Prognostic Value of P Wave for Developing Atrial Fibrillation

Hideki Hayashi and Minoru Horie
Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Otsu, Shiga, Japan

1. Introduction
The prevalence of atrial fibrillation (AF) increases as age advances, especially over 65 years old.\textsuperscript{1,2} Given AF occurs, the risk of mortality increases because AF is able to cause thromboembolism and heart failure.\textsuperscript{3-5} In industrialized countries, a number of patients with AF need medical care, which has brought a social problem in terms of medical expenses. Therefore, it is so important to prevent the occurrence of AF and predict who more likely develop AF. Epidemiological studies\textsuperscript{6-8} revealed that the risk factors for AF development are aging, gender, valvular heart disease, hypertension, chronic lung disease, and left atrial size, and so forth. In addition, smoking\textsuperscript{9} and obesity\textsuperscript{10} are closely associated with the development of AF. Needless to say, 12-lead ECG is used ubiquitously in clinical practice to evaluate patients and provides information on the presence of structural heart disease and heart rhythm abnormality. Moreover, P-wave morphological characteristics deserve noting that the pattern of atrial depolarization is normal or ill. In this chapter, we focus on the relation between P-wave characteristics and AF occurrence.

2. P Mitrale and AF
The P wave reflects electrical depolarization of both the right atrium (RA) and the left atrium (LA). When the P wave is biphasic in lead V\textsubscript{1} (Figure 1), the positive initial portion and the negative terminal portion of the P wave represent depolarization of the RA and the LA, respectively.\textsuperscript{11, 12} Since the early description of an asynchrony of atrial depolarization by Reynolds,\textsuperscript{13} several studies reported P-wave abnormality suggesting LA enlargement.\textsuperscript{14-16} In 1964, Morris et al.\textsuperscript{17} advanced this concept as representing LA overload (LAO). They proposed that P terminal force >0.04 second in duration and >0.1 mV in depth at lead V\textsubscript{1} was associated with hemodynamically strained LA in various valvular heart diseases. The magnitude of the negative terminal portion of the P wave, calculated as the algebraic product of the duration and amplitude (P terminal force) in precordial lead V\textsubscript{1}, was significantly larger in patients with various valvular heart diseases than in normal subjects. In their study, the P terminal force was associated with mitral valve area and increased LA pressure. The magnitude of the P terminal force has been shown to be associated with LA enlargement as revealed by transthoracic echocardiography.\textsuperscript{18, 19} These findings suggest that the negative terminal portion of the P wave in lead V\textsubscript{1} is a sign of pressure and volume...
overload in the LA, which may lead to structural and functional remodeling in the LA. Because AF often occurs and/or recurs in the remodeled LA, the increased P terminal force may underlie the generation of AF.

Fig. 1. Twelve-lead ECG showing P mitrale in lead V1.

The increased P terminal force is observed not only in valvular heart diseases but also in other heart diseases, including hypertension, myocardial infarction, and cardiomyopathy. As patients with such disorders likely suffer from AF, the increased P terminal force in lead V1 has been considered a probable precursor to development of AF. The terminal portion of the P wave in lead V1 has been associated with electrical depolarization of the LA alone in humans and in dogs. Using angiocardiography, Miller and Spertus showed a correlation of marked negative component in leads V1 and V2 with LA enlargement. Subsequently, Morris et al showed a significant correlation of the magnitude of P terminal force with severity of hemodynamic abnormality. The P terminal portion in lead V1 is composed of several factors: (1) anatomic shift of the LA to the posterior side by hemodynamic strain, (2) enlarged LA size, (3) LA hypertrophy, and (4) reduced conduction velocity in the LA. These factors are also attributed to prolonged P-wave duration. Ishida et al studied relation of LAO with development of AF. They found that the rate of AF development was significantly higher in patients with LAO (P terminal force ≥ 0.06 second × 0.2 mV in lead V1) than in control subjects. In addition, the area of initial portion of P wave in lead V1 was larger in patients who developed AF than in those who did not. These findings showed that an increased magnitude of P-wave initial force in lead V1 was associated with a higher rate of AF development. This finding suggests that when a substrate develops in the RA in addition to the LA, susceptibility to the development of AF may increase.

The P-wave features of LAO reflect basic mechanisms underlying AF occurrence in terms of electrophysiologic and structural remodeling of the atrium that predisposes to the
development of AF. Increased P-wave duration results from either slow conduction or an enlarged atrium. The former shortens wavelength, and the latter provides a sufficient area for reentry to occur. These pathophysiologic changes are linked to the maintenance of AF. Increased intracardiac pressure of the left ventricle may cause LA remodeling, which is likely to occur in patients with structural heart disease. Disturbed transmitral blood flow due to elevated diastolic pressure in the left ventricle may induce heterogeneous distribution of the atrial refractory period. Structural remodeling, as occurs with interstitial fibrosis and connexin redistribution, causes anisotropic conduction or discontinuous propagation. In hypertrophied atrial myocytes, triggered activity, such as early and delayed afterdepolarizations, is prone to occur, thus AF ensuring in the remodeled atrium.

3. P Pulmonale and AF

It was reported that chronic obstructive pulmonary disease (COPD) complicated AF. A recent study acknowledged that multivariate analysis revealed that heart failure, advanced age, prior cerebrovascular events, COPD, and hypertension were independently associated with progression of paroxysmal to persistent AF in pharmacologically treated patients. When chronic obstructive pulmonary disease (COPD) develops, intimal thickening of arterioles, intravascular thrombosis, loss of capillaries occur in addition to perivascular inflammation and fibrosis, causing pulmonary hypertension. Under these pathophysiological conditions, the right atrial pressure increases, which results in right atrial enlargement, being responsible for P pulmonale. In an autopsy study, Berliner and Master reported that subjects with isolated left atrial hypertrophy had normal P-wave amplitude; while those with biatrial hypertrophy had an increase in P-wave amplitude, although in four cases of isolated right atrial hypertrophy, no P-wave abnormalities were noted. Caird and Wilcken found a right atrial abnormality at autopsy in patients with COPD. Tall P waves with the amplitude $\geq 0.25$ mV in inferior leads have been regarded as an ECG sign representing RA overload (RAO). Typically, patients with COPD exhibit vertical P-wave axis with peaked P wave in leads II, III, and aVF (P pulmonale) (Figure 2).

![Fig. 2. Twelve-lead ECG showing P pulmonale in inferior leads.](www.intechopen.com)
It was reported that P pulmonale was associated with impaired pulmonary function worsens.\textsuperscript{42} Asad et al.\textsuperscript{43} reported that P-wave amplitude in inferior leads decreased in most patients with COPD after the acute exacerbations subsided. Saha et al.\textsuperscript{44} reported that right atrial enlargement or increased right atrial pressure or both are important factors for the change of the P waves in cor pulmonale. However, little correlation between P pulmonale and abnormality of ventilator function in patients with chronic bronchitis was reported\textsuperscript{38}. Maeda et al.\textsuperscript{45} measured intracardiac pressure using Swan-Ganz catheter in patients with P pulmonale. In these, no significant increase of intracardiac pressure in right-sided chambers was found. However, there was a significant inverse relation between the presence of P pulmonale and the cardiothoracic ratio. These findings indicated that a vertical anatomical position of the heart was attributed to generation of P pulmonale in COPD rather than hemodynamic stress in the right-sided chambers.

As mentioned above, traditional ECG criteria for P pulmonale are increased amplitudes of P waves \(\geq 2.5\) mm in leads II, III, and aVF. Such characteristics, however, have been criticized as nonspecific for COPD. Chou and Helm\textsuperscript{46} used the term "pseudo P pulmonale" to explain cases where left atrial forces contributed to increased P-wave amplitude in lead II, indicating that P pulmonale is not so specific as has been generally believed. Alternative criteria were proposed for identifying RAO. Macruz et al.\textsuperscript{47} investigated that the ratio of P-wave duration to PR interval (P/PR) in normal subjects and patients with RAO and LAO. In RAO, the P/PR increases because of increased transit time from the sinus node to the atrioventricular node. In LAO, the terminal portion of the P wave is delayed because of the prolonged transit time of the depolarization impulse through the enlarged left atrial wall. Hence, the P-wave duration is prolonged, but P-R interval remains unchanged, resulting in the P/PR above the normal limit. Several investigators studied the feasibility of the RAO criteria by determining the size of the RA on imaging. Reeves et al.\textsuperscript{48} determined RA size with two-dimensional echocardiography using the apical four-chamber view. They found that RA enlargement was present only in 18\% of patients with P pulmonale. However, a qR pattern in lead V\textsubscript{1} was a significant marker for detecting RA enlargement and a positive linear correlation of RA size with the ratio of total QRS amplitude in lead V\textsubscript{2} compared with lead V\textsubscript{1}. Kaplan et al.\textsuperscript{49} determined the size of the right atrium using quantitative two-dimensional echocardiography in patients with right atrial enlargement. They found that traditional ECG criteria for RAO were insensitive. Instead, a P wave height \(>0.15\) mV in lead V\textsubscript{2} and, a QRS axis \(>90\) degree and an R/S ratio \(>1\) in lead V\textsubscript{1} in the absence of complete right bundle branch block best predicted right atrial enlargement. Recently, Tsao et al.\textsuperscript{50} compared anatomic atrial enlargement as determined by volumetric cardiovascular magnetic resonance with ECG findings concurrent to criteria of RAO. They found that the presence of at least one ECG criteria for P pulmonale is sensitive but not specific for anatomic enlargement.

### 4. Atrial conduction delay and AF

Delayed inter- or intra-atrial conduction time predisposes subjects to the development of AF.\textsuperscript{51-53} Histology marked by interstitial fibrosis,\textsuperscript{54-56} uncoupling of muscle bundle,\textsuperscript{57} altered distribution of gap junction,\textsuperscript{58, 59} and inflammation\textsuperscript{60} underlies slow conduction, giving rise to P wave prolongation. Several studies\textsuperscript{61-68} determined P-wave duration. The maximum P-wave duration varied approximately from 90 ms to 120 ms. Prolonged P-wave duration is a useful predictor of AF development.\textsuperscript{63, 69} Prolonged P-wave duration phenotypically represent conduction delay in the atria (Figure 3). A positive correlation between advancing
age and P-wave duration was noted. Slowed interatrial conduction velocity has been demonstrated in a cohort with a history of AF, underscoring the importance of atrial conduction delay. Many studies reported intimate association of P-wave duration and occurrence of AF. In addition to P-wave duration, P-wave dispersion, as is reflected as the interval between the longest and the shortest duration of P wave in any of 12-lead ECG leads, is an invariable maker in relation to AF occurrence and recurrence. Both indices are associated with conventional risk factors of AF. Patients with uncontrolled hypertension had significantly prolonged P-wave duration and increased P-wave dispersion as compared to controls or controlled hypertension. Likewise, patients with diabetes had significantly prolonged P-wave duration and increased P-wave dispersion as compared to normal controls. Several studies showed that individuals with obesity had significantly prolonged P-wave duration and increased P-wave dispersion as compared with control groups. Because those risk factors are independently related to AF occurrence, P-wave duration can be used as a noninvasive marker predicting AF occurrence.

Fig. 3. Twelve-lead ECG showing prolonged P-wave duration of 156 ms.

Intraatrial and interatrial conduction delay prolongs duration of P wave and affects configuration of P wave. Although P-wave duration on 12-lead ECG is able to be measured by computerized assessment, signal averaging technique of body surface ECG provides ability to detect small amplitudes <1 µV of P wave. Since electrograms are composed by hundreds of data points in signal averaging ECG (SAECG), the onset and offset of P wave are appreciated with high reliability and accuracy. The filtered P-wave duration by SAECG was significantly longer in patients with paroxysmal AF than in controls, and the amplitude of atrial late potential for the last 10-20 ms of P wave significantly lower in patients with paroxysmal AF than in controls. Thus, patients at risk for paroxysmal AF can be evaluated by SAECG while in sinus rhythm. The role of P-wave SAECG was further investigated. Prolonged P wave on SAECGs was associated with recurrence of AF after cardioversion and occurrence of AF after cardiothoracic surgery. In addition, P-wave duration on SAECG was longer in hypertensive patients with paroxysmal AF than in those without. Prolonged P-wave duration on SAECG exerted to predict future transition from paroxysmal to persistent AF.
5. Conclusion

P-wave measures can be noninvasively obtained from patients having any disease, if they have sinus rhythm. In clinical practice, it is possible to utilize data of ECG recordings for various study designs such as cross-sectional, case-control, and intervention studies. Therefore, the P-wave analysis needs to be used not only for a diagnostic tool but also to evaluate the prognostic value for AF development in the future study.

6. References


Atrial Fibrillation-Basic Research and Clinical Applications is designed to provide a comprehensive review and to introduce outstanding and novel researches. This book contains 22 polished chapters and consists of five sections: 1. Basic mechanisms of initiation and maintenance of atrial fibrillation and its pathophysiology, 2. Mapping of atrial fibrillation and novel methods of signal detection. 3. Clinical prognostic predictors of atrial fibrillation and remodeling, 4. Systemic reviews of catheter-based/surgical treatment and novel targets for treatment of atrial fibrillation and 5. Atrial fibrillation in specific conditions and its complications. Each chapter updates the knowledge of atrial fibrillation, providing state-of-the-art for not only scientists and clinicians who are interested in electrophysiology, but also general cardiologists.

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Phone: +86-21-62489820
Fax: +86-21-62489821