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P-wave dispersion and atrial electromechanical delay in patients with inflammatory bowel disease

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SOUHRN

Kontext: Nespecifické střevní záněty (inflammatory bowel disease, IBD) představují skupinu zánětlivých onemocnění, k jejichž rozvoji dochází u vnímavých jedinců s nadměrnou imunitní odpovědí na různé antigeny nebo faktory okolního prostředí. Starší studie navrhly jako možný časný marker fibrilace síní parametr elektromechanické zpoždění síní (electromechanical delay, EMD). Cílem této studie bylo zhodnotit elektromechanické vlastnosti síní pacientů s IBD, měřené dopplerovským ultrazvukem a současně elektrokardiograficky (EKG).
Materiál a metody: Do studie bylo zařazeno 35 pacientů s IBD a 21 dobrovolníků srovnatelného věku a pohlaví. Elektromechanické vlastnosti síní byly měřeny transthorakální echokardiografií a povrchovým EKG. Vypočítávaly se disperze vlny P (P wave dispersion, PWD), elektromechanické zpoždění (electromechanical delay, EMD) v šíření vzruchu mezi síněmi, EMD v šíření vzruchu v levé síni i EMD v šíření vzruchu v pravé síni.
Výsledky: Do studie bylo zařazeno celkem 35 pacientů s IBD (54 % muži; 19 s ulcerózní kolitidou, 16 s Crohnovou chorobou, průměrný věk 43,97 ± 13,98 roku). Ve skupině pacientů byla ve srovnání s kontrolní skupinou PWD delší a doba trvání vlny P kratší. Trvání EMD mezi síněmi (laterální-trikuspidální-PA) i v rámci levé síně (laterální-septální-PA) bylo ve skupině pacientů delší.
Závěr: U pacientů s IBD byly ve srovnání s kontrolní skupinou hodnoty PWD, EMD síní a EMD v levé síni delší. Vzhledem k predispozici jedinců s IBD ke vzniku epizod arytmií síní lze uvedené parametry použít k vyhledávání vysoce rizikových jedinců.

Keywords:
Atrial fibrillation
Electromechanical delay
Inflammatory bowel disease
P-wave dispersion

ABSTRACT

Background: Inflammatory bowel disease (IBD) is a group of inflammatory diseases that occur with excessive immune response against various antigens or environmental factors in sensitive individuals. Atrial electro-mechanic delay (EMD) was suggested as an early marker of atrial fibrillation in previous studies. The objectives of this study were to evaluate atrial electromechanical properties measured by tissue doppler imaging and simultaneous electrocardiography (ECG) tracing in patients with inflammatory bowel disease.
Materials and methods: Thirty-five patients with inflammatory bowel disease (IBD), and 21 healthy volunteers, matched for age and sex, were enrolled in the study. Atrial electromechanical properties were measured by using transthoracic echocardiography and surface ECG. P wave dispersion (PWD), interatrial electro-mechanic delay (EMD), left intraatrial EMD, right intraatrial EMD were calculated.
Results: A total of 35 patients with IBD (54% males; 19 with ulcerative colitis, 16 with Crohn's disease, mean age 43.97 ± 13.98 years) were included in the study. In the patient group, PWD was longer and the P min time was shorter as compared to the control group. Both interatrial (lateral-tricuspid-PA) and left intraatrial (lateral-septal-PA) EMD times were longer in the patient group.
Conclusion: In patients with IBD, PWD, interatrial EMD and left intraatrial EMD were prolonged as compared to the control group. As IBD patients have predisposition to atrial arrhythmic events, those parameters may be used to predict high-risk individuals.

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Introduction

Inflammatory bowel disease (IBD) is a group of inflammatory diseases that occur with excessive immune response against various antigens or environmental factors in sensitive individuals. It has a chronic course, involves remission and exacerbation periods and is frequently accompanied by systemic findings.[1,2] It is composed of two main subgroups including ulcerative colitis (UC) and Crohn's disease (CD). Extraintestinal involvement may develop with a rate of > 40% in IBD.[3] One of the extraintestinal involvement is cardiovascular system, which may present as pericarditis, pericardial effusion, myocarditis, endocarditis, cardiomyopathy, predisposition to thromboembolic events, acute myocardial infarction due to coronary artery thrombosis or complete heart block.[3,4]

Atrial fibrillation (AF) is the most common permanent rhythm disorder[5,6] and a significant cause of morbidity and mortality.[7,8] Previous studies have suggested that inflammation may play a role in AF recurrence by triggering oxidative stress.[9]

Prolongation of intra-/interatrial conduction time and heterogeneous expansion of sinus impulses are the electrophysiological components of AF development.[10] All of those parameters refer to heterogeneous conduction of the electrical activity and previous studies have shown that presence of atrial electromechanical delay (EMD) and prolonged P wave dispersion (PWD) were associated with increased risk of AF.[11] Previously, Efe et al have showed that atrial electromechanical conduction is prolonged in IBD in active phase of disease.[12] AF and its relation with atrial EMD times in chronic phase of inflammatory bowel disease has not been studied yet. In our study, we aimed to evaluate P-wave dispersion and atrial electromechanical delay in patients with inflammatory bowel disease.

Methods

Study group

35 patients with IBD who were not in the active period were included in this study. Age and gender matched 21 healthy individuals, were included as control group. Presence of diabetes mellitus, hypertension, hyperlipidemia and smoking were interrogated. The study was initiated after obtaining approval from the ethics committee of our hospital.

Individuals who used anti-arrhythmic drugs, who had a history of AF, structural cardiac disease, permanent cardiac pacemaker, hyperthyroidism, hypothyroidism, primary cardiomyopathy, ischemic cardiomyopathy, heart failure (ejection fraction <50%), who had left ventricular segmental wall movement disorder, moderate-severe valve stenosis, severe valve failure, atrioventricular conduction disorder or bundle branch block, electrolyte disorder, renal failure, whose P wave's starting and ending could not be clearly evaluated on ECG or who had insufficient quality of imaging on echocardiography were not included in the study. The study complied with the principles of the Declaration of Helsinki and was approved by the local ethics committee.

Definitions

The waist circumference was measured around the top of the iliac crest in centimeter and body weight was measured at fasting period as kilogram. Body mass index was calculated according the formula: the weight(kg)/square of the height (m^2).

Echocardiography

For echocardiographic examination 2.5–3.5 MHz transducer was used (GE-Vingmed Vivid 7 Ultrasound AS, Horten, Norway). Standard echocardiographic measurements were performed considering the guideline of the American Echocardiography Association. The measurements were performed in the left lateral decubitus position using parasternal long and short axis and apical windows. With a simultaneous single-derivation ECG, the average of 3 cardiac beats in the sinusal rhythm was obtained.

On tissue Doppler examination, adjusting the spectral pulsed Doppler signal filters up to Nyquist limit of 15–20 cm/s and using optimal gain. The monitor's flow rate was adjusted to 50–100 mm/s to optimize the image of myocardial velocities. On apical four-chamber view, the pulse tissue Doppler volume sample was obtained from the left ventricular lateral mitral ring, septal mitral ring and right ventricular tricuspid ring. On the simultaneous ECG recording, the time between the start of the P-wave and the start of the tissue Doppler late diastolic wave (A') was labeled as PA (Fig. 1). The measurements were obtained from the lateral mitral ring (lateral-PA), septal mitral ring (septal-PA) and right ventricular tricuspid ring (tricuspid-PA). The difference between the lateral and tricuspid-PA (lateral–tricuspid-PA) was defined as interatrial electromechanical delay (EMD); the difference between the septal and tricuspid-PA (septal–tricuspid-PA) was defined as right intraatrial EMD and the difference between the lateral and septal-PA (lateral-septal-PA) was defined as left intraatrial EMD.

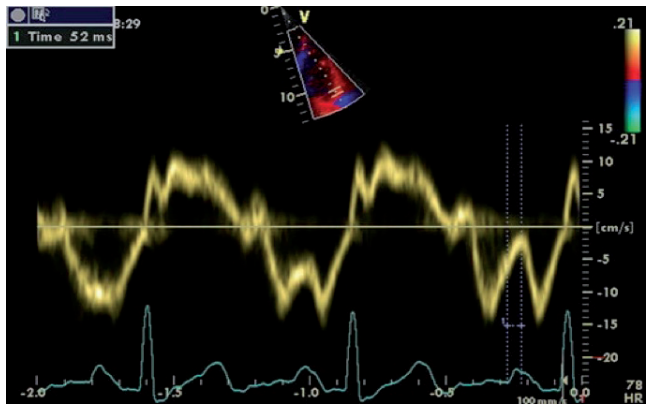

Fig. 1 – Measurement of the PA interval by tissue Doppler echocardiography. On superficial electrocardiography, the time interval between the start of the P wave and the late diastolic wave (A') obtained on tissue Doppler recording was taken.

Electrocardiography and P-wave dispersion

A 12-derivation ECG recording was performed in the supine position at a rate of 25 mm/s with an amplitude of 10 mm/mV after a 20-minute resting period. The starting point of the first wave observed upwards or downwards from the

isoelectrical line was considered the starting point of the P wave. The point of return of the wave back to the isoelectrical line was considered the end of the P wave. The time of the P wave for each derivation was determined by using digital measurement device for approximately 3 P wave times. The longest P wave time (P-max) and the shortest P wave time (P-min) in any derivation on 12-derivation ECG were measured; the difference between P-max and P-min was determined as P-wave dispersion.

Statistical analysis

Descriptive statistics of the parametric variables were expressed as mean ± standard deviation and the categorical variables were expressed as patient number (n) and percentage (%). For comparison of the control group with the patient group, Independent t-test was used for parametric variables and chi-square test was used for categorical variables. In cases where the assumptions of the chi-square test could not be provided, Fisher's exact test was used. Pearson correlation coefficient was used in measurement of the relation between two parametric variables. All statistical analyses were performed using the SPSS 20.0 (IBM Corporation) statistical package program. The *p* values obtained as a result of the tests were evaluated at a significance level of $\alpha = 0.05$.

Results

A total of 35 patients with IBD (54% males; 19 UC, 16 CD, mean age 43.97 ± 13.98) were included in the study. As control group, 21 age and gender-matched healthy individuals were included (71% males; mean age 40.14 ± 10.24 years). Demographic data, clinical characteristics, laboratory and echocardiographic findings of the study patients are summarized in Table I. The clinical characteristics of the groups were similar aside from diastolic blood pressure, which was significantly higher in the patient group as compared to control group. C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were higher in the patient group as well as the platelet count.

The results of the ECG and Doppler evaluation of the electromechanical delay are shown in Table 2. In the patient group, PWD was longer (45.40 ± 11.21 ms and 30.76 ± 9.99 ms, $p < 0.05$) and the P-min time was shorter (54.46 ± 9.83 ms and 69.14 ± 7.11 ms, $p < 0.05$) as compared to the control group. P-max values were similar in both groups. On tissue Doppler examination, the lateral and septal PA times were longer in the IBD group compared to the control group (lateral PA 69.86 ± 11.32 ms and 56.24 ± 9.93 ms, $p < 0.05$; septal PA 45.06 ± 7.98 ms and 38.38 ± 9.96 ms, $p = 0.008$). Tricuspid PA was similar in both groups.

Both interatrial (lateral-tricuspid-PA) and left intraatrial (lateral-septal-PA) EMD times were longer in the patient group (34.46 ± 10.79 ms and 25.43 ± 7.52 ms, $p = 0{,}001$; 24.80 ± 9.31 ms and 17.86 ± 7.35 ms, $p = 0{,}001$, respectively). The right intraatrial EMD time was similar in both groups.

Correlation analysis is summarized in Table 3. No statistically significant correlation was found between disease duration, inflammatory biomarker and PWD and EMD. Also, there was no significant correlation between PWD and EMD.

Table 1 – Demographic data, clinical characteristics, laboratory and basal echocardiographic findings of the patient and control groups

	Control group (n = 21)	Patient group (n = 35)	*p* value
Age (years)	40.14 ± 10.24	43.97 ± 13.98	0.281
Gender (female) (n, %)	6 (% 28.6)	17 (% 48.6)	0.141
Waist circumference (cm)	91.59 ± 9.68	94.97 ± 12.90	0.345
Body mass index (kg/m^2)	25.49 ± 3.44	26.07 ± 6.36	0.701
Systolic blood pressure (mmHg)	116.43 ± 14.92	119.06 ± 17.08	0.562
Diastolic blood pressure (mmHg)	71.48 ± 6.29	77.69 ± 11.62	***0.028****
White blood cell (10^9/L)	6.71 ± 2.37	7.22 ± 2.26	0.453
Platelet (× 10^3/L)	256 ± 42	296 ± 76	***0.019****
CRP (mg/L)	2.05 ± 2.02	8.41 ± 5.48	***< 0.001****
ESR (mm/h)	5.53 ± 4.38	16.03 ± 7.88	***< 0.001****
Diabetes mellitus	0 (% 0)	2 (% 5.7)	0.523
Hypertension	2 (% 9.5)	6 (% 17.1)	0.430
Hyperlipidemia	2 (% 9.5)	5 (% 14.3)	0.700
Smoking	0 (% 0)	2 (% 5.7)	0.523
Echocardiography			
E Velocity (cm/s)	70.65 ± 17.04	70.14 ± 20.30	0.930
A Velocity (cm/s)	53.24 ± 11.75	62.94 ± 20.20	0.073
IVSd (cm)	8.62 ± 1.20	8.23 ± 1.47	0.311
LVIDd (mm)	44.57 ± 3.15	43.86 ± 4.12	0.498
LVIDs (mm)	29.57 ± 4.29	27.74 ± 3.32	0.080
Diameter of left atrium (cm)	33.00 ± 3.75	32.83 ± 3.56	0.865

CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; IVSd – diastolic interventricular septum diameter; LVIDd – left ventricular end diastolic dimension; LVIDs – left ventricular end systolic dimension; * $p < 0.05$ statistically significant, values expressed as mean ± standard deviation or number and frequency n (%).

Table 2 – Descriptive statistics and results of the analyses

	Control group (n = 21)	Patient group (n = 35)	*p* value
P-max (ms)	99.90 ± 11.08	99.86 ± 16.68	0.991
P-min (ms)	69.14 ± 7.11	54.46 ± 9.83	***< 0.001****
PWD (ms)	30.76 ± 9.99	45.40 ± 11.21	***< 0.001****
Lateral PA (ms)	56.24 ± 9.93	69.86 ± 11.32	***< 0.001****
Septal PA (ms)	38.38 ± 9.96	45.06 ± 7.98	***< 0.01****
Tricuspid PA (ms)	30.81 ± 8.71	35.40 ± 8.14	0.052
Interatrial EMD (ms)	25.43 ± 7.52	34.46 ± 10.79	***0.001****
Right intraatrial EMD (ms)	7.57 ± 4.05	9.66 ± 5.80	0.154
Left intraatrial EMD (ms)	17.86 ± 7.35	24.80 ± 9.31	***< 0.01****

*$p < 0.05$, EMD – electromechanical delay; PWD – P wave dispersion.

Table 3 – Results of the correlation analysis

		r	*p* value
Disease period	P wave dispersion (ms)	0.123	0.480
	Interatrial EMD (ms)	0.246	0.154
	Left intraatrial EMD (ms)	0.206	0.236
P wave dispersion	Left intraatrial EMD	0.222	0.156
	Interatrial EMD	0.156	0.251
CRP	P wave dispersion	0.133	0.349
	Left intraatrial EMD	0.250	0.074
	Interatrial EMD	0.243	0.083

CRP – C-reactive protein; EMD – electromechanical delay.

Discussion

In our study, PWD, lateral-PA, septal-PA, interatrial EMD and left intraatrial EMD times were significantly longer in the patients with IBD in chronic phase. This study showed that in patients with inflammatory bowel disease had disturbed atrial electromechanical properties.

AF is the most common arrhythmia in clinical practice and previous studies reported the relation of AF in the setting of acute and chronic systemic inflammation.[13] Predisposition to AF may also be observed in patients with IBD on an inflammatory background. Moreover, there is a tendency to hypercoagulation in IBD and venous thromboembolic events are significant causes of morbidity and mortality.[14–16] Since patients with IBD carry a risk of AF and AF-related thromboembolic events, prevention of complications may be provided with early treatment.

Prolongation of intraatrial and interatrial conduction times of the sinusal impulses may develop as a result of electrical and mechanical changes in the atria. Non-homogeneous conduction can be determined by P-wave period on surface ECG. Since P-wave localizations on surface ECG corresponds different parts of the atria, regional delays in atrial depolarization cause heterogeneities in P-wave times. In a study by Dilaveris et al., PWD was longer while the mean P-wave and P-min times were shorter in hypertensive patients with a history of AF as compared to the individuals with sinus rhythm.[17] In addition, a PWD of >40 ms had a sensitivity of 83%, a specificty of 85% and a positive predictive value of 89% in determining paroxysmal AF.[17] In line with our findings, no significant difference was found in P-max and P-min times on ECG in individuals with IBD, while PWD was significantly longer than control group in a cross-sectional study.[18] It can be concluded that PWD is a convenient and inexpensive tool and may be used to identify individuals who are prone to atrial arrhythmias in the light of the studies mentioned above.

Our findings indicate that the time between the electrical impulses in the atria and occurrence of mechanical contractions was prolonged in patients with IBD. The EMD times in different conditions have been evaluated previously. Interatrial and intraatrial EMD times were longer in a study that investigated the patients with paroxysmal AF.[19,20] In a study by Ari et al. atrial EMDs were longer in patients with AF recurrence than in sinus rhythm, prolonged atrial EMD were independent predictors of AF recurrence in patients with persistent AF.[21] Post-cardioversion atrial EMD durations predict recurrence of AF at 1-month follow-up. Evranos et al. showed that predictors of AF recurrence after AF ablation with cryoballon are prolonged left intraatrial EMD and lateral PA times. Left intraatrial EMD is a better predictor than PA lateral.[11] Electrophysiologically, delayed intraatrial conduction time has been shown to be a trigger for the initiation of the reentry circuit; a major cause of AF and atrial flutter.[22] Several studies reported the accuracy and feasibility of the tissue Doppler echocardiography imaging in measurement of atrial conduction times.[20,22]

Systemic inflammation plays a significant role in the pathogenesis of AF.[23–25] Whether inflammation is a cause for occurrence of AF or an outcome of AF is unknown. Inflammation causes formation of arrythmogenic substrates by stimulating fibrosis and structural changes.[26] Previously, Acar et al. investigated atrial EMD and PWD times in patients with familial Mediterranean fever.[27] They reported significant correlation between serum CRP levels, EMD and PWD times. The authors suggested that the frequency of atrial arrhythmias might be increased due to inflammation. From Danish nationwide registries in the IBD patients they found that in persistent activity periods and during flares are re-

lated increased AF risk, but in remission periods they didn't find any increased risk for AF.[28] In our study, we included IBD patients who were not in active period, but inflammatory parameters (CRP and ESR) were higher than control groups, and the periodical frequency of inflammation and persistent activity periods of patients who were included into the study hadn't been taken into consideration. In our study, no correlation was observed between the disease duration, CRP level, PWD and EMD times. We did not evaluate the activation/remission periods of the IBD or anti-inflammatory therapies, which may have affected our results.

Limitations

This is a single center study; therefore, our results may not reflect the properties of the general population. The sample size is limited. Computer-based calculation systems were not used for calculation of PWD, P-max and P-min times. The activation/remission times, and immunosuppressive treatment agents administered during these periods could not be evaluated, which may have affected the degree of systemic inflammation. Since the patients were not followed up prospectively, it is not clear if the prolongation of PWD and atrial EMD would cause atrial arrhythmic events in the future. Larger prospective studies are needed to elucidate the predictive role of these parameters for development of atrial arrhythmia.

Conclusion

In patients with IBD, PWD, interatrial EMD and left intraatrial EMD were prolonged as compared to the control group. As IBD patients have predisposition to atrial arrhythmic events, those parameters may be used to predict high-risk individuals. Incorporation of these noninvasive measures to the clinical practice may pursue early treatment options and prevent AF-related complications.

Conflict of interest
None.

Funding body
None.

References

1. Bernstein CN, Blanchard JF, Rawsthorne P, Yu N. The prevalence of extraintestinal diseases in inflammatory bowel disease: a population-based study. Am J Gastroenterol 2001;96:1116–1122.
2. Williams H, Walker D, Orchard TR. Extraintestinal manifestations of inflammatory bowel disease. Curr Gastroenterol Rep 2008;10:597–605.
3. Danese S, Papa A, Saibeni S, et al. Inflammation and coagulation in inflammatory bowel disease: The clot thickens. Am J Gastroenterol 2007;102:174–186.
4. Bansal D, Chahoud G, Ison K, et al. Pleuropericarditis and pericardial tamponade associated with inflammatory bowel disease. J Ark Med Soc 2005;102:16–19.
5. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285:2370–2375.
6. Stewart S, Hart CL, Hole DJ, McMurray JJ. Population prevalence, incidence, and predictors of atrial fibrillation in the Renfrew/Paisley study. Heart 2001;86:516–521.
7. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002;113:359–364.
8. Kirchhof P, Auricchio A, Bax J, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J 2007;28:2803–2817.
9. Hadi HA, Alsheikh-Ali AA, Mahmeed WA, Suwaidi JM. Inflammatory cytokines and atrial fibrillation: current and prospective views. J Inflamm Res 2010;3:75–97.
10. Daubert JC, Pavin D, Jauvert G, Mabo P. Intra- and interatrial conduction delay: implications for cardiac pacing. PACE 2004;27:507–525.
11. Evranos B, Aytemir K, Oto A, et al. Predictors of atrial fibrillation recurrence after atrial fibrillation ablation with cryoballoon. Cardiol J 2013;20:294–303.
12. Efe TH, Cimen T, Ertem AG, et al. Atrial Electromechanical Properties in Inflammatory Bowel Disease. Echocardiography 2016;33:1309–1316.
13. Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a risk factor for atrial fibrillation. Circulation 2003;108:3006–3010.
14. Solem CA, Loftus EV, Tremaine WJ, Sandborn WJ. Venous thromboembolism in inflammatory bowel disease. Am J Gastroenterol 2004;99:97–101.
15. Novacek G, Weltermann A, Sobala A, et al. Inflammatory bowel disease is a risk factor for recurrent venous thromboembolism. Gastroenterology 2010;139:779–787, 787 e1.
16. Irving PM, Pasi KJ, Rampton DS. Thrombosis and inflammatory bowel disease. Clin Gastroenterol Hepatol 2005;3:617–628.
17. Dilaveris P, Stefanadis C. P-wave dispersion and atrial fibrillation risk: methodological considerations. Am J Cardiol 2011;107:1405.
18. Dogan Y, Soylu A, Eren GA, et al. Evaluation of QT and P wave dispersion and mean platelet volume among inflammatory bowel disease patients. Int J Med Sci 2011;8:540–546.
19. Cui QQ, Zhang W, Wang H, et al. Assessment of atrial electromechanical coupling and influential factors in nonrheumatic paroxysmal atrial fibrillation. Clin Cardiol 2008;31:74–78.
20. Omi W, Nagai H, Takamura M, et al. Doppler tissue analysis of atrial electromechanical coupling in paroxysmal atrial fibrillation. J Am Soc Echocardiogr 2005;18:39–44.
21. Ari H, Ari S, Akkaya M, et al. Predictive value of atrial electromechanical delay for atrial fibrillation recurrence. Cardiol J 2013;20:639–647.
22. Shimizu A, Centurion OA. Electrophysiological properties of the human atrium in atrial fibrillation. Cardiovasc Res 2002;54:302–314.
23. Conen D, Ridker PM, Everett BM, et al. A multimarker approach to assess the influence of inflammation on the incidence of atrial fibrillation in women. Eur Heart J 2010;31:1730–1736.
24. Boos CJ, Anderson RA, Lip GY. Is atrial fibrillation an inflammatory disorder? Eur Heart J 2006;27:136–149.
25. Schnabel RB, Larson MG, Yamamoto JF, et al. Relation of multiple inflammatory biomarkers to incident atrial fibrillation. Am J Cardiol 2009;104:92–96.
26. Kirchhof P, Bax J, Blomstrom-Lundquist C, et al. Early and comprehensive management of atrial fibrillation: proceedings from the 2nd AFNET/EHRA consensus conference on atrial fibrillation entitled 'research perspectives in atrial fibrillation'. Europace 2009;11:860–885.
27. Acar G, Akcay A, Sayarlioglu M, et al. Assessment of atrial conduction time in patients with familial Mediterranean fever. PACE 2009;32:308–313.
28. Kristensen SL, Lindhardsen J, Ahlehoff O, et al. Increased risk of atrial fibrillation and stroke during active stages of inflammatory bowel disease: a nationwide study. Europace 2014;16:477–484.