

# Correlation of the Monocyte/High-Density Lipoprotein Ratio, Red Blood Cell, Hemoglobin and Combined Lower Extremity Atherosclerosis in Patients with Essential Hypertension

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**Abstract:** This study aims to explore the correlation between the monocyte/high-density lipoprotein ratio (MHR), red blood cell (RBC), hemoglobin (Hb) levels, and lower limb atherosclerosis (AS) in patients diagnosed with essential hypertension (EH). A total of 310 EH patients admitted to the General Medical Department of the Second Affiliated Hospital of Guilin Medical College between July 2021 and December 2022 were selected for this analysis. The patients were categorized into four groups based on the severity of lower limb AS: the AS1+EH group (simple EH) included 90 patients; the AS2+EH group (EH with intimal thickening of the lower extremity arteries) comprised 42 patients; the AS3+EH group (EH with lower extremity arterial plaques) consisted of 90 patients; and the AS4+EH group (EH with lower extremity arterial stenosis) included 88 patients. Age, history of coronary heart disease, white blood cells (WBC), RBC, Hb, monocytes, platelets, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), indirect bilirubin (IBIL), and MHR were all statistically significant across the four groups. Specifically, the counts of RBC and Hb in the AS1+EH, AS2+EH, AS3+EH, and AS4+EH groups exhibited a decreasing trend, while age showed an increasing trend. WBC, monocytes, platelets, and MHR demonstrated an overall increasing trend; however, a decrease was observed in the AS3+EH group compared to the AS1+EH group ( $P < 0.05$ ). In contrast, no statistically significant differences were found in gender, direct bilirubin (DBIL), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) ( $P > 0.05$ ). Spearman rank correlation analysis indicated that in patients with lower limb AS, MHR exhibited a positive correlation with WBC, monocytes, platelets, and TG. Conversely, MHR showed a negative correlation with RBC, TC, HDL, and LDL. Additionally, MHR was correlated with age, Hb, ALT, AST, and TBIL; however, DBIL and IBIL were not found to be related. Multivariate logistic regression analysis indicated that increasing age, along with decreasing RBC and Hb levels, are risk factors for grades 3 to 4 lower AS in patients with EH. Additionally, an elevated MHR was identified as a risk factor specifically for grade 4 lower limb AS in these patients. The parameters MHR, RBC, and Hb are correlated with the severity of lower limb AS in EH patients. Notably, RBC and Hb levels decline as the severity of lower limb AS increases, particularly in patients classified with grades 3 to 4. Conversely, MHR levels rise with increasing severity of lower extremity AS, primarily observed in patients with grade 4.

**Keywords:** Essential Hypertension, Lower Extremity Atherosclerosis, Monocyte/High-Density Lipoprotein Ratio, Red Blood Cell, Hemoglobin

## 1. Introduction

Hypertension is one of the most prevalent chronic diseases. In my country, there are approximately 245 million individuals affected by hypertension, with essential hypertension (EH) constituting over 95% of these cases [1]. The incidence of essential hypertension among the elderly in my country ranges from 38.2% to 57.6% [2], and this prevalence continues to rise annually. Atherosclerosis (AS) of the lower extremities is a common complication associated with senile hypertension, with an incidence rate

reaching 20% in individuals over the age of 65 [3]. In severe instances, amputation may be necessary [4], leading to significant challenges in patients' daily lives. The monocyte/high-density lipoprotein ratio (MHR) is significantly associated with various cardiovascular diseases and serves as a novel inflammatory marker for atherosclerosis [5]. Additionally, red blood cells are intricately linked to the progression of atherosclerosis [6]. Hemoglobin (Hb) has been identified as an independent risk factor for both severe and moderate forms of atherosclerosis [7]. Currently, there is a paucity of domestic literature addressing the relationships among MHR, red blood cells (RBC), Hb, and the incidence of lower limb atherosclerosis (AS) in patients with EH. This article aims to investigate the correlation between peripheral blood levels of MHR, RBC, and hemoglobin in EH patients, and their association with the occurrence of lower limb AS, thereby offering new targets for prevention and treatment.

## **2. Methods**

### **2.1 General materials**

A total of 310 patients diagnosed with EH were admitted to the General Medical Department of the Second Affiliated Hospital of Guilin Medical College between July 2021 and December 2022. This cohort comprised 162 male patients and 148 female patients, with an average age of  $67.56 \pm 10.63$  years, ranging from 38 to 89 years. The inclusion criteria encompass patients diagnosed with EH for the first time, as well as those with a prior diagnosis of EH, in accordance with the diagnostic criteria outlined in the 2018 revised version of the Chinese Guidelines for the Prevention and Treatment of Hypertension [8]. This research protocol received approval from the Medical Ethics Committee of the Second Affiliated Hospital of Guilin Medical College, and all research participants voluntarily provided informed consent prior to the commencement of the experiment. Exclusion criteria included patients with a history of drug abuse, malignant tumors, respiratory system diseases, digestive system diseases, rheumatic immune system diseases, neurological and mental health disorders, endocrine system diseases, infectious diseases, and those who were uncooperative or provided incomplete information.

### **2.2 Data collection**

Gender and age of the study participants were collected.

### **2.3 Blood pressure and physical measurements**

After the study subjects rested for 15 minutes, professional nurses measured the blood pressure in both upper limbs using a standardized Omron blood pressure monitor. The side with the higher blood pressure was recorded as the measurement result. Each measurement was separated by a 5-minute interval, and the final result was determined by averaging the two measurements. If the difference in diastolic or systolic blood pressure between the two sides exceeded 5 mmHg, a third measurement was conducted, with the final result based on the average of all three measurements.

### **2.4 Blood tests and biochemical indicators**

All research subjects were instructed to undergo a strict 8-hour fasting period, after which cubital venous blood was drawn at 7:00 AM the following day. The XN-9000 fully automatic hematology analyzer from Sysmex, Japan, was utilized to measure white blood cells (WBC), RBC, Hb, monocytes, and platelets. Additionally, the Swiss Roche C702 fully automatic biochemistry instrument was employed to assess alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). The monocyte/high-density lipoprotein ratio (MHR) was calculated using the formula  $MHR = \text{monocyte}/HDL$ .

### **2.5 Ultrasound of lower extremity arteries**

A senior sonographer utilized the PHILIPS-EPIQ color Doppler ultrasound instrument to examine the arteries of both lower extremities of the study subjects. Prior to the examination, subjects were permitted to rest for 15 minutes. During the examination, patients were positioned supine, ensuring that no pressure was applied to the lower limbs, and the angle between the ultrasound beam and the blood flow was maintained at less than 60°. The examination assessed the diameters, intima-media thickness,

presence of plaques, number and volume of plaques, and the degree of vascular stenosis in the common femoral artery, deep femoral artery, superficial femoral artery, popliteal artery, anterior tibial artery, posterior tibial artery, and dorsalis pedis artery of both lower limbs. AS was categorized into four grades based on the severity of lower limb AS: grade 1 indicates no AS with normal arteries; grade 2 reflects arterial intima-media thickening (intima-media  $\geq 1$  mm) without plaque; grade 3 denotes the presence of arterial plaque with a degree of stenosis of the arterial lumen  $<50\%$ ; and grade 4 indicates a degree of stenosis of the arterial lumen  $\geq 50\%$ . Based on these criteria, the study subjects were classified into four groups: 90 cases in the AS1+EH group (simple EH), 42 cases in the AS2+EH group (EH combined with intimal thickening of the lower limb arteries), 42 cases in the AS3+EH group (EH combined with lower limb arterial plaques), and 88 cases in the AS4+EH group (EH combined with lower extremity arterial stenosis).

## 2.6 Statistical analysis

Statistical analysis was conducted using SPSS 26.0 software. Measurement data that conform to a normal distribution are expressed as ( $\bar{x} \pm s$ ), with analysis of variance employed for comparisons among multiple groups. For non-normally distributed measurement data, values are presented as M (P25, P75), and the Kruskal-Wallis H test is utilized for comparisons across multiple groups. Enumeration data are expressed as [cases (%)], with the chi-squared test applied for comparison among multiple groups. Spearman rank correlation analysis was performed to explore correlations. Multivariate logistic regression was used to analyze the influencing factors of lower limb AS in EH patients. The value of  $<0.05$  was considered statistically significant.

## 3. Results

### 3.1 Comparison of general clinical data and laboratory test indexes between the four groups of patients

Age, history of coronary heart disease, WBC, RBC, Hb, monocytes, platelets, ALT, AST, TBIL, IBIL, and MHR were all statistically significant across the four groups. Specifically, the counts of RBC and Hb in the AS1+EH, AS2+EH, AS3+EH, and AS4+EH groups exhibited a decreasing trend, while age showed an increasing trend. WBC, monocytes, platelets, and MHR demonstrated an overall increasing trend; however, a decrease was observed in the AS3+EH group compared to the AS1+EH group ( $P < 0.05$ ). In contrast, no statistically significant differences were found in gender, history of type 2 diabetes, smoking, alcohol consumption, DBIL, TC, TG, HDL, and LDL ( $P > 0.05$ ). (see Table 1)

Table 1: Comparison of general clinical data and laboratory test indexes between the four groups of patients

variate	AS1+EH group (n=90)	AS2+EH group (n=42)	AS3+EH group (n=90)	AS4+EH group (n=88)	$t/t'/\chi^2/z$	P
Gender (male/female)	40/50	25/17	44/46	53/35	5.71	0.125
Age(years)	60(55,67)	64(57,70)	71(67,77)	74(68,81)	84.263	0.000
history of coronary heart disease(n[%])	10 (11.2%)	8 (19.0%)	23(25.6%)	38(43.2%)	24.892	0.000
history of type 2 diabetes (n[%])	56(62.9%)	30(71.4%)	66(73.3%)	60(68.2%)	2.432	0.488
Smoking (n[%])	10(11.2%)	5(11.9%)	7(7.8%)	10(11.4%)	0.923	0.820

alcohol consumption (n[%])	12(13.5%)	5(11.9%)	6(6.7%)	11(12.5%)	2.524	0.471
WBC( $\times 10^9/L$ )	6.78 (5.49,8.51)	6.83 (5.67,7.92)	6.46 (5.41,7.93)	7.75 (6.14,9.28)	13.228	0.004
RBC( $\times 10^9/L$ )	4.45 (4.18,4.76)	4.39 (3.97,4.68)	4.27 (3.83,4.57)	3.79 (3.29,4.29)	47.515	0.000
monocyte count ( $\times 10^9/L$ )	0.50 (0.37,0.62)	0.51 (0.42,0.72)	0.48 (0.40,0.59)	0.63 (0.48,0.80)	29.090	0.000
Hb (g/L)	130.50 (119.00,142.00)	130.50 (116.50,139.25)	122.50 (115.00,134.00)	109.00 (97.00,127.50)	44.530	0.000
Platelets ( $\times 10^9/L$ )	229.50 (188.25,280.50)	230.50 (184.00,295.00)	213.50 (182.00,244.00)	254 (198.50,301.25)	12.892	0.005
ALT (U/L)	17.45 (12.20,24.63)	15.90 (12.60,24.55)	12.95 (10.08,17.68)	16.00 (11.22,24.73)	13.212	0.004
AST (U/L)	18.50 (15.30,22.03)	16.65 (13.38,21.23)	17.00 (14.25,20.90)	19.95 (14.10,27.43)	9.263	0.026
TBIL (umol/L)	8.25 (6.18,10.50)	8.50 (6.50,11.30)	6.80 (5.35,9.87)	7.05 (4.75,10.98)	9.285	0.026
DBIL (umol/L)	3.55 (2.68,4.70)	3.5 (2.78,4.93)	3.25 (2.30,4.20)	3.30 (2.40,5.20)	2.837	0.417
IBIL (umol/L)	4.75 (3.20,6.10)	4.65 (3.50,6.63)	3.70 (2.88,5.50)	3.35 (2.23,5.33)	17.679	0.001
TC (mmol/L)	4.72 (3.99,5.38)	4.32 (3.68,5.52)	4.55 (3.92,5.30)	4.28 (3.41,5.18)	6.301	0.098
TG (mmol/L)	1.78 (1.17,2.65)	1.45 (1.05,2.68)	1.75 (1.04,2.83)	1.69 (1.12,2.08)	1.804	0.614
HDL (mmol/L)	1.12 (0.95,1.34)	1.18 (1.01,1.31)	1.16 (1.01,1.44)	1.06 (0.91,1.24)	7.573	0.056
LDL (mmol/L)	2.88 (2.22,3.50)	2.59 (2.07,3.65)	2.88 (2.12,3.38)	2.62 (1.83,3.32)	3.337	0.343
MHR	0.42 (0.32,0.59)	0.44 (0.38,0.62)	0.41 (0.31,0.56)	0.60 (0.43,0.85)	37.14	0.000

### 3.2 Correlation analysis of MHR, cystatin C and other indicators

Spearman rank correlation analysis indicated that in patients with lower limb AS, MHR exhibited a positive correlation with WBC, monocytes, platelets, and TG. Conversely, MHR showed a negative correlation with RBC, TC, HDL, and LDL. Additionally, MHR was correlated with age, Hb, ALT, AST, and TBIL; however, DBIL and IBIL were not found to be related. (see Table 2)

Table 2: Correlation of MHR and other indicators

variate	platelets		WBC		RBC		Hb	
	r	P	r	P	r	P	r	P
MHR	0.117	0.039	0.478	0.000	-0.116	0.004	-0.093	0.102

variate	TC		TG		HDL		LDL	
	r	P	r	P	r	P	r	P
MHR	-0.152	0.007	0.200	0.000	-0.553	0.000	-0.146	0.010

variate	age		monocyte count		AST		ALT	
	r	P	r	P	r	P	r	P
MHR	0.034	0.547	0.814	0.000	-0.071	0.211	0.079	0.165

variate	TBIL		DBIL		IBIL	
	r	P	r	P	r	P
MHR	-0.032	0.574	0.001	0.987	-0.074	0.192

### 3.3 Analysis of factors affecting lower extremity AS in EH patients with comorbidities

The presence or absence of lower limb AS was designated as the dependent variable (assignment: yes=1, no=0). Age, RBC, Hb, and MHR—indicators that exhibited statistically significant differences in single-factor analysis—were employed as independent variables (all indicators were assigned values based on actual measured values). Multivariate logistic regression analysis revealed that age, elevated MHR, and decreased levels of RBC and Hb were identified as risk factors for lower limb AS in patients with EH ( $P < 0.05$ ). (see Table 3)

Table 3: Multifactorial Logistic Regression Analysis of Lower Extremity AS Occurrence in EH Patients

variate	$\beta$	SE	Wald $\chi^2$	P	OR	95%CI
age	0.1	0.015	44.328	0.000	1.105	(1.073,1.138)
RBC	-0.729	0.188	15.081	0.000	0.482	(0.334,0.697)
Hb	-0.034	0.008	20.018	0.000	0.966	(0.952,0.981)
MHR	1.578	0.579	7.412	0.006	4.843	(1.556,15.079)

### 3.4 Analysis of factors affecting EH patients with combined grade 2-4 lower extremity AS

The AS grade of the lower limbs was utilized as the dependent variable, with the assignment of AS grades as follows: AS grade 1 = 1, AS grade 2 = 2, AS grade 3 = 3, and AS grade 4 = 4. All indicators that demonstrated statistical significance in the univariate analysis were employed as independent variables. The results of the multivariate logistic regression analysis indicated that increasing age, along with decreasing levels of RBC and Hb, were identified as risk factors for progression from grade 3 to grade 4 lower limb AS in patients with EH. Additionally, an increased MHR was found to be a risk factor specifically for grade 4 lower limb AS in this patient population ( $P < 0.05$ ). (see Table 4)

*Table 4 Multifactorial Logistic Regression Analysis of Combined Grade 2-4 Lower Extremity AS in Patients with EH*

variate	AS2+EH group					
	$\beta$	SE	Wald $\chi^2$	P	OR	95%CI
age	0.025	0.02	1.634	0.201	1.026	(0.987,1.067)
RBC	-0.233	0.306	0.579	0.447	0.792	(0.435,1.443)
Hb	-0.018	0.012	2.439	0.118	0.982	(0.960,1.005)
MHR	1.347	0.849	2.514	0.113	3.844	(0.728,20.305)

variate	AS3+EH group					
	$\beta$	SE	Wald $\chi^2$	P	OR	95%CI
age	0.133	0.022	35.782	0.000	1.142	(1.093,1.192)
RBC	-0.727	0.283	6.611	0.010	0.484	(0.278,0.841)
Hb	-0.026	0.01	6.422	0.011	0.974	(0.954,0.994)
MHR	-0.435	0.795	0.300	0.584	0.647	(0.136,3.070)

variate	AS4+EH group					
	$\beta$	SE	Wald $\chi^2$	P	OR	95%CI
age	0.131	0.021	38.928	0.000	1.14	(1.094,1.187)
RBC	-1.469	0.284	26.751	0.000	0.230	(0.132,0.402)
Hb	-0.055	0.010	30.840	0.000	0.947	(0.929,0.965)
MHR	3.448	0.769	20.115	0.000	31.433	(6.966,141.824)

## 4. Discussion

AS refers to an inflammatory reaction that occurs when the walls of blood vessels in the lower limbs are injured. With the acceleration of an aging population, the incidence of lower limb AS is

increasing annually. Patients with EH who develop lower limb AS may experience symptoms such as intermittent claudication, ischemic ulcers, and gangrene in the later stages. This study found that an increase in MHR, along with a decrease in RBC and Hb, is associated with the severity of lower limb AS in EH patients. Therefore, monitoring MHR, RBC, and Hb serves as convenient screening and preventive indicators for the early detection of lower limb AS in EH patients.

When the vascular endothelium is damaged, a significant number of monocytes become activated. These cells adhere tightly to the surface of the vascular endothelium with the aid of adhesion factors, migrate through the endothelial gaps to the subendothelium in response to chemokines, and subsequently differentiate into macrophages. With the assistance of scavenger receptors, macrophages engulf oxidized LDL, transforming into macrophage-derived foam cells, which promotes the development of AS[9]. HDL plays an anti-atherosclerotic role by facilitating the reverse transport of cholesterol and inhibiting the activation and proliferation of monocytes [10]. Univariate analysis in this study revealed that monocyte levels significantly increased with the severity of AS in the lower limbs, and this difference was statistically significant. Furthermore, Spearman rank correlation analysis indicated a positive correlation between the MHR and monocyte levels. A study by Huang Xingjie et al. [11] found that patients with EH and carotid atherosclerosis (CAS) exhibited significantly higher levels of monocytes compared to the normal control group, with these differences being statistically significant. This finding aligns with the results of the current study. Additionally, this study observed that MHR levels generally increased with the severity of lower limb AS, particularly in EH patients with grade 4 lower limb AS. Ding Yan et al. [12] reported that MHR rises with the degree of lower extremity arterial stenosis, identifying high MHR as a risk factor for the development of lower extremity arterial stenosis. Similarly, Tu Zhenxing et al. [13] found a positive correlation between MHR and lower limb arterial severity scores, which corresponds with the findings of this study. Furthermore, Li Zhichao et al. [14] categorized patients with type 2 diabetes mellitus (T2DM) and lower limb arteriosclerosis obliterans (ASO) into four groups based on MHR quartiles. They noted that the incidence of ASO increased with higher MHR levels, establishing MHR as an independent risk factor for ASO in T2DM patients, and demonstrating a positive correlation with ASO, which is consistent with the results of this study. Univariate analysis in this study indicated that monocyte and MHR levels in the AS3+EH group were lower compared to those in the AS1+EH group. Given that patients in the AS3+EH group may initiate lipid-lowering therapy earlier, future studies should aim to collect a larger sample size and refine the timing of medication initiation for this patient population. The findings of this study are promising, particularly since the early symptoms of EH in patients with lower limb AS are often subtle, leading many to miss the opportunity for early diagnosis. In contrast to traditional biomarkers such as interleukin-8, interleukin-6, and tumor necrosis factor, MHR offers advantages including ease of use, low cost, immediate availability, and repeatable detection. These characteristics make it suitable for promotion within primary medical institutions, facilitating early detection of affected patients. For individuals presenting with plaque or stenosis in the lower limbs, prompt administration of statins is recommended to manage lipid levels and stabilize plaques. In cases of severe stenosis, early interventional treatment should be considered to mitigate the risk of necrosis or amputation of the lower limbs.

Red blood cell membranes contain a significant amount of free cholesterol, which plays a crucial role in plasma lipid metabolism and is involved in reverse cholesterol transport (RCT) [15]. This process is vital for the formation and progression of AS. The rupture of RBC leads to the release of heat shock protein 70, which inhibits the expression of ABCA1 and ABCG1 via the JNK/Elk-1 pathway, thereby promoting the progression of AS in ApoE<sup>-/-</sup> mice [16]. The primary function of Hb is to ensure an adequate supply of oxygen to body tissues. Tissue hypoxia and alterations in blood flow patterns resulting from low Hb levels may contribute to the development of AS [17]. Within atherosclerotic plaques, Hb is readily self-oxidized to oxidized Hb in a highly oxidative environment and reacts with nitric oxide (NO) to produce high-iron Hb and inert nitrates. Both of these processes diminish the bioavailability of NO within plaques, leading to increased intercellular adhesion and, consequently, accelerating the AS process [18]. This study found that as the severity of EH in patients with lower limb AS increases, the levels of RBC and Hb gradually decrease, particularly in those with EH combined with grade 3 to 4 lower limb AS. Research conducted by Hong et al. [19] demonstrated that Hb levels were negatively correlated with the absolute necrotic core volume of AS plaques in patients suffering from coronary heart disease, suggesting that lower Hb levels are associated with a greater plaque burden. Consequently, low Hb levels may significantly influence the pathophysiological processes underlying the occurrence and progression of AS, as well as being closely related to the vulnerability of coronary plaques, which aligns with the findings of this study. Delbosc et al. [20] reported in a rabbit aortic AS model that RBCs can infiltrate the arterial wall during the AS plaque stage and be

phagocytosed by smooth muscle cells, mirroring the observations in this study. Therefore, during the treatment of patients with EH and lower limb AS, actively increasing RBC and Hb levels may help delay the progression of AS, presenting a potential new therapeutic target for managing these patients. However, the sample size of this study was limited, and there was a lack of subsequent follow-up with this patient population. Thus, the degree of increase in RBC and Hb levels, as well as the underlying reasons for their decrease, warrant further investigation in future studies.

Age is an independent risk factor for AS [21]. As age increases, smooth muscle cells in blood vessels proliferate, migrate, and secrete substantial amounts of extracellular matrix, resulting in decreased blood vessel elasticity, vascular lumen expansion, and vascular remodeling, which ultimately contributes to the development of AS [22]. Single-factor analysis in this study revealed a sequential increase in the age of patients across the four groups, with statistically significant differences observed. Multivariate logistic regression analysis indicated that increasing age elevates the risk of lower limb AS in both the AS3+EH and AS4+EH groups. Consistent with the findings of Zhang Cuntai et al. [23], the incidence of AS rises with age. Thus, advancing age is an unavoidable risk factor for patients with EH to develop lower limb AS. Consequently, elderly patients should be encouraged to manage and control other modifiable risk factors actively.

Univariate analysis in this study indicated that the differences in WBC and platelet levels among the four patient groups were statistically significant. Additionally, Spearman rank correlation analysis revealed a positive correlation between MHR and both WBC and platelet counts. The onset and progression of AS are associated with chronic inflammation and intra-plaque hemorrhage [24]. WBC counts reflect the inflammatory response, while variations in platelet levels can lead to bleeding within the body. Therefore, administering moderate anti-inflammatory treatment to patients with lower extremity AS, along with controlling platelet counts when necessary, may help to slow or reverse the progression of AS in patients with EH.

Single-factor analysis in this study revealed statistically significant differences in ALT, AST, TBIL, and IBIL among the four patient groups. Additionally, Spearman rank correlation analysis indicated no correlation between MHR and the liver function markers ALT, AST, TBIL, DBIL, and IBIL. In cases where EH patients are combined with lower limb AS, abnormal liver function may occur. If necessary, hepatoprotective drugs, such as diammonium glycyrrhizinate and magnesium isoglycyrrhizinate, may be administered. The relationship between MHR and liver function will be further investigated through multi-center data in future studies.

## 5. Limitations

This study has several limitations: (1) It is a small-sample, single-center cohort study, and the findings require further validation through multi-center, large-sample studies; (2) The baseline data lacks information on C-reactive protein, reticulocyte count, and pro-erythropoietin levels, which may introduce residual confounding factors in the analysis of relevant data, including erythropoietin, folic acid, vitamin B12, and iron levels. Future research should aim to address these potential confounding factors to better evaluate the relationship between RBC, Hb levels, and EH in conjunction with lower limb AS; (3) This study does not include data related to dietary factors, or the use of antihypertensive and lipid-lowering medications. We aim to further investigate the influencing factors affecting EH patients with concurrent lower limb AS by increasing the sample size.

## 6. Conclusion

In summary, MHR, RBC, and Hb levels are correlated with the severity of lower limb AS in patients with EH. Specifically, RBC and Hb levels decrease as the severity of lower limb AS increases, particularly in patients with grades 3 to 4. Conversely, MHR increases with the severity of lower extremity AS in EH patients, predominantly in those classified as grade 4. Given that MHR, RBC, and Hb assessments are straightforward to perform in primary care settings, they can facilitate disease screening and tiered management in the early stages. In the long term, these measures may help alleviate the financial burden on patients and enhance their quality of life.

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Monocytes/high density lipoprotein and lower extremity atherosclerosis in patients with essential



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