

Atrial Conduction Disorders

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Abstract: Atrial conduction disorders result from impaired propagation of cardiac impulses from the sinoatrial node through the atrial conduction pathways. Disorders affecting interatrial conduction alter P-wave characteristics on the surface electrocardiogram. A variety of P-wave indices reflecting derangements in atrial conduction have been described and have been associated with an increased risk of atrial fibrillation (AF) and stroke. Interatrial block (IAB) is the most well-known of the different P-wave indices and is important clinically due to its ability to predict patients who are at risk of the development of AF and other supraventricular tachycardias. P-Wave Axis is a measure of the net direction of atrial depolarization and is determined by calculating the net vector of the P-wave electrical activation in the six limb-leads using the hexaxial reference system. It has been associated with stroke and it has been proposed that this variable be added to the existing CHA2DS2-VASc score to create a P2-CHA2DS2-VASc score to improve stroke prediction. P-Terminal Force in V1 is thought to be an epiphenomenon of advanced atrial fibrotic disease and has been shown to be associated with a higher risk of death, cardiac death, and congestive heart failure as well as an increased risk of AF. P-wave Dispersion is defined as the difference between the shortest and longest P-wave duration recorded on multiple concurrent surface ECG leads on a standard 12-lead ECG and has also been associated with the development of AF and AF recurrence. P-wave voltage in lead I (PVL1) is thought to be an electrocardiographic representation of cardiac conductive properties and, therefore, the extent of atrial fibrosis relative to myocardial mass. Reduced PVL1 has been demonstrated to be associated with new-onset AF in patients with coronary artery disease and may be useful for predicting AF. Recently a risk score (the MVP risk score) has been developed using IAB and PVL1 to predict atrial fibrillation and has shown a good predictive ability to determine patients at high risk of developing atrial fibrillation. The MVP risk score is currently undergoing validation in other populations. This section reviews the different P-wave indices in-depth, reflecting atrial conduction abnormalities.

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1. INTRODUCTION

Atrial conduction disorders result from impaired propagation of cardiac impulses from the sinoatrial node through the atrial conduction pathways. They have received a great deal of attention in the literature owing to their ability to lead to atrial fibrillation (AF) and stroke. Careful analysis of the P-wave on the surface ECG is essential in the identification of these disorders. During sinus rhythm, atrial conduction originates within the sinoatrial node. Once the electrical impulse exits the sinoatrial node, right atrial activation typically proceeds rapidly along the crista terminalis and moves anteriorly towards the inferior portion of the right atrium, where it meets the atrioventricular node. Simultaneously, rapid propagation of the atrial impulse across the interatrial

septum occurs, allowing for near synchronous atrial activation. Interatrial electrical impulse propagation occurs most commonly *via* the Bachmann region, with other less common areas of conduction having been described at the level of the fossa ovalis and the coronary sinus [1, 2]. Following conduction across the Bachmann region (both endo- and epicardially), the left atrium depolarizes in a cranio-caudal direction with the last area of atrial activation typically being the inferolateral left atrium. This pattern of spread produces the normal P-wave on the surface ECG, which is upright in lead II and typically in leads I, aVL and aVF, has a mean frontal plane axis of approximately 60 degrees, is monophasic, and has a duration of less than 120ms [3]. Disorders affecting interatrial conduction can alter these P-wave characteristics on the surface electrocardiogram. A variety of P-wave indices reflecting derangements in atrial conduction have been described. These indices and their prognostic significance are reviewed.

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1.1. Interatrial Block

Interatrial block is the most well-known of the different P-wave indices. It has been the focus of increasing interest since it was first described in 1979 by Antoni Bayes de Luna due to its ability to predict AF and other supraventricular tachycardias [4, 5]. Interatrial block represents a conduction block between the two atria, and similar to other blocks, is divided into degrees. Partial (first degree) IAB is defined as a prolongation of the P-wave ≥ 120 milliseconds without any other significant abnormality. Advanced (third degree) IAB is defined as prolongation of the P-wave ≥ 120 milliseconds with a biphasic P wave in any of the inferior leads [6]. Second degree interatrial block occurs when both partial and advanced interatrial block are intermittently present in the same recording which can also show normal P-wave duration [6]. Partial interatrial block is common in the general population and increases in prevalence with increasing age. Its prevalence has been described as nearly 40% in septuagenarians and over 50% in octogenarians [7, 8]. Partial IAB is significantly more common than advanced IAB. The conduction abnormalities seen in IAB are thought to be mediated by a block of interatrial conduction through the Bachmann region. The importance of the Bachmann region has been demonstrated experimentally in canine models, with interruption reproducing the classic ECG findings of advanced IAB, as well as from electrophysiological studies involving human subjects [9, 10]. More recently, a new experimental model using open-chest anesthetized healthy adult swine and direct application of ice at the transverse sinus of the pericardium where the Bachmann's region is located demonstrated gradual and reversible IAB in the absence of structural atrial disease, which demonstrates that IAB is an independent phenomenon and not necessarily related to left atrial enlargement [11]. Partial IAB is thought to occur when interatrial conduction continues to conduct *via* a partially blocked Bachmann region, resulting in a prolonged P-wave with a normal upright morphology in the inferior leads. Advanced IAB is thought to be the result of a complete conduction block of the Bachmann region, with the left atrium being activated in a caudo-cranial direction from the level of the coronary sinus, resulting in a prolonged and biphasic P-wave in the inferior leads [12]. Although the exact pathophysiologic mechanisms responsible for IAB have not been fully elucidated, fibrosis of the Bachmann region is thought to play a causative role in the development of this condition [13, 14]. Correlation of IAB on surface ECG and localized fibrosis in the Bachmann region by cardiac MRI has been demonstrated [15, 16]. Interatrial block has been shown to be both a progressive phenomenon and may, in certain cases, be reversible [17, 18]. IAB is frequently found in patients with left atrial enlargement (LAE) but is an independent phenomenon as demonstrated by its experimental reproducibility in animal models with structurally normal hearts. Right and particularly left atrial enlargement can cause prolongation of the P-wave on surface ECG and can cause significant changes in P-wave morphology. The ECG pattern of IAB can be distinguished from LAE in patients with structurally normal atria by careful examination of lead V1. In IAB without associated LAE, the P loop on vectorcardiography

does not move so clearly backwards as shown in Figure 8, which results in a much smaller negative P-wave component in lead V1 [19]. IAB is thought to occur in many patients with LAE and the term atrial abnormalities has been proposed to describe this association [19]. IAB can also be difficult to distinguish from atrial ectopic beats occurring at the level of the crista terminalis or lower. Careful examination of the low lateral leads V5-V6 for positive P-wave can help to distinguish IAB from junctional atrial rhythms [20].

IAB is important clinically due to its ability to predict patients who are at risk of the development of AF and other supraventricular tachycardias. A recent meta-analysis evaluated the ability of interatrial block to predict new-onset atrial fibrillation [21]. Sixteen studies were included with a total population size of 18,204 patients (mean age 56 ± 13 , 48% male) and a mean follow-up period of 15.1 years. IAB was found to predict new-onset AF (HR 2.42, 95% CI 1.44-4.07; $p=0.001$). Interestingly, partial IAB did not reach statistical significance in this analysis while advanced IAB was strongly predictive of new-onset AF. This may be due to partial IAB being an intermediate phenotype of a progressive interatrial conduction block. A registry of IAB is currently ongoing to better define the association between IAB and AF [22]. Its results were recently presented and a manuscript has been submitted. There is currently no recommendation to change anticoagulation practices based on the presence of IAB. However, IAB should alert clinicians that a patient may be at higher risk for the development of AF and to monitor patients appropriately.

1.2. Abnormal P-Wave Axis

P-Wave axis is a measure of the net direction of atrial depolarization and is determined by calculating the net vector of the P-wave electrical activation in the six limb-leads using the hexaxial reference system. An abnormal P-wave axis is defined as a P-wave vector outside of 0 to 75 degrees. Abnormal P-wave axis has been shown to be associated with the development of AF and with ischemic stroke [23, 24]. In a recent study of 2,229 patients from the ARIC (Atherosclerosis Risk in Communities) combined with 700 patients from the MESA (Multi-Ethnic Study of Atherosclerosis), abnormal P-wave axis was shown to be associated with an increased risk of ischemic stroke and significantly improved the risk prediction of the CHA2DS2-VASc score [25]. The ARIC and MESA cohorts are large prospective epidemiological studies involving separate communities in the United States. It has been proposed that this variable be added to the existing CHA2DS2-VASc score to create a P2-CHA2DS2-VASc score, thereby improving stroke prediction. While this shows promise to further improve stroke risk prediction, further replication and validation studies in diverse cohorts are needed to test this score in different populations prior to it entering wide-spread clinical practice.

1.3. P-Terminal Force in V1

P-Terminal Force in V1 (PTFV1) was first identified as a concept in 1964 and has been of continued interest since [26]. PTFV1 is defined as the product of the duration (in se-



Fig. (1). Measurement of P-Terminal Force in V1 (the product of the duration (in seconds) and amplitude (in millimeters) of the negative terminal deflection of the P-wave in lead V1). (A higher resolution / colour version of this figure is available in the electronic copy of the article).

conds) and amplitude (in millimeters) of the negative terminal deflection of the P-wave in lead V1 (Fig. 1) [27]. PTFV1 is thought to be an epiphenomenon of advanced atrial fibrotic disease [28]. PTFV1 has been shown to highly correlate with left atrial enlargement [29]. PTFV1 has been associated with a higher risk of death, cardiac death, and congestive heart failure as well as an increased risk of AF [27, 30]. A recent meta-analysis demonstrated that PTFV1 is an independent predictor of ischemic stroke [30].

1.4. P-Wave Dispersion

P-wave dispersion (Pd) is defined as the difference between the shortest and longest P-wave duration recorded on multiple concurrent surface ECG leads on a standard 12-lead ECG. Pd is thought to be a marker of inhomogeneous atrial conduction. Pd has been shown to be associated with the development of atrial fibrillation and atrial fibrillation recurrence [31]. Pd has also been found to be increased in coronary artery disease, hypertension, valvular heart disease and congestive heart failure [31]. Currently, most of the existing data on Pd has been derived from small retrospective studies and large prospective trials are needed to further validate Pd as a risk marker [31].

1.5. P-wave Voltage in Lead I (PVL1)

P-wave voltage in lead I (PVL1) is thought to be an electrocardiographic representation of cardiac conductive properties and, therefore, the extent of atrial fibrosis relative to my-

ocardial mass [32]. P-wave voltage depends on the direction of electrical propagation relative to the measured lead axis, myocardial mass as well as any intervening substrates. A significant association has been demonstrated between reduced PVL1 and displaced conduction in the Bachmann's region determined by left-atrial voltage and activation maps [33]. Reduced PVL1 has been demonstrated to be associated with new-onset AF in patients with coronary artery disease and may be useful for predicting atrial fibrillation.

1.6. MVP Score (Morphology-Voltage-P-wave Duration)

Our group has recently developed a risk score for atrial fibrillation using the P-wave variables of P-wave morphology, P-wave voltage in lead I and P-wave duration (Fig. 2) [34]. Patients were assigned 0-2 points in each of the categories of morphology, voltage and duration and then classified according to total points into low, medium and high-risk groups. The score was then tested in a population of patients (n = 676) undergoing non-emergent coronary angiography. The high-risk and medium-risk groups were found to have a significantly increased risk of developing atrial fibrillation compared to the low-risk group during the follow-up period of ~3 years (OR 2.4, 95% confidence interval [CI] 1.3-4.4; p = 0.006 and OR 2.1, 95% CI 1.4-3.27; p = 0.009, respectively). The high-risk group had a significantly shorter mean time to AF (258 weeks; 95% CI 205-310 weeks) compared to the intermediate-risk group (278 weeks; 95% CI 252-303 weeks) and low-risk group (322 weeks 95% CI

307-338 weeks; $p = 0.005$). The score is currently undergoing validation in other populations to determine its ability to predict incident AF and its generalizability.

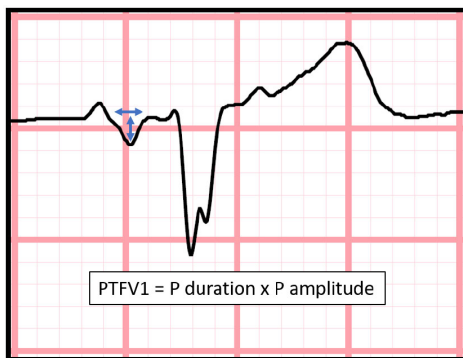


Fig. (2). Component Variable Measurements of the MVP ECG Risk Score. P-Wave Duration (measured in milliseconds) and Morphology (normal or biphasic) are measured in the inferior leads and P-Wave Voltage (in millivolts) is measured in Lead I. *Reproduced with permission from Alexander B, Mildon J, Hazim B, et al. New electrocardiographic score for the prediction of atrial fibrillation: The MVP ECG risk score (morphology-voltage-P-wave duration). Ann Noninvasive Electrocardiol. 2019;24(6):1-7. © 2019 Wiley Periodicals, Inc. [34] (A higher resolution / colour version of this figure is available in the electronic copy of the article).*

CONCLUSION

The P-wave indices as markers of impaired interatrial conduction have been associated with an increased risk of incident AF and stroke. AF is a complicated pathophysiological process that is considerably more complex than the previously widely-accepted stasis hypothesis [35]. Recent evidence from the ASSERT and IMPACT trials has demonstrated a lack of a temporal relationship between AF episodes and incident stroke. As a high percentage of patients were not in AF prior to their thromboembolic event, it is likely that there are other mechanisms involved besides stasis in the generation of thromboembolism in AF [36, 37]. It has been proposed that AF may be a result of, or can lead to, atrial cardiomyopathy, a complex condition of structural, architectural, contractile and electrophysiological changes in the atria, which itself may be the substrate of stroke [38, 39]. P-wave indices may serve as electrocardiographic markers of this atrial cardiomyopathy, a concept which has been incorporated into the design of recent trials [40]. While advanced imaging such as magnetic resonance imaging and three-dimensional echocardiography may be used to diagnose atrial cardiomyopathy, the value of atrial conduction abnormalities on the surface ECG remains relevant to identify patients who are at high risk of this condition and at risk for subsequent thromboembolic events such as stroke. For clinicians, P-wave indices can serve as markers of patients who are at a higher risk of developing atrial fibrillation and may benefit from increased surveillance. Moreover, as these measurements are all taken from the surface ECG, it is possible that these measurements could be programmed into a compu-

terized ECG interpretation algorithm, automating the detection of these markers of the disordered atrial conduction.

LIST OF ABBREVIATIONS

AF	= Atrial Fibrillation
ARIC	= Atherosclerosis Risk in Communities Study
ECG	= Electrocardiogram
IAB	= Interatrial Block
LAE	= Left Atrial Enlargement
MESA	= Multi-Ethnic Study of Atherosclerosis
MRI	= Magnetic Resonance Imaging
MVP Score	= Morphology-Voltage-P-Wave Duration Score
Pd	= P-Wave Dispersion
PTFV1	= P-Wave Terminal Force in V1
PVL1	= P-Wave Voltage in Lead I

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CONFLICT OF INTEREST

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