Original Article

Investigation of Routine Blood Parameters for Predicting Embolic Risk in Patients with Nonvalvular Atrial Fibrillation

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Abstract

Introduction: Nonvalvular atrial fibrillation (NV-AF) is an important risk factor for cardiac thromboembolic disorders. However, there is not an exact biomarker for evaluating risk in these patients. In this study, we aimed to investigate the routine blood test and inflammatory markers in NV-AF patients with or without embolic complications. **Materials and Methods:** Routine complete blood count (CBC) and a clinical biochemistry analysis of 214 NV-AF patients (151 with embolic complication and 63 without embolic complication) were recorded retrospectively. Obtained results compared between NV-AF with embolic group and NV-AF without an embolic group. **Results:** The most of the CBC and biochemical markers were found as similar ($P > 0.05$) between groups except white blood cell count, lymphocyte ratio (Lym%), neutrophil ratio (Neu%), eosinophil ratio (Eus%), neutrophil count (Neu), mean corpuscular hemoglobin concentration, blood urea nitrogen, cholesterol, low-density lipid, sodium (Na), total bilirubin, direct bilirubin, plasma iron levels, and neutrophil to lymphocyte ratio (NLR) ($P < 0.05$). **Conclusion:** The inflammatory markers, especially NLR, seem to be useful for embolic risk stratification in NVAF patients.

Keywords: Embolic risk, neutrophil to lymphocyte ratio, nonvalvular atrial fibrillation, routine blood markers

Introduction

Nonvalvular atrial fibrillation (NV-AF) leads to disturbance of hearth functions that are occurred due to irregular atrial rhythm and noncoordinate consecutive contraction with cardiac ventricles. Because of irregular blood flow between atriums to ventricles, blood pooling is developed in atriums which can be forming blood clot.[1,2] Moreover, it is known that NV-AF increases stroke risk 5-fold when compared with overall age groups. Therefore, anticoagulation is essential for preventing AF-related thromboembolic events.[2,3] Especially, previously described Virchow's triads all steps that predisposing to hypercoagulable state is occur in NV-AF. Flow abnormalities that related with the loss of atrial systole and ineffective ventricle filling resulted with atrial stasis. AF predisposing factors such as hypertension lead to second step, vessel wall abnormalities with corrupted endothelial functions. As the last stage of the Virchow triad, abnormal procoagulant activity also occurs through blood components.[2-6] Furthermore, incremental fibrinolytic activity and circulating procoagulant microparticles were detected in NV-AF patients.[4] However, literature includes insufficient data that presents to the differences of blood parameters between NV-AF with acute arterial embolus and NV-AF without any embolic complication.

In the current study, we aimed to compare the routine blood parameters between NV-AF with acute arterial embolus and NV-AF without any embolic complication.

Materials and Methods

After the determination of preliminary study protocol, ethical approval was obtained from the local ethical committee of university. The patients who admitted to our clinic with NV-AF scanned from the hospital records between June 2017 and March 2019. The demographic data and routine blood parameters of patients were recorded retrospectively.

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The patients were divided into two groups as following criteria:

First group (n = 63) diagnosed as NV-AF (only newly diagnosed patients with NV-AF without any antiaggregant or anticoagulant treatment were included to this group).

Second group (n = 151) admitted with peripheral embolus due to the NV-AF who has not treated with antiaggregant or anticoagulant treatment previously.

Exclusion criteria

Previously, antiaggregant or anticoagulant treatment for NV-AF or any other disease; any other diagnosed disease that predisposing for thrombosis; patients with intravascular drug usage such as chemotherapy utilization; patients with hematological disorders excluded from the study.

The demographic data and routine blood parameter levels were recorded retrospectively both two groups. After data collection, complete blood parameters (white blood cell [WBC] count, red blood cell [RBC] count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin [MCH], MCH concentration [MCHC], platelet count, RBC distribution width, plateletcrit, mean platelet volume, platelet distribution width, lymphocyte ratio [Lym%], lymphocyte count [Lym], neutrophil ratio [Neu%], neutrophil count [Neu], monocyte ratio [Lym%], monocyte count [Lym], eosinophil ratio [Eus%], eusinophly count [Eus], basophile ratio [Ba%], and basophile count [Ba]) and routine biochemical parameters (fasting blood glucose, blood urea nitrogen, creatinine, cholesterol [Chol], triglyceride, low density lipid [LDL], high-density lipid, alanine aminotransferase, aspartate aminotransferase [AST], total bilirubin, direct bilirubin, alkaline phosphatase, total protein [PRT], albumin, ferrum, gamma-glutamyl transpeptidase, amylase, sodium [Na], potassium [K], Calcium [Ca], C-reactive protein [CRP], unsaturated iron-binding capacity, plasma iron levels, and neutrophil to lymphocyte ratio [NLR]) were investigated from the blood samples.

Statistical analyses

Data were assessed with the SPSS software statistical program (Version 15.0, SPSS Inc., Chicago, Illinois, USA). Whole continuous variables were expressed as mean ± standard deviation (SD), and the categorical variables were expressed with percentages. The normally distributed independent parameters were compared with Mann–Whitney U-test and nonnormal variables were compared with Student's t-test. Chi-square tests were used for comparing nonparametric values. $P < 0.05$ was approved as statistically significant.

Results

The embolic events were most commonly detected at female gender ($P = 0.000$). Both diabetes mellitus and hyperlipidemia were lower in patients with embolic events. The groups were similar in according to mean ages (70.67 ± 9.91 vs. 67.23 ± 16.33 years). The comparison of mean demographic data presented in Table 1.

Table 1: The comparison of demographic data between groups

	NV-AF without embolic events (n=63), n (%)	NV-AF with embolic events (n=151), n (%)	P*
Male	23 (36.5)	105 (69.5)	0.000
Age (mean±SD)	70.67±9.91	67.23±16.33	0.121
DM	38 (60.3)	32 (21.2)	0.005
HL	12 (19.0)	7 (4.6)	0.001

*P<0.05 means statistically significant. NV-AF: Nonvalvular atrial fibrillation, DM: Diabetes mellitus, HL: Hyperlipidemia, SD: Standard deviation

The majority of complete blood parameters and biochemical markers were found as similar between groups ($P > 0.05$). However, WBC count, lymphocyte ratio (Lym%), neutrophil ratio (Neu%), eosinophil ratio (Eus%), neutrophil count (Neu), MCHC, blood urea nitrogen, Chol, LDL, sodium (Na), total bilirubin, direct bilirubin, plasma iron levels, and NLR statistically different between groups ($P < 0.05$). The mean ± SD values of blood markers and statistical comparison between groups were presented in Table 2. The main significant values were obtained at inflammatory markers and markedly incremental NLR levels observed in patients with embolic events due to the NVAF.

Discussion

Although many predictors evaluated for AF risk in patient groups formerly, in according to our knowledge, current literature has a lack of subgroup analyze about embolic and nonembolic events. In our study, we divided to NVAF patients in according to presenting embolic symptoms and compared their demographic and simple blood markers findings. Our results indicated that the simple inflammatory markers are higher in patients with embolic events. Especially NLR, currently published risk marker for cardiovascular many diseases, was found as a significant marker for the differentiation of NVAF patients with or without peripheral embolus.

Previous reports indicate some routine biomarkers for following the cardioembolic events in different situations. For instance, increased blood urea levels mean dehydration and disrupted renal functions that related with increased thrombotic tendency. Kim *et al*. suggested that elevated blood urea nitrogen levels are related with high-risk venous embolism in acute ischemic stroke patients.[7] In another study, Gary *et al*. claimed that critical ischemia is related with higher blood urea nitrogen levels.[8] Furthermore, as comprehensively described in previous reports, higher hyperlipidemic conditions were related with increased risk of atherothrombotic events and because of this all cardiovascular risk groups routinely checking up for blood lipid profiles. Both ischemic (thromboembolic or atherosclerotic) and mechanical or functional (AF, etc.) cardiometabolic disorders were associated with higher plasma lipid levels.[9,10] By the way, the main routine biomarkers that associated with higher

Table 2: The comparison of blood markers between groups

Blood markers	Mean±SD		*P*
	NVAF without emboly (*n*=63)	NVAF with emboly (*n*=151)	
WBC	7.69±3.46	11.24±8.71	0.002
RBC	4.50±0.59	4.41±0.98	0.532
HGB	12.92±1.65	12.97±2.74	0.885
HCT	39.53±4.67	38.65±8.45	0.438
MCV	87.18±9.79	88.22±7.09	0.386
MCH	28.83±2.56	29.61±2.77	0.057
MCHC	32.68±0.97	33.54±1.60	0.000
PLT	229.00±74.91	232.40±105.31	0.816
MPV	9.36±0.98	8.85±7.77	0.604
RDW	15.36±1.82	15.54±2.66	0.611
PCT	0.21±0.067	0.25±0.897	0.726
PDW	15.55±2.963	14.86±2.41	0.080
LY1	25.30±9.47	17.47±8.97	0.000
NE1	62.21±14.65	71.00±13.75	0.000
MO1	7.33±2.97	7.41±4.33	0.885
EO1	2.42±1.52	1.23±1.33	0.000
BA1	2.08±9.078	1.40±4.50	0.463
LY	2.09±2.54	2.00±2.92	0.832
MO	0.80±1.21	0.96±1.48	0.455
NNE	5.09±3.07	7.79±4.77	0.000.
BA	0.08±0.06	0.20±1.09	0.365
Glucose	127.90±60.70	130.27±72.68	0.827
Blood urea nitrogen	40.62±16.14	50.84±32.53	0.022
Creatinine	0.93±0.30	1.47±2.29	0.068
Choll	186.11±54.37	157.42±21.89	0.002
TG	148.48±129.95	108.20±55.83	0.067
LDL	112.51±41.00	89.92±25.58	0.004
HDL	50.05±13.46	49.62±17.46	0.907
AST	22.45±14.03	73.10±287.05	0.174
ALT	24.08±23.64	38.67±97.83	0.257
Total bil	0.98±1.17	0.43±0.47	0.006
Direct bil	0.44±0.73	0.17±0.07	0.014
ALP	76.33±31.57	89.94±38.00	0.406
PRT	6.26±1.10	6.61±1.24	0.642
Albumin	3.97±0.58	3.65±0.48	0.053
Ferrum	76.83±29.39	60.16±24.10	0.026
Iron binding capacity	248.55±61.31	218.86±60.89	0.091
GGTP	34.43±31.52	33.79±23.29	0.932
Amylase	62.78±33.61	55.87±16.55	0.274
Na+	139.43±3.37	137.72±4.56	0.012
K+	71.26±518.02	4.49±0.083	0.173
Ca+	10.56±11.10	8.79±0.82	0.095
CRP	2.11±3.54	0.10±0.07	0.267
NLR	3.10±2.10	6.21±5.99	0.000

NV-AF: Nonvalvular atrial fibrillation, SD: Standard deviation, WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelet, MPV: Mean platelet volume, RDW: RBC distribution width, PCT: Plateletcrit, PDW: Platelet distribution width, BA: Basophile count, TG: Triglyceride, LDL: Low-density lipid, HDL: High-density lipid, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, PRT: Total protein, GGTP: Gamma-glutamyl transpeptidase, Na^+: Sodium, K^+: Potassium, Ca^+: Calcium, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio

thrombotic risk are inflammatory biomarkers such as WBC, lymphocyte ratio (Lym%), neutrophil ratio (Neu%), eosinophil ratio (Eus%), neutrophil count (Neu), MCHC, and/or NLR. WBC was found as an independent predictor for major thrombosis in platelet disorders.[11] Vilalta *et al*. found that higher leukocyte counts are interacted with increased risk of venous thromboembolism.[12] Coller presented a report that declares strong association with incremental risk for ischemic vascular disease and increased leukocyte count. Moreover, he overviewed many reports of the relation of leukocytosis with acute thrombotic event, involving elevated WBC levels related with higher vascular complications in myocardial, cerebrovascular, and blood disorders.[13] Recently, the ratio of inflammatory biomarkers is more frequently investigated for getting more sensitivity to detecting disease conditions. The NLR is one of the popular examples for these ratio investigations. The predictive role of this marker was shown in many cardiovascular events. Aktimur *et al*. investigated NLR in acute mesenteric ischemia patients and they showed elevated NLR values in these patients.[14] Kaya *et al*. studied this marker in patients with coronary artery disease, and they reported that there is a relation between atherosclerosis severity and NLR levels.[15] In another study, the prognostic role of NLR was investigated in acute decompensated heart failure and in according results of this study; NLR was shown as a predictive marker for prognosis of acute decompensated heart failure.[16] In a systematic review and meta-analyses, it was suggested that NLR can be beneficial for cardiovascular disease management.[17]

Furthermore, inflammatory biomarkers were investigated in AF and CRP, interleukin-6, and NLR were found as predictors for outcomes in patients with AF.[18] Ertaş *et al*. investigated NLR in patients with nonvalvular AF, and they claimed that increased NLR levels are strongly associated with thromboembolic stroke in these patients.[19]

Conclusion

It seems to be routine inflammatory biomarkers can be useful for determining the embolic risk in patients with NV-AF. In addition, the popular biomarker NLR can be more significant predictor for embolic risk such these patients. These results should be confirmed bigger cohort populations.

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Conflicts of interest

There are no conflicts of interest.

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