INTRODUCTION

Atrial fibrillation (AF), characterized by irregular R-R intervals and absence of ‘p’ wave in 12-lead surface electrocardiography (ECG), is still among the important causes of mortality and morbidity despite the developments in current treatment methods and the use of new generation drugs.1-3 In the classification made according to the current guideline, the beginning and ending style of the palpitation are taken into account. Nevertheless, the beginning and ending style of the palpitation are taken into account. Nevertheless, the beginning and ending style of the palpitation are taken into account.

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consideration. According to this, there are five groups; (a) first detected, (b) paroxysmal, (c) persistent, (d) long-term persistent, and (e) permanent AF. Among these types, p wave is not observed in surface ECG in patients with permanent AF, instead, fibrillatory waves are observed. If the atrial tissue is still able to maintain its viability, it is said that coarse F waves can be seen in surface ECG as a reflection of atrial contraction.

In patients with atrial fibrillation, the left atrium (LA) and left atrial appendix (LAA) have been shown as the main source of thromboembolism. In the literature, left atrial size and left atrial appendix functions are closely associated with coarse F waves. There are contradictory results related to thromboembolism in studies evaluating patients with AF with and without coarse F wave. In some studies, it has been mentioned that thromboembolic complications are less common in patients with coarse F waves, while in some studies it has been reported that they may be unrelated or these complications are detected more in these patients.

According to our opinion, since p wave will not be detected in ECG in patients with permanent AF, coarse F waves, which are the indicators of viability and contractility in the atrium, become more important on thromboembolic events compared to other types of AF. For this reason, we hypothesized that it will be a more accurate approach to investigate the effect of coarse F waves on morbidity in patients with permanent AF.

In our study we aimed to investigate the effect of coarse F wave on thromboembolic events in patients with permanent AF.

2 | METHODS

2.1 | Study population

In our study, 511 patients with permanent AF who applied to our arrhythmia outpatient clinic between January 2015 and December 2019 were retrospectively screened. Since AF patients with heart failure and mitral valve stenosis tend to have thromboembolism, we thought that the net effect of coarse F waves could not be evaluated and we did not include these patients in the study. We excluded 183 patients from the study because hospital records of 85 patients were insufficient (ECG, laboratory tests, or follow-up information), 24 patients had mitral valve stenosis, 34 patients had hemorrhagic cerebrovascular events (CVE), 30 patients had heart failure (HF), and 10 patients had kidney and liver failure. A total of 328 patients with permanent AF were included in the study. Demographic data and drug using were recorded. Dabigatran 110 or 150 mg 2 × 1, rivaroxaban 15 or 20 mg 1 × 1, edoxaban 30 or 60 mg 1 × 1, and apixaban 2.5 or 5 mg 2 × 1 were considered as new oral anticoagulant (NOAC). CHA2DS2-VASc (congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke, vascular disease, age 65-74 years, and gender category) score was calculated for all patients.

2.2 | Evaluation of laboratory findings

Renal function tests, lipid parameters, high sensitive CRP (hs-CRP), uric acid, thyroid function tests, prothrombin time–international normalized ratio (PT-INR), and complete blood count results were recorded from routine blood tests.

2.3 | Electrocardiographic evaluation

The 12-lead surface ECGs of the patients (Nihon Kohden, Cardiofax V; model ECG-1550K, 25mm/sec speed and 1mv/10mm standard) were evaluated independently by two cardiologists (YKI and HK). Fibrillatory waves with an amplitude ≥ 0.5 mm in lead V1 was considered as the coarse F wave. T wave or U wave was carefully distinguished to avoid artifacts (Figures 1 and 2).

2.4 | Echocardiographic evaluation

From echocardiographic (Phillips Healthcare, DA Best, Netherlands) data, ejection fraction (EF), left ventricular diastole and end-systolic diameters (LVDD, LVDS), and left atrium diameter (LAD) were recorded.

2.5 | Thromboembolic event evaluation

Embolism or thrombus caused by atherosclerosis in large arteries, cardiac-induced embolism, and small vessel occlusion (lacune) were accepted as embolic events. From the hospital records; Thromboembolic event evaluated by computed brain tomography (BBT), magnetic resonance imaging (MRI), color
doppler ultrasonogrophy (RDUS), or physical examination findings.

2.6 | Statistical analysis

The variables were divided into two categories, categorical and continuous. Categorical data were shown as numbers and percentages and compared with the chi-square test. Whether continuous variables show normal distribution was calculated by the Kolmogrov-Smirnov test. Continuous variables were shown with mean and standard deviation. Normally distributed continuous variables were compared with independent simple T test, while non-normally distributed variables were compared with Man–Whitney test. Binominal logistic regression analysis was performed with the variables P < .05 and independent predictors for thromboembolic events were determined. Statistics were made in SPSS 20.0 (SPSS Inc, Chicago, IL, United States) in Windows operating system. P < .05 was considered statistically significant.

3 | RESULTS

According to our results, 46 (14.0%) of the patients were detected with thromboembolic events and 282 (86%) of them without thromboembolic events. Among the patients with thromboembolic events, 4 (1.2%) had acute artery occlusion, others were CVE. When the demographic data are compared between the two groups; in the group of patients with thromboembolic events, the mean age (P < .001) and the number of patients with hypertension (P < .001) and a history of CAD (P = .003) were significantly higher, follow-up durations (5.5 ± 0.9 vs 4.6 ± 2.1 years, P = .156) and other findings were similar (Table 1). When the pharmacological treatment used by the patients were compared, the number of patients using warfarin was significantly lower in the group of patients with thromboembolic events (P = .025), other pharmacological treatment were similar (Table 2). When the laboratory parameters of both groups were compared, there was no significant difference (Table 3). When electrocardiographic and echocardiogarphic data were compared, the number of patients with coarse F wave in surface ECG was significantly lower in the group of patients with thromboembolic events (P = .001), other findings were similar (Table 4). In binominal logistic regression analysis with significant parameters, age (OR: 1.105, 95% CI: 1.066-1.145, P < .001), HT (OR: 2.831, 95% CI: 1.266-6.331, P = .011), and coarse F wave (OR: 0.290, 95% CI: 0.126-0.670, P = .004) were determined as independent predictors for thromboembolic events (Table 5). When 144 patients with coarse F waves (43.9%) and 184 patients without it were compared, the number of patients with hypertension, hyperlipidemia, and thrombembolic events was higher in the group without the coarse F wave (P = .004, P = .005, and P = .001, respectively), left atrium size increased significantly (P = .001), and other findings were similar (Table 6).

4 | DISCUSSION

In our study where we investigated the effect of coarse F wave on thromboembolic events in surface ECG in patients with permanent AF, we found several important results. The most important of these is that thromboembolic event appears less in patients with a coarse F wave. In this study, patients with heart failure and mitral valve stenosis, which are directly related to thromboembolic events, were excluded, and the relationship between the coarse F wave and thromboembolic events was clearly determined. In addition, thromboembolic events were found to be closely related to age and HT.

Compared to other types of AF, patients with permanent AF usually do not show p waves showing atrial contraction at all, instead thin

**TABLE 1** Comparison of patients’ demographic findings

| Variable                        | Group with thromboembolic events (n = 282) | Group without thromboembolic events (n = 46) | P value |
|---------------------------------|-------------------------------------------|---------------------------------------------|---------|
| Age (yr)                        | 72.3 ± 8.5                                | 60.7 ± 10.8                                 | <0.001  |
| Male gender, n (%)              | 18 (39.1)                                 | 153 (54.3)                                  | 0.057   |
| Systolic blood pressure (mm Hg) | 122.5 ± 18.9                               | 124.8 ± 18.7                                | 0.446   |
| Diastolic blood pressure (mm Hg)| 77.9 ± 15.0                                | 80.7 ± 11.2                                 | 0.232   |
| BMI (kg/m²)                     | 27.2 ± 6.1                                | 27.4 ± 7.7                                  | 0.801   |
| Smoking, n (%)                  | 10 (21.7)                                 | 81 (28.7)                                   | 0.327   |
| DM, n (%)                       | 19 (41.3)                                 | 79 (28.0)                                   | 0.068   |
| HT, n (%)                       | 36 (78.3)                                 | 135 (47.9)                                  | <0.001  |
| HPL, n (%)                      | 16 (34.8)                                 | 51 (18.1)                                   | 0.009   |
| CAD, n (%)                      | 9 (19.6)                                  | 18 (6.4)                                    | 0.003   |
| AF duration, n (yr)             | 5.5 ± 0.9                                 | 4.6 ± 2.1                                   | 0.1     |
| CHA₂DS₂-VASc score, n           | 3.5 ± 1.4                                 | 3.1 ± 0.9                                   | 0.377   |

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CHA₂DS₂-VASc, congestive heart failure, hypertension, age, diabetes mellitus, stroke, vascular disease, gender category; DM, diabetes mellitus; HT, hypertension; HPL, hyperlipidemia.
Fibrillatory waves may appear in surface ECG. In some patients, the amplitude of these fibrillatory waves is >0.1 mm, which is called the coarse F wave. In our opinion, in these patients who have been diagnosed with AF for a long time, coarse F waves, which are an indicator of the ability of viable atrium tissue to contract, may cause a shaking by causing contraction in the left atrium and left atrial appendix, which is the main source of thrombogenicity. Thus, one or more beats cause blood flow and venous stasis may decrease in LA and LAA. In previous studies, the results supporting our opinion were obtained. There are also studies suggesting that coarse F waves may reflect atrial hypertrophy and increased thromboembolic event. Owing to the reduction in venous stasis in the left atrium and LAA, thrombogenicity has decreased and therefore, in our study, patients with coarse F wave may have seen less thromboembolic events.

Nakagawa et al investigated hemostatic abnormality and LAA dysfunction with fibrillatory wave amplitude in patients with chronic non-rheumatic AF. In this study, it was stated that cerebral embolism was found less in patients with a coarse F wave. It is also stated that fine fibrillatory waves in V1 lead are a useful parameter that can be used in LAA dysfunction. Although the results of this study are compatible with the results of our study, LAA was not evaluated with transesophageal echocardiography (TEE) in our

| Table 2 | Comparison of patients' medications |
|---|---|
| Patients with thromboembolic events (n = 46) | Patients without thromboembolic events (n = 282) | P |
| Warfarine (n, %) | 21 (45.7) | 178 (63.1) | .025 |
| NOAC (n, %) | 13 (28.3) | 80 (28.4) | .988 |
| ACE-ARB (n, %) | 16 (34.8) | 128 (45.4) | .179 |
| Calcium channel blocker (n, %) | 6 (13.0) | 40 (14.2) | .836 |
| B blocker (n, %) | 35 (76.1) | 183 (64.9) | .136 |
| Furosemid (n, %) | 5 (10.9) | 35 (12.4) | .767 |
| Amiodarone (n, %) | 7 (15.2) | 57 (20.2) | .428 |
| Statin (n, %) | 7 (15.2) | 47 (16.7) | .806 |
| Digoxin (n, %) | 14 (30.4) | 74 (26.2) | .552 |
| ASA (n, %) | 23 (50.0) | 169 (59.9) | .205 |

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; NOAC, Novel oral anticoagulant.

| Table 3 | Comparison of patients' laboratory findings |
|---|---|
| Patients with thromboembolic events (n = 46) | Patients without thromboembolic events (n = 282) | P |
| WBC (uL) | 7.2 ± 2.3 | 7.4 ± 2.6 | .604 |
| Hemoglobin (mg/dL) | 13.6 ± 2.3 | 13.5 ± 1.9 | .885 |
| BUN (mg/dL) | 31.5 ± 10.3 | 32.3 ± 21.5 | .798 |
| Cr (mg/dL) | 0.8 ± 0.3 | 0.8 ± 0.2 | .254 |
| Na (mmol/L) | 138.1 ± 3.1 | 138.7 ± 3.1 | .138 |
| K (mmol/L) | 4.4 ± 0.5 | 4.2 ± 0.5 | .078 |
| Total cholesterol (mg/dL) | 189.5 ± 42.5 | 183.9 ± 36.4 | .409 |
| LDL (mg/dL) | 128.6 ± 31.1 | 126.5 ± 35.7 | .731 |
| HDL (mg/dL) | 40.4 ± 9.9 | 42.2 ± 12.5 | .399 |
| Triglyceride (mg/dL) | 160.1 ± 70.9 | 178.8 ± 92.9 | .268 |
| Hs-CRP (mg/L) | 3.4 ± 3.6 | 2.3 ± 2.8 | .065 |
| Uric acid (mg/dL) | 7.1 ± 2.5 | 6.9 ± 2.2 | .615 |
| T4 (ng/dL) | 1.3 ± 0.2 | 1.3 ± 0.3 | .957 |
| TSH (uIU/dL) | 1.8 ± 1.4 | 1.9 ± 1.5 | .752 |
| PT-INR, (n) | 2.6 ± 0.8 | 2.7 ± 0.7 | .859 |

Abbreviations: BUN, blood urea nitrogen; Cr, creatinin; HDL, high-density lipoprotein; Hs-CRP, high-sensitive C-reactive protein; Htc, hematocrit; LDL, low-density lipoprotein; PT-INR, prothrombin time–international normalized ratio; TSH, thyroid stimulation hormone; WBC, white blood cells.
with mitral stenosis, the enlargement of the left atrium will be in-
mitral stenosis. With the increase in left atrial pressure in patients
are contrary to our study, is that it was performed in patients with
F waves. The greatest disadvantage of this study, whose results
LA and LAA of the patients with coarse F waves tend to expand,
Therefore, thromboembolism will appear more frequently with in-
progression. Blackshear et al stated that the LAA function and velocity
latory waves were associated with unsuccessful CV and poor pro-
success and AF progression were examined, high-amplitude fibril-
latory waves by slowing intraatrial conduction.18 There are also drug studies that mention that antiarrhythmic drugs such as
procainamide, ibutilide, flecainide, and amiodarone reduce fibrilla-
tory waves in patients with persistent AF who underwent catheter
This decrease in frequency of coarse F waves with age coincides with our study, but the follow-up times were similar in our study between the two groups. There are studies mentioning that coarse F wave can be used in both relapse and long-term follow-up in patients with persistent AF who underwent catheter ablation.15,16 In a study by Cheng et al, in which cardioversion (CV) success and AF progression were examined, high-amplitude fibrillatory waves were associated with unsuccessful CV and poor progression. Blackshear et al stated that the LAA function and velocity are not correlated with the coarse F waves because they cannot simultaneously evaluate coarse F waves and LAA functions.18 There are also drug studies that mention that antiarrhythmic drugs such as procainamide, ibutilide, flecainide, and amiodarone reduce fibrillatory waves by slowing intraatrial conduction.17,18 In our study, such an effect cannot be mentioned since the number of patients using antiarrhythmic drug (amiodarone) is similar.

In addition, in our study, warfarin use was found to be less associated with thromboembolic events in univariate analyzes, and also could not be detected as an independent marker in multivariate analysis. In a retrospective study by Shpak et al, it was stated that more ischemic events were detected in patients using NOAC. In another large-scale retrospective study, it was stated that no significant difference was found between NOAC and warfarin use in terms of ischemic events and embolism.20 It was observed that warfarin and NOAC use were similar in terms of thromboembolic events, consistent with previous studies.

4.1 | Limitations

Since our study was retrospective, a maximum of 3-4 surface ECG recordings in the patient file records could be examined. If longer continuous recordings could have been examined, the number of AF patients with coarse waves might have been found to be increased. Age and hypertension are known risk factors for thromboembolism. In patients with atrial fibrillation, it would be more logical to select individuals from similar age and hypertensive patient groups, to have a stronger claim for that coarse F waves are

### Table 4: Comparison of patients’ electrocardiographic and echocardiographic findings

| | Patients with thromboembolic events (n = 46) | Patients without thromboembolic events (n = 282) | P |
|---|---|---|---|
| Coarse F wave, n (%) | 10 (21.7) | 134 (47.5) | .001 |
| EF (%) | 57.7 ± 6.5 | 56.9 ± 6.3 | .693 |
| LVDD (mm) | 49.8 ± 3.6 | 47.2 ± 4.6 | .084 |
| LVSD (mm) | 29.9 ± 5.1 | 30.7 ± 3.8 | .490 |
| Left atrial diameter, (mm) | 50.8 ± 5.6 | 48.8 ± 5.3 | .092 |

Abbreviations: EF, ejection fraction; LVDD, left ventricle end-diastolic diameter; LVDS, left ventricle end-systolic diameter.

### Table 5: Independent predictors for thromboembolic events

| | Odds ratio | 95% confidence interval | P |
|---|---|---|---|
| Age | 1.105 | 1.066-1.145 | <.001 |
| HPL | 0.689 | 0.278-1.704 | .689 |
| HT | 2.831 | 1.266-6.331 | .011 |
| HPL | 1.452 | 0.587-3.593 | .420 |
| CAD | 2.430 | 0.904-6.530 | .078 |
| Warfarin | 0.609 | 0.282-1.315 | .207 |
| Coarse F wave | 0.290 | 0.126-0.670 | .004 |

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; HT, hypertension; HPL, hyperlipidemia.
protective from thromboembolism. Since our patients are generally >60 years old, the presence of atheroma plaques in the carotid or vertebral arteries as a source of thromboembolism has not been examined. Some of our patients may have had thromboembolism for this reason. In addition, according to multivariate analysis, many known parameters associated with thromboembolic events associated with coarse F wave may have caused overfitting.

## 5 | CONCLUSION

The coarse F waves in surface ECG in permanent AF patients may be a sign of good prognosis in terms of thromboembolic events. If coarse F waves are absent on the surface ECG of the patient, the patient should be followed closely and more attention should be paid for anticoagulation. If these patients were using coumadin, PT-INR monitoring should be done more closely.

## DISCLOSURE

The authors have not conflicts of interest. The study was approved by Adana City Hospital Institutional Review Board, number 467, and date 22.05.2019.
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