

Interatrial Block in the Modern Era

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Abstract: Interatrial block (IAB; P-wave duration ≥ 110 ms), which represents a delay in the conduction between the atria, is a pandemic conduction abnormality that is frequently underappreciated in clinical practice. Despite its comprehensive documentation in the medical literature, it has still not received adequate attention and also not adequately described and discussed in most cardiology textbooks. IAB can be of varying degrees and classified based on the degree of P-duration and its morphology. It can transform into a higher degree block and can also manifest transiently. IAB may be a preceding or causative risk factor for various atrial arrhythmias (esp. atrial fibrillation) and also be associated with various other clinical abnormalities ranging from left atrial dilation and thromboembolism including embolic stroke and mesenteric ischemia. IAB certainly deserves more attention and prospective studies are needed to formulate a standard consensus regarding appropriate management strategies.

Keywords: Interatrial block, bachmann's bundle, review, thromboembolism, atrial arrhythmia, P-wave duration.

INTRODUCTION

Interatrial conduction delay and its importance as leading to atrial fibrillation was described as early as 1916 by Bachmann *et al.* [1], however it has still not received adequate coverage in textbooks and remains poorly perceived in clinical practice [2].

DEFINITION

The normal transit time for electrical impulses generated in the sinus node to be conducted throughout the right and left atrium (RA and LA) is less than 110 ms which represents the P-wave duration on surface ECG. Interatrial block is defined as prolonged conduction time between the RA and LA due to impulse delay or blockage, probably most often but not exclusively in the Bachmann bundle (BB), resulting in prolonged P-wave duration (≥ 110 milliseconds) (Fig. 1).

NORMAL PHYSIOLOGY

Four right to left atrial conduction pathways have been described – Bachmann's bundle (BB), muscular bundles on the inferior atrial surface near the coronary sinus (CS), trans-septal fibers in the fossa ovalis and posteriorly in the vicinity of the right pulmonary veins [3-7]. BB functions as the principal relay in humans with a conduction speed of approximately 177cm/s [8-9]. The theory of possible interatrial specialized conduction tissue was first proposed by Lewis *et al.* in 1914 and described by Bachmann in 1916 [1]. With time, this specialized conduction band was famously known as Bachmann's bundle (BB). It is easily seen as a trapezoidal band-like structure of collimated muscle fiber coursing on

the atrial walls in front of the superior vena cava and straddles the convexities of the atrial walls, connecting them in the superior quadrant of the interatrial sulcus [10]. Tapanainen *et al.* studied the conduction pathways in patients with paroxysmal atrial fibrillation during sinus rhythm; most of the patients (72%) demonstrated solitary conduction, most commonly through the BB (69%) followed by an area near the fossa ovalis (19%) and CS ostium (11%) [11].

P-WAVE AND IAB

The P-wave which denotes atrial depolarization is initiated by right atrial activity following the sinus node stimulus, and then continued by left atrial activity until it reaches the PR segment following completion of biatrial activation. A World Health Organization/ International Society and Federation of Cardiology task force defined normal P wave duration as less than 110 milliseconds [12]. Interatrial block (IAB) is due to impulse slowing or blockage of conduction between the atria. This delay causes a wide P wave (≥ 110 milliseconds) often with a bifid notch representing the electrical gap between right and left atrial activation [13]. With more advanced disease, the electrical impulse from the sinus node is directed towards the AV node and then reflected caudo-cranially to the left atrium resulting in a biphasic 'P' wave in inferior leads [13].

PREVALENCE OF IAB

The prevalence of IAB has been shown to increase with age with only 9% in those less than 35 years, [14] to 40-60% at ages over 50 years [15-17]. Prevalence of IAB in classic textbooks seems lower than in recent reports and the likely reason could be that the previous reports were based solely on lead II measurement of P wave duration [17]. Considerable under-diagnosis of IAB utilizing lead II only for P wave duration and morphology, [18] has been reported and also

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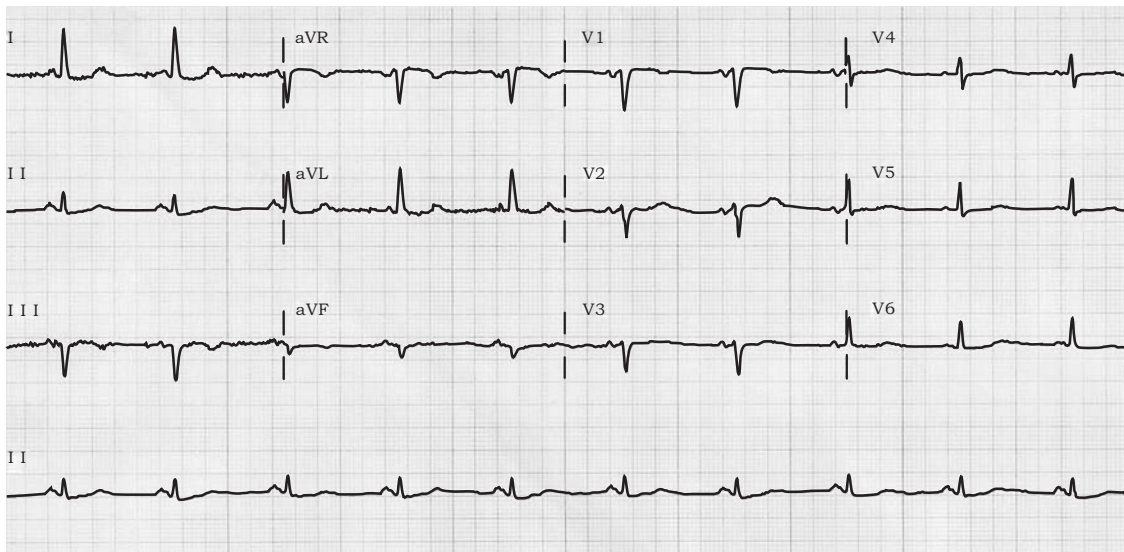


Fig. (1). ECG shows the presence of interatrial block. P-wave duration is wide (> 110 ms) and bifid.

the importance of 12-lead analysis for its correct recognition has been emphasized [19]. Lead II and precordial leads V3-V6 were noted to show IAB most consistently [14, 19]. Ariyarajah *et al.* suggested re-evaluation of the normal range for P wave duration based on the findings in a study of 500 consecutively numbered electrocardiograms in a university hospital for better bedside diagnosis accepting the fact that it might still not be possible to detect all IAB with manual estimation at bedside [20]. The mode P wave duration was 120 ms among those diagnosed with IAB and the prevalence remained comparable to previous studies in an outpatient setting with a cut-off of ≥ 110 ms [15, 16, 19, 20].

PATHOPHYSIOLOGY OF IAB

The pathological findings consistently seen with IAB were intracellular destruction and replacement with glycogen and collagen deposition in-between the cells disturbing the close mosaic architectural pattern seen in normal atrial musculature [21]. The P wave duration was found to correlate with the amount of collagen deposition between the cells, the longest P wave durations having more collagen deposition [21]. The collagen deposition disrupting the normal atrial current flow was consistently seen in patients with P wave duration of more than 140 ms [21].

In spite of IAB prevalence increasing with age, [14-17] the exact pathogenesis has not been elucidated. Various comorbidities including coronary artery disease, hypertension, and diabetes mellitus have been proposed to be the pathogenesis; however none of them showed a statistically significant correlation with progression of the IAB [22]. The cause of IAB could be ischemic [23] or inflammatory or infiltrative versus likely degenerative from the fact that its incidence increases with age [23-25]. Overstretch of the atrial wall secondary to congestive heart failure and hypervolemia were also shown to cause IAB based on the reversal of IAB with diuretic therapy [26].

CORRELATION WITH LEFT ATRIAL MECHANICS

Though IAB represents electromechanical dysfunction which could be multi-factorial and left atrial enlargement

means anatomical enlargement [27], they are frequently considered together under the term 'left atrial abnormality' and the association has also been studied in retrospective population analysis [28]. A formula based on a study proved to predict LA size in the echocardiographic parasternal long axis view. LA size (in millimeters) = $2.47 \pm 0.29 \times$ P-wave duration (in milliseconds) [28].

On the contrary and interestingly, these both can occur as separate entities. It has also been shown that patients with IAB and LAE will have a poorly contractile left atrium as compared to patients with LAE alone [29]. Poor LA systolic indices in IAB have correlated well quantitatively with the delay in LA activation compared with patients without IAB [29]. P wave duration more than 110 ms for diagnosis of left atrial enlargement has been shown to have a high sensitivity (90%) with negative predictive value of 74% using cardiac magnetic resonance (CMR) imaging as the comparative gold standard [30]. IAB potentially may induce LAE by mistiming the atrial contraction against a closed or closing mitral valve raising the shear force, which in turn can induce an increased left atrial dilatation [31].

GRADING OF INTERATRIAL BLOCK

In analogy to other conduction delays, IAB may be graded as first, second and third degrees or partial and advanced IAB [32, 33]. Partial IAB is synonymous to first degree IAB whereas the term advanced IAB encompasses both second and third degree IAB. The distinction is based on the P-wave duration and more importantly, the P-wave morphology. IAB with bifid P wave (notched P-wave) in leads I, II, III and aVF, is considered to represent partial or first degree IAB, as they represent normal propagation with a conduction delay [32]. P-wave morphology in V1 in partial IAB often presents with a negative mode or a biphasic mode where negative phase is less evident than in cases of associated left atrial enlargement (LAE) [32] (Fig. 2a-2b). Third degree IAB refers to those with biphasic P waves (\pm P-waves) in inferior leads (II, III and aVF), indicating caudo-cranial left atrial activation, usually due to a fixed block in the normal route of conduction [34] (Fig. 2c). The positive mode of P-waves in leads II, III and

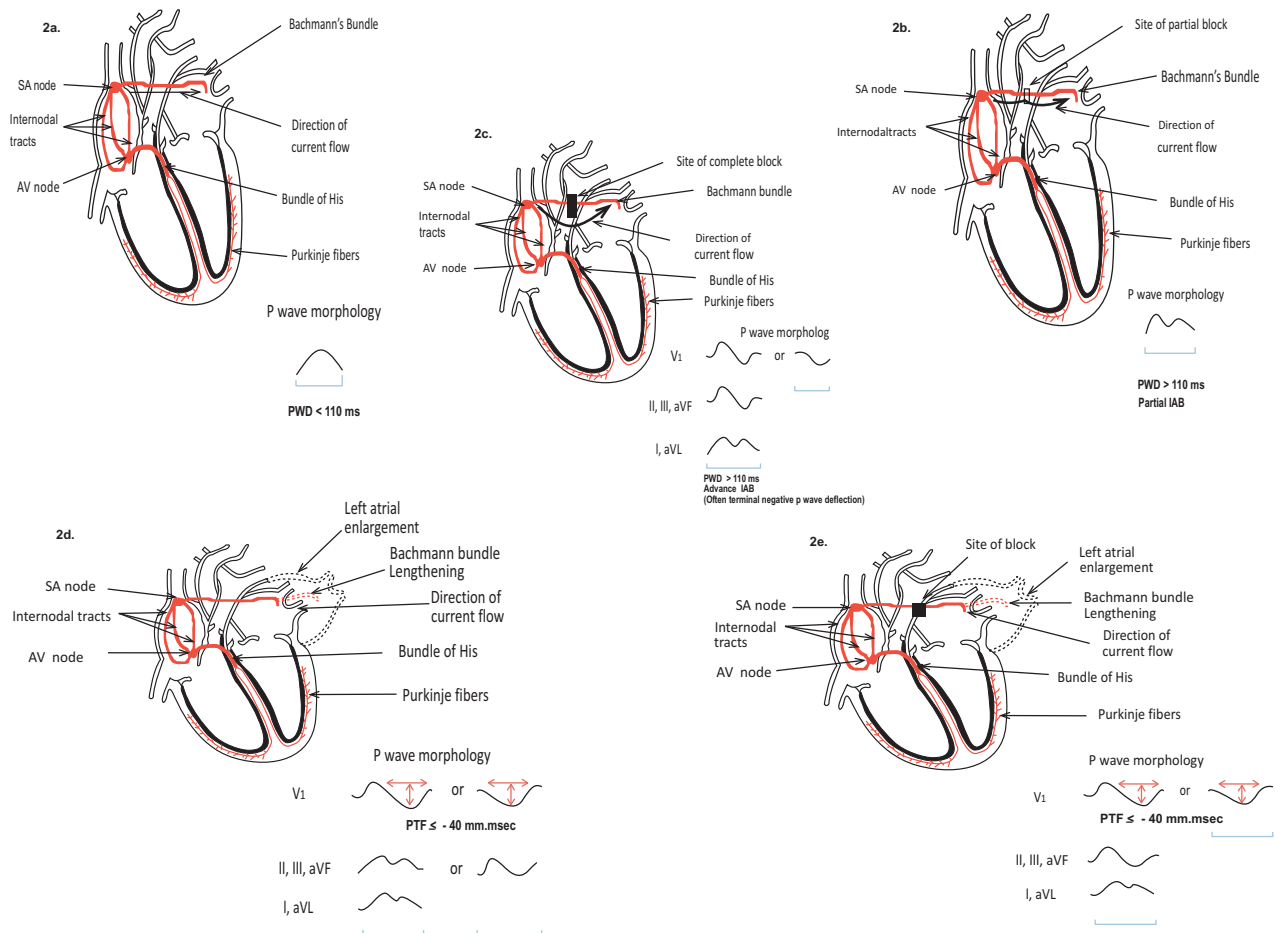


Fig. (2). (2a). Interatrial conduction traverses from the right to left atrium, through a normal conduction pathway. P-wave duration < 110 ms. (2b). A conduction delay across the Bachmann's bundle producing a first degree or partial IAB, with P-wave duration > 110 ms. Impulse however travels through the normal conduction pathway, though with a delay. (2c). There is a complete block in the normal interatrial conduction pathway resulting in a third degree IAB. Impulse propagates through an alternate pathway with caudocranial activation of the left atrium producing a biphasic (\pm) P wave in the inferior leads. Terminal negative loop of P-wave in lead V1 is often wider as compared with a partial IAB. (Third degree advanced IAB often co-exists with left atrial enlargement). (2d). This schematic illustration shows the interatrial conduction delay resulting from a pure left atrial enlargement without the presence of an underlying conduction block. Stretching of conduction fibers lead to an increased interatrial conduction time, resulting in an increased P-duration. P-waves are often bifid/notched (not biphasic) in leads I, II, III and aVF. Terminal P-force (P-tf) in V1 is often ≤ 40 mm.ms. (2e). Patient has LAE with an underlying complete interatrial conduction block. This is often a more practical clinical situation in the presence of an increased P-duration (>120 ms) with LAE, as an underlying advanced IAB often co-exists with LAE. P-waves are biphasic (\pm) in inferior leads and bifid in leads I and aVL. P-tf in V1 is often ≤ 40 mm.ms.

aVF may sometimes not be well seen because of underlying fibrosis and the diagnosis of junctional rhythm due to an apparently negative P wave in inferior leads may be made [32]. P-wave in V1 in advanced IAB often has a negative terminal P-loop (negative P-loop) which is more prominent than that in partial IAB (i.e. with a more backward direction) [32]. Finally, a changing P-wave morphology noticed in a single recording, that the first component of the P wave maintains its spatial orientation while the final component shows noticeable modifications in its morphology and duration, is considered as second degree IAB. This pattern has also been shown to be consistently seen with atrial aberrancy [35]. The bizarre and prolonged configuration of P-wave following an atrial premature complex due to the alteration of atrial refractory period due to concealed atrial conduction, was originally defined by Chung and is famously known as Chung's phenomenon [36]. Bayes

de Luna later named this as second degree IAB. IAB with morphology of third degree blockade is frequently accompanied by paroxysmal atrial arrhythmias, especially atrial flutter in patients with cardiomyopathies and with valvular heart disease [34, 37-39]. This association is often considered as an ECG clinical syndrome [37-39]. A biphasic P wave in V1 with a terminal negative phase enclosing an area equal to 1 small square on the ECG grid (≥ 40 milliseconds x 1 mm; that is P-terminal force in V1 of ≤ -40 mm.ms), is highly specific for LAE [40] (Fig. 2d). Also, an advanced IAB often co-exists with LAE and especially the terminal P-wave force is greater in these patients (Fig. 2e). A prospective study on patients with first degree IAB could throw more light on the mechanism of propagation of the block and correlation with left atrial mechanics potentially enabling us to find ways to retard or halt the progression with therapy.

IAB AND ATRIAL ARRHYTHMIAS

IAB has been consistently associated with reentrant atrial arrhythmias, especially atrial fibrillation (AF) [34, 41]. Bayés de luna *et al.* showed that the incidence of atrial tachyarrhythmias was more pronounced in the group who had advanced IAB along with LAE than the control group with only LAE or LAE with partial interatrial conduction block [34]. Progression from paroxysmal to chronic AF was consistently seen in populations with more prolonged duration of the P wave [42].

The possible mechanisms for induction of atrial arrhythmias in IAB stems from 2 basic studies. Rensma *et al.* demonstrated that changes in wavelength in the atrial impulse had an inverse correlation with initiation of tachyarrhythmias (wavelength = refractory period x conduction velocity) [43]. In the same study, premature beats were shown to have a shorter wavelength depending on the degree of prematurity observed in chronically instrumented conscious dog hearts. During the analysis of rabbit atrial myocardium for the leading circle concept by Allesie *et al.*, a sustained period of circus movement tachycardia was produced by the induction of a single properly timed premature impulse [44]. Hence in the setting of a fixed interatrial block and retrograde conduction, variation in the refractory period and conduction velocity in the atrial myocardium forms a suitable substrate for induction and sustenance of atrial tachyarrhythmia.

IAB AND THROMBOEMBOLISM

A weak and enlarged left atrium frequently found either associated with or as a result of IAB, predisposes to thrombus formation and subsequent thromboembolism [28, 29]. In 2005, Lorbar *et al.* showed an 80% prevalence of IAB in patients with embolic stroke by retrospective analysis, which is exceptionally high compared to the prevalence in the general population [45]. Chhabra *et al.* found an 88.9% prevalence of IAB in patients diagnosed with acute mesenteric ischemia, which is again about twice the average prevalence in the general population [46].

Given the strong evidence from retrospective studies for IAB as a risk factor for embolic phenomena, a question of prophylactic anticoagulation has been raised in a few studies [46-47]. However, given the high incidence of IAB in the general population, further prospective randomized studies are warranted for risk stratification and identifying the patient population with IAB who will benefit from prophylactic anticoagulation.

IAB AND MYOCARDIAL ISCHEMIA

Another interesting aspect of IAB confirming its multifactorial etiology is its anticipated role in diagnosing ischemic heart disease. Myrianthefs *et al.* studied the P wave duration during the recovery period after exercise treadmill stress tests (ETT) in patients with documented coronary artery disease [48]. They found that inclusion of P wave duration as an additional parameter for ETT interpretation increased the sensitivity of the test from 57% to 75% with a slight reduction in specificity from 85 to 77%. Increases in P wave duration (>20ms) from baseline in patients with IAB during exercise tolerance tests was also shown to be in-

versely related to the Duke Prognostic Score predicting survival in patients with coronary artery disease by Ariyarahaj *et al.* in 2006 [49]. This variation during the exercise stress test indicates its role in predicting ischemic heart disease. Another study revealed a higher incidence of IAB in patients with evidence of cardiac ischemia than in patients without evidence of ischemia who underwent ETT [50]. The study concluded that accounting the new onset IAB and worsening of preexistent IAB in combination with other parameters for positive ETT, increases the sensitivity and accuracy for diagnosing ischemic heart disease [50].

Attempts to identify the culprit vessel for IAB angiographically have revealed contradictory results. In 1992, 3-channel electrocardiographic holter monitoring during angioplasty induced myocardial ischemia revealed a statistically significant increase in P wave duration during balloon inflation in the left anterior descending and left circumflex arteries [51]. Balloon inflation in the right coronary artery was not found to significantly increase P wave duration. However in another recent retrospective study, Ariyarahaj *et al.* found that in patients with IAB at rest and coronary artery disease, the right coronary artery was predominantly affected [52].

IAB AND OBSTRUCTIVE SLEEP APNEA (OSA)

The prevalence of cardiac arrhythmias especially atrial arrhythmias is significantly higher in patients with OSA as compared to the general population [53]. There is an independent significant association between increased P wave duration (IAB) and severity of OSA based on apnea-hypopnoea index as shown by recent studies [54-56]. P wave dispersion is also increased in patients with moderate to severe OSA [57]. These studies to a certain extent explain the mechanism of increased incidence of atrial arrhythmias in OSA. The increased P wave duration and dispersion could be a result of the atrial remodeling in OSA caused by associated pathophysiological mechanisms viz. pulmonary hypertension, systemic hypertension and atrial overload, which eventually act as a substrate for atrial arrhythmias.

IAB AND ALL CAUSE MORTALITY

The relation between quantitative electrocardiography and mortality in populations is widely accepted in the literature. Prolonged QRS duration is an independent predictor of cardiovascular mortality in patients with underlying structural heart disease. Similarly, the relation between sudden death and QT prolongation is an established fact.

However, there is a recent upsurge in reviewing the association of P wave indices with all-cause mortality as well as cardiovascular mortality. A National Health and Nutrition Examination Survey (NHANES) revealed that increased P wave duration was the only P wave index significantly associated with increased cardiovascular mortality [58]. Though increased P wave duration frequently accompanies disease ailments like diabetes, hypertension and metabolic syndrome, the results from NHANES study emphasize IAB as a subclinical disease and merits elucidation as a marker of risk for adverse outcomes (Fig. 3). Certainly, further prospective research would be paramount to

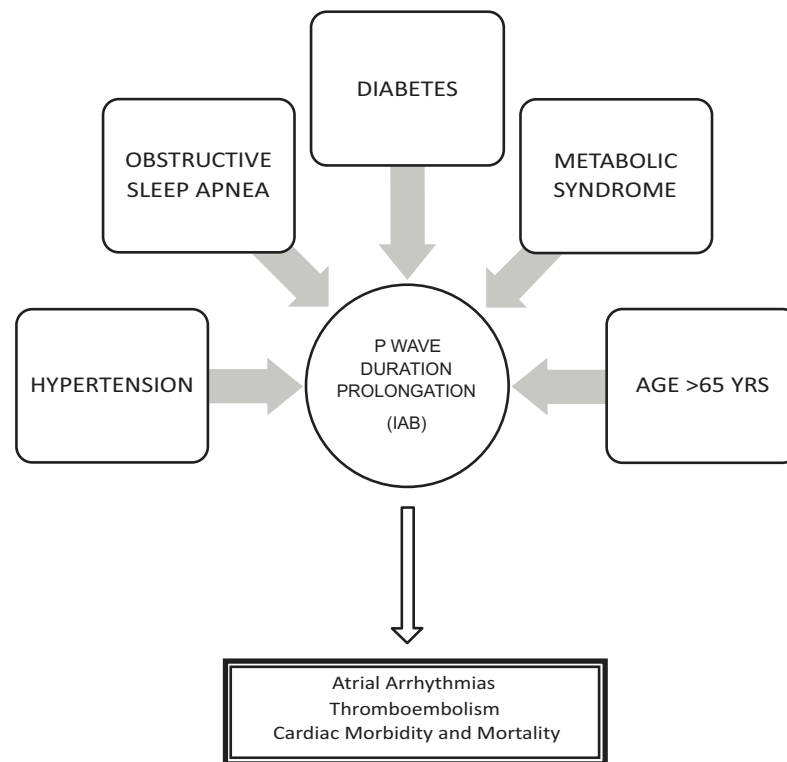


Fig. (3). A schematic description of IAB, its associated risk factors and outcomes.

clearly define IAB as an independent cardiovascular and all-cause mortality risk predictor.

IAB AND MISCELLANEOUS ASSOCIATIONS

The exact mechanism of interatrial conduction delay is furthermore plagued by its association with varied conditions. Systemic inflammatory and infectious pathologies can alter atrial electrophysiology leading to the development of interatrial block [59]. Atrial tissue in diabetic subjects demonstrates persistent oxidative stress compared with nondiabetics [60]; which can potentially play a role in the development of interatrial conduction delay. In addition, diseases that can directly involve the BB viz. secundum type atrial septal defect, interatrial septal lymphoma, septal hypertrophy and amyloidosis can prolong the duration of interatrial conduction [61-63]. Dynamic and fixed lengthening of atrial conduction fibers in hypervolemia and valvular heart disease can also impair atrial conduction leading to IAB.

CONTROVERSIES IN TERMINOLOGY

There are several controversies regarding the terminology of interatrial block (IAB) which we attempt to clarify in this section. The term "Intra-atrial" (not inter-atrial) block was in practice as early as before 1946 and was originally coined by Katz where he referred intra-atrial block to a prolonged P-wave duration (>120 ms) [64]. The subsequent literature reported intra-atrial block as a delay in the impulse conduction within the atrium leading to an altered P-wave morphology [65-67]. Some authors used the term 'complete intra-atrial block' to refer the existence of more than one pacemaker in one atrium (usually two-impulse forming cen-

ters). The term interatrial block was used by several authors to define a delay or a block in the impulse conduction between the two atria, however both these terms have been used exchangeably.

Waldo *et al.* first demonstrated in canine experiments that after the transection of anterior internodal tract, the P-wave duration increased significantly though morphology and polarity remained the same. However, transection of the BB not only caused increased P-duration but also distorted its polarity and morphology [68]. With the advent of modern electrophysiology and the knowledge gained about this subject over the last few decades, one can conceptually project that a notched and prolonged P wave morphology without change in polarity may resemble partial or first degree inter-atrial block as previously described in our review. Thus, this suggests that the term partial IAB may encompass intra-atrial blocks. The most recent literature reports have preferably used the term interatrial block which along with left atrial enlargement is usually referred as left atrial abnormality. Practically, there is a significant overlap between the two entities and given the similar morphology between intra-atrial block and partial interatrial block (IAB), its differentiation on a surface ECG is impractical. We thus do suggest and advocate the use of the term "IAB" for the sake of uniformity.

With increasing understanding of the electrical pathways in the atria and interatrial conduction, we are at the junction where we should start considering a broader terminology for interatrial block. The simplest way to measure atrial conduction is to measure P wave duration on the surface EKG. The anatomic length of the longest pathway to complete atrial conduction has a major impact on the P wave duration. Other

less important factors are atrial conduction velocity and the origin of the atrial impulse.

The term interatrial block simply suggests that there is a breach/block in the interatrial conduction pathway which may not be true in all cases. In atrial enlargement, there is stretching of the atrial conducting fibers which increases the travelling distance for the current, thereby increasing the duration of conduction, provided the velocity of the electrical current remains uniform. This increase in duration of conduction brings about an apparent increase in P wave duration and by definition interatrial block. However the real issue in this scenario is delayed conduction rather than a true block (Fig. 4). On the contrary, one must however remember that the most common cause of increased P-wave duration in LAE is due to an underlying IAB and not merely the increase in the length of conduction pathways [27].

The commonest expressway for interatrial conduction is the Bachmann bundle and thereby makes it the most common culprit in interatrial block. Increased P wave duration could certainly be possible based on the relative origin of the site of impulse to sinus node- origin of the Bachmann bundle complex with a normal P vector. This by definition will be erroneously termed as interatrial block if P wave duration happens to be more than 110 ms.

It is high time to consider using a wider terminology which will suggest a broader meaning. And more importantly, the terminology should be uniform.

COMMON MYTHS AND UNDER-KNOWN FACTS ABOUT IAB

1. Is IAB the same entity as LAE?

Answer: No. IAB implies to an impaired electrical conduction or a conduction delay between the atria as compared to LAE which is an anatomical problem ("enlarged left

atrium"). Many patients have IAB (esp. partial IAB) without associated LAE. Advanced IAB (with often biphasic P-waves in the inferior leads) frequently accompanies LAE.

2. Can advanced IAB with P-wave duration > 120 ms occur without LAE?

Answer: Yes. Though advanced IAB and LAE frequently co-exist, prolonged P-duration > 120 ms can be present in the elderly and disease conditions like acute pericarditis, acute MI or heart failure exacerbation without left atrial enlargement. In fact, P-wave may often be very long in these conditions as in LAE, but the P-loop does not so clearly backwards as in a figure 8 shape, which results in a much smaller negative P-component in V1.

3. What are the two most likely common mechanisms of prolonged P-wave duration in LAE? Which mechanism is more common?

Answer: Prolonged P-wave duration in LAE occurs due to the stretching of conduction fibers (as the current has to go across a longer distance) and due to an underlying conduction block (IAB). Underlying IAB is more commonly the cause for an increased P-duration in LAE than the stretching of conduction fibers.

4. What are the common sites of electrical impulse block in an advanced IAB?

Answer: The electrical impulse is blocked in the upper and middle part of interatrial septum, in the BB zone and/or in the upper part of left atrium, resulting in caudocranial left atrial activation. Studies have observed that in patients with sinus node disease and intra-atrial conduction delay at the posterior angle of Koch, low interatrial pacing is superior compared to right atrial appendage pacing in preventing progression to persistent or permanent AF and is associated with

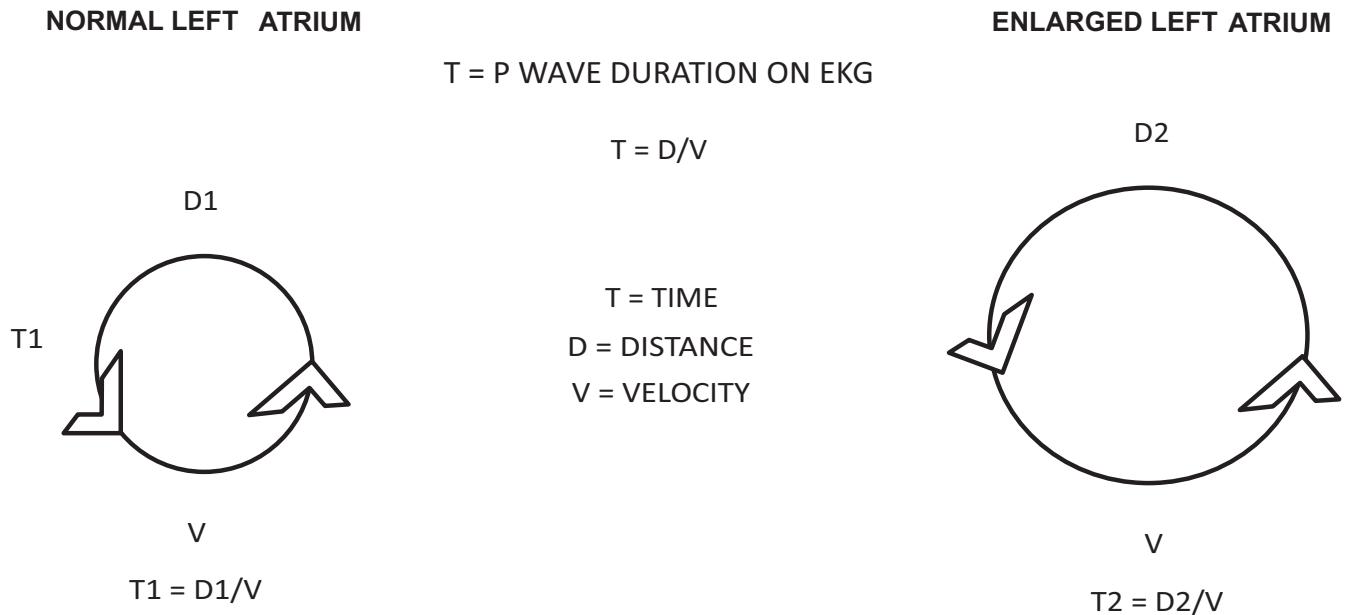


Fig. (4). A schematic representation of interatrial electrical conduction in normal and enlarged atria. Enlargement of the left atrium increases the overall distance for impulse conduction from the right to left atria. Provided the velocity of conduction remains constant, the time for conduction to cross the distance is increased which manifests as an interatrial conduction block (IAB) on the surface ECG.

the shortest atrial activation time compared with other atrial septal pacing sites in patients with IAB [32, 69, 70].

5. Advanced IAB always occurs as a result of fixed conduction block?

Answer: No. An advanced IAB may not exclusively be due to a complete or fixed block. Ariyaratjah *et al.* had reported spontaneous regression from advanced to partial IAB and resolution of advanced IAB to partial IAB with graded exercise during treatment with a β -adrenergic blocker [71].

THERAPEUTIC INTERVENTIONS FOR IAB

Medical Therapy

The multi-factorial etiology of IAB and its close correlation with risk factors for primary atherosclerotic disease [22] gives a clue that a better control of the risk factors should aid in its primary and secondary prevention. Angiotensin-converting enzyme (ACE) inhibitors have been shown to facilitate electrical defibrillation in patients with persistent AF and also reduce signal averaged P wave duration post cardioversion [72]. The likely mechanism considered was suppression of fibrosis by cytokine modulation and prevention of atrial remodeling [33, 73]. Angiotensin II receptor blockers have also been shown to inhibit the shortening of the effective refractory period during rapid atrial pacing in dogs [74]. This experiment also supports an inverse relation between wavelength and initiation of atrial tachyarrhythmia [43]. This has also been demonstrated in small prospective studies where valsartan was found to be more effective in preventing recurrence of atrial fibrillation and the same was attributed to greater reduction of P wave dispersion [75]. In another similar study telmisartan was found to be more effective than ramipril in reducing the P-wave dispersion in hypertensive patients [76]. Bayes de Luna *et al.* suggested that anti-arrhythmic treatment prevents recurrence of atrial tachyarrhythmia [77]. Again, the large prevalence of IAB in the general population precludes initiation of therapeutic interventions (like anticoagulation) in all patients diagnosed with IAB. Large prospective studies are needed to risk stratify the group and identify populations for therapeutic intervention.

Non-medical Therapies

Resynchronization therapy for atrial flutter with high degree inter-atrial block has been studied as early as 1994 by Daubert *et al.* [78]. They suggested bi-atrial pacing would prevent recurrence of atrial flutter by avoiding retrograde conduction. In an animal model Becker *et al.* proved that the number of atrial fibrillation episodes decreased with an increasing number of pacing sites [79]. Saksena *et al.* showed that dual-site right atrial pacing along with antiarrhythmics was superior to right atrial and supportive pacing in patients with symptomatic atrial fibrillation [80]. Cardiac resynchronization therapy for heart failure has also been shown to improve P wave duration and left ventricular systolic function [81]. Though the mechanical options for controlling morbidity from advancing interatrial block are attractive and promising, large randomized controlled trials are needed for guidelines to be initiated for the same.

CONFLICT OF INTEREST

The authors confirm that this article's content has no conflict of interest.

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