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Original Article

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Monocyte-to-High-Density Lipoprotein Ratio Predicts the Outcome of Acute Ischemic Stroke

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Aim: Monocyte-to-high-density lipoprotein ratio (MHR) recently emerged as an inflammatory marker and has been reported to be a novel prognostic indicator of cardiovascular diseases. However, the relationship between MHR and prognosis of acute ischemic stroke (AIS) remains unclear.

Methods: Consecutive AIS patients were prospectively identified from January 2015 to December 2017. Functional outcome was evaluated by the modified Rankin Scale (mRS). Poor outcome was defined as of mRS 3-6. Multivariate logistic regression analysis was conducted to evaluate the relationship between MHR and poor outcome.

Results: A total of 1090 AIS patients within 24 hours of the onset of symptoms were recruited. MHR was higher in poor outcome group compared to that in good outcome group [0.53 (0.37-0.69) vs. 0.48 (0.33-0.60), $P=0.007$]. Multivariate logistic regression analysis indicated that higher MHR level was independently associated with the poor outcome at 3 months (OR 2.58, 95% CI, 1.21-5.51, $P=0.015$), especially the stroke subtype of large artery atherosclerosis (OR 2.52, 95% CI, 1.03-6.19, $P=0.034$). Receiver operating curve (ROC) analysis showed that the area under the ROC curves for MHR was 0.67 and the best predictive cutoff value of MHR was 0.51, with a sensitivity of 62.3% and a specificity of 66.5%.

Conclusions: MHR may be a significant and independent predictor of poor functional outcome in patients with AIS.

Key words: Stroke, Prognosis, Monocytes, High-density lipoprotein, Risk factors

Introduction

Despite the improvement in antithrombotic therapy and the reinfusion strategy, the prognosis of patients with acute ischemic stroke (AIS) is still unsatisfactory[1, 2]. Increasing interest focuses on the identification of new prognostic markers to better enable the categorization of patients who are at higher risk for poor outcome. Recent studies have reported that inflammation plays an important role in the process of ischemic stroke[3]. Some inflammatory factors, including neutrophil-to-lymphocyte ratio (NLR)[4], C reactive protein (CRP)[5], and D-dimer[6], have been identified through the study of AIS. Monocytes (MONO) are a type of leukocytes that play an important role in the post-ischemic inflammation[7]. Monocytes were recruited to the ischemic area in the early stages of inflammatory response when AIS occurs, which promoted the damage of blood-brain barrier by releasing inflammatory mediators[8, 9]. In addition, high-density lipoprotein cholesterol (HDL-C) counteracts these pro-inflammatory and prooxidant effects of monocytes by preventing the migration of macrophages and oxidation of LDL molecules and by promoting the efflux of cholesterol from these cells, thus inhibiting the inflammatory process and reducing the

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risk of atherosclerotic events[10-12].

Monocyte-to-HDL-C ratio (MHR), which was calculated by dividing the absolute monocyte count by the absolute HDL-C count, has emerged as a novel inflammation marker and reported to be strongly associated with cardiovascular events[13]. Previous studies have shown that admission MHR values were independently correlated with increasing risk of disability or death in patients with intracerebral hemorrhage[14]. Another investigation of 466 patients with AIS found that high MHR was independently correlated with a 30-day mortality[15]. Nevertheless, to our knowledge, few studies have investigated the association between MHR and function prognosis in AIS. Therefore, more prospective cohort and large sample size studies are needed to explore this relationship. It may therefore be useful to know the level of MHR to identify those at higher risk of poor outcome and to perform further potential intervention.

In this study, we aimed to evaluate the relationship between MHR and 3-month function prognosis in patients with AIS.

Material and Methods

Patients and Methods

Patients included in this study were from the database of the Henan Province Stroke Registry at the First Affiliated Hospital of Zhengzhou University[16] from January 2015 to December 2017. Ischemic stroke was diagnosed according to World Health Organization-defined criteria[17], based on clinical data, patient history, and neuroimaging results (computed tomography or magnetic resonance imaging).

Exclusion criteria were as follows: (1) time from onset to admission over 24 hours; (2) patients without complete clinical data; (3) having a history of cancer, use of an immunosuppressant, or hematologic disease; (4) severe hepatic or renal diseases; (5) major trauma, surgery, or lost to follow-up; (6) immune diseases/chronic inflammatory diseases; and (7) chronic lung disease. This study was approved by the First Affiliated Hospital of Zhengzhou University, and informed consent was obtained from all participating patients or their immediate family members in this study.

Data Collection

Baseline data of the patients were recorded in paper-based case report forms. Demographic characteristics such as age, gender, smoking (defined as continuous or cumulative smoking ≥ 6 months or at least 6 months every day; passive smoking refers to nonsmokers inhaling the smoke from smokers' breath for at least 15 minutes per day for more than 1 day per week), and statin use history. The stroke risk factors included history of stroke (defined as medical record-confirmed history of ischemic, hemorrhagic stroke or subarachnoid hemorrhage), diabetes mellitus (including history of diabetes mellitus and newly diagnosed diabetes), hypertension (defined as history of hypertension and newly diagnosed hypertension), dyslipidemia (defined as low HDL-C and high triglycerides; the cutoff values were selected at HDL-C <40 mg/dl and triglyceride $\geq$ 200 mg/dl in both men and women), coronary heart disease (CHD) (including myocardial infarction and angina pectoris), and atrial fibrillation. Trained neurologists assessed the baseline stroke severity of neurologic impairment within 24 hours after admission using the National Institutes of Health Stroke Scale (NIHSS).

Laboratory examinations, including blood cell counts and lipid profiles, were routinely obtained within 24 hours of fasting upon admission to the hospital. The blood cell counts and lipid profiles included white blood cell (WBC), neutrophil, MONO, lymphocyte, total cholesterol (CHO), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and HDL-C.

Follow-Up and Outcome

The patient outcomes were evaluated by the modified Rankin Scale (mRS). Good and poor outcomes were identified by mRS $\leq$ 2 and mRS >2. Clinical follow-up was completed for most patients. Follow-up results were recorded by telephone interview. Telephone interviewers were not involved in the registry and were blinded to the baseline data.

Statistical Analysis

Continuous variables were expressed as mean ± SD or median which were analyzed by independent student's *t*-test or Mann-Whitney *U* test. Categorical variables were presented as numbers which were analyzed using χ^2 test or Fisher's exact test. Multivariate logistic regression analysis was conducted to assess the association between MHR and the prognosis. The receiver operating characteristic (ROC) analysis was further conducted to evaluate the ability of the MHR, MONO, and HDL to predict the outcome. Two-tailed p values of <0.05 were considered significant. All statistical analyses were performed using SPSS 19.0 software.

Results

Baseline Characteristics

A total of 1,293 AIS patients within 24 hours of the onset of symptoms were consecutively recruited

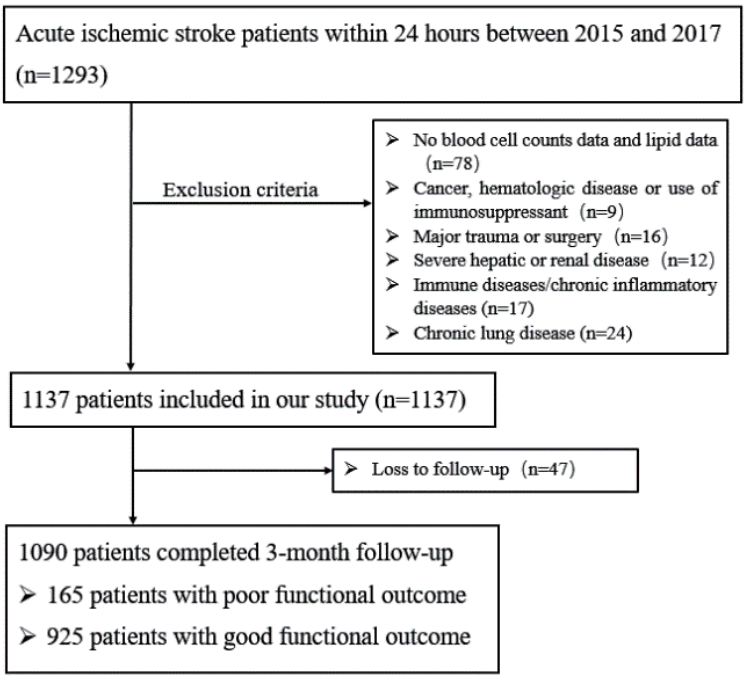

Fig. 1. Patients flowchart of the cohort

(**Fig. 1**), and 203 patients were excluded during the study period: 78 patients who had incomplete clinical data, 47 patients who were lost to follow-up, 62 patients who had other diseases, and 16 patients who had undergone trauma or surgery. By the time of a 3-month follow-up, 1090 patients were finally enrolled in this study. Comparison of the baseline characteristics between included and excluded patients showed no significant differences except history of hypertension (**Supplemental Table 1**).

During the 3-month follow-up, 925 patients had a good outcome and 165 patients had a poor outcome. The baseline clinical data of two groups are shown in **Table 1**. MHR [0.53 (0.37-0.69) vs. 0.48 (0.33-0.60), $P=0.007$] was significantly higher in the poor outcome group (**Fig. 2**). Compared with good outcome group, patients with a poor outcome were significantly older (64.13 ± 12.21 vs. 59.32 ± 12.64, $P=0.001$), were female (38.2% vs. 31.2%, $P=0.037$), had higher NIHSS score at admission ($P<0.001$), and had a prior history of smoking (41.1% vs. 34.5%, $P=0.018$), statin use (9.1% vs. 5.5%, $P=0.034$), CHD (17.2% vs. 10.8%, $P=0.013$), and stroke (30.1% vs. 20.9%, $P=0.007$). As for laboratory parameters, neutrophil [5.21 (4.02-6.69) vs. 4.93 (3.62-5.71), $P=0.017$], TG [1.12 (0.88-1.70) vs. 1.35 (0.95-1.84), $P=0.012$], HDL-C [1.03 (0.89-1.22) vs. 1.09 (0.93-1.29), $P=0.036$], and MONO [0.55 (0.43-0.67) vs. 0.51 (0.41-0.63), $P=0.027$] reached statistical significance. However, no significant intergroup differences were observed in terms of WBC, lymphocyte, CHO, LDL-C, and history of hypertension, dyslipidemia, and diabetes mellitus between good and poor outcome group.

Association between MHR at Admission and Functional Prognosis at 3 Months after Stroke

Multivariate logistic analysis showed that the MHR (OR 2.58, 95% CI, 1.21-5.51, $P=0.015$) was independently associated with the 3-month poor outcome after the adjustment for age, gender, NIHSS score at admission, and history of stroke, atrial fibrillation, coronary heart disease, hypertension, diabetes mellitus, neutrophil, triglyceride, smoking, and statin use. The MONO (OR 2.21, 95% CI, 1.05-4.68, $P=0.038$) remained significantly associated, but not HDL-C (**Table 2; Supplemental Table 2**).

As shown in **Supplemental Table 3**, after multivariable adjustment, odds ratios (95% confidence intervals) for the highest quartile of MHR were 1.64 (1.06-2.54) for primary outcome, 1.97 (0.49-2.99) for death, 3.34 (1.56-4.61) for disability, and 1.07 (1.03-1.09) for 1-U higher mRS score, compared with the lowest quartile of MHR. Every 1-SD increase of MHR level was not positively associated with poor outcomes among patients with ischemic stroke ($P=0.125$).

TOAST subgroup analysis showed that high

Table 1. Clinical and demographic characteristics of the study population in relation to 3-month outcomes

Characteristics	Good outcome (n=925)	Poor outcome (n=165)	P Value
Age, y	59.32 ± 12.64	64.13 ± 12.21	0.001
Male	636 (68.8%)	102 (61.8%)	0.037
Smoking	315 (34.5%)	67 (41.1%)	0.018
Statin use history	51 (5.5%)	15 (9.1%)	0.034
NIHSS score at admission	3 (2-5)	8 (4-12)	<0.001
Hypertension	539 (58.3%)	109 (65.8%)	0.059
CHD	99 (10.8%)	29 (17.2%)	0.013
Atrial fibrillation	41 (4.5%)	19 (11.5%)	0.004
Diabetes mellitus	182 (19.7%)	43 (25.8%)	0.057
Stroke	192 (20.9%)	51 (30.1%)	0.007
Dyslipidemia	97 (10.4%)	17 (10.2%)	0.949
WBC, 10^9/L	7.21 (5.91-8.41)	7.61 (6.43-8.71)	0.062
Neutrophil, 10^9/L	4.93 (3.62-5.71)	5.21 (4.02-6.69)	0.017
Lymphocyte, 10^9/L	1.73 (1.41-2.14)	1.71 (1.11-1.97)	0.059
MONO, 10^9/L	0.51 (0.41-0.63)	0.55 (0.43-0.67)	0.027
CHO, mmol/L	4.19 (3.49-4.87)	4.15 (3.47-4.99)	0.695
TG, mmol/L	1.35 (0.95-1.84)	1.12 (0.88-1.70)	0.012
LDL-C, mmol/L	2.67 (2.10-3.24)	2.55 (1.92-3.26)	0.280
HDL-C, mmol/L	1.09 (0.93-1.29)	1.03 (0.89-1.22)	0.036
MHR	0.48 (0.33-0.60)	0.53 (0.37-0.69)	0.007

NIHSS, National Institutes of Health Stroke Scale; CHD, coronary heart disease; WBC, white blood cell, MONO, monocyte; CHO, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein; HDL-C, high-density lipoprotein and MHR, monocyte to high-density lipoprotein ratio.

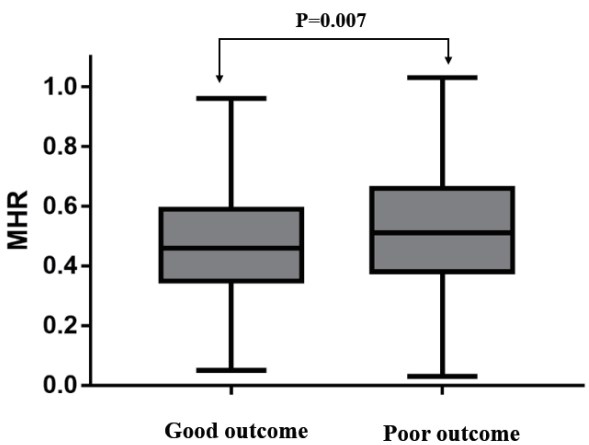

Fig. 2. Comparison of MHR between good and poor outcome in AIS patients

MHR was significantly associated with the 3-month poor outcome among stroke patients of LAA subtype (OR 2.52, 95% CI, 1.03-6.19, P=0.034) (**Table 3**). There was no statistical significance for the other types.

The receiver operating characteristic analysis and area under the curve (AUC) with respect to the outcome are shown in **Fig. 3**. The best discriminating variable was the MHR [AUC 0.67; 95% CI (0.64-0.69)], which showed the highest AUC value than those of MONO [AUC 0.61; 95% CI (0.59-0.64); P=0.021] and HDL-C [AUC 0.56; 95% CI (0.53-0.60); P<0.001]. The best predictive cutoff value was 0.51, with a sensitivity of 62.3% and a specificity of 66.5%. However, there is no significance between MONO and HDL-C counts (P=0.106).

Discussion

In this study, we found that high value of MHR was associated with risks of poor outcomes within 3 months after AIS. Furthermore, the MHR represented a readily available prognostic predictor and outperformed the predictive value of the MONO and HDL-C in the current analysis.

As shown in various pathologic conditions, AIS is a local event of vascular occlusion resulting in the deprivation of oxygen and nutrients, initiating a local inflammatory immune response[18, 19]. In ischemic brain damage, tissue infiltration with MONO occurs at least 72 h after injury onset, with the peak reaching 7 days after injury[20, 21]. Damaged tissue expresses chemokine receptors on the endothelial cell surfaces and interacts with leukocyte receptors, including monocyte/macrophage lineage CD11b+cells[22]. Under stimulation of oxidized LDL (ox-LDL), blood mono-

Table 2. Univariate and multivariate logistic regression analyses depicting the associations of MONO, HDL-C and MHR with 3-month outcomes of AIS

	Univariate logistic regression analysis			Multivariate logistic regression analysis*		
Variables	OR	95% CI	*P* Value	OR	95% CI	*P* Value
MONO, 10^9/L	2.76	1.10-6.93	0.030	2.21	1.05-4.68	0.038
HDL-C, mmol/L	0.52	0.29-0.92	0.045	0.56	0.28-1.09	0.088
MHR	2.42	1.20-4.87	0.013	2.58	1.21-5.51	0.015

*Adjustment for age, gender, NIHSS score at admission, history of stroke, history of atrial fibrillation, history of coronary heart disease, history of hypertension, history of diabetes mellitus, neutrophil, triglyceride, smoking, statin use history; MONO, monocyte; HDL-C, high-density lipoprotein; MHR, monocyte to high-density lipoprotein ratio.

Table 3. Before and after adjusted odds ratio analysis between presence of high MHR in stroke subtypes

	Before adjusted odd ratio			After adjusted odd ratio		
stroke subtypes	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Large artery atherosclerosis	2.99	1.26–5.73	0.023	2.52	1.03-6.19	0.034
Small artery disease	0.82	0.67–1.45	0.713	0.98	0.83-1.17	0.872
Cardioembolic stroke	1.01	0.47-1.46	0.509	1.15	0.74–1.55	0.815
Stroke of other determined etiology	0.85	0.50-1.47	0.568	1.04	0.88–1.67	0.921
Stroke of undetermined etiology	1.05	0.64–1.28	0.314	1.04	0.91–1.52	0.576

*Adjustment for age, gender, NIHSS score at admission, history of stroke, history of atrial fibrillation, history of coronary heart disease, history of hypertension, history of diabetes mellitus, neutrophil, triglyceride, smoking, statin use history;

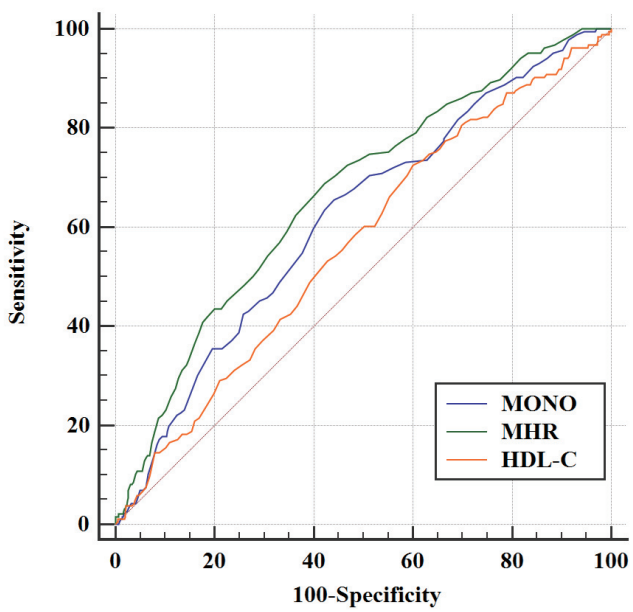

Fig. 3. Comparison of predictive power between MHR, MONO, and HDL in 3-month prognosis of patients with AIS

MHR [AUC 0.67; 95% CI (0.64–0.69)] showed the highest AUC value than those of MONO [AUC 0.61; 95% CI (0.59-0.64); $p=0.021$] and HDL-C [AUC 0.56; 95% CI (0.53-0.60); $p<0.001$]

cytes adhered to endothelial cells differentiated into macrophages. Macrophages not only gobble up ox-LDL and turn into foam cells but also secrete interleukin-1 (IL-1β), tumor necrosis factor-α (TNF-α), and other inflammatory factors[23, 24]. Animal studies have demonstrated the association of monocyte count with the extent of inflammation. Qiao *et al.*[25], who investigated inflammation in macrophage colony-stimulating factor-deficient mice, reported a gene dosage-related reduction in atherosclerosis correlated with a decrease in blood monocyte counts. In clinical studies, monocyte activation was also observed in peripheral blood after stroke, especially during the acute phase of ischemic stroke[26]. A study from Europe reported that baseline monocytes positively correlated with stroke severity and disability across all time points in a 90-day follow-up[27]. Another study showed that a number of monocytes and plasma MCP-1 level could be clinical prognostic biomarkers as early indicator of severity of illness in patients with AIS[28]. These are consistent with our findings. On the other hand, HDL-C represents well-known anti-inflammatory and antioxidant as well as antithrombotic effects; these activities have been shown in accordance with both the quality and quantity of HDL-C[29, 30]. Moreover, it has been confirmed that HDL-C particles exhibited anti-inflammatory effects on human monocytes by inhibiting activation of CD11b[31, 32]. Other studies have shown that the inhibitory effect of HDL-C may

be related to the signaling pathway mediated by scavenger receptor class B type I and sphingosine-1-phosphate receptor[7, 11].

Recently, the MHR as a novel marker to reflect inflammation was relatively more stable than single blood parameters[33, 34]; therefore, it may be more valuable than monocyte or HDL-C counts alone in the prediction of various diseases including cardiovascular and cerebrovascular diseases. Several studies reported that high MHR had a linear association with the rates of cardiovascular events and mortality. The pioneering study of Kanbay *et al.*[35] investigated that higher MHR has been associated with worse cardiovascular prognosis and independent predictor of major cardiovascular events in chronic kidney disease. Following this study, Shoujiang You[36] reported this marker in acute intracerebral hemorrhage population and suggested that MHR was independently associated with disability or death at hospital discharge and at 3 months post-stroke. A study by Asli Bolayir[15] enrolled 466 patients who were referred to clinic within the first 24 hours of symptom presentation and diagnosed with AIS; the findings demonstrated that high MHR was independently correlated with a 30-day mortality. Another investigation of 3,798 Chinese patients scheduled for selective coronary angiography found that MHR, as a novel inflammation-based marker, seemed to be an independent predictor of severity of coronary artery disease and future cardiovascular events in patients with ACS[37]. However, to our knowledge, few studies have investigated the association between MHR and prognosis in AIS. Therefore, more prospective cohort and large sample size studies are needed to further confirm this relationship.

In addition, the etiological mechanism of different subtypes AIS is different, which is important for the treatment and evaluation of prognosis. The etiological mechanism of large artery atherosclerosis (LAA) stroke is atherosclerosis[38]. MHR, as an inflammatory factor, may play a role in cell proliferation, macrophage chemotaxis, neutrophil exudation, oxidative stress, and other processes[39]. MHR may promote the formation of foam cells by activating the release of macrophage inflammatory mediators and may also affect the formation and development of atherosclerotic plaques by inhibiting the adhesion of smooth muscle cells to the matrix and other processes[39, 40]. In this study, high MHR level was associated with all stroke subtypes, especially the stroke subtype of large artery atherosclerosis. So far, there has been no study on the relationship between MHR and prognosis of different subtypes of stroke. We hypothesize that MHR may not equally contribute to subsequent stroke events among stroke patients of LAA and other subtypes.

There were several limitations in our study. First, our study is a single center and selection bias was unavoidable. Second, MONO and HDL-C concentrations were only collected once; thus there was a lack of dynamic data. Finally, some important inflammatory factors, including C reactive protein, procalcitonin, and erythrocyte sedimentation rate, were not routinely screened among included patients. For these reasons, more detailed and extensive prospective studies are required in the future.

Conclusion

In summary, our findings suggested that MHR may be a significant and independent predictor of unfavorable functional outcome in patients with AIS.

Acknowledgments

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Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contribution

Project development: Dr. Yuming Xu and Dr. Bo Song; Writing (original draft preparation): Dr. Hongbing Liu; Data analysis: Dr. Lu Zhao; Dr. Hui Fang and Dr. Bo Song; English editing help: Dr. Kai Liu; Dr. Yuan Gao; Data collection: Dr. Hongbing Liu; Dr. Lulu Pei; Figures and Tables: Dr. Yusheng Li; Dr. Shilei Sun and Dr. Jun Wu;

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Supplemental Table 1. Baseline characteristics of study patients with acute ischemic stroke

Characteristics	Enrolled (n=1,090)	Excluded (n=203)	P Value
Age, y	60.09 ± 12.78	60.42 ± 11.80	0.803
Male	714 (62.9%)	61 (54.5%)	0.074
Smoking	417 (38.3%)	65 (32.2%)	0.217
Statin use history	66 (6.1%)	18 (8.9%)	0.668
NIHSS score at admission	3 (2-6)	3 (1-6)	0.868
Hypertension	604 (53.3%)	71 (63.4%)	0.030
CHD	119 (10.5%)	22 (12.7%)	0.059
Atrial fibrillation	57 (5%)	14 (8.5%)	0.148
Diabetes mellitus	198 (17.5%)	299 (18.3%)	0.610
Stroke	209 (18.4%)	30 (18.9%)	0.702
Dyslipidemia	78 (6.9%)	11 (6.5)	0.633
WBC, 10^9/L	7.51 (6.31-8.51)	7.61 (6.13-9.67)	0.608
Neutrophil, 10^9/L	5.10 (3.91-6.11)	5.15 (3.88-7.21)	0.471
Lymphocyte, 10^9/L	1.71 (1.31-2.11)	1.65 (0.95-2.15)	0.638
MONO, 10^9/L	0.56 (0.48-0.63)	0.61 (0.45-0.79)	0.333
CHO, mmol/L	4.07 (3.46-4.77)	4.16 (3.11-4.70)	0.571
TG, mmol/L	1.37 (1.01-2.01)	1.35 (0.91-1.89)	0.309
LDL-C, mmol/L	2.49 (1.93-3.06)	2.63 (1.75-3.18)	0.742
HDL-C, mmol/L	1.06 (0.91-1.24)	1.06 (0.89-1.33)	0.923
MHR	0.48 (0.35-0.61)	0.46 (0.34-0.64)	0.934

NIHSS, National Institutes of Health Stroke Scale; CHD, coronary heart disease; WBC, white blood cell, MONO, monocyte; CHO, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein; HDL-C, high-density lipoprotein and MHR, monocyte to high-density lipoprotein ratio.

Supplemental Table 2. Multivariate logistic regression analysis predicting the 3-month outcomes

		Multivariate logistic regression analysis*		
Model	Independent variable	OR	95% CI	P Value
Model 1 (with MONO and HDL-C)	Age, y	1.03	1.02-1.05	0.001
	Male	1.66	1.13-2.43	0.010
	Smoking	1.34	1.03-1.71	0.026
	Statin use history	1.58	1.01-2.54	0.042
	NIHSS score at Admission	1.78	1.14-2.78	0.011
	History of hypertension	1.18	0.81-1.74	0.388
	History of atrial fibrillation	1.40	0.72-2.69	0.320
	History of stroke	1.52	1.02-2.27	0.039
	History of CHD	1.29	0.78-2.14	0.318
	History of diabetes mellitus	1.17	0.76-1.78	0.477
	Neutrophil, 10^9/L	1.11	1.02-1.20	0.016
	TG, mmol/L	0.81	0.65-1.01	0.057
	MONO, 10^9/L	2.21	1.05-4.68	0.038
	HDL-C, mmol/L	0.56	0.28-1.09	0.088
Model 2 (with MHR)	Age, y	1.03	1.01-1.04	0.001
	Male	1.38	0.96-1.99	0.084
	Smoking	1.27	1.01-1.65	0.016
	Statin use history	1.71	1.11-2.34	0.049
	NIHSS score at Admission	1.68	1.07-2.63	0.024
	History of hypertension	1.20	0.84-1.73	0.314
	History of atrial fibrillation	1.38	0.72-2.62	0.332
	History of stroke	1.30	0.89-1.90	0.184
	History of CHD	1.20	0.74-1.96	0.461
	History of diabetes mellitus	1.25	0.84-1.87	0.266
	Neutrophil, 10^9/L	1.17	1.09-1.25	0.001
	TG, mmol/L	0.81	0.66-0.99	0.043
	MHR	2.58	1.21-5.51	0.015

NIHSS, National Institutes of Health Stroke Scale; CHD, coronary heart disease; WBC, white blood cell, MONO, monocyte; CHO, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein; HDL-C, high-density lipoprotein and MHR, monocyte to high-density lipoprotein ratio.

Supplemental Table 3. Odds ratios and 95% confidence intervals of primary and secondary outcomes associated with MHR, as a categorical variable, after acute ischemic stroke onset

Outcomes	MHR				
	Quartile 1 <0.345	Quartile 2 0.345-0.451	Quartile 3 0.451-0.602	Quartile 4 ≥ 0.602	*P* Trend
Primary outcome					
Death and major disability (mRS, 3–6)					
No. of cases (%)	41 (14.5%)	35 (12.3%)	49 (17.3%)	62 (21.8%)	
Multivariable adjusted model*	1.00	0.82 (0.51-1.34)	1.23 (0.78-1.94)	1.64 (1.06-2.54)	0.016
Secondary outcomes					
Death					
No. of cases (%)	6 (2.1%)	7 (2.4%)	5 (1.8%)	10 (3.5 %)	
Multivariable adjusted model	1.00	1.22 (0.49-2.99)	1.58 (0.67-3.71)	1.97 (0.49-2.99)	0.028
Death or disability (mRS, 2-6)					
No. of cases (%)	88 (24.2%)	76 (20.9%)	94 (25.8%)	106 (29.1%)	
Multivariable adjusted model	1.00	0.73 (0.51-1.04)	1.19 (0.84-1.68)	3.34 (1.56-4.61)	0.033
Modified Rankin Scale**					
0 (no symptoms)	118 (41.4%)	125 (44.1%)	109 (38.4%)	112 (39.2%)	
1 (no significant disability despite symptoms)	98 (34.4%)	100 (35.1%)	102 (35.8%)	90 (31.7%)	
2 (slight disability)	28 (9.7%)	24 (8.6%)	24 (8.5%)	21 (7.3%)	
3 (moderate disability)	17 (5.8%)	13 (4.6%)	24 (8.4%)	29 (10.2%)	
4 (moderately severe disability)	14 (4.9%)	9 (2.8%)	13 (4.6%)	14 (4.9%)	
5 (severe disability)	5 (1.7%)	7 (2.5%)	7 (2.5%)	9 (3.2%)	
6 (dead)	6 (2.1%)	7 (2.4%)	5 (1.8%)	10 (3.5%)	
Multivariable adjusted model	1.00	1.43 (1.19-1.67)	1.60 (1.36-1.84)	1.07 (1.03-1.09)	0.125

*Adjustment for age, gender, MONO, HDL-C; NIHSS score at admission, history of stroke, history of atrial fibrillation, history of coronary heart disease, history of hypertension, history of diabetes mellitus, neutrophil, triglyceride, smoking, statin use history;
*Odds of a 1-U higher modified Rankin Scale score MHR, monocyte to high-density lipoprotein ratio.