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Review

Advanced interatrial block as a substrate of supraventricular tachyarrhythmias: a well recognized syndrome☆,☆☆,★

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Abstract Interatrial blocks (IABs) are well described and accepted in the scientific community. In the last four decades major discoveries were made including its physiopathology, ECG presentation, classification and association with atrial tachyarrhythmias (advanced IAB). This article will briefly review the state of the art on the understanding of advanced IAB as an electrical substrate for atrial tachyarrhythmias as well as the future directions.

Keywords: ECG; Interatrial block; Atrial tachyarrhythmia

Introduction

The interatrial block (IAB) occurs due to a delay of conduction between the right and left atrium, including the zone of the Bachmann bundle (BB), and usually an important part of mid and high septum/left atrium [1,2]. As it happens with other types of heart blocks, IAB may be partial (first degree) or advanced (third degree). In the second degree IAB, transient widening of the P-wave in the same ECG recording, may be seen.

In partial IAB (Fig. 1A, B) the stimulus is delayed in some part of the zone of the atria already mentioned, yielding a wider and bimodal P-wave with duration of 120 ms or more. The first case was published by Bachmann in 1941 [3] and he also published the description of the bundle [4]. Many years later the group of Spodick [5,6] published several papers stressing the concept that partial IAB constitutes a not well known and poorly perceived pandemic and that more attention should be paid to this condition as it could be possibly associated to a higher risk of embolic stroke.

In the advanced form of IAB (Fig. 1C), the stimulus is totally blocked in the Bachmann bundle but it also involves, as we have stated, the area near it, and usually part of the left atrium. However some part of left atrium especially latero posterior zone is retrogradely activated from the mid/lower part of the septum in a caudocranial direction. This results in a wider P-wave (usually more than 120 ms) and the last part of the P-wave is negative in the inferior leads due to retrograde conduction, which explains the ± morphology in leads II, III, and VF. In lead II the second part of the P-wave may be isodiphasic [7].

Although left atrial enlargement is common in patients with advanced IAB [8,9] one should consider the following: a) the ECG pattern of partial and advanced IAB may appear intermittently with and without relation to changes in heart rate: b) there are cases of partial and even advanced IAB without left atrial enlargement and c) the ECG pattern of IAB may be reproduced experimentally in cases with normal structural chambers [10].

In this review manuscript, we will discuss the early evidence shown by different articles published by our group and validated by other authors, that the presence of the ECG pattern of advanced IAB is strongly associated with supraventricular arrhythmias (atrial flutter and fibrillation; AF). This association constitutes a syndrome [11] that has been named Bayes' syndrome in recognition to the one that has investigated all aspects associated with this condition [12,13].

Review

This article is an extension of a presentation that Dr Antoni Bayés de Luna delivered in Bratislava, Slovakia; during the 41st International Congress of Electrocardiology.

We will briefly review the following aspects: 1) the ECG–VCG diagnostic criteria of advanced IAB; 2) the

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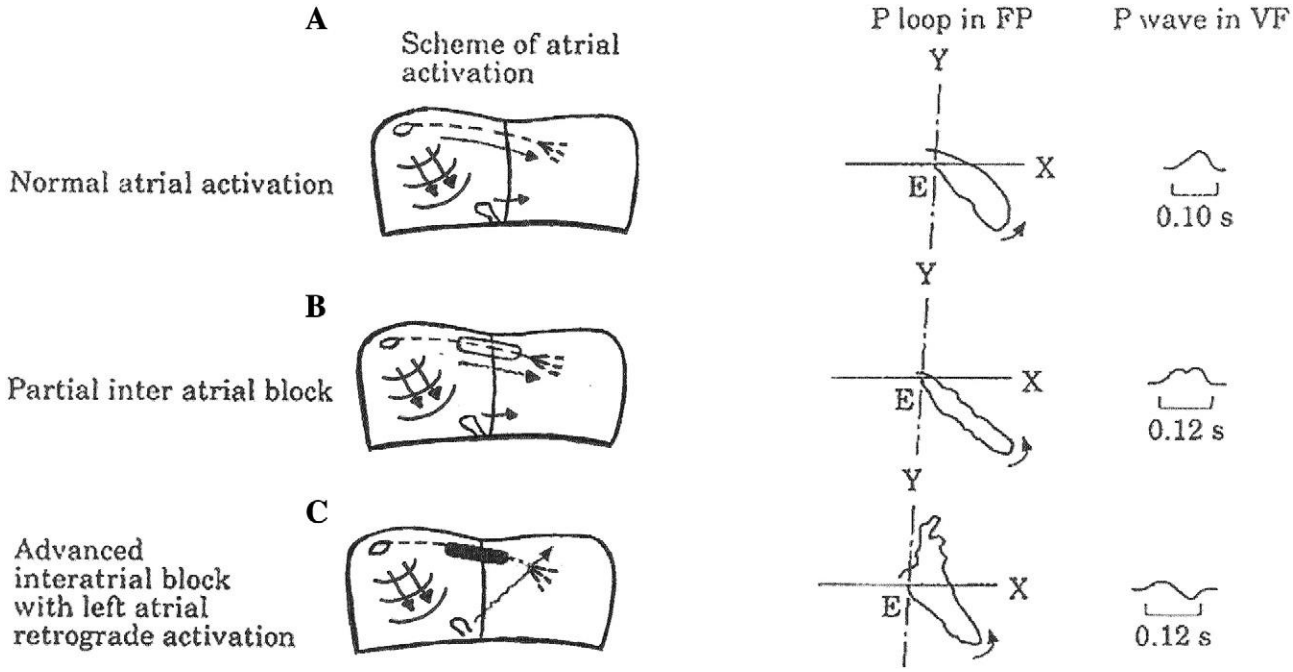

Fig. 1. Left: Scheme of atrial activation in a normal P-wave (A), in presence of partial IAB (B), and of advanced IAB (C). Right: Characteristics of the P loop and P-wave in each case. We want to note that in normal conditions, the breakthrough in left atrium also occurs at the level of coronary sinus. The dotted line shows that the Bachmann bundle is the preferential way of interatrial conduction. The remaining atrial activation is performed without preferential pathways. The primary left atrium breakthrough is in the Bachmann bundle, and also often in the fossa ovalis area (see arrow).

prevalence and clinical significance of advanced IAB; 3) the identification of the syndrome; 4) the efforts to prevent the syndrome and arrhythmia recurrences; 5) how to proceed in different clinical situations, 6) recent research in this topic and 7) future directions.

ECG–VCG diagnostic criteria for advanced IAB

The first case of advanced IAB was published by Puech in 1956 [14], in his excellent monograph "L'activite electrique auriculare" demonstrating with oesophageal leads the correlation of the caudocranial activation of the left atrium in cases of ± P-waves in leads II, III, and VF. In the 70's, some cases (including our first paper) were published [15,16]. Later on, Bayés de Luna et al., published a large series of 83 cases with detailed ECG and VCG criteria (Table 1) with oesophageal leads and intracavitary recordings, demonstrating the sequence of activation (Fig. 2) [7].

The diagnosis of advanced IAB is not difficult, if careful attention is paid to the morphological aspects of the P-wave in leads II, III and VF which may require magnification of the images. Special attention should be given to measure the P-wave onset and offset in 3 lead ECG recording devices on simultaneous beats, as the first part of the P-wave could be isodiphasic or nearly isodiphasic in some leads probably due to fibrosis (Table 1). Finally if the caudocranial activation of the left atrium is directed around −30º, what assures the diagnosis of retrograde left atrium activation, the P-wave seems only positive in lead II but presents a second part isodiphasic because falls in the limit between the positive and negative hemi-field of this lead. Furthermore, in VL the P-wave is usually clearly −/+ as it represents a mirror pattern of lead III, and in lead V1 (and often also in leads V2–V3) the morphology is ± usually with a great negative component of the P-wave, due to frequently associated left atrial enlargement (also known as P-negative force).

Prevalence of advanced IAB

The prevalence of advanced IAB was of 1‰ in the global population of young/middle age people, and 2% among patients with valvular heart disease and cardiomyopathies [7].

In an in-hospital population, Spodick identified the prevalence of IAB (most likely partial IAB) in 47% of the screened population (1000 patients), being highly prevalent in the subgroup above 60 years of age [17].

Advanced IAB may develop progressively, changing from normal P-wave to partial and finally to advanced ECG pattern [7,18].

In the initial studies [7,16], a high prevalence of supraventricular arrhythmias in patients with advanced IAB was detected, leading to further investigations.

Identification of the syndrome

Bayés de Luna et al. [11] reported a series of patients with long-term follow-up to better characterize the incidence of atrial tachyarrhythmias in patients with advanced IAB (16 patients) and compared them with patients with partial IAB (22 patients) but similar echocardiographic parameters. The advanced IAB group presented a higher incidence of atrial flutter/fibrillation (15/16, 93.7%) during a 30-month follow-up compared with the control group with partial IAB (6/22, 27.7%) ($p < 0.0001$) (Fig. 3). At one year of follow-up, the incidence of arrhythmias was 80% and 20% respectively.

Table 1
Diagnostic criteria of advanced IAB.

1) Surface ECG:
   - P ± II, III, VF. In lead II the P wave can be only + with isodiphasic last part, if the P axis is around -30º. On the other hand, in II, III, and VF, in presence of atrial fibrosis, the P wave may be recorded as negative, but in a 3 channel recording device may be seen that in lead I the P wave starts earlier. Therefore, the first part is isodiphasic.
   - P ≥ 120 msec.
   - Open angle (usually > 90º) between the 2 parts of the P wave.
2) Orthogonal ECG:
   - P ± in Y lead with a negative mode duration ≥ 40 msec.
3) VCG:
   - More than 40 msec. above X or Z axis
   - P loop duration ≥ 110 msec.
   - Open angle in FP and RSP
   - Slurrings and delays in the last part of the loop
4) Oesophageal ECG:
   - H.O.L. = P wave -/+ with delayed inscription
   - L.O.L. = P wave ±
5) Interacavitary ECG:
   - Craneocaudal sequence in RA
   - Caudocraneal sequence in LA (combined with oesophageal ECG)

HOL: High oesophageal lead. LOL: Low oesophageal lead. RA: Right atrium. LA: Left atrium.

Additionally, Holter monitoring showed that the prevalence of frequent premature atrial contractions (more than 60/h) was much more frequent in advanced (75%) than in partial (25%) IAB.

In 1999 Bayés de Luna et al., published a review paper in which they summarized all previous research published in this topic; suggesting that the association between advanced IAB and atrial tachyarrhythmias should constitute a syndrome [19].

Since then, different groups have confirmed this association [20–22], and a recent consensus on IAB has expanded on diagnostic criteria and clinical associations of advanced IAB with atrial arrhythmias [8], confirming that this association is a unique syndrome [20,21].

Should we prevent atrial arrhythmias in patients with IAB?

The strong relationship between advance IAB and atrial flutter/fibrillation led us to investigate the possible role of preventing atrial arrhythmias using antiarrhythmic drugs [23]. A small study of 32 patients with advanced IAB was compared to receive either an antiarrhythmic drug or placebo. A significant reduction of AF recurrences was observed in a long term follow-up in the group receiving prophylactic antiarrhythmic medication [23]. Despite this small series, this study should be considered a pioneer on the idea to treat patients at early stages when advanced IAB is detected, in order to reduce the incidence of atrial arrhythmias. This hypothesis needs to be confirmed with larger studies.

We have not tested the possible benefits of antithrombotic therapy in this group (advanced IAB) as the presence of documented AF is still needed, to start anticoagulation. However, as an interesting hypothesis, it could be reasonable to consider anticoagulation if the CHADS2 score is > 1 [24] and the patient presents with advanced IAB. Again, anticoagulation in high risk patients but without documented AF has yet to be proved beneficial. This hypothesis needs to be tested before making any recommendations.

Several studies with despair results have tried to re-synchronize the atriums with bi-atrial pacing. There is still no consensus whether this technique reduces the incidence of AF and this technique did not prove to be superior to sequential pacing [25].

How to proceed in different clinical situations based on available data.

1. Patients with the ECG pattern but without any evidence of previous tachyarrhythmias (no evidence of the syndrome)
   - It is premature to make any general recommendation for prophylactic antiarrhythmic treatment based on available data. In the case of very frequent premature atrial contractions and/or self limited runs of atrial flutter/fibrillation further antiarrhythmic treatment should be considered. We could also recommend close follow-up of these patients using long-term monitoring (i.e. Holter monitoring, external loop recorders) in order to capture a first (even short) episode of AF to make further therapeutic recommendations.
   - The link between IAB and stroke was studied by Spodick and his group (most of the patients with partial IAB), who demonstrated a strong association [6,26]. Careful selection of patients for oral anticoagulation should be given to those with advanced IAB, again, based on their CHADS2 score [24] and presence of documented arrhythmia.
2. Patients that already have presented the syndrome but remain in sinus rhythm
   - Antiarrhythmic drugs should be considered and antithrombotic treatment, according to their CHADS2 score as deemed necessary [24].
   - Advanced therapies to control for AF (i.e. left atrial ablation, pacing) should be considered according to guidelines and on an individual basis.
3. Patients with the syndrome and persistent atrial fibrillation
   - Rate vs. rhythm control (either drugs or ablation) should be considered on individual basis. The presence of advanced IAB was reported to be associated with increase AF recurrence after AF ablation [27].

Recent research on these topic

We would like to briefly review some of the important contributions that different groups have published on this topic. Special attention should be paid to the group of Dr. Spodick from USA that investigated several aspects of IAB and specifically its relation to stroke [6,26] and to the electromechanical dysfunction of the left atrium associated to IAB [4–6]. Daubert's group from France, studied different aspects of atrial pacing associated with the presence of advanced IAB [24]. Garcia-Cosio's group from Spain performed interesting studies using intracardiac mapping, demonstrating the retrograde activation of the left atrium in these patients [28,29]. Platonov and Holmqvist studied the characteristics of the P-wave morphology according to the

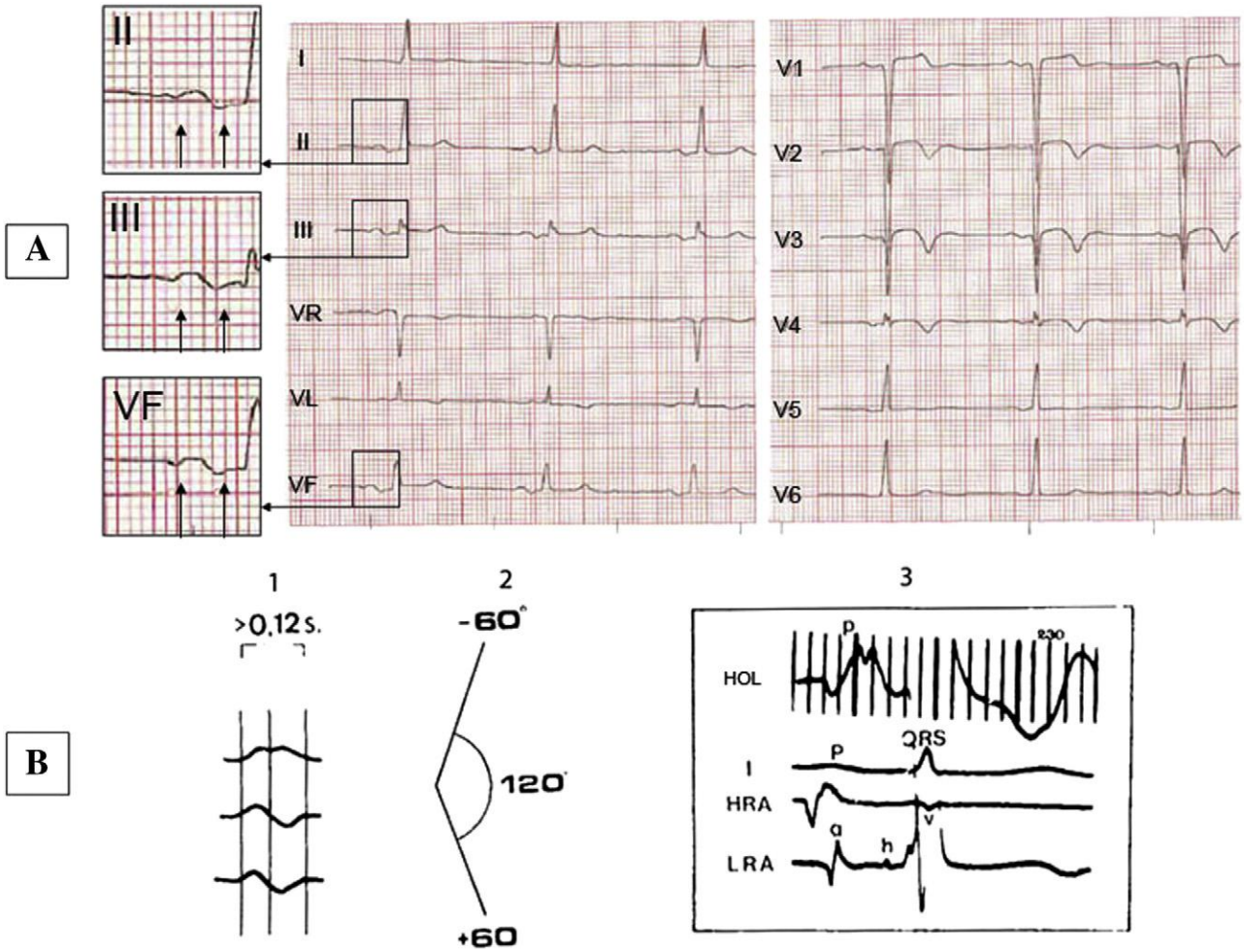

Fig. 2. **A**. Typical ECG of advanced interatrial block (P-wave ± in leads II, III, and VF and duration > 120 ms) in a patient with ischemic cardiomyopathy. When amplified, the beginning and end of the P-wave can be seen in three leads II, III and VF. **B. 1**: P-wave with ± morphology in leads I, II, and III depicting advanced IAB with retrograde conduction to the left atrium. **2**: Note how the ÄP and the angle between the direction of the activation in the first and second parts of the P-wave are measured, **3**: High intra-oesophageal ECG (HE) and endocavitary recordings (HRA: high right atrium; LRA: low right atrium) demonstrate that the electrical stimulus moves first downwards (HRA–LRA) and then upwards (LRA–HE), **4**: Location of bipolar leads to follow the course of activation is shown. HRA: high right atrium; LRA: low right atrium; HEL: high oesophageal lead; CSp and CSd: coronary sinus proximal and distal.

way of atrial activation and the relation of this pattern with atrial fibrillation [30–32].

In the last 3 years, the groups of Baranchuk and Conde from Canada/Argentina have contributed to the knowledge of the syndrome [12,13]. Their recent contributions expanded knowledge in the following areas: a) the presence of advanced IAB was a strong predictor of new atrial flutter/fibrillation post cavotricuspid isthmus ablation for typical atrial flutter [33]; b) the presence of advanced IAB in patients with Chagas' disease implanted with defibrillators; was a strong predictor of new AF in the follow-up [34]; c) the presence of advanced IAB is highly prevalent in patients with sleep apnea [35] and this probably could explain the higher incidence of AF in these patients; d) the presence of advanced IAB predicted AF recurrence after pharmacological cardioversion [36]; d) treatment with CPAP could induced reverse atrial remodelling and resolution of IAB [37] and e) the presence of advanced IAB did not predict post-CABG AF [38].

Future directions

It is our intention to call attention to the association of advanced IAB, which can be easily recognized in a surface 12-lead ECG with atrial arrhythmias (specifically AF). Future investigations (some of them ongoing studies of our international collaboration group) should be considered:

1. To create an International Registry, this would allow for longitudinal follow-up of these patients. To determine the incidence of supraventricular and ventricular arrhythmias, complications, and mortality, and to decide, according to the findings, the need of trials to investigate the need to consider preventive antiarrhythmic treatment and/or antithrombotic agents.
2. To perform studies to evaluate IAB and its association with atrial arrhythmias in different clinical settings including: a) after electrical cardioversion (larger observational studies); b) cardiac surgery for aortic and mitral

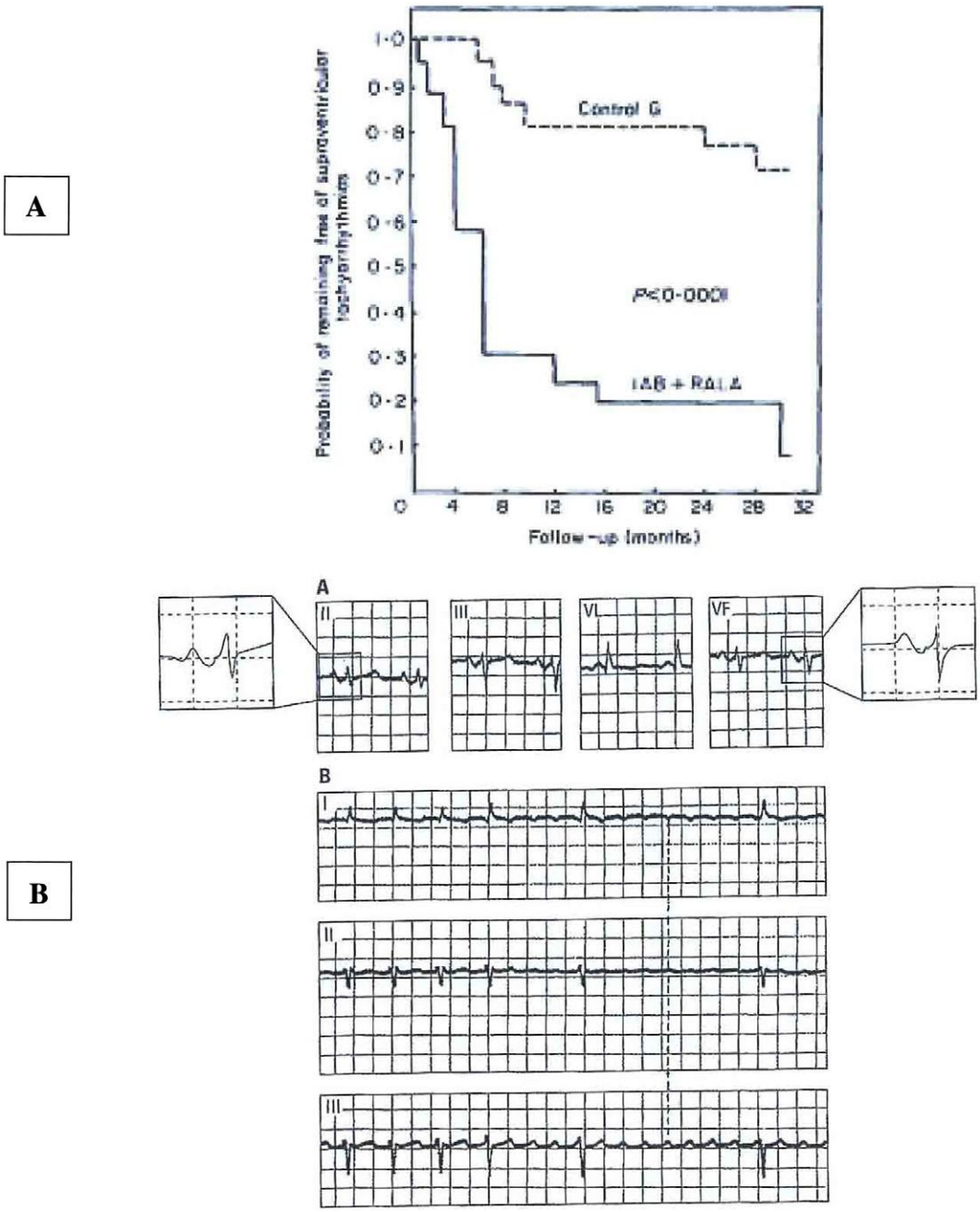

Fig. 3. **A**. Analysis of the probability of remaining free of supraventricular tachyarrhythmias in patients with advanced IAB and controls (partial IAB). The statistical difference is very important ($p < 0.0001$). **B**. Typical morphology of advanced IAB and retrograde activation of the left atrium, in sinus rhythm. The polarity of the flutter waves indicates atypical left atrial flutter (negative in lead I and positive in II and III).

valve replacement (ongoing); c) in patients with heart failure; d) in patients with hypertrophic cardiomyopathy and other forms of less frequent cardiomyopathies and e) in athletes.
3. To obtain a direct clinical evidence of slowing or complete block in the Bachmann bundle.
4. To determine the prevalence of IAB is special populations (i.e. atrial septum abnormalities, hemodialysis (ongoing), cryptogenic stroke, patients with fibrotic diseases).
5. To study the correlation by cardiac MR between advanced IAB ECG pattern and extensions of atrial fibrosis.
6. To test the hypothesis that early intervention with antiarrhythmic drugs may represent a reduction in the incidence of new AF
7. To determine whether patients with CHADS2 score >1 and advanced IAB, regardless the documentation of AF, would benefit from oral anticoagulation

Conclusions

1. Interatrial blocks are a separate entity from atrial enlargement and may be of first (partial), third degree (advanced), or second degree (intermittent).
2. Advanced interatrial block presents a clear ECG pattern ($P \geq 120$ ms with a ± morphology in leads II, III and VF). This ECG pattern may be transient, it may present

simultaneously without left atrial enlargement (or not), and it may be reproduced experimentally.
3. Although all IABs are more frequently associated with atrial arrhythmia, its incidence is much higher in advanced IABs when compared with partial IABs.
4. The presence of advanced IAB associated with supraventricular arrhythmias constitutes a true syndrome now termed as Bayes' syndrome.
5. Further studies will help in characterizing the syndrome in different clinical scenarios.

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