**Name of Journal: *World Journal of Clinical Cases***

**ESPS Manuscript NO: 29984**

**Manuscript Type: Minireviews**

**Bayés syndrome and acute cardioembolic ischemic stroke**

Arboix A *et al*. Bayés syndrome and acute stroke

**Adrià Arboix, Lucía Martí, Sebastien Dorison, María-José Sánchez**

**Adrià Arboix,** Division of Cerebrovascular, Universitat de Barcelona, 08029 Barcelona, Spain

**Adrià Arboix,** **Lucía Martí,** Department of Neurology, Hospital Universitari del Sagrat Cor, 08029 Barcelona, Spain

**Sebastien Dorison, María José Sánchez,** Medicine School, Universidad de los Andes, 111711 Bogotá, Colombia.

**Author contributions:** All the authors contributed to the manuscript.

**Conflict-of-interest** **statement:** The authors declare no conflicts of interest regarding this manuscript.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Correspondence to: Adrià Arboix, MD, PhD,** Division of Cerebrovascular, Department of Neurology, Hospital Universitari del Sagrat Cor, Universitat de Barcelona, Viladomat 288, 08029 Barcelona, Spain. [aarboix@hscor.com](mailto:aarboix@hscor.com)

**Telephone:** +34-93-4948940

**Fax:** +34-93-4948906

**Received:** September 2, 2016

**Peer-review started:** September 6, 2016

**First decision:** September 29, 2016

**Revised:** October 10, 2016

**Accepted:** December 7, 2016

**Article in press:**

**Published online:**

**Abstract**

Bayés syndrome is an under-recognized clinical condition characterized by advanced interatrial block. Bayés syndrome is a subclinical disease that manifests electrocardiographically as a prolonged *P* wave duration > 120 ms with biphasic morphology ± in the inferior leads. The clinical relevance of Bayés syndrome lies in the fact that is a clear arrhythmological syndrome and has a strong association with supraventricular arrhythmias, particularly atypical atrial flutter and atrial fibrillation. Likewise, Bayés syndrome has been recently identified as a novel risk factor for non-lacunar cardioembolic ischemic stroke and vascular dementia. Advanced interatrial block can be a risk for embolic stroke due to its known sequelae of left atrial dilation, left atrial electromechanical dysfunction or atrial tachyarrhythmia (paroxysmal or persistent atrial fibrillation), conditions predisposing to thromboembolism. Bayés syndrome may be responsible for some of the unexplained ischemic strokes and shall be considered and investigated as a possible cause for cryptogenetic stroke. In summary, Bayés syndrome is a poorly recognized cardiac rhythm disorder with important cardiologic and neurologic implications.

**Key words:** Bayés syndrome; Cardioembolic stroke; Electrophysiological processes; Cardiovascular risk factors; Heart conduction system

**© The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Bayés syndrome is an under-recognized cardiac rhythm disorder with significant cardiologic and neurologic implications. It constitutes a genuine arrhythmological syndrome characterized by advanced interatrial block. Bayés syndrome is a key predictor of higher risk of new-onset atrial fibrillation and it is independently associated with an increased risk for non-lacunar cardioembolic stroke. Likewise, can be the cause of some cryptogenic strokes, and be related to clinically silent cerebral ischemia and vascular cognitive impairment, or even, vascular dementia.

Arboix A, Martí L, Dorison S, Sánchez MJ. Bayés syndrome and acute cardioembolic ischemic stroke. *World J Clin Cases* 2016; In press

**INTRODUCTION**

Bayés syndrome is an under-recognized cardiological condition characterized by advanced interatrial block. Although it has yet to receive adequate coverage in textbooks and remains poorly perceived in clinical practice, Bayés syndrome represents a novel risk factor for cardioembolic ischemic stroke[1,2].

The principal goal of this mini-review is to expand and update knowledge of the little-known relationship between Bayés syndrome and acute ischemic cardioembolic stroke.

It should be noted that cardioembolic ischemic stroke accounts for one-quarter of all cerebral infarcts[3], is the most severe ischemic stroke subtype with a low prevalence of absence of neurological dysfunction at hospital discharge and a non-negligible risk of early embolic recurrence (1%-10%)[4-7], and has the highest in-hospital mortality (6%-27%)[3,4,8].

Compared to non-cardioembolic stroke, the percentage of female sex (54.3% *vs* 34.6%) and very old patients (≥ 85 years) (28.5% *vs* 18.3%) is more frequent. This may be explained by the increasing prevalence of atrial fibrillation with age. In the Framingham study, a growing population attributable risk of stroke due to atrial fibrillation with age was found, with a prevalence of atrial fibrillation of 1.8% in patients aged 60-69 years, 4.8% in those aged 70-79 years, and 8.8% in the 80 to 90 year group[9]. Similarly, the increased frequency of cardioembolic infarcts in women compared to non cardioembolic, which are more frequent in men, may also be related to increasing age observed in the industrialized societies, where women represent the majority of elderly people due to their higher life expectancy[10].

In the Sagrat Cor Hospital of Barcelona Stroke Registry (Table 1), which is one of the first stroke data banks of Catalonia and Spain, the short prognosis of patients with cardioembolic cerebral infarction is poorer compared to other subtypes of cerebral infarction with higher in-hospital mortality (21.9% vs 8.2%), whereas symptom free at discharge are less frequent (14.3% *vs* 19.9%)[7].

Recent studies have shown that Bayés syndrome is a key independent factor of cardioembolic cerebral ischemia[1,2], although there is still a need of high level of clinical suspicion in order to diagnose it. Early and proper diagnosis of Bayés syndrome is desirable and necessary, since patients will require closer clinical surveillance, and possibly accompanying antiarrhythmic and antithrombotic preventive therapies.

**CONCEPT AND DEFINITIONS**

In analogy to other cardiac conduction delays, atrial conduction abnormalities should be divided into partial and advanced interatrial blocks (aIAB) or Bayés syndrome. The syndrome of advanced interatrial conduction block due to conduction impairment in Bachmann’s bundle, results in delayed and retrograde activation of the left atrium that signifies a conduction delay between the left and right atria, and it is associated with a high incidence of atrial tachyarrhythmias, especially a particular and specific form of atypical atrial flutter or atrial fibrillation[11,12].

The first case of inter-atrial block was described by Bachmann in 1941[13]. Later, in 1971, Castillo and Vernant emphasized that when a *P* wave with plus/min (biphasic) morphology is observed in leads II, III, and avF, the atrial stimulus is blocked in the upper part of the septum[14]. Finally, between 1979 and 1985, Bayés *et al*[15,16] precisely analyzed the prevalence, pathological associations, and profile of the arrhythmias associated with aIAB, thereby defining a distinct and well-defined anatomo-electrical entity. Dr Bayés de Luna contribution was fundamental in demonstrating the association between advanced interatrial block and supraventricular arrhythmias, thus confirming a well-defined arrhythmic syndrome. The consensus of naming this association with the eponymous Bayés syndrome has recently been accepted by the scientific community in honor of Dr Antoni Bayés de Luna, the great Catalan master of clinical electrocardiography[1,17,18], for his contribution to the understanding of the natural history of this cardiac syndrome. However, Bayés syndrome remains an under-recognized clinical condition.

Bayés de Luna described the electrocardiographic pattern for identifying IAB and classified the types of block that occur at the atrial level. The distinction is based on the *P*-wave duration, and more important, the *P*-wave morphology: a partial block, indicated by a *P*-wave duration of 120 ms or more, and bifid *P* wave (notched *P*-wave) in leads II, III and aVF (Figure 1). If the interatrial block is advanced, also, the *P* wave is prolonged (duration 120 ms or more), but the second part of the P wave in inferior leads becomes negative (biphasic pattern or *P*-wave plus/min morphology) because of the retrograde activation of the left atrium (*P*-wave ± in II, III, and aVF) (Figure 2)[19-21].

It should be noted that, initially, IAB may occur transiently and may be reversible. It may be classified as first-degree (partial), second-degree (transient interatrial block or atrial aberrancy), or third-degree (advanced).There is consensus on considering transient interatrial block as a marker of electromechanical dysfunction of the left atrium and a risk factor for recurrence of atrial fibrillation[11,15].

Although the diagnosis of interatrial block is frequently associated with left atrial enlargement (LAE), there are some cases, especially of first-degree IAB, without this association. Therefore, it should be noted that IAB is a separate entity from atrial enlargement[11,22].

The prevalence of interatrial block is age-dependent, increasing from 5.4% at < 20 years old to 60% at > 50; in the same way, advanced IAB increases from 0.1% to 2% in patients with heart valve disease and cardiomyopathy[23,24]. The increased age-related risk may be probably due to atrial fibrosis which would result in impaired atrioventricular conduction through the atria. However, the exact pathogenesis has not been elucidated and various comorbidities, including coronary heart disease, arterial hypertension, and diabetes mellitus, have been proposed. The cause of IAB may be likely degenerative because of the increased incidence with age[11].

**ASSOCIATION OF INTERATRIAL BLOCK WITH SUPRAVENTRICULAR ARRHYTHMIAS**

The Bayés syndrome is a clear arrhythmological syndrome. Advanced IAB is a key predictor for high risk of new-onset atrial fibrillation after a successful cavo-tricuspid isthmus ablation in patients with typical atrial flutter[11,25].

A clinical study reported that 90% of patients with atrial fibrillation recurrence at one year had advanced IAB, and multivariate analysis demonstrated that persistent IAB was a predictor of AF recurrence. Advanced IAB is a useful marker to identify subjects who are at high risk for developing atrial fibrillation, and is a pre-atrial fibrillation condition associated with premature atrial beats[24].

Practical consequences and clinical implications of Bayés syndrome are the high incidence of atrial extrasystoles and paroxysmal supraventricular tachyarrhythmia, especially in patients with valvular heart disease or cardiomyopathy. A control group of patients with similar clinical states and left atrial size by echocardiography showed much lower incidence of these arrhythmias[11]. Bayés *et al*[26] also suggested that antiarrhythmic treatment prevents recurrences of atrial tachyarrhythmia in these cases.

There are currently no evidence-based recommendations on the most appropriate therapeutic approach for Bayés syndrome in any of the different cardiologic or neurologic guidelines for primary or secondary prevention of cerebral ischemia. A clinical case of a patient with Bayés syndrome reported antiarrhythmic treatment with amiodarone and anticoagulant administration with acenocoumarol[27].

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[11]. Increased P wave duration is the only P wave index significantly associated with increased cardiovascular mortality. Therefore, IAB as a subclinical disease merits elucidation as a marker of risk for adverse outcomes.

**A NEW RISK FACTOR FOR CEREBRAL INFARCT AND VASCULAR DEMENTIA**

Recently, Bayés syndrome has been shown to be a predictor of cardioembolic stroke[28]. There are three main consequences of advanced IAB: Firstly, IAB is a substrate for sustained AF, and the association between AF and advanced IAB has been demonstrated. Secondly, IAB results in poor left atrium (LA) contractility due to a delayed depolarization which can result in LA dysfunction. Such a delay has hemodynamic consequences including raised LA pressure and LA dilatation, which again is a substrate for AF. Thirdly, IAB may be associated with structural factors as a result of left atrium enlargement, although it may occur in patients with normal left atrium size[11].

As a result, advanced IAB could be a risk for embolic stroke due to its known sequelae of left atrial dilation, LA electromechanical dysfunction or atrial tachyarrhythmias, conditions which predispose to the formation of echocontrast, and may serve as a nidus for thrombi or microthrombi, and thus increase the risk for cardioembolic events. Because IAB predicts atrial fibrillation, patients with IAB may intermittently be in atrial fibrillation (paroxysmal atrial fibrillation), causing embolization[3,11].

Ariyarajah *et al*[2] analyzed 293 patients with cerebral infarct, 85 of them cardioembolic, and reported that 88% of cardioembolic infarcts showed sinus rhythm and 61% of these had advanced IAB, concluding that IAB could be a novel risk factor for embolic stroke.

In an analysis of ARIC (Atherosclerosis risk in Communities Study) advanced IAB was independently associated with an increased risk for ischemic stroke, thus definitively confirming IAB as a novel risk factor for cardioembolic ischemic stroke[29].

Cotter *et al*[30] reported an increased incidence of interatrial block in younger adults with cryptogenic stroke and patent foramen ovale, suggesting atrial arrhythmias as a possible cause of unexplained ischemic stroke in these patients. In another study, atrial fibrillation detected by implantable loop recorders in unexplained stroke was identified in 25.5% of cases, and AF was independently associated with interatrial conduction block[31].

In a clinical study the CHADS2 and CHADS2DS2-VASCc scores could predict the risk of ischemic stroke or TIA in patients with IAB without atrial fibrillation[32].

However, the association of Bayés syndrome and ischemic stroke is limited to non-lacunar cardioembolic infarcts[33,34]. Lacunar infarcts are an ischemic stroke subtype related mainly to hypertension and diabetes[35,36]. Ischemic stroke of unusual causes accounted for 5% of ischemic strokes and the association of advanced IAB in this ischemic stroke subtype is improbable[37].

By contrast, it is important to highlight that about 10%-30% of ischemic strokes remain cryptogenic despite reasonably thorough evaluations[38,39]. A possible explanation for this is that IAB may be responsible for some of the unexplained strokes.

Furthermore, atrial fibrillation is independently associated with an increased risk of vascular dementia. In a clinical study conducted in centenarians, the rate of dementia was 48% in subjects with a normal P wave, 60%in those with partial IAB, and 81% in those with advanced IAB and 90% in those with atrial fibrillation[40].

Table 2 shows the most relevant published studies about IAB as a cardiovascular risk factor and acute ischemic stroke[41-43].

**FUTURE RESEARCH**

Recognition of Bayés syndrome is not merely an academic issue. It allows selecting high-risk patients for which pharmacological therapy could be beneficial. Open questions remain to be addressed with well-designed clinical trials including whether antiarrhythmic and/or anticoagulant drugs could be used in patients with advanced IAB without atrial tachyarrhythmias to prevent both AF and embolic stroke.

Additional epidemiological studies would be needed to define the possible connection between Bayés syndrome and clinically silent cerebral infarctions, small vessel disease, cognitive impairment of vascular type or dementia.

**CONCLUSION**

Bayés syndrome is a poorly recognized cardiac rhythm disorder with important clinical implications. Bayés syndrome is a pre-atrial fibrillation condition and should be considered a novel and important risk factor for cardioembolic stroke and vascular cognitive impairment.

**ACKNOWLEDGMENTS**

We thank Drs J Massons, E Comes, M Oliveres, for their assistance in this study and Dr Antoni Bayés-Genís for allowing us to use the illustrative ECG of Figure 1 and the scheme of the anatomo-electrophysiologic features of the Bayés syndrome of Figure 2.

**REFERENCES**

1 **Bacharova L**, Wagner GS. The time for naming the Interatrial Block Syndrome: Bayes Syndrome. *J Electrocardiol* 2015; **48**: 133-134 [PMID: 25620789 DOI: 10.1016/j.jelectrocard.2014.12.022]

2 **Ariyarajah V**, Puri P, Apiyasawat S, Spodick DH. Interatrial block: a novel risk factor for embolic stroke? *Ann Noninvasive Electrocardiol* 2007; **12**: 15-20 [PMID: 17286646 DOI: 10.1111/j.1542-474X.2007.00133.x]

3 **Arboix A**, Alio J. Acute cardioembolic cerebral infarction: answers to clinical questions. *Curr Cardiol Rev* 2012; **8**: 54-67 [PMID: 22845816 DOI: 10.2174/157340312801215791]

4 **Weir NU**. An update on cardioembolic stroke. *Postgrad Med J* 2008; **84**: 133-42; quiz 139-40 [PMID: 18372484 DOI: 10.1136/pgmj.2007.066563]

5 **MacDougall NJ**, Amarasinghe S, Muir KW. Secondary prevention of stroke. *Expert Rev Cardiovasc Ther* 2009; **7**: 1103-1115 [PMID: 19764863 DOI: 10.1586/erc.09.77]

6 **Khoo CW**, Lip GY. Clinical outcomes of acute stroke patients with atrial fibrillation. *Expert Rev Cardiovasc Ther* 2009; **7**: 371-374 [PMID: 19379061 DOI: 10.1586/erc.09.11]

7 **Arboix A**, Vericat MC, Pujades R, Massons J, García-Eroles L, Oliveres M. Cardioembolic infarction in the Sagrat Cor-Alianza Hospital of Barcelona Stroke Registry. *Acta Neurol Scand* 1997; **96**: 407-412 [PMID: 9449481 DOI: 10.1111/j.1600-0404.1997.tb00307.x]

8 **Arboix A**, García-Eroles L, Massons J, Oliveres M. Predictive clinical factors of in-hospital mortality in 231 consecutive patients with cardioembolic cerebral infarction. *Cerebrovasc Dis* 1998; **8**: 8-13 [PMID: 9645975 DOI: 10.1159/000015809]

9 **Wolf PA**, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; **22**: 983-988 [PMID: 1866765 DOI: 10.1161/01.STR.22.8.983]

10 **Arboix A**. Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke. *World J Clin Cases* 2015; **3**: 418-429 [PMID: 25984516 DOI: 10.12998/wjcc.v3.i5.418.]

11 **Chhabra L**, Devadoss R, Chaubey VK, Spodick DH. Interatrial block in the modern era. *Curr Cardiol Rev* 2014; **10**: 181-189 [PMID: 24827803 DOI: 10.2174/1573403X10666140514101748]

12 **Ariyarajah V**, Apiyasawat S, Fernandes J, Kranis M, Spodick DH. Association of atrial fibrillation in patients with interatrial block over prospectively followed controls with comparable echocardiographic parameters. *Am J Cardiol* 2007; **99**: 390-392 [PMID: 17261404 DOI: 10.1016/j.amjcard.2006.08.043]

13 **Bachmann G**. The significance of splitting of the P-wave in the electrocardiogram. *Ann Intern Med* 1941; **14**: 1702-1709 [DOI: 10.7326/0003-4819-14-9-1702]

14 **Castillo A**, Vernant P. [Disorders of intraauricular conduction due to block of Bachman's bundle]. *Arch Mal Coeur Vaiss* 1971; **64**: 1490-1503 [PMID: 5001535]

15 **Bayes de Luna AJ**. [Block at the auricular level]. *Rev Esp Cardiol* 1979; **32**: 5-10 [PMID: 441485]

16 **Bayes de Luna A**, Fort de Ribot R, Trilla E, Julia J, Garcia J, Sadurni J, Riba J, Sagues F. Electrocardiographic and vectorcardiographic study of interatrial conduction disturbances with left atrial retrograde activation. *J Electrocardiol* 1985; **18**: 1-13 [PMID: 3156200]

17 **Conde D**, Baranchuk A. What Cardiologist must know about Bayés Syndrome. *Rev Argent Cardiol* 2014; **82**: 237-239

18 **Conde D**, Baranchuk A. [Interatrial block as anatomical-electrical substrate for supraventricular arrhythmias: Bayés syndrome]. *Arch Cardiol Mex* 2014; **84**: 32-40 [PMID: 24529591 DOI: 10.1016/j.acmx.2013.10.004]

19 **Bayés de Luna A**, Cladellas M, Oter R, Torner P, Guindo J, Martí V, Rivera I, Iturralde P. Interatrial conduction block and retrograde activation of the left atrium and paroxysmal supraventricular tachyarrhythmia. *Eur Heart J* 1988; **9**: 1112-1118 [PMID: 3208776]

20 **Bayés de Luna A**, Guindo J, Viñolas X, Martinez-Rubio A, Oter R, Bayés-Genís A. Third-degree inter-atrial block and supraventricular tachyarrhythmias. *Europace* 1999; **1**: 43-46 [PMID: 11220539 DOI: 10.1053/eupc.1998.0006]

21 **Bayés de Luna A**, Platonov P, Cosio FG, Cygankiewicz I, Pastore C, Baranowski R, Bayés-Genis A, Guindo J, Viñolas X, Garcia-Niebla J, Barbosa R, Stern S, Spodick D. Interatrial blocks. A separate entity from left atrial enlargement: a consensus report. *J Electrocardiol* 2012; **45**: 445-451 [PMID: 22920783 DOI: 10.1016/j.jelectrocard.2012.06.029]

22 **Tse G**, Lai ET, Yeo JM, Yan BP. Electrophysiological Mechanisms of Bayés Syndrome: Insights from Clinical and Mouse Studies. *Front Physiol* 2016; **7**: 188 [PMID: 27303306 DOI: 10.3389/fphys.2016.00188]

23 **Jairath UC**, Spodick DH. Exceptional prevalence of interatrial block in a general hospital population. *Clin Cardiol* 2001; **24**: 548-550 [PMID: 11501606 DOI: 10.1002/clc.4960240805]

24 **O'Neal WT**, Zhang ZM, Loehr LR, Chen LY, Alonso A, Soliman EZ. Electrocardiographic Advanced Interatrial Block and Atrial Fibrillation Risk in the General Population. *Am J Cardiol* 2016; **117**: 1755-1759 [PMID: 27072646 DOI: 10.1016/j.amjcard.2016.03.013]

25 **Mehrzad R**, Spodick DH. Interatrial block: a virtual pandemic requiring attention. *Iran J Med Sci* 2014; **39**: 84-93 [PMID: 24644376]

26 **Bayés de Luna A**, Oter MC, Guindo J. Interatrial conduction block with retrograde activation of the left atrium and paroxysmal supraventricular tachyarrhythmias: influence of preventive antiarrhythmic treatment. *Int J Cardiol* 1989; **22**: 147-150 [PMID: 2914739 DOI: 10.1016/0167-5273(89)90061-2]

27 **Baranchuk A**, Bayes-Genis A. Bayés' Syndrome. *Rev Esp Cardiol (Engl Ed)* 2016; **69**: 439 [PMID: 26948392 DOI: 10.1016/j.rec.2015.12.013]

28 **Hughes TM**, Worrall BB. Acute interatrial block is a distinct risk factor for ischemic stroke. *Neurology* 2016; **87**: 344-345 [PMID: 27343065 DOI: 10.1212/WNL.0000000000002905]

29 **O'Neal WT**, Kamel H, Zhang ZM, Chen LY, Alonso A, Soliman EZ. Advanced interatrial block and ischemic stroke: The Atherosclerosis Risk in Communities Study. *Neurology* 2016; **87**: 352-356 [PMID: 27343071 DOI: 10.1212/WNL.0000000000002888]

30 **Cotter PE**, Martin PJ, Pugh PJ, Warburton EA, Cheriyan J, Belham M. Increased incidence of interatrial block in younger adults with cryptogenic stroke and patent foramen ovale. *Cerebrovasc Dis Extra* 2011; **1**: 36-43 [PMID: 22566981 DOI: 10.1159/000327346]

31 **Cotter PE**, Martin PJ, Ring L, Warburton EA, Belham M, Pugh PJ. Incidence of atrial fibrillation detected by implantable loop recorders in unexplained stroke. *Neurology* 2013; **80**: 1546-1550 [PMID: 23535493 DOI: 10.1212/WNL.0b013e31828f1828]

32 **Wu JT**, Wang SL, Chu YJ, Long DY, Dong JZ, Fan XW, Yang HT, Duan HY, Yan LJ, Qian P. CHADS2 and CHA2DS2-VASc Scores Predict the Risk of Ischemic Stroke Outcome in Patients with Interatrial Block without Atrial Fibrillation. *J Atheroscler Thromb* 2016; Epub ahead of print [PMID: 27301462 DOI: 10.5551/jat.34900]

33 **Lorbar M**, Levrault R, Phadke JG, Spodick DH. Interatrial block as a predictor of embolic stroke. *Am J Cardiol* 2005; **95**: 667-668 [PMID: 15721117 DOI: 10.1016/j.amjcard.2004.10.059]

34 **Chhabra L**. Importance of P-wave indices in stroke. *Int J Cardiol* 2016; **203**: 962-963 [PMID: 26625321 DOI: 10.1016/j.ijcard.2015.11.102]

35 **Arboix A**, Font A, Garro C, García-Eroles L, Comes E, Massons J. Recurrent lacunar infarction following a previous lacunar stroke: a clinical study of 122 patients. *J Neurol Neurosurg Psychiatry* 2007; **78**: 1392-1394 [PMID: 17615167 DOI: 10.1136/jnnp.2007.119776]

36 **Arboix A**, López-Grau M, Casasnovas C, García-Eroles L, Massons J, Balcells M. Clinical study of 39 patients with atypical lacunar syndrome. *J Neurol Neurosurg Psychiatry* 2006; **77**: 381-384 [PMID: 16484649 DOI: 10.1136/jnnp.2005.071860]

37 **Arboix A**, Bechich S, Oliveres M, García-Eroles L, Massons J, Targa C. Ischemic stroke of unusual cause: clinical features, etiology and outcome. *Eur J Neurol* 2001; **8**: 133-139 [PMID: 11430270 DOI: 10.1046/j.1468-1331.2001.00180.x]

38 **Palomeras Soler E**, Fossas Felip P, Casado Ruiz V, Cano Orgaz A, Sanz Cartagena P, Muriana Batiste D. The Mataró Stroke Registry: a 10-year registry in a community hospital. *Neurologia* 2015; **30**: 283-289 [PMID: 24953407 DOI: 10.1016/j.nrl.2014.01.004]

39 **Purroy F**, Montaner J, Molina CA, Delgado P, Ribo M, Alvarez-Sabín J. Patterns and predictors of early risk of recurrence after transient ischemic attack with respect to etiologic subtypes. *Stroke* 2007; **38**: 3225-3229 [PMID: 17962602 DOI: 10.1161/STROKEAHA.107.488833]

40 **Martínez-Sellés M**, Massó-van Roessel A, Álvarez-García J, García de la Villa B, Cruz-Jentoft AJ, Vidán MT, López Díaz J, Felix Redondo FJ, Durán Guerrero JM, Bayes-Genis A, Bayes de Luna A. Interatrial block and atrial arrhythmias in centenarians: Prevalence, associations, and clinical implications. *Heart Rhythm* 2016; **13**: 645-651 [PMID: 26520207 DOI: 10.1016/j.hrthm.2015.10.034]

41 **Pirinen J**, Putaala J, Aro AL, Surakka I, Haapaniemi A, Kaste M, Haapaniemi E, Tatlisumak T, Lehto M. Resting 12-lead electrocardiogram reveals high-risk sources of cardioembolism in young adult ischemic stroke. *Int J Cardiol* 2015; **198**: 196-200 [PMID: 26163917 DOI: 10.1016/j.ijcard.2015.06.095]

42 **Enriquez A**, Sarrias A, Villuendas R, Ali FS, Conde D, Hopman WM, Redfearn DP, Michael K, Simpson C, De Luna AB, Bayés-Genís A, Baranchuk A. New-onset atrial fibrillation after cavotricuspid isthmus ablation: identification of advanced interatrial block is key. *Europace* 2015; **17**: 1289-1293 [PMID: 25672984 DOI: 10.1093/europace/euu379]

43 **Ariyarajah V**, Apiyasawat S, Najjar H, Mercado K, Puri P, Spodick DH. Frequency of interatrial block in patients with sinus rhythm hospitalized for stroke and comparison to those without interatrial block. *Am J Cardiol* 2007; **99**: 49-52 [PMID: 17196461 DOI: 10.1016/j.amjcard.2006.07.060]

**P-Reviewer:** Aggarwal A, Petix NR, Petretta M, Said SAM **S-Editor:** Qiu S **L-Editor: E-Editor:**

**Table 1 Demographic, cerebrovascular risk factors, neuroimaging and outcome in the first-ever cardioembolic stroke versus first-ever non-cardioembolic cerebral infarct population**

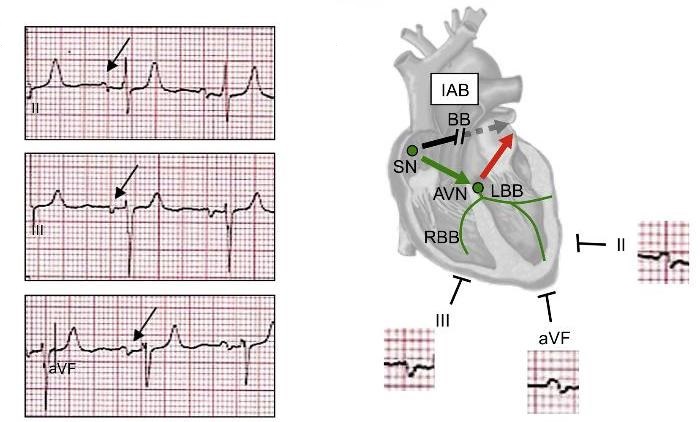
|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Cardioembolic stroke**  ***n* = 575** | **Non-cardioembolic cerebral infarct1**  ***n* = 1.507** | ***P* value** |
| Age, years, mean (SD) | 78.96 (9.39) | 73.45 (12.8) | 0.0001 |
| Age strata, yr |  |  | 0.0001 |
| < 65 | 44 (7.6) | 285 (18.9) |  |
| 65-74 | 116 (20.2) | 405 (26.9) |  |
| 75-84 | 251 (43.7) | 557 (37.0) |  |
| ≥ 85 | 164 (28.5) | 260 (17.3) |  |
| Sex |  |  | 0.0001 |
| Males | 199 (34.6) | 788 (52.3) |  |
| Females | 373 (65.4) | 719 (47.7) |  |
| Hypertension | 291 (50.6) | 835 (55.4) | 0.049 |
| Diabetes | 103 (17.9) | 368 (24.4) | 0.002 |
| Atrial fibrillation | 433 (75.3) | 176 (11.7) | 0.0001 |
| Heavy smoking (> 20 cigarettes/day) | 23 (4.0) | 184 (12.2) | 0.0001 |
| ACM vascular topography | 391 (68.0) | 703 (46.6) | 0.0001 |
| Ecocardiography | 363 (63.1) | 598 (39.7) | 0.0001 |
| Symptom-free at discharge | 82 (14.3) | 300 (19.9) | 0.003 |
| In-hospital death | 126 (21.9) | 123 (8.2) | 0.0001 |
| Transfer to convalescent/rehabilitation units | 89 (15.5) | 154 (10.2) | 0.001 |
| Length of stay, days, median (interquartile range) | 15 (10-24) | 11 (8-19) | 0.0001 |
| Prolonged hospital stay > 12 d | 330 (57.4) | 650 (43.1) | 0.0001 |

Data expressed as numbers and percentages in parenthesis. **1**Atherothrombotic, *n* = 565; lacunar, *n* = 566; essential, *n* = 280; unusual, *n* = 96.

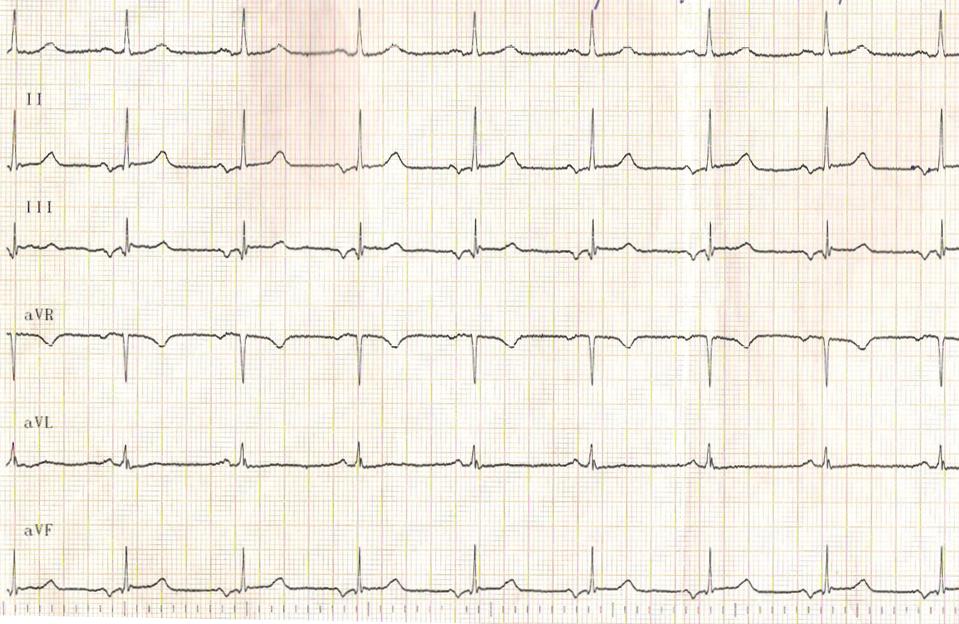
**Table 2 Main studies of Interatrial Block as a cerebrovascular risk factor or as a predictor for acute ischemic stroke (period 1979-2016)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Study type** | **n** | **Age**  **(yr)** | **Gender** | **Inclusion criteria** | **Exclusion criteria** | **Confounding factors** | **Parameters evaluated** | **Results** |
| Wu *et al*[32] | Retrospective cohort | 1,046 | 63 ± 10 | 612 males  434 females | - Patients hospitalized in Zhengzhou University People's Hospital for diagnosis and treatment between March 1 and March 31 of 2010  - ECG  - Presence of IAB | - History of AF  - Patients under anticoagulant treatment  - Missing data for calculation of CHADS₂ and CHA₂DS₂-VASc scores  - Lost to follow-up | - Congestive Heart Failure  - Hypertension  - Diabetes Mellitus  - Previous strokes/ TIA  - Coronary Artery Disease  - PCI during index admission  - CABG during index admission  - Tobacco consumption  - LVEF  - LA diameter  - Medication Use | - Conduction lengths  - CHADS₂ and CHA₂DS₂-VASc scores  - Apparition of Stroke (Hemorrhagic or Ischemic) | - Mean follow-up of 4.9 ± 0.7 years  - 0.8% hemorrhagic stroke  - 5.3% presented ischemic stroke or TIA  - Ischemic stroke or TIA increased with CHADS₂ score: 0.37, 0.85, 0.96 and 1.92 per 100-person years for scores of 0, 1, 2, and > 3 respectively.  - CHA₂DS₂-VASc scores correlated with Ischemic stroke or TIA (0.19, 0.59, 0.76, 0.88, and 2.0 for scores of 0, 1, 2, 3, and > 4 respectively)  - Cut-off points: > 3 for CHADS₂, > 4 for CHA₂DS₂-VASc  Conclusion: CHADS₂ and CHA₂DS₂-VASc scores may be predictors of risk of ischemic stroke or TIA in patients with IAB without atrial fibrillation |
| Martinez-Selles *et al*[40] | Case-control | 80 | 101.4 ± 1.5 | 21 males  59 females | - Patients from the Cardiac and Clinical Characterization of Centenarians (4C) Registry | - Hospitalized patients | - Dementia  - Perceived health status score  - Previous stroke  - Mitral regurgitation  - Systolic Dysfunction  - Left atrial diameter > 40mm | - Conduction lengths  - ECG measurements  - Short Portable Mental Status Questionnaire  - Premature atrial beats | - IAB group showed higher rate of previous stroke than normal P wave and AF groups  - Premature atrial beats were more frequent in advanced IAB than normal *P*-wave  - Mitral regurgitation could play an important role in IAB  Conclusion: advanced IAB is a pre-atrial fibrillation condition associated with premature atrial beats. Atrial arrhythmias and IAB occurred more frequently in centenarians than in septuagenarians. |
| O'Neal *et al*[24] | Retrospective cohort | 14,716 | 54 ± 5.8 | 6,622 males  8,094 females | - Patients enrolled in the Atherosclerosis Risk in Communities (ARIC) Study  - Recruited between 1987 and 1989 | - Patients with prevalent stroke or AF at baseline  - Race other than black or white  - Black participants from Washington County and Minneapolis | - Black  - Tobacco use  - Diabetes  - LDL cholesterol level  - BMI  - Hypertension  - Antihypertensive medication  - Coronary heart disease  - Heart failure | - Conduction lengths  - Presence of stroke  - Stroke type | - Incidence rate of ischemic stroke was higher in aIAB (8.05/1000 person-years *vs* 3.14; *P* < 0.0001)  Conclusion: aIAB was associated with incident ischemic stroke |
| O'Neal *et al*[29] | Retrospective cohort | 14,625 | 54 ± 5.8 | 6,581 males  8,044 females | - Patients enrolled in the Atherosclerosis Risk in Communities (ARIC) Study  - Recruited between 1987 and 1989 | - Participants with AF at baseline  - Missing baseline covariates  - Missing follow-up data  - Race other than black or white  - Black participants from Washington County and Minneapolis | - Black  - Tobacco consumption  - Diabetes  - LDL cholesterol level  - BMI  - Hypertension  - Antihypertensive medication  - Coronary heart disease  - Heart failure | - Conduction lengths | - Total of 262 aIAB (69 baseline, 193 new)  - 1,929 AF cases were identified  - aIAB patients presented an AF incidence of 29.8/1000 *vs* 6.8/1000 of non-aIAB; HR = 3.09 (*P* < 0.0001)  Conclusion: aIAB is a useful marker to identify high risk subjects for developing atrial fibrillation |
| Pirinen *et al*[41] | Case-control | 690 | 15 - 49 | 438 males  252 females | - Correct diagnosis of IS  - Part of the Helsinki Young Stroke Study | - Unknown stroke date  - Outpatient treatment only  - No ECG OR only take on the day of stroke in ER OR no ECG between day of stroke and 14 d after | - Obesity  - Hypertension  - Tobacco use  - Dyslipidemia  - CHF  - Preexisting AF  - DM1, DM2  - Composite of Cardiovascular Disease | - Arrhythmia types  - Conduction lengths  - Stroke etiology | Most Common ECG abnormalities:  - T-wave inversion (LVH (14%),  - prolonged *P*-wave (13%),  - prolonged QTc (12%).  - Most ECG abnormalities in the Stroke Etiology Subgroups: HRCE, LAA and SVD  Conclusion: Routine ECG provides useful information for directing the work-up of a young IS patient. In addition to AF, P-terminal force in particular showed a strong association with etiology of high-risk source of cardioembolism |
| Enriquez *et al*[42] | Prospective cohort | 187 | 67 ± 10.7 | *not reported* | - Patients with typical atrial flutter (AFI) with no prior history of AF referred for CTI ablation | - Patients that had received repeat ablations or did not demonstrate a bidirectional block | *not reported* | - Conduction lengths  - Ejection fraction  - Holter monitoring  - Device interrogations | - Advanced IAB was detected in 18.2% of patients  - Left atrium was larger in aIAB (46.2 ± 5.9 *vs* 43.1 ± 6.0 mm; *P* = 0.01)  - 35.8% of patients developed new-onset AF  - AF was greater in patients with aIAB (64.7% *vs* 29.4%; *P* < 0.001)  Conclusion: Advanced interatrial block is a key predictor for high risk of new-onset AF after a successful CTI ablation in patients with typical AFl. |
| Cotter *et al*[31] | Retrospective  cohort | 51 | 17 - 73 | 28 males  23 females | - ILR implanted after unexplained ischemic stroke  - Brain imaging consistent with embolism  - Arterial imaging  - Structural cardiac imaging and rhythm monitoring  - 50 d of continuous monitoring | - TIA  - Documented cause of stroke before ILR implantation  - Intrinsic small-vessel disease cause  - Atheromatosis stenosis > 50% or dissection  - High-risk cardiac embolic source  - No AF detected in 24h - Holter | *not reported* | - Rhythm monitoring  - ECG  - Conduction lengths  - CHADS₂ and CHA₂DS₂-VASc scores | - 25.5% of cases had AF  - IAB more prevalent in patients with AF (*P* = 0.02)  - AF patients larger LA volumes (*P* =0.025)  - Mean AF duration was 6 minutes.  Conclusion: In patients with unexplained stroke atrial fibrillation was detected by implantable loop recorders in 25.5%. IAB was an independent predictor of AF. |
| Cotter *et al*[30] | Case-control | 78 | 24 - 55 | 49 males  29 females | - ≤ 55 years at time of stroke  - index cerebral infarct with no cause found  - CT or MRI imaging, cervical vascular imaging, ECG and rhythm monitoring | - Poor quality data | *not reported* | - Conduction lengths  - PFO status  - A-S-C-O Classification | - IAB more frequent in cases than controls (40 *vs* 13%) (*P* < 0.05).  - 74.6% of stroke showed PFO (70.3% large)  - No statistical difference of *P*-wave length (with *vs* without PFO)  Conclusion: In young patients with unexplained stroke, particularly those with patent foramen ovale atria l dysfunction is a possible mechanism of stroke |
| Ariyarajah *et al*[43] | Case-control | 66 | 60 - 87 | 39 males  27 females | - Definitive acute or subacute cerebral infarct  - Probable embolic origin | - No 12-lead ECG during 14 d post infarct  - Non-sinusal rhythm detected in ECG | - Hypertension  - Valvulopathies  - Cardiomyopathies  - Tobacco Use  - Dyslipidemia  - Diabetes Mellitus  - Hyper/Hypothyroidism  - COPD  - Florid Heart Failure  - Cardiac Catheterization  - Myocardial Infection  - Valvuloplasty  - Previous strokes/ TIA  - History of AF/Flutter  - CAD | - Echocardiogram  - Conduction lengths | - 61% IAB prevalence  - CAD paroxistically more present in control, perhaps due to atherosclerotic origin  - LA more prevalent in IAB group, with greater LA thrombi (83% *vs* 0%)  Conclusion: IAB could be a risk factor for embolic stroke due to its known sequelae of left atrial dilation and electromechanical dysfunction that predispose to thrombosis. |
| Ariyarajah *et al*[2] | Case-control | 228 | 30 - 102 | 118 males  110 females | - Studied for suspicion of stroke\* with CT Scan and MRI | - No 12-lead ECG during 14 d post infarct | - Hypertension  - Valvulopathies  - Cardiomyopathies  - Tobacco Use  - Dyslipidemia  - Diabetes Mellitus  - Hyper/Hypothyroidism  - COPD  - Florid Heart Failure  - Cardiac Catheterization  - Myocardial Infection  - Valvuloplasty  - Previous strokes/ TIA  - History of AF/Flutter  - CAD | - Conduction lengths  - Stroke etiology | - 61% IAB embolic *vs* 40% non-embolic (*P* = 0.006)  - Hypertension for embolic stroke (*P* < 0.0001)  Conclusion: IAB could be a novel risk for embolic stroke |
| Ariyarajah *et al*[12] | Prospective cohort | 32 | 66 - 94 | 15 males  17 females | - Saint Vincent Hospital general patients (Dec. 15, 2004 to Jan. 14, 2005)  - Resting ECG obtained on admission  - Existing 2-dimensional transthoracic echocardiograms  - Sinus rhythm | *not reported* | - Mitral or tricuspid valvular disease  - Hypertension  - Coronary artery disease  - Hyperlipidemia  - Diabetes mellitus  - History of AF/Flutter  - ACEI use  - Beta-blocker use  - Statins use | - Conduction lengths  - LA dimension  - LVEF  - Cardiovascular events (heart failure, peripheral embolism, transient ischemic attack, stroke, atrial tachyarrhythmias) | - Coronary disease was more prevalent in the IAB group  - Cardiovascular events were overall most significant in IAB, except for stroke, TIA, peripheral arterial embolism and atrial flutter  Conclusion: In patients with comparable echocardiographic parameters, IAB remained associated with atrial fibrillation after 15-months follow-up. |
| Lorbar *et al*[33] | Retrospective  cohort | 104 | 22 - 101 | 58 males  46 females | - St Vincent Hospital (Jan. 2000 to Dec. 2001) patients with ICD codes for embolic stroke  - Diagnosis of embolic ischemic stroke or TIA by a neurologist with or without imaging techniques | - Cerebrovascular events non ICD codes  - Dementia, seizure, hypertensive encephalopathy, subdural hematoma, dizziness, vertigo, psychosis, and headache | not reported | - Conduction lengths  - ECG patterns | - 41% history of AF, or newly diagnosed AF  - 80% normal sinus rhythm patients showed IAB on concurrent ECG  Conclusion: IAB may represent a new factor for stroke. |
| Jairat *et al*[23] | Prospective cohort | 1000 | 24-94 | 585 males  415 females | - Saint Vincent Hospital general patients | not reported | not reported | - Conduction lengths  - ECG patterns | - 32.8% of all patients showed IAB  - 41.1% of sinus rhythm patients showed IAB  Conclusion: Patients with IAB must be followed for atrial enlargement, potential thrombosis, and the onset of atrial fibrillation |

ACEI: Angiotensin converting enzyme inhibitor; AF: Atrial fibrillation; aIAB: Advanced intraatrial block; BMI: Body Mass Index; CABG: Coronary artery bypass grafting; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CHF: Chronic heart failure; CT: Computed tomography; CTI: Cavotricuspid isthmus; DM1: Diabetes mellitus 1; DM2: Diabetes mellitus 2; ECG: Electrocardiogram; ER: Emergency room; HR: Hazard Ratio; HRCE: High-risk source of cardioembolism; IAB: Intraatrial block; ILR: Implantable loop recorder; IS: Ischemic stroke; LA: Left atrium; LAA: Large artery atherosclerosis; LDL: Low density lipoprotein; LVEF: Left ventricular ejection fraction; LVH: Left ventricle hypertrophy; MRI: Magnetic resonance imaging; PCI: Percutaneous coronary intervention; PFO: Permeable foramen ovale; SVD: Small-vessel disease; TIA: Transient ischemic attack.

****

**Figure 1 Scheme of the anatomo-electrophysiologic features of the Bayés syndrome[27].** AVN: AV node; BB: Bachmann bundle; IAB: Interatrial block; LBB: Left bundle branch; RBB: Right bundle branch; SN: Sinus node.



**Figure 2 A 55-year-old male diagnosed with Bayés syndrome, with a history of paroxysmal atrial fibrillation showing normal values of echocardiographic measurements, except for a discrete left atrial enlargement (40 mm).** ECG shows the presence of advanced interatrial block. *P*-wave duration is wide (120 ms) and biphasic in inferior leads (II, III and aVF). ECG: Electrocardiogram.