27] Tunca Çağatay, Taş Alperen, Demirtaş İnci Saadet. The role of the HALP score in determining the severity of lower extremity peripheral arterial disease. Vascular, 2025 :17085381251330370.
[28] GONG P, LIU Y, GONG Y, et al. The association of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and lymphocyte to monocyte ratio with post-thrombolysis early neurological outcomes in patients with acute ischemic stroke[J]. J Neuroinflammation, 2021,18(1):51.

[29] WALLENTIN L, ERIKSSON N, OLSZOWKA M, et al. Plasma proteins associated with cardiovascular death in patients with chronic coronary heart disease: A retrospective study[J]. PLoS Med, 2021,18(1):e1003513.
[30] BIANCHI V E. Impact of Nutrition on Cardiovascular Function[J]. Curr Probl Cardiol, 2020,45(1):100391.
[31] LAI T, LIANG Y, GUAN F, et al. Trends in hemoglobin-to- red cell distribution width ratio and its prognostic value for all-cause, cancer, and cardiovascular mortality: a nationwide cohort study[J]. Sci Rep, 2025,15(1):7685.
[32] ZHAO D, JIAO H, ZHONG X, et al. The association between serum albumin levels and related metabolic factors and atrial fibrillation: A retrospective study[J]. Medicine (Baltimore), 2022,101(44):e31581.
[33] STOKES K Y, GRANGER D N. Platelets: a critical link between inflammation and microvascular dysfunction[J]. J Physiol, 2012,590(5):1023-1034.
[34] ZUO L, DONG Y, LIAO X, et al. Low HALP (Hemoglobin, Albumin, Lymphocyte, and Platelet) Score Increases the Risk of Post-Stroke Cognitive Impairment: A Multicenter Cohort Study[J]. Clin Interv Aging, 2024,19:81-92.
[35] Wang Haixu, Zhou Zeming, Liu Xiaoxin, Chen Ying. Anti-inflammatory diets might mitigate the association between sedentary behaviors and the risk of all-cause deaths. Nutr Metab (Lond), 2025, 22(1):11.
[36] ANTAR R, FARAG C, XU V, et al. Evaluating the baseline hemoglobin, albumin, lymphocyte, and platelet (HALP) score in the United States adult population and comorbidities: an analysis of the NHANES[J]. Front Nutr, 2023, 10: 1206958.
[37] PAN H, LIN S. Association of hemoglobin, albumin, lymphocyte, and platelet score with risk of cerebrovascular, cardiovascular, and all-cause mortality in the general population: results from the NHANES 1999-2018[J]. Front Endocrinol (Lausanne), 2023,14:1173399.
[38] CHEN L, DENG H, CUI H, et al. Inflammatory responses and inflammation-associated diseases in organs[J]. Oncotarget, 2018,9(6):7204-7218.