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The Predictive Value of Inflammatory Indices and CHA2DS2-VASc Score for NOAF in Covid-19 Patients and the Effect of NOAF on in-Hospital Outcomes

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Abstract

Introduction: It has been reported that atrial fibrillation (AF) is frequently observed in patients with severe COVID-19. Various mechanisms may be involved in the pathogenesis of AF in these patients. COVID-19 infection increases susceptibility to atrial AF acutely during the infectious stages and sometimes in the post-convalescence period.

Materials and Methods: The current retrospective multicenter review consists of consecutive patients hospitalized for COVID-19-related infection in 3 different medical centers. Patients hospitalized for COVID-19 infection between September 2021 and February 2022 were studied.

Results: The incidence of New-onset AF (NOAF) was 7.8%. N/L ratios on days 1, 3, and 7 were significantly higher in the NOAF group. In-hospital all-cause mortality, embolic events, and major bleeding were significantly higher in the NOAF group. Hospital stay was significantly longer in the NOAF group.

Conclusions: CHA2DS2VASc score, D-Dimer, and N/L ratio are independent predictors of NOAF in COVID-19 patients. NOAF is associated with worse clinical features during hospitalization in terms of more bleeding events, death, and embolic events. NOAF is also associated with a longer hospital stay.

Key words: New-onset atrial fibrillation; COVID-19; inflammatory indices

Introduction

COVID-19 was initially recorded in China and declared as a pandemic by the World Health Organization on March 12, 2020. (1) Among the WHO's current recommendations, people with mild respiratory symptoms should be encouraged to isolate themselves, and social distancing is emphasized and these recommendations apply even to countries with no reported cases. Cohort studies from various countries suggest that risk factors and prognoses for COVID-19 patients might not be representative of other geographic regions, as they could be influenced by specific public health conditions or race-related factors. (2) Cardiac arrhythmias, including life-threatening ventricular arrhythmias, could arise from the direct impact of COVID-19 or from the systemic effects of the disease and the potential side effects of drugs used for its treatment (3). Data from hospitalized patients indicate that COVID-19 infection increases susceptibility to atrial fibrillation (AF) acutely during the infectious stages and sometimes in the post-convalescence period. (4) New-onset AF exacerbates the prognosis of patients dealing with serious illnesses. (5) This arrhythmia is common in contexts involving acute conditions such as myocardial infarction, cardiac surgeries, or infections, where it is associated with a heightened risk of complications and mortality. (6) While atrial fibrillation is a frequent cause of stroke, the risk of developing thromboembolic events appears to be higher in COVID-19. (7) Previous studies have indicated that COVID-19 is a risk factor for both arterial and venous thrombotic events. (8) The management of AF in clinical practice, including the use of antithrombotic therapies, does not significantly deviate from routine management of COVID-19. (9) For these patients,

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a delicate balance must be maintained between the risks of embolism and bleeding. Various parameters within the CHA2DS2-VASc score, such as congestive heart failure (CHF), hypertension (HT), advanced age, female gender, and diabetes mellitus (DM), are closely associated with the development of AF. In this study, our objectives encompass determining the incidence of newly diagnosed AF among COVID-19 patients in our region, assessing the impact of newly diagnosed AF on hospital stay duration, stroke occurrence, bleeding episodes, and mortality, as well as evaluating the predictive value of inflammatory parameters and the CHA2DS2-VASc score for newly diagnosed AF.

Materials and Methods

The present retrospective multicenter study encompassed 436 consecutive patients who were admitted to three different medical centers in Elazığ, and Ağrı, Türkiye due to COVID-19-related infections. Access to medical records was granted by hospital administrations for the purpose of retrospective analysis, which aimed to inquire about patients' past medical histories and initiated treatments. The methodology leans towards retrospective analysis, leveraging existing data and patient records to investigate the incidence and characteristics of AF development in COVID-19 patients, along with associated outcomes such as embolic events and bleeding episodes. The patients' files were requested from the archive and their anamnesis notes, treatment protocols, and admission and follow-up ECGs were examined. Daily follow-up notes were reviewed through the system and compared with the records in the file. Laboratory and radiological images and consultation notes were searched through the hospital system. The study focused on patients hospitalized for COVID-19 infection between September 2021 and February 2022. Inclusion criteria were set as age greater than 18 years and a confirmed diagnosis of COVID-19 through polymerase chain reaction. For comparison purposes, two distinct groups were formed: the new-onset AF (incipient AF) group, comprising consecutive patients exhibiting "de novo" AF upon hospitalization; and a control group of patients without a history of AF who were previously hospitalized for COVID-19 during the same period. These groups were defined as incipient AF and control groups to investigate the role of new-onset AF. Exclusion criteria involved patients with any cancer diagnosis, moderate-to-severe mitral stenosis (identified through history and physical examination), individuals with mechanical valve prostheses, and those with a prior AF diagnosis. Clinical and treatment data were collected. Electrocardiogram (ECG) monitoring was conducted for all patients upon initial hospitalization and continued daily during their stay. Additionally, ECGs were recorded in response to palpitations, dizziness, and chest pain. Both groups received COVID-19 treatment according to the hospital's ongoing protocol and the Ministry of Health's recommendations, including hydroxychloroquine and azithromycin, antiviral medications if necessary, dexamethasone, and oxygen support, without differentiation between the groups unless contraindicated.

As standard treatment for all patients;
- Oxygen support
- Dexamethasone 6 mg once a day
- Azithromycin 500 mg once a day
-enoxaparin 4000 sc once a day
- Hydroxychloroquine 400 mg twice a day on the first day, 200 mg twice a day for the next 4 days

The first ECG was administered within the initial 10 minutes of admission, and continuous ECG monitoring was employed throughout hospitalization to detect arrhythmias. AF defined as the absence of discernible P waves for a minimum of 30 seconds, an irregular R-R interval, and an indistinct isoelectric line. Development of AF during hospitalization in patients without a prior history of AF who presented with sinus rhythm upon admission was defined as New-onset AF (NOAF). Clinical follow-up was conducted throughout hospitalization, with particular attention to anticoagulation therapy. A systemic embolic event was defined as a combination of ischemic stroke, systemic embolism, and pulmonary embolism that occurred without any invasive intervention. Ischemic stroke was investigated in cases of sudden-onset focal neurological deficits without identifiable non-vascular causes. Documentation, either clinical or radiological, was required to confirm embolic events.The diagnosis of major bleeding was made according to the criteria determined by the International Thrombosis and Haemostasis Society(ISTH) (10). Major bleeding encompassed fatal bleeding, bleeding into critical organs, or bleeding causing a hemoglobin drop of ≥ 2 g/dL.

Table 2: Events during hospitalization in patients with COVID-19

Variable	New Onset AF (n:34)	Control Group (n:402)	p value
Age, years	66.0 ± 12.5	59.1 ± 16.1	0.004
Gender, Female/Male	16/18	210/192	0.561
Diabetes Mellitus	6 (17.6)	113 (28.2)	0.182
Previous CAD, n (%)	6 (17.6)	52 (12.9)	0.434
Smoking, n (%)	5 (14.7)	38 (9.5)	0.323
Hypertension, n (%)	13 (38.5)	173 (43.0)	0.580
Congestive Heart Failure	3 (8.8)	20 (5.0)	0.331
Previous Stroke/Systemic Embolism	2 (5.9)	21 (5.2)	0.861
Previous Bleeding	4 (11.8)	13 (3.2)	0.014
Renal Dysfunction	4 (11.8)	14 (3.5)	0.020
Abnormal Liver Function	3 (8.8)	12 (3.0)	0.070
CHA_2DS_2VASc	1.9 ± 0.9	1.3 ± 0.6	0.001
HAS-BLED	1.1 ± 0.3	1.1 ± 0.4	0.570
Anticoagulation Therapy	5 (14.7)	11 (2.7)	0.000
Blood Pressure on admission (mmHg)			
Systolic	116.1 ± 15.6	119.1 ± 14.7	0.287
Diastolic	73.9 ± 12.5	73.3 ± 10.8	0.781
Heart rate, beats/min	85.7 ± 14.5	80.9 ± 15.4	0.075
Blood parameters			
Serum glucose, mg/Dl	116.6 ± 46.0	134.3 ± 62.5	0.047
Troponin	19.9 ± 18.1	10.2 ± 10.7	0.011
D-Dimer	2.4 ± 2.5	0.8 ± 1.3	0.001
CRP	52.6 ± 38.5	32.3 ± 31.5	0.005
Hemoglobine (g/dl)	13.9 ± 1.4	13.6 ± 1.9	0.328
White blood cell count, x 10^9/L	11.0 ± 2.7	7.0 ± 3.3	0.399
Platelet count, x 10^9/L	218.4 ± 130.6	197.2 ± 84.8	0.358
N/L at day 1	4.7 ± 1.2	3.1 ± 0.6	0.000
N/L at day 3	8.3 ± 1.8	5.7 ± 1.0	0.000
N/L at day 7	13.8 ± 1.1	9.9 ± 1.3	0.000
eGFR, mL/min/1.73 m2	77.3 ± 26.4	85.6 ± 18.1	0.087

Dataexpressed mean ± SD and percentage (%) for categorical variables.

Table 1: Baseline characteristics of patients in groups

Variable	*New Onset AF (n:34)*	*Control Group (n:402)*	*p value*
Embolic Events, n (%)	5 (14.7)	15 (3.7)	0.003
Bleeding Events, n (%)	4 (11.8)	3 (0.7)	0.000
All-cause mortality, n (%)	7 (20.6)	14 (3.5)	0.000
Hospital length of stay, days	12.8 ± 6.0	8.4 ± 3.6	0.000

Dataexpressed mean ± SD and percentage (%) for categorical variables. **CAD:** Coronary artery disease; **eGFR:** estimated Glomerular Filtration Rate; **CRP:** C-reactive protein; **N/L:** Neutrophil-Lymphocyte ratio; n: number

Ethical consent: The study was started with the permission of the ethics committee of the Fırat University Medical Faculty Non-Interventional Research Ethics Committee (17.04.2023-15649). All procedures were conducted in accordance with Declaration of Helsininki.

Statistical analysis: Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. We report continuous data as mean and standard deviation. We compared continuous variables using Student t-test between groups. Categorical variables were summarized as percentages and compared with the Chi-square test. The effects of different variables on left ventricular dysfunction were calculated in univariate analysis for each. The variables for which the unadjusted P value was <0.10 in logistic regression analysis were identified as potential risk

markers and included in the full model. We reduced the model by using backward elimination multivariate logistic regression analyses and we eliminated potential risk markers by usinglikelihood ratio tests. A two-sided $P < 0.05$ was considered as significant and confidence interval (CI) was 95%. All statistical analyses were performed using SPSS version 21 (SPSS, Inc., Chicago, Illinois).

Results

Following the application of exclusion criteria, 32 out of the initially considered 436 patients were identified to have NOAF. The calculated incidence of NOAF was 7.8%. The patients underwent thorough assessment based on their fundamental characteristics, clinical conditions, and laboratory measurements. The essential characteristics of the patient cohort, as assessed per the predefined groups, are outlined in Table 1. Patients within the NOAF group was notably older. Renal dysfunction was more pronounced among individuals in the NOAF group. While no significant distinction was observed between the groups regarding the history of chronic diseases, a higher incidence of bleeding history was recorded within the NOAF group.

Table 3: Effects of various variables on New onset AF in multivariate logistic regression analyses

Variables	OR	95% CI	*P value*
Age	0.985	0.933 –1.040	0.586
CHA2DS2VASc	2.665	1.115 – 6.371	0.028
Systolic BP	0.966	0.919 – 1016	0.179
Troponin	1.007	0.998 – 1017	0.109
D-Dimer	1.714	1.272 – 2309	<0.001
CRP	1018	0.999 – 1038	0.059
N/L 1	8.383	2.637– 26.652	<0.001
N/L 3	4.035	2.184 – 7.492	<0.001
N/L 7	12.455	3.457 – 34.298	<0.001
Bleeding event	0.578	0.043 – 7.852	0.681
Renal Dysfunction	1.018	0.040 – 25.630	0.992

OR: Odds ratio, **CI:** Confidence interval, **BP:** Blood Pressure; **N/L:** Neutrophil-Lymphocyte ratio; **CRP:** C-reactive protein

Despite a higher CHA2DS2-VASc score in the NOAF group, no significant variance was detected between the groups concerning the HAS-BLED score. Rates of anticoagulant treatment application were greater in the NOAF group. In terms of laboratory analysis, lower glucose levels were found in the NOAF group. Conversely, D-dimer, C-reactive protein (CRP), and troponin values were significantly elevated within the NOAF group. Notably, the neutrophil-to-lymphocyte (N/L) ratios on days 1, 3, and 7 were markedly higher in the NOAF group. Within-hospital all-cause mortality, occurrence of embolic events, and major bleeding incidents were notably higher in the NOAF group. Correspondingly, the duration of hospital stays was significantly extended in the NOAF group (refer to Table 2). In the context of multivariate analysis, the CHA2DS2-VASc score, D-Dimer levels, and N/L ratio were found as independent risk factors for NOAF (see Table 3). Regarding in-hospital all-cause mortality, solely the N/L ratio on day 7 emerged as an independent risk factor according to the multivariate analysis (see Table 4).

Discussion

The present study reveals the following key findings:

1. CHA2DS2-VASc score, D-Dimer, and N/L ratio are independent predictors of NOAF in COVID-19 patients.
2. New-onset AF is associated with worse clinical outcomes during hospitalization including increased in events, mortality, and embolic events.
3. New-onset AF is linked to a prolonged hospital stay.
4. The incidence of NOAF among COVID-19 patients in our region is 7.8%.

Emerging epidemiological evidence from hospitalized patients indicates that COVID-19 infection acutely elevates the susceptibility to atrial fibrillation (AF) during the infectious stages

Table 4: Effects of various variables on All-cause mortality in multivariate logistic regression analyses

Variables	OR	95% CI	*P value*
Age	1.007	0.970 – 1.046	0.706
CHA2DS2VASc	0.913	0.430 – 1.938	0.813
Systolic BP	1.035	0.999 – 1.072	0.054
Troponin	0.989	0.946 - 1034	0.618
D-Dimer	1.046	0.778 – 1.406	0.768
CRP	0.981	0.963 – 1.000	0.045
N/L at day 1	0.717	0.381 – 1.351	0.304
N/L at day 3	1.031	0.714 – 1.492	0.868
N/L at day 7	3.069	2.019 – 4.665	<0.001
Renal dysfunction	0.609	0.036 – 10.374	0.732
Bleeding	1.269	0.085 – 18.844	0.863

OR: Odds ratio, **CI:** Confidence interval **BP:** Blood Pressure; **N/L:** Neutrophil-Lymphocyte ratio; **CRP:** C-reactive protein

and potentially even post-convalescence. AF has been observed in 17% of COVID-19 patients admitted to intensive care units in the US. (11) Similarly, studies by Mountantonakis SE et al. (12) indicated that AF occurred in 17.6% of patients hospitalized with COVID-19, with 12.5% of these patients having no prior history of AF. Reports by Bhatia et al. (3) demonstrated 25 episodes of atrial fibrillation during 700 episodes of SARS-CoV-2 infection. García-Granja PE et al. (13) noted that 10% of SARS-CoV-2 patients developed atrial fibrillation during hospitalization. In a study conducted in Turkey, the incidence of NOAF was 5%, although the mean age and CHA2DS2-VASc score were higher. (14) In our study, the incidence of NOAF in COVID-19 patients was 7.8%, likely higher than the aforementioned study due to the consideration of quarantine period data in our country. A study in Denmark indicated a 47% decrease in NOAF frequency during the quarantine period. (15) Meanwhile, Rahimi et al. (16) reported an NOAF incidence of 8.3%, similar to our study. Our findings are consistent with studies of AF in other critically ill patients, where the incidence of NOAF has been reported to range from 6% to 12%. (17) The presence of AF, particularly new-onset AF, is independently associated with higher in-hospital mortality. (12) Reports from the SEMI-COVID-19 records highlighted that 11% of patients had a history of AF, with a 41% mortality rate in this patient group. (18) Our study similarly found higher all-cause mortality in the NOAF group. This may be attributed to elevated CRP, troponin, and D-dimer levels, which are indicators of disease severity. Studies have indicated that high D-dimer levels, in conjunction with ECG anomalies like AF, could be associated with elevated mortality in COVID-19 patients. (19) In our study, the NOAF group exhibited higher troponin levels, consistent with other COVID-19 studies that linked elevated troponin levels to poor outcomes. (20) New-onset AF has been shown to significantly prolong hospital stays in COVID-19 patients. (16) Our study aligns with this observation, revealing that the presence of NOAF leads to extended hospitalization. The hypercoagulative status during SARS-CoV-2 infection likely influences AF-related thromboembolic events. (21) Recent reports suggest that NOAF independently predicts embolic events in COVID-19 patients. (22) The American Heart Association and the European Society of Cardiology recommend anticoagulant use, including heparin, in hospitalized COVID-19 patients with concurrent AF. (23) Our study, while showing a higher rate of anticoagulant use in the NOAF group, found a higher prevalence of embolic events in line with previous studies. The development of embolic events in NOAF may be linked to thrombotic tendencies in severe COVID-19 patients. (7) In patients receiving full-dose anticoagulation, a higher incidence of bleeding has been reported alongside a reduced incidence of embolism. (24) Al-Samkari et al. (25) analyzed bleeding and thrombotic complication rates in a multicenter cohort of critically ill and non-critically ill COVID-19 patients, with a major bleeding rate of 2.3%. Our study identified higher bleeding rates in the NOAF group, aligning with previous studies. However, the potential influence

of higher anticoagulant usage in the NOAF group should be considered, necessitating further comprehensive research to directly evaluate bleeding rates in COVID-19 patients with NOAF. Inflammation is an important factor in the development of NOAF, independent of traditional risk factors. (26) Inflammatory markers like CRP, interleukin-6, and tumor necrosis factor-alpha have been linked to development of AF in patients with ischemic heart disesase or renal disease. (27) Our study found higher CRP and N/L ratios in the NOAF group, consistent with prior research. The N/L ratio has previously been shown to predict NOAF in diverse patient populations. (28) Kelesoglu et al. (14) reported higher N/L ratios in the NOAF group of COVID-19 patients, consistent with our study, where the N/L ratio, along with D-dimer levels and CHA2DS2-VASc score, emerged as independent risk factors for NOAF in the COVID-19 patient population. Furthermore, we found that the N/L ratio at day 7 is a predictor of all-cause mortality in COVID-19 patients. Studies have indicated that the incidence of NOAF in AMI increases with higher $CHADS_2$ scores. (29) Similarly, in elderly individuals, the CHA2DS2-VASc score, together with hs-CRP, has been shown to predict NOAF development in ACS patients. (30) Our study concurs with these findings, as the CHA2DS2-VASc score, along with D-dimer levels and the N/L ratio, emerged as predictors of NOAF in COVID-19 patients.

Study limitations: Several limitations need to be acknowledged in the context of this study. The potential influence of unmeasured third variables, including other unknown inflammatory parameters, cannot be entirely excluded. The primary limitations of this study stem from its relatively modest experience and the consequently small number of patients. Although our findings hold relevance, they serve to encourage further investigations with larger sample sizes.

Conclusions

Our study is unique in demonstrating that N/L ratios at days 1, 3, and 7 serve as independent risk factors for NOAF in COVID-19 patients. Additionally, the N/L ratio at day 7 emerges as a predictor of all-cause mortality in COVID-19 patients.

Ethics approval: This study was approved by Fırat University Ethics Committee(17.04.2023-15649) in accordance with the International Code of Ethics and the Declaration of Helsinki.(2013)

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References

1. WHO. WHO announces COVID-19 outbreak a pandemic. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Published 2020.
2. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. linical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054-1062.
3. Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, al. COVID-19 and cardiac arrhythmias. Heart Rhythm 2020;17(9):1439-1444.
4. Seecheran R, Narayansingh R, Giddings S, Rampaul M, Furlonge K, Abdool K, et al. Atrial Arrhythmias in a Patient Presenting With Coronavirus Disease-2019 (COVID-19) Infection. J Investig Med High Impact Case Rep 2020;8:2324709620925571.
5. Moss TJ, Calland JF, Enfield KB, Gomez-Manjarres DC, Ruminski C, DiMarco JP, et al. New-Onset Atrial Fibrillation in the Critically Ill. Crit Care Med 2017;45(5):790-797.
6. Steinberg BA, Zhao Y, He X, Hernandez AF, Fullerton DA, Thomas KL, et al. Management of postoperative atrial fibrillation and subsequent outcomes in contemporary patients undergoing cardiac surgery: insights from the Society of Thoracic Surgeons CAPS-Care Atrial Fibrillation Registry. Clin Cardiol 2014;37(1):7-13.
7. Llitjos JF, Leclerc M, Chochois C, Monsallier JM, Ramakers M, Auvray M, et al. High incidence of venous

thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost 2020;18(7):1743-1746.
8. Zhang L, Feng X, Zhang D, Jiang C, Mei H, Wang J, et al. Deep Vein Thrombosis in Hospitalized Patients With COVID-19 in Wuhan, China: Prevalence, Risk Factors, and Outcome. Circulation 2020;142(2):114-128.
9. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37(38):2893-2962.
10. Schulman S, Kearon C; Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost 2005;3(4):692-694.
11. Colon CM, Barrios JG, Chiles JW, McElwee SK, Russell DW, Maddox WR, et al. Atrial Arrhythmias in COVID-19 Patients. JACC Clin Electrophysiol 2020;6(9):1189-1190.
12. Mountantonakis SE, Saleh M, Fishbein J, Gandomi A, Lesser M, Chelico J, et al. Atrial fibrillation is an independent predictor for in-hospital mortality in patients admitted with SARS-CoV-2 infection. Heart Rhythm 2021;18(4):501-507.
13. García-Granja PE, Veras C, Aparisi Á, Amat-Santos IJ, Catalá P, Marcos M, et al. Atrial fibrillation in patients with SARS-CoV-2 infection. Med Clin 2021;157(2):58-63.
14. Kelesoglu S, Yilmaz Y, Ozkan E, Calapkorur B, Gok M, Dursun ZB, et al. New onset atrial fibrillation and risk factors in COVID-19. J Electrocardiol 2021;65:76-81.
15. Holt A, Gislason GH, Schou M, Zareini B, Biering-Sørensen T, Phelps M, et al. New-onset atrial fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of 5.6 million people. Eur Heart J 2020;41(32):3072-3079.
16. Rahimi FS, Afaghi S, Tarki FE, Omran HS, Nasirpour MH. Risk factors, thromboembolic events, and clinical course of New-Onset Atrial Fibrillation among COVID-19 hospitalized patients: A multicenter cross-sectional analysis in Iran. Health Sci Rep 2022;5(6):e813.
17. Walkey AJ, Greiner MA, Heckbert SR, Jensen PN, Piccini JP, Sinner MF, et al. Atrial fibrillation among Medicare beneficiaries hospitalized with sepsis: incidence and risk factors. Am Heart J 2013;165(6):949-955.e3.
18. Azaña Gómez J, Pérez-Belmonte LM, Rubio-Rivas M, Bascuñana J, Quirós-López R, Taboada Martínez ML, et al. Mortality risk factors in patients with SARS-CoV-2 infection and atrial fibrillation: Data from the SEMI-COVID-19 registry. Med Clin 2022;159(10):457-464.
19. Chen J, Wang Y, Wang J, Chen L, Luo Q, Wang B, et al. Coronavirus disease 2019 death prediction by electrocardiographic abnormalities and elevated D-dimer levels. Front Cardiovasc Med 2022;9:948347.
20. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis 2020;63(3):390-391.
21. Bilaloglu S, Aphinyanaphongs Y, Jones S, Iturrate E, Hochman J, Berger JS. Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System. JAMA 2020;324(8):799-801.
22. Pardo Sanz A, Salido Tahoces L, Ortega Pérez R, González Ferrer E, Sánchez Recalde Á, Zamorano Gómez JL. New-onset atrial fibrillation during COVID-19 infection predicts poor prognosis. Cardiol J 2021;28(1):34-40.
23. The Task Force for the management of COVID-19 of the European Society of Cardiology. European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis. European Heart Journal 2022;43(11):1033–1058.
24. Uribarri A, Núñez-Gil IJ, Aparisi Á, Arroyo-Espliguero R, Maroun Eid C, Romero R, et al. Atrial fibrillation in patients with COVID-19. Usefulness of the CHA2DS2-VASc score: an analysis of the international HOPE COVID-19 registry. Rev Esp Cardiol 2021;74(7):608-615.
25. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, et al. COVID-19 and coagulation: bleeding and

thrombotic manifestations of SARS-CoV-2 infection. Blood 2020;136(4):489-500.
26. Issac TT, Dokainish H, Lakkis NM. Role of inflammation in initiation and perpetuation of atrial fibrillation: a systematic review of the published data. J Am Coll Cardiol 2007;50(21):2021-2028.
27. Marcus GM, Whooley MA, Glidden DV, Pawlikowska L, Zaroff JG, Olgin JE. Interleukin-6 and atrial fibrillation in patients with coronary artery disease: data from the Heart and Soul Study. Am Heart J 2008;155(2):303-309.
28. Wagdy S, Sobhy M, Loutfi M. Neutrophil/Lymphocyte Ratio as a Predictor of In-Hospital Major Adverse Cardiac Events, New-Onset Atrial Fibrillation, and No-Reflow Phenomenon in Patients with ST Elevation Myocardial Infarction. Clin Med Insights Cardiol 2016;10:19-22.
29. Huang SS, Chan WL, Leu HB, Huang PH, Chen JW, Lin SJ. Association between CHADS2 score and the preventive effect of statin therapy on new-onset atrial fibrillation in patients with acute myocardial infarction. PLoS One 2013;8(8):e74709.
30. Fu Y, Pan Y, Gao Y, Yang X, Chen M. Predictive value of CHA2DS2-VASc score combined with hs-CRP for new-onset atrial fibrillation in elderly patients with acute myocardial infarction. BMC Cardiovasc Disord 2021;21(1):175.