Turk Kardiyol Dern Ars 2021;49(3):206-213 doi: 10.5543/tkda.2020.92345

ORIGINAL ARTICLE

Comparison of clinical features and conventional echocardiographic characteristics of patients with heart failure with mid-range ejection fraction with and without interatrial block

İnteratriyal bloğu olan ve olmayan sınırda ejeksiyon fraksiyonlu kalp yetersizliği olan hastaların klinik özellikleri ile konvansiyonel ekokardiyografik özelliklerinin karşılaştırılması

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ABSTRACT

Objective: Heart failure with mid-range ejection fraction (HFmrEF) has been proposed as a distinct heart failure (HF) phenotype. Interatrial block (IAB) is a conduction delay between the atria and is associated with cardiovascular disease. Although there are several studies examining the effect of IAB in patients with HF with reduced ejection fraction and HF with preserved ejection fraction, a literature review did not reveal any study investigating the clinical importance of the presence of IAB in patients with HFmrEF. Thus, the aim of this research was to evaluate clinical characteristics of HFmrEF with and without IAB.

Methods: A total of 520 consecutive patients with HFmrEF in sinus rhythm who were examined at outpatient clinics were enrolled in the study (244 patients with IAB and 276 patients without IAB). Surface 12-lead standard electrocardiograms (ECGs) were recorded. Clinical characteristics, echocardiographic examination results, and laboratory values of the patients were recorded.

Results: The mean age of the patients was 67.4±11.1 years, and 76.1% were male. The patients with IAB had more comorbidities, including hypertension, diabetes mellitus, and stroke/transient ischemic attack. A statistically significant, strong, positive linear correlation was observed between P-wave duration and age, systolic blood pressure, and left atrial volume index (r=0.718, p<0.001; r=0.704, p<0.001; and r=0.725, p<0.001, respectively).

Conclusion: To the best of our knowledge, the present study is the first to evaluate the clinical relevance of IAB in HFmrEF. Adding this simple ECG marker to the clinical evaluation could add significantly to the management of HFmrEF. IAB can be used to identify high-risk HFmrEF patients, as well as to guide follow-up and appropriate treatment.

ÖZET

Amaç: Sınırda ejeksiyon fraksiyonlu kalp yetersizliği (SEF-KY) ayrı bir kalp yetersizliği (KY) fenotipi olarak önerilmiştir. İnteratriyal blok (İAB) her iki atriyum arasında bir iletim gecikmesidir ve kardiyovasküler hastalıklar ile ilişkilidir. Düşük ejeksiyon fraksiyonlu kalp yetersizliği (DEF-KY) ve korunmuş ejeksiyon fraksiyonlu kalp yetersizliği (KEF-KY) hastalarında İAB'nin etkisini inceleyen birkaç çalışma olmasına rağmen, SEF-KY hastalarında İAB varlığının klinik önemini araştıran bir çalışma bulamadık. Bu nedenle, İAB eşlik eden ve etmeyen SEF-KY'nin klinik özelliklerini değerlendirmeyi amaçladık.

Yöntemler: Sinüs ritminde olan, polikliniğe başvuran ardışık 520 SEF-KY hastası (244 İAB olan ve İAB olmayan 276 hasta) çalışmaya dahil edildi. On iki derivasyonlu standart yüzey EKG'ler kaydedildi. Hastaların klinik özellikleri, ekokardiyografik incelemeleri ve laboratuvar değerleri kaydedildi.

Bulgular: Hastaların ortalama yaşı 67.4±11.1 yıldı ve %76.1'i erkekti. İAB olanlarda hipertansiyon (HT), diyabetes mellitus (DM) ve inme/geçici iskemik atak gibi daha fazla komorbidite vardı. P-dalga süresi ve yaş, sistolik kan basıncı ve sol atriyum volüm indeksi (LAVI) arasında istatistiksel olarak anlamlı güçlü pozitif doğrusal korelasyon gözlendi (sırasıyla, r=0.718, p<0.001; r=0.704, p<0.001; ve r=0.725, p<0.001).

Sonuç: Bu çalışma SEF-KY'de İAB'nin klinik önemini değerlendiren ilk çalışmadır. Bu uygulanabilir ve basit EKG belirtecinin klinik değerlendirmeye eklenmesinin SEF-KY'in yönetimine önemli ölçüde yol gösterebileceğini düşünüyoruz. İAB, yüksek riskli SEF-KY hastalarını tanımlamak, takip etmek ve uygun tedaviyi yönlendirmek için kullanılabilir.

Received: May 29, 2020 *Accepted:* October 21, 2020 *Online:* December 22, 2020
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The incidence of heart failure (HF) has reached pandemic proportions, is associated with a significant morbidity and mortality burden, and continues to grow.[1] Despite recent important advances in treatment, the prognosis of patients with HF remains poor, and is worse than some cancers.[2,3] In 2016, the European Society of Cardiology (ESC) included a new entity of HF with mid-range ejection fraction (HFmrEF) as clinical syndrome characterized by typical symptoms and signs of HF, a left ventricular ejection fraction (LVEF) of 40% to 49%, elevated natriuretic peptide levels, and documentation of structural heart disease.[4] The prevalence of HFmrEF has been estimated at 12% to 24% of all patients with HF.[5,6] This LVEF range is less well studied than HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). The clinical features and outcomes of HFmrEF remain unclear.

Interatrial block (IAB), a conduction delay over the Bachmann bundle, is characterized by the presence of a prolonged P-wave duration that exceeds 120 milliseconds on a 12-lead surface electrocardiogram (ECG).[7] IAB is known to be associated with atrial fibrillation (AF), atrial tachyarrhythmia, left atrial (LA) electromechanical dysfunction, thromboembolic ischemic stroke, and increased cardiovascular mortality.[8–10] Therefore, it is important to identify the presence of IAB in patients at risk for such clinical scenarios.

Although there are several studies examining the effects of IAB and P-wave indices in patients with HFrEF and HFpEF, a review of the literature did not reveal any study investigating the clinical importance of the presence of IAB in patients with HFmrEF. Since the clinical management in cases of HFmrEF may differ in patients with IAB, the objective of the present study was to evaluate clinical characteristics of HFmrEF with and without IAB.

METHODS

Study population

This was a single-center, cross-sectional, observational study. A total of 520 consecutive patients with HFmrEF in sinus rhythm who presented for a routine checkup and were examined at outpatient clinics between January 2018 and June 2019 were enrolled. In all, there were 244 patients with IAB [IAB (+) group] and 276 patients without IAB [IAB (-) group]. The exclusion criteria were age <18 years, acute coronary syndrome during previous 3 months, severe systemic inflammatory disease, permanent AF, liver failure, malignancy, the use of a cardiotoxic agent, LVEF of <40% or >49% (HFrEF and HFpEF), use of anti-arrhythmic drugs (including class I drugs, amiodarone, and sotalol), thyroid dysfunction, congenital heart disease, or poor ECG quality. The study was approved by the Uşak University Faculty of Medicine Ethics Committee (date: 01.07.2020, decision no: 152-05-23). Written, informed consent was obtained from all of the patients included in the study.

Abbreviations:

AF	*Atrial fibrillation*
a-IAB	*Advanced IAB*
ASE	*American Society of Echocardiography*
BMI	*Body mass index*
CI	*Confidence interval*
COPD	*Chronic obstructive pulmonary disease*
DBP	*Diastolic blood pressure*
DM	*Diabetes mellitus*
ECG	*Electrocardiogram*
ESC	*European Society of Cardiology*
HF	*Heart failure*
HFmrEF	*Heart failure with mid-range ejection fraction*
HFpEF	*HF with preserved ejection fraction*
HFrEF	*HF with reduced ejection fraction*
HLP	*Hyperlipidemia*
HT	*Hypertension*
IAB	*Interatrial block*
LA	*Left atrium*
LAVI	*Left atrial volume index*
LVEF	*Left ventricular ejection fraction*
MPV	*Mean platelet volume*
NYHA	*New York Heart Association*
PAD	*Peripheral artery disease*
p-IAB	*Partial IAB*
SBP	*Systolic blood pressure*
TIA	*Transient ischemic attack*

Demographic and clinical evaluation of the patients

Baseline demographic characteristics of the study population were recorded. Hypertension (HT) was defined by a previous diagnosis of HT or the presence of a systolic blood pressure (SBP) of ≥140 mmHg or a diastolic blood pressure (DBP) of ≥90 mmHg. Hyperlipidemia (HLP) was defined as a baseline total cholesterol level of >200 mg/dL or current treatment with statins and/or lipid-lowering agents. Diabetes mellitus (DM) was defined as a fasting plasma glucose level of ≥126 mg/dL or a plasma glucose level of ≥200 mg/dL 2 hours after a 75-mg oral glucose tolerance test or a glycated hemoglobin result of ≥6.5%, or use of antidiabetic medications. Chronic obstructive pulmonary disease (COPD) was defined by a previous diagnosis of COPD or the use of medication for COPD. Peripheral artery disease (PAD) was defined by an ankle-brachial index value of <0.9 or previous percutaneous intervention/surgery for PAD. Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2). Cigarette smoking was defined as smoking ≥1 cigarette a day. The symptoms and physical examination findings of the patients were recorded. Primary etiologies (ischemic/non-ischemic heart disease, valvular diseases, etc.) causing HFmrEF were also recorded. Blood samples were taken from all of the participants after 12 to 14 hours of fasting.

Echocardiographic assessment

Echocardiographic imaging was performed in accordance with the American Society of Echocardiography (ASE) criteria from the parasternal long-axis, parasternal short-axis, and apical 4-chamber views in the left lateral position, and a subcostal view in the supine position with single-lead ECG monitoring.[11] All of the patients underwent 2-dimensional transthoracic echocardiographic (HD11 XE Ultrasound system; Philips Medical Systems International B.V., Best, Netherlands) evaluation with a 1.5–4.0 MHz transducer. Standard 2-dimensional, M-mode, pulsed Doppler measurements were performed according to the most recent recommendations for cardiac chamber quantification in adults. LA volume and LVEF were assessed using the modified Simpson biplane method. LA volume was measured using standard apical 4-chamber views at end-systole just before mitral valve opening. The LA borders were traced using planimetry. The borders were defined by the walls of the LA, excluding pulmonary veins and the left atrial appendage. The biplane method of disks was used to calculate the LA volume. The LA volume index (LAVI) was calculated by dividing the LA volume by the body surface area.[12] The mitral flow waves (E and A) via pulsed-wave Doppler in the apical 4-chamber view and the peak velocity were measured according to the recommendations of the ASE.

Electrocardiogram analysis

Surface 12-lead standard ECGs were recorded for each patient with a 25 mm/second paper speed at 10 mm/mV amplitude (Cardiofax M ECG-1350; Nihon Kohden Corp., Tokyo, Japan). ECG images were amplified 8 times and P-wave duration was measured blindly using semiautomatic digital calipers in all 12 leads to acquire the longest duration. All of the measurements were repeated 3 times and average values were calculated. The onset of the P-wave was the point of initial upward or downward deflection from the ECG baseline, and the P-wave endpoint was determined as the point where the waveform returned to baseline. Partial IAB (p-IAB) was defined as a P-wave duration of more than 120 milliseconds without biphasic morphology in the inferior leads, and advanced IAB (a-IAB) was defined as a P-wave duration longer than 120 milliseconds with biphasic morphology in the inferior leads.[7] In the current study, there were 210 (86.1%) patients with p-IAB and 34 (13.9%) patients with a-IAB. All of the ECG measurements were analyzed by 2 cardiologists who were blinded to all other data.

Measurement reproducibility

The intraclass correlation coefficient for interobserver comparisons of LA diameter, LAVI, LVEF, and P-wave duration was 0.92 [95% confidence interval (CI): 0.89–0.94], 0.91 (95% CI: 0.87–0.95), 0.88 (95% CI: 0.86–0.90), and 0.93 (95% CI: 0.90–0.96), respectively, while the intraobserver comparison was 0.89 (95% CI: 0.87–0.91), 0.90 (95% CI: 0.86–0.94), 0.92 (95% CI: 0.89–0.95), and 0.91 (95% CI: 0.88–0.94), respectively.

Statistical analysis

SPSS Statistics for Windows, Version 25.0 software (IBM Corp., Armonk, NY, USA) was used for the data analysis. Normally distributed continuous data were expressed as mean±SD. Continuous variables that were not normally distributed were expressed as the median (minimum-maximum), and categorical variables were expressed as numbers and percentages. The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test and the variance homogeneity was evaluated using the Levene test. An independent samples t-test was used with the bootstrap results when comparing the quantitative data of 2 independent groups, and the Mann-Whitney U test was used with the Monte Carlo results. To compare categorical variables, the Pearson chi-squared and Fisher exact tests were applied using the exact results. Pearson correlation analysis was performed to examine the relationship between P-wave duration and clinical characteristics, echocardiographic data, and biochemical values. Variables were examined with a 95% confidence level. A p value of <0.05 was considered statistically significant.

RESULTS

The baseline clinical characteristics of the study population are presented in Table 1. The mean age of

Table 1. Comparison of baseline clinical characteristics of patients with and without interatrial block

	IAB (-) group (n=276)			IAB (+) group (n=244)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			65.3±11.5			69.2±10.8	<0.001[a]
Male gender	208	75.3		189	77.4		0.068[b]
Body mass index (kg/m^2)			28.2±3.2			28.8±3.4	0.135[a]
Heart rate (bpm)			73.7±14.8			74.1±15.3	0.228[a]
P-wave duration (ms)			98.6±8.2			127.5±6.3	<0.001[a]
NYHA class III/IV	39	14.1		45	18.4		0.024[b]
Pulmonary congestion	145	52.5		134	54.9		0.179[b]
Peripheral edema	106	38.4		98	40.1		0.059[b]
Hypertension	175	63.4		168	68.8		<0.001[b]
Diabetes mellitus	98	35.5		101	41.3		0.008[b]
Hyperlipidemia	68	24.6		61	25		0.416[b]
Prior stroke/TIA	24	8.6		31	12.7		<0.001[b]
COPD	34	12.3		29	11.8		0.538[b]
Chronic kidney disease	40	14.4		37	15.1		0.332[b]
Peripheral artery disease	57	20.6		62	25.4		0.015[b]
Smoking	98	35.5		90	36.8		0.484[b]
Systolic blood pressure (mmHg)			124.5±30.3			135.2±31.5	<0.001[a]
Diastolic blood pressure (mmHg)			80.6±10.5			81.4±10.2	0.257[a]
Primary etiology							
Ischemic heart disease	228	82.6		203	83.1		0.845[b]
Non-ischemic dilated cardiomyopathy	34	12.3		28	11.4		0.141[b]
Other 2	14	5.1		13	5.5		0.396[b]

[a]Independent samples t-test (bootstrap); [b]Pearson chi-squared test (exact). COPD: Chronic obstructive pulmonary disease; IAB: Interatrial block; NYHA: New York Heart Association; TIA: Transient ischemic attack; SD: Standard deviation.

the patients was 67.4±11.1 years, and 397 (76.1%) of the patients were male. There was a larger proportion of men in both groups. The mean BMI of the patients was 28.5±3.3 kg/m^2. The patients with IAB were older than those without IAB [IAB (+): 69.2 years, IAB (-): 65.3 years; p<0.001]. The patients with IAB had more comorbidities, including HT, DM, stroke or transient ischemic attack (TIA), and PAD than those without IAB (p<0.001, p=0.008, p<0.001, and p=0.015, respectively). There were more patients with New York Heart Association (NYHA) class III/IV in the IAB (+) group than in the IAB (-) group (p=0.024). In the present study, it was observed that HFmrEF was frequently caused by ischemic heart disease in both groups (82.8%). There were no significant differences between groups in terms of gender, BMI, heart rate, DBP, smoking, pulmonary congestion, peripheral edema, or history of HLP, chronic kidney disease, or COPD, (Table 1).

In the echocardiographic evaluation, the LA was larger and the LAVI was significantly higher in the IAB (+) group than in the IAB (-) group (p=0.001, p<0.001, respectively). There were more patients with moderate-to-severe mitral regurgitation in the IAB (+) group than in the IAB (-) group (p<0.001) (Table 2).

The laboratory examination revealed that the mean platelet volume (MPV) and platelet distribution width values were significantly higher in the IAB (+) group than in the IAB (-) group (p<0.001 and p=0.003, respectively) (Table 3).

A strong, statistically significant, positive linear correlation was observed between P-wave duration and age, SBP, and LAVI (r=0.718, p<0.001; r=0.704,

Table 2. Comparison of echocardiographic findings of the patients with and without interatrial block

	IAB (-) group (n=276)			IAB (+) group (n=244)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Left ventricular ejection fraction (%)			45.2±3.3			44.7±3.5	0.322[a]
Left ventricular septal wall thickness (mm)			9.1±1.2			9.3±1.1	0.505[a]
Posterior wall thickness (mm)			8.6±1.2			8.5±1.2	0.498[a]
Left ventricular end-diastolic diameter (mm)			55.7±11.4			56.2±10.7	0.215[a]
Left ventricular end-systolic diameter (mm)			38.5±4.8			39.2±4.4	0.452[a]
Left atrium diameter (mm)			36.6±4.4			38.5±4.6	0.001[a]
Left atrial volume index (ml/m^2)			38.5±19.1			42.3±18.2	<0.001[a]
E/A			1.24±0.4			1.18±0.6	0.235[a]
Lateral e′ (cm/s)			10.7±3.6			10.5±3.3	0.202[a]
Septal e′ (cm/s)			8.1±1.6			8.4±1.9	0.117[a]
TAPSE (mm)			23.8±3.1			22.7±3.5	0.424[a]
Mitral regurgitation moderate–severe	81	29.3		100	40.9		<0.001[b]
Tricuspid regurgitation moderate–severe	62	22.4		60	24.5		0.114[b]
Aortic stenosis moderate–severe	7	2.5		7	2.8		0.162[b]

[a]Independent samples t-test (bootstrap); [b]Pearson chi-squared test (exact). IAB: Interatrial block; SD: Standard deviation.

Table 3. Comparison of laboratory findings of the patients with and without interatrial block

	IAB (-) group (n=276)	IAB (+) group (n=244)	*p*
Fasting glucose (mg/dL)[1]	112.4±24.5	121.2±22.3	0.082[a]
Creatinine (mg/dL)[1]	1.28±0.5	1.35±0.7	0.424[a]
Total cholesterol (mg/dL)[1]	177.2±30.4	181.5±35.3	0.191[a]
Triglyceride (mg/dL)[1]	150.7±42.4	148.5±44.6	0.212[a]
High-density lipoprotein cholesterol (mg/dL)[1]	38.4±9.5	37.7±9.2	0.55[a]
Low-density lipoprotein cholesterol (mg/dl)[1]	106.8±39.2	115±35.5	0.095[a]
N-terminal pro-B-type natriuretic peptide (pg/mL)[2]	1890 (396–3225)	2134 (480–3750)	0.122[b]
Hemoglobin (g/dL)[1]	14.3±1.5	13.6±1.8	0.345[a]
Platelet (x1000) (K/uL)[2]	227 (98–360)	242 (110–402)	0.263[b]
Plateletcrit (%)[1]	0.24±0.02	0.26±0.01	0.174[a]
Mean platelet volume (fL)[1]	9.2±1.3	11.7±1.5	<0.001[a]
Platelet distribution width (%)[1]	13.5±5.4	16.2±5.2	0.003[a]

[1]Mean±Standard deviation; [2]Median (minimum-maximum). [a]Independent samples t-test (bootstrap); [b]Mann-Whitney U test (Monte Carlo). IAB: Interatrial block.

p<0.001; and r=0.725, p<0.001, respectively) (Table 4).

DISCUSSION

In the current study, we evaluated clinical characteristics of HFmrEF patients with and without IAB. It was determined that older age and greater SBP and LAVI values were significantly associated with prolongation of P-wave duration. To the best of our knowledge, the present study was the first to focus on evaluating the clinical relevance of IAB in HFmrEF.

Several studies have suggested that HFrEF and HFpEF are distinct pathophysiological syndromes.[13]

Table 4. Correlation between P-wave duration and clinical characteristics, echocardiographic data, and biochemical values

	P-wave duration	
	r	*p*
Age	0.718	<0.001
NYHA class III/IV	0.183	0.106
Systolic blood pressure	0.704	<0.001
Prior stroke/TIA	0.609	0.001
Left atrium diameter	0.573	0.008
LAVI	0.725	<0.001
Mitral regurgitation moderate–severe	0.252	0.045
Mean platelet volume	0.413	0.026

Pearson correlation analysis. LAVI: Left atrial volume index; NYHA: New York Heart Association; TIA: Transient ischemic attack.

HFrEF is generally characterized predominantly by systolic dysfunction and HFpEF by diastolic dysfunction, although varying degrees of overlap are often seen. The ESC guidelines suggest that patients with HFmrEF are likely have mild systolic dysfunction as well as diastolic dysfunction.[4] It is not clear whether HFmrEF is a separate clinical entity or a "transition zone" between HFrEF and HFpEF. Therapies for patients with HFmrEF are uncertain, as clinical trials have not directly targeted this population, yet there may be some tools to guide the clinical management of patients with HFmrEF.

HF is known to cause endothelial dysfunction and atrial fibrosis due to overstretching of the atrium.[14] Atrial fibrosis is considered the main pathophysiological mechanism leading to IAB. IAB is an easily detectable finding on ECG. Therefore, the presence or absence of IAB in patients with HFmrEF may be useful in clinical management.

Our study revealed significant differences in some demographic and clinical characteristics (age, NYHA class III/IV, HT, DM, TIA/prior stroke, and SBP) of HFmrEF patients with and without IAB. Aging affects the cardiac conduction system through increased atrial myocardial fibrosis. IAB is related to atrial fibrosis, which produces a slowing of electrical conduction and atrial activation.[15] Atrial fibrosis probably plays a pivotal role in the increase of IAB prevalence with age; moreover, fibrosis is associated with age and is a risk factor for stroke.[16] Similar to reports in the literature, in our study, the patients with IAB were older than those without IAB (69.2 years, 65.3 years, respectively; p<0.001), and there were more patients with stroke/TIA in the IAB (+) group than in the IAB (-) group (p<0.001). These results suggest that it might be appropriate to follow the development of AF in HFmrEF patients with IAB closely.

The ischemic etiology of patients with HFmrEF seems to be similar to that of those with HFrEF. In the Swedish heart failure registry of 42,987 patients, the ischemic heart disease percentages were 60% HFrEF, 61% HFmrEF, and 52% HFpEF.[5] In our study, an ischemic etiology was common in patients with HFmrEF (82.8%), but no significant difference was observed between the IAB (+) and IAB (-) groups. The reason for the higher rate of ischemic etiology in our study compared with other studies may be that patients with HFmrEF and comorbid conditions such as coronary artery disease, HT, and DM were more frequent among the routine outpatient clinic visits that made up the study.

There are several studies investigating IAB in patients with HFrEF. Abdellah et al.[17] demonstrated that P-wave dispersion and IAB were prevalent in patients with HFrEF and significantly associated with low LVEF, paroxysmal AF, poor functional capacity, hospitalization, and mortality. In the Bayes' Syndrome-HF study, Escobar-Robledo et al.[18] found that advanced IAB predicted new-onset AF and ischemic stroke in patients with HF. Similarly, in the present study, the IAB (+) patients had poor functional capacity and a history of stroke was more common. However, our study included evaluation of IAB in the new clinical entity of HFmrEF.

It has been established that LA diameter and the LAVI have key roles in predicting new-onset AF and/or recurrence of AF after radiofrequency ablation.[19] Bruun Pedersen et al.[20] investigated several echocardiographic parameters for predicting AF in patients with TIA. They observed that echocardiographic measurements of LA and LV size and function could noninvasively predict AF in patients with TIA and could potentially be used to guide AF monitoring strategy. In another study, Ariyarajah et al.[21] reported that IAB was associated with several pathophysiologic impairments that result in LA electromechanical dysfunction. They showed that the degree of conduction delay and IAB were directly correlated with LA enlargement. In our study, the HFmrEF patients with IAB had a significantly larger LAVI compared with the patients without IAB, and the LAVI was directly correlated with P-wave duration. We also noted that HFmrEF patients with IAB had a significantly larger LA and the frequency of moderate-to-severe mitral regurgitation was greater in the HFmrEF patients with IAB compared with the patients without IAB, and these were directly correlated with P-wave duration.

MPV, an indicator of platelet activation, has an independent effect on the pathophysiology of atherosclerosis and thrombosis in the presence of other risk factors. It has been reported that the MPV was higher in cases of acute coronary syndrome, ischemic stroke, and congestive heart failure.[22,23] In the current study, the MPV values were higher in the HFmrEF patients with IAB as well as the frequency of TIA/stroke. The association of ischemic stroke and high MPV value is consistent with literature findings.

The risk factors for IAB, AF, and stroke appear to be very similar, and the underlying pathogenesis is likely due to myocardial fibrosis and atrial remodeling. Given the association with LA enlargement and electromechanical atrial dysfunction, IAB may facilitate the anatomical-electrical substrate for thrombus formation and embolism. Our results suggest that IAB, a simple ECG finding, may be useful to identify high-risk HFmrEF patients, consideration of early anticoagulation treatment, and helpful in follow-up.

Limitations

The present study has several limitations. Magnification of the P-wave using a computer-based system might have provided more accurate data for the measurement of P-wave duration. The cross-sectional design of our study limited distinguishing causality between HFmrEF and IAB. In addition, since these patients do not have required follow-up, we do not have information regarding any new onset AF in the IAB (+) group. Finally, this study did not include patients with HFpEF or HFrEF. Additional large-scale, multicenter studies with follow-up are needed to validate our findings.

Conclusion

To the best of our knowledge, the present study was the first to evaluate the clinical relevance of IAB in HFmrEF. We found that older age and increased systolic BP and LAVI values were significantly associated with of P-wave prolongation. We think that adding this simple ECG marker to the clinical evaluation could serve as a significant guide in the management of HFmrEF.

The visual summary of the article can be seen in Appendix 1.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Uşak University School of Medicine (Approval Date: July 1, 2020; Approval Number: 152-05-23).

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - M.D., İ.K.; Design - M.D.; Supervision - M.D., İ.K.; Materials - M.D., İ.K.; Data - M.D., İ.K.; Analysis - M.D.; Literature search - M.D.; Writing - M.D.; Critical revision - İ.K.

Funding: No funding was received for this research.

Conflict-of-interest: None.

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Keywords: Heart failure with mid-range ejection fraction; interatrial block; P-wave duration.

Anahtar sözcükler: Sınırda ejeksiyon fraksiyonlu kalp yetersizliği; interatriyal blok; P dalgası süresi.

Appendix 1. Visual summary of the article