

# Role of electrophysiological study in patients with syncope and bundle branch block

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**Background:** The finding of bundle branch block (BBB) in patients with syncope suggests that paroxysmal atrioventricular block (AVB) or ventricular tachyarrhythmia (VT) may be the cause of syncope. Guidelines for cardiac pacing and cardiac resynchronization therapy have been recommended to perform electrophysiological study (EPS) for confirming main cause of syncope. Therefore, the aim of our study was to evaluate the role of EPS in patients with syncope and BBB. **Materials and Methods:** We evaluated 133 patients (mean age  $63 \pm 13.8$  years) with past history of syncope and BBB from April 2002 to December 2010 who referred to Arrhythmia clinic in two tertiary care centers. All patients underwent EPS on admission time. The frequency distributions of AVB and VT in patients were determined. **Results:** Left bundle branch block was diagnosed in 184 (82.1%) patients. 133 of them had preserved left ventricular ejection fraction (LVEF  $\geq 45\%$ ) that in 91 (68.4%) of those, EPS finding was normal. In 41 (30.8%) patients AVB was reported. In 2 (1.5%) patients VT and atrioventricular nodal reentrant tachycardia were seen. Coronary artery disease was more common in patients with AVB and abnormal EPS finding ( $P = 0.02$ ). **Conclusion:** Ventricular tachyarrhythmia was a rare electrophysiological finding in those with syncope, bifascicular block, and preserved LVEF. Considering cost-effect benefit, pacemaker or implantable loop recorder implantation is suggested; however, EPS may not be necessary to perform before permanent pacemaker implantation.

**Key words:** Atrioventricular block, electrophysiological study, left bundle branch block, permanent pacemaker implantation, syncope, ventricular tachyarrhythmia

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## INTRODUCTION

Atrioventricular block (AVB) may develop in patients with bundle branch block (BBB). The risk of developing AVB increases up to 17% in patients with syncope and BBB during 42 months follow-up.<sup>[1]</sup> In addition, patients with BBB and syncope have an unusually high incidence of cardiac disease and sudden cardiac death (SCD), which is mostly among patients with left bundle branch block (LBBB) and cardiac disease specially heart failure.

Implantable cardioverter defibrillator (ICD) is recommended in patients with syncope and severe left ventricular (LV) dysfunction. Syncope in those with preserved LV function may occur due to advanced His-Purkinje disease or ventricular tachyarrhythmia (VT), therefore according to permanent pacemaker implantation (PPM) Guideline published in 2007, complete electrophysiological study (EPS) was recommended to exclude a VT as a cause of syncope because the therapies are different.<sup>[2-6]</sup> In recent investigations, the prevalence of bradyarrhythmias

is more reported in in patients with BBB.<sup>[7,8]</sup> The aim of this study was to investigate the role of VT study, determining predictors of abnormal EPS, and risk of SCD in patients with BBB, preserved LV function (it was defined on the basis of a left ventricular ejection fraction [LVEF]  $>45\%$  by echocardiography) and syncope.

## Study population

In a retrospective study, 224 patients with BBB and syncope between April 2002 and December 2009 were evaluated at two tertiary referral centers; Rajaie Cardiovascular Medical and Research Centre, Heshmat Cardiovascular Medical and Research Center, Rash University of Medical Sciences. Baseline information, including age, underlying disease, sex, and cardiovascular medication ( $\beta$ -blocker, Ca<sup>+2</sup>-blocker, digoxin, and anti-arrhythmic agents) was reviewed from medical records. Patients with LVEF  $\leq 45\%$ , congenital heart disease, Q-wave myocardial infarction (MI), and neuromuscular disease were excluded (91). Palpitation, sweating, nausea, vomiting, dizziness, and blurred vision were considered as

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prodromal symptoms. Patients were followed every 3-6 month at our outpatient syncope clinic. Syncope may occur due to effective drugs on conduction system. It is necessary to discontinue them before EPS. All medications were discontinued for 5 half-life as in all EPS study the drugs should be discontinued.

## MATERIALS AND METHODS

### Study protocol

All participants underwent EPS. An EPS was considered normal in the absence of one of abnormal sinus node recovery time (SNRT), baseline His bundle to the ventricle (HV) interval (the conduction time from the HV)  $\geq 70$  ms, His-Purkinje block demonstrated during incremental atrial pacing or after procainamide administration and induction of sustained monomorphic ventricular tachycardia (SMMVT) or Supraventricular tachycardia with programmed electrical stimulation. The EPS included measurement of corrected SNRT; HV interval at baseline and under stress by incremental atrial pacing and procainamide infusion (10 mg/kg over 10 min); inducibility of ventricular arrhythmia by means of programmed ventricular stimulation in two drive cycle length (600,400) with three extra stimuli. EPS was considered normal in the absence of one of abnormal SNRT, baseline HV interval (the conduction time from the HV)  $\geq 70$  ms, His-Purkinje block demonstrated during incremental atrial pacing or after procainamide administration and induction of SMMVT or supraventricular tachycardia with programmed electrical stimulation.<sup>[9,10]</sup> Inform consent was taken from all the patients and all they were satisfy with the procedural process.

### Statistical analysis

Data were expressed as mean  $\pm$  standard deviation if continuous and as counts and percent if categorical. Data analysis was performed using SPSS software package (version 15, SPSS, Inc., Chicago, IL, USA). Continuous variable were compared with ANOVA. Categorical data were compared with Chi-square. Differences in proportions were compared using Chi-square analysis for categorical variable and independent Student's *t*-test for continuous variables.  $P < 0.05$  were considered as statistically significant.

## RESULTS

A total of 133 patients (92 male, mean age;  $63 \pm 13.8$  years) met the inclusion criteria for analysis. All the patients were in sinus rhythm. Mean LVEF was  $52.34 \pm 2.73$ %. The follow-up duration was  $3.7 \pm 2.24$  years. Eight patients were lost to follow-up. Abnormal EPS finding was more observed in patients with  $>2$  syncope episodes during last 6 months ( $P = 0.001$ ). Coronary artery disease (CAD) was more common in patients with AVB and abnormal EPS

**Table 1: Baseline demographic characteristics**

Baseline characteristics	All patients (n = 133)
Age (mean $\pm$ SD, years)	Mean=62.6 $\pm$ 14
Sex (male/female)	92/41
Follow-up period (years, %)	3.7 $\pm$ 2.24
Sinus rhythm	128 (96.24)
LBBB/RBBB + IVCD	110/23
First degree AVB (n, %)	31 (23)
LVEF (mean $\pm$ SD)	52.34 $\pm$ 2.73
Number of syncope (mean $\pm$ SD)	3 $\pm$ 1.09 (1-6)
Patients with $>2$ syncope and at least one syncope during last 6 months (n, %)	50 (37)
Prodromal symptoms before syncope (n, %)	65 (48)
Lost data during follow-up (n, %)	8 (6.1)

The results are presented as mean  $\pm$  SD (range) or number (%) where applicable. LBBB = Left bundle branch block; RBBB = Right bundle branch block; SD = Standard deviation; IVCD = Intraventricular conduction defect; AVB = Atrioventricular block; LVEF = Left ventricular ejection fraction

**Table 2: Clinical characteristics of the patients with normal and abnormal EPS**

Demographic data and clinical variables	Normal EPS (n = 91 (%))	Abnormal EPS (n = 131 (%))	P value
Age (years)	62.6 $\pm$ 13.8	62 $\pm$ 17.7	NS
Sex (male/female)	20/44	21/48	NS
Number (mean $\pm$ SD) of syncope	2.6 $\pm$ 0.90	3.3 $\pm$ 1.15	0.01
$>2$ syncope episodes with at least one syncope during last 6 months	13 (14.28)	37 (28.24)	0.001
Prodromal symptoms (n)	40 (15.38)	25 (19.8)	0.01
Persistent AVB at the end of follow-up	8 (8.79)	30 (2.29)	$<0.001$
CAD	20 (21.97)	32 (24.42)	0.021

SD = Standard deviation; CAD = Coronary artery disease; AVB = Atrioventricular block; EPS = Electrophysiological study.  $P < 0.05$  considered as the level of significance. The results are presented as mean  $\pm$  SD (range) or number (%) where applicable

finding ( $P = 0.02$ ). Baseline and clinical characteristics of these patients are depicted in Tables 1 and 2.

Of the 133 patients, 110 (82.7%) patients had LBBB. Mean LVEF was  $52.34 \pm 2.78$ %. His-Purkinje (HV) interval  $\geq 70$  ms and/or AVB were seen in 45 (40%) of the patients before procainamide infusion and in 61 (55%) of them after drug challenge test. 34 (30.9%) patients had AVB. SMMVT and ventricular flutter were inducible in one and two patients, respectively. 48 (44%) patients had prodromal symptoms. Palpitation was reported by 12 (11%) patients and two of them had sudden onset palpitation with inducible SMMVT in one and atrioventricular nodal reentrant tachycardia another patient in EPS. The number of syncopal attacks was more in patients with abnormal finding in EPS or occurrence of AVB during follow-up ( $P = 0.001$ , and  $P = 0.01$ , respectively).

Out of 34 patients with AVB after high right atrial pacing or after procainamide infusion, 27 (79.4%) of them had HV interval  $<100$  ms and only 7 (20.6%) patients had HV interval

>100 ms ( $P=0.001$ ). Forty-five (40%) patients with LBBB and preserved LVEF had ischemic etiology.

Permanent pacemaker implantation was recommended in all patients without inducible ventricular tachycardia. Ten patients refuse pacemaker implantation. Therefore, implantable loop recorder (ILR) was implanted for five patients. Complete AVB was detected in two patients with ILR. ICD was implanted for those with ventricular tachyarrhythmia. Two of three patients received inappropriate discharge during follow-up.

Of the 133 patients, 23 had right bundle branch block (RBBB). EPS was normal in 16 (69.6%) patients. Six patients with abnormal EPS had first degree AVB and/or left anterior hemiblock. EPS was normal in 10 patients with pure RBBB. Prodromal symptoms were reported by 11 (48%) patients. In this group, LVEF was  $52.7 \pm 2.13$  and CAD was detected in 7 (30%) patients ( $P = 0.021$ ). Pacemaker was implanted for those with abnormal EPS.

All pacemakers were evaluated every 6 months. Persistent AVB was defined as presence of complete heart block, 2:1 AVB, or advanced AVB during periodic pacemaker analysis. Persistent AVB was detected in 38 patients at the end of follow-up.

## DISCUSSION

The main finding of this study was the inducibility of VT in patients with syncope, BBB and normal LV function. Even though according to some studies, VT will be found in one-third to one half of patients with wide QRS and syncope.<sup>[11,12]</sup> However, regarding to this study it's a rare finding in patients with normal LV systolic function. This difference may be due to consideration of both LV dysfunction and preserved LV systolic function for sample population. It was shown that in patients with BBB and normal EPS, and implantation of ILR was shown that most recurrent syncope episodes are due to prolonged a systolic pauses, mainly attributable to sudden onset paroxysmal AVB.<sup>[1-4,13,14]</sup> This study demonstrated a significant relationship between clinical variables such as sudden onset palpitation, absence of prodromal, and recent frequent episodes of syncope (defined as more than two syncope episodes with at least one syncope during last 6 months) and abnormal EPS. Consistent with our study, other investigators demonstrated relationship between some clinical variables and arrhythmic causes of syncope.<sup>[7,8]</sup> Presence of CAD in our patients depicts more advances His-Purkinje disease.

Since the high-incidence of short-term AVB in patients with syncope and BBB who have a normal HV conduction time, an acceptable strategy could be to implant a PPM rather

than a loop recorder (Class 2).<sup>[1]</sup> Abnormal HV interval or induction of AVB by programmed atrial stimulation with or without procainamide stress test identify high risk patients for spontaneous AVB and syncope in future, but normal EPS does not exclude the development of AVB. Previous studies demonstrated that patients with BBB and syncope are at risk of SCD and permanent pacemaker cannot reduce the risk of SCD. However, our study shows that SMMVT and SCD are rare findings in patients with BBB and syncope in EPS and during follow-up, respectively. We can interpret this discrepancy somehow by normal LV function and exclusion of those with history of Q-wave MI in study group. The pathologic substrate for patients with VT associated with CAD is usually a prior MI resulting in wall motion abnormality. The greater wall motion abnormality, the higher-incidence of aneurysm formation; and lower EF, the more likely is development of SMM VT and SCD.<sup>[2]</sup>

## Study limitation

The principal limitations of this study include its retrospective design. The other limitation of this study was the fact that we had no prolonged follow-up for patients with normal EPS finding.

## CONCLUSION

Ventricular tachyarrhythmia was a rare electrophysiological finding in those with syncope, bifascicular block, and preserved LVEF. Considering cost-effect benefit, pacemaker or ILR implantation is suggested; however, EPS may not be necessary to perform before PPM. According to our findings, pacemaker or ILR implantation is suggested and may not necessary to perform EPS before PPM.

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## AUTHOR'S CONTRIBUTION

NN collected the data. AK collected the data. SS examined the patients and case selection. MH examined the patients and case selection. AG case selection, EPS, managing the patients. MAR data collection. AA EPS of the patients, leader of the project. MH provide scientific writing of the manuscript, editing and submitting the paper.

## REFERENCES

1. McAnulty JH, Rahimtoola SH, Murphy E, DeMots H, Ritzmann L, Kanarek PE, *et al.* Natural history of "high-risk" bundle-branch block: Final report of a prospective study. *N Engl J Med* 1982;307:137-43.

2. Vardas PE, Auricchio A, Blanc JJ, Daubert JC, Drexler H, Ector H, *et al.* Guidelines for cardiac pacing and cardiac resynchronization therapy. The task force for cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology. Developed in collaboration with the European Heart Rhythm Association. *Europace* 2007;9:959-98.
3. Brignole M, Menozzi C, Moya A, Garcia-Civera R, Mont L, Alvarez M, *et al.* Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. *Circulation* 2001;104:2045-50.
4. Donato P, Brignole M, Alboni P, Menozzi C, Raviele A, Del Rosso A, *et al.* A standardized conventional evaluation of the mechanism of syncope in patients with bundle branch block. *Europace* 2002;4:357-60.
5. Eriksson P, Wilhelmsson L, Rosengren A. Bundle-branch block in middle-aged men: Risk of complications and death over 28 years. The Primary prevention study in Göteborg, Sweden. *Eur Heart J* 2005;26:2300-6.
6. Task Force for the Diagnosis and Management of Syncope, European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA), Heart Rhythm Society (HRS), Moya A, *et al.* Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J* 2009;30:2631-71.
7. Martí-Almor J, Cladellas M, Bazán V, Delclós J, Altaba C, Guijo MA, *et al.* Novel predictors of progression of atrioventricular block in patients with chronic bifascicular block. *Rev Esp Cardiol*. 2010;63:400-8.
8. Tabrizi F, Rosenqvist M, Bergfeldt L, Englund A. Long-term prognosis in patients with bifascicular block-the predictive value of noninvasive and invasive assessment. *J Intern Med* 2006;260:31-8.
9. Fazelifar AF, Ashrafi P, Haghjoo M, Haghghi ZO, Abkenar HB, Ashour A, *et al.* Predictors of ventricular tachycardia induction in syncopal patients with mild to moderate left ventricular dysfunction. *Cardiol J* 2009;16:327-31.
10. García Civera R, Sanjuán Máñeza R, Ruiz Granell R, Morell Cabedo S, Carlos Porres Azpíroz J, Ruiz Ros V, *et al.* Diagnostic accuracy of a protocol in the evaluation of unexplained syncope. *Rev Esp Cardiol* 2001;54:425-30.
11. Krahn AD, Morillo CA, Kus T, Manns B, Rose S, Brignole M, *et al.* Empiric pacemaker compared with a monitoring strategy in patients with syncope and bifascicular conduction block-Rationale and design of the syncope: Pacing or recording in the later years (SPRITELY) study. *Europace* 2012;14:1044-8.
12. Gaggioli G, Bottoni N, Brignole M, Menozzi C, Lolli G, Oddone D, *et al.* Progression to 2d and 3d grade atrioventricular block in patients after electrostimulation for bundle-branch block and syncope: A long-term study. *G Ital Cardiol* 1994;24:409-16.
13. Sud S, Klein GJ, Skanes AC, Gula LJ, Yee R, Krahn AD. Predicting the cause of syncope from clinical history in patients undergoing prolonged monitoring. *Heart Rhythm* 2009;6:238-43.
14. Task Force members, Brignole M, Vardas P, Hoffman E, Huikuri H, Moya A, *et al.* Indications for the use of diagnostic implantable and external ECG loop recorders. *Europace* 2009;11:671-87.

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