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Coexistent coronary artery disease in Indian patients undergoing permanent pacemaker implantation (PPI) for symptomatic bradyarrhythmia



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ABSTRACT

Background: The cause-effect of conduction disturbance in chronic lesion of coronary arteries is complicated. This study was designed to evaluate coexistent CAD in patients with symptomatic bradyarrhythmia to find common anatomic basis for conduction disturbances and its relationship to conventional coronary risk factors.

Methods: In this prospective observational study, 929 patients who admitted for symptomatic bradyarrhythmia requiring permanent pacemaker implantation were included. All included patients underwent coronary angiography and were divided into groups based on angiographic findings. Association between conduction disturbances and these groups were analyzed.

Results: A total of 929 patients with mean age of 63.1 years were included in our study. We found age ≥ 50 years, male sex, presence of diabetes and hypertension as statistically significant predictors of abnormal coronary angiography. Obstructive CAD ($\geq 50\%$ stenosis) was found in 34.4% patients. Prevalence of single vessel disease, double vessel disease and triple vessel disease was 15.3%, 10.2% and 8.9% respectively. Severe coronary obstruction ($\geq 90\%$ obstruction) was found in 16.25% patients. Revascularization was advised in three fourth of cases of obstructive CAD. Approximately two third of patients didn't have significant obstruction in coronaries supplying the conduction system. Type 4 was the commonest anatomy in obstructive CAD. SA Nodal artery was found more diseased in patients of SSS with p value of 0.01.

Conclusion: Obstructive CAD was found in one third of patients undergoing PPI. Age ≥ 50 years, male sex, diabetes and hypertension were found significantly correlated with presence of CAD and may act as important markers for the judgment of further coronary evaluation.

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1. Introduction

Most common cause of symptomatic bradycardia are sinus node dysfunction or AV conduction block at the level of AV node, his

bundle or purkinje fibers. These conduction abnormalities are often due to sclerodegenerative processes or extrinsic pathological conditions damaging the conduction system.

Bradyarrhythmias and conduction disturbances are well recognized complications of acute myocardial infarction (MI). They are induced by either autonomic imbalance or ischemia & necrosis of the conduction system. But the effect of chronic lesion of coronary arteries on conduction system is complex & not known.

Some studies have done histopathological examination of conduction system which suggested role of broad spectrum of pathological processes in coronary artery disease in major conduction

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disturbances and its variable clinical presentation.¹ These histopathological changes are nonspecific & cannot explain the underlying disorder as these changes can be seen in many pathological conditions like hypertension, congenital heart diseases, myocardial diseases or coronary atherosclerosis.²

Coronary angiography is the gold standard test for diagnosis of atherosclerotic coronary artery disease. It is not a routine practice to do coronary angiography prior to permanent pacemaker implantation in all patients with symptomatic bradyarrhythmia. Few small studies have investigated association between conduction disturbance & coronary atherosclerosis.^{2–6} These studies showed 15–70% association of chronic coronary artery disease in chronic conduction disorders.^{7–10} Coexistence of CAD with symptomatic bradycardia has major effects on prognosis & long term plan of care in form of either medication or revascularization. Significant prevalence of CAD with conduction disorders found in these studies needs to be further investigated in large samples to identify risk factors, specific coronary artery lesions, anatomy of branches supplying the conduction system & extent of coronary atherosclerotic diseases.

Epidemiology of CAD in India is different from western population with particular causes of concern like its accelerated build up, the early age of disease onset in the population & high case fatality rate.¹¹ This study was designed to evaluate coexistent CAD in patients with symptomatic bradyarrhythmia to find common pathological anatomic basis for conduction disturbances and its relationship to conventional coronary risk factors in Indian population. Only few Indian studies are available who have addressed this issue.² Data of this study will help in estimating the burden of chronic CAD in Indian patients with conduction disturbances undergoing PPI.

2. Methods

2.1. Study design

Our study is prospective observational study. We prospectively studied 1055 consecutive patients who presented to our institute with symptomatic bradyarrhythmia and required insertion of permanent pacemaker implantation between January 2016 to September 2020. The study was approved by institutional ethics committee.

2.2. Study population

A total of 1055 patients underwent permanent pacemaker insertion during study period. These patients were subjected to following inclusion and exclusion criteria. 929 patients fulfilling these criteria were included in the study.

2.3. Inclusion criteria

- Age more than or equal to 40 years with symptomatic bradycardia fulfilling ACC/AHA/HRS 2018 guidelines for requirement of permanent pacemaker insertion.
- Patients who gave consent for coronary angiography prior to pacemaker insertion

2.4. Exclusion criteria

- Acute coronary syndrome
- History of Drugs (Beta blockers, non-dihydropyridine calcium channel blockers, digoxin, antiarrhythmic drugs, lithium, methyl dopa, risperidone, cisplatin, interferon) or toxins intake

- Electrolyte abnormality/Metabolic/endocrine causes
- Hypothermia/Vagotonic causes
- Infectious causes/Inflammatory/infiltrative Myocarditis
- Congenital heart diseases
- Contra-indications for coronary angiography (history of contrast agent allergy; renal dysfunction with serum creatinine >1.8 mg/dL; coagulopathies; sepsis)
- Patients who did not give consent for the study

3. Methods

The clinical parameters, demographic data, electrocardiogram and echocardiographic findings were collected for all the patients. A detailed history of symptoms was recorded. Diagnosis of sinus node dysfunction, second degree AV-block, high grade AV block, complete heart block, trifascicular or bifascicular block or junctional bradyarrhythmias were made based on 12 lead ECG findings or ECG evidence on holter monitoring. Only in selected cases of bifascicular or trifascicular block and junctional bradycardia, diagnostic electrophysiology study was done to decide further plan of management. Details of underlying cardiac disease, blood pressure, fasting blood glucose and fasting lipid profile were measured. The conventional coronary risk factors including male sex, age, diabetes mellitus (DM), hypertension, dyslipidemia (total cholesterol ≥ 200 mg/dL or LDL cholesterol ≥ 130 mg/dL or triglycerides ≥ 150 mg/dL, or HDL cholesterol ≤ 40 mg/dL), smoking (Our definition of smoking risk factor requires at least 10 years exposure to tobacco with at least 10 cigarettes per day), obesity (body mass index >30 kg/m²), family history of CAD and physical inactivity were recorded.

3.1. Coronary angiography

Coronary angiography was performed during the same session or one day prior to pacemaker implantation. A total of 3–4 views for left coronary artery and two views for right coronary artery were taken. The coronary angiography was reviewed by two independent experienced cardiologists unaware of the patient's general data. The Coronary angiographic study included measurement of diameter and stenosis severity, visual qualitative assessment of flow particularly the blood supply to territories that supply conduction system (proximal LAD, Right coronary artery and Left Circumflex coronary artery) were documented. Luminal stenosis was calculated as visual estimation of the percentage of diameter reduction in diseased segment compared to the proximal disease free reference segment. More than or equal to 50% stenosis in left main coronary artery (LMCA), either one of three major coronary arteries including the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA) or their first-order branches was considered as obstructive CAD. While less than 50% stenosis in either one of three major coronary arteries was considered as non obstructive CAD. Stenosis of vessels were further divided into mild (50–70%), moderate (70–90%) and severe ($\geq 90\%$) stenosis. Obstructive CAD in the arteries supplying the conduction system was subclassified into type I to type IV as per Mosseri's classification.¹² The sinus nodal artery (SNA) and atrio-ventricular nodal artery (AVNA) were identified. Significant disease with flow compromise was defined as more than 50% stenosis in the nodal artery or its feeding artery proximal to the origin.

3.2. Statistical analysis

All statistical studies were carried out using IBM SPSS program vs. 20. The patients were divided into groups based on their coronary angiographic findings. Quantitative variables were expressed

as the mean ± standard deviation and qualitative variables were expressed as percentage (%). Parametric values between two groups were performed using the independent sample *t*-test or chi-square test, as appropriate. Categorical variables were compared using the chi-square test. A nominal significance was taken as a two tailed *p* value < 0.05.

4. Results

4.1. Baseline characteristics

Out of total 929 patients included in the study, 503 were male & 426 were female. Mean age of patients was 67.79 ± 24.71 years (with range of 40–92 years). Diagnosis of CHB was made in 67% patients, SSS in 13.1% patients, 2nd degree AV- block or high grade AV block in 9.8% patients, bifascicular or trifascicular block in 7% patients & junctional bradycardia in 3.1% patients.

4.2. Coronary risk factors and its relation to coronary angiography

Coronary risk factors and its relation to coronary angiography have been given in Table 1. Regarding coronary risk factors, we found male sex (63.7% vs. 36.3%; *p* < 0.0001), age more than or equal 50 years (95.44% vs. 4.56%; *p* = 0.0002), hypertension (35.5%

v/s 26.2%; *P* = 0.003), diabetes (19% v/s 8.1% *P* < 0.0001) and presence of both hypertension & diabetes (14.9% v/s 6.5%; *P* = 0.0001) as statistically significant risk factors for having abnormal coronary angiography.

4.3. Coronary angiography pattern of study population

Out of 929 patients who underwent coronary angiography, 447 patients (48.10%) had normal coronary angiography, 162 patients (17.44%) had non-obstructive (<50% obstruction) coronary artery disease & 320 patients (34.44%) had obstructive coronary artery disease (stenosis ≥50%).

Coronary angiographic profile of patients has been given in Table 2. Incidence of obstructive CAD was 28.46% (177 patients) in patients with CHB, 51% (63 patients) in SSS, 45.05% in second degree or high grade AV block, 33.84% bifascicular or trifascicular AV block & 58.62% in patients with junctional bradycardia.

In terms of number of vessels involved, 142 patients (15.29%) had single vessel disease, 95 patients (10.22%) had double vessel disease & 83 patients (8.93%) had triple vessel disease.

We classified obstructive CAD in three groups according to the severity of obstruction which is given in Table 3. Out of 320 patients of obstructive CAD, coronary revascularization either in form of percutaneous revascularization or coronary artery bypass grafting

Table 1
Conventional coronary risk factors.

Variables	Normal CAG N = 447(48.10%)	Abnormal CAG N = 482 (51.9%)	<i>P</i> value
Age			
<50 years	42(9.40%)	22(4.56%)	0.0002
≥50 years	314(70.25%)	460(95.44%)	
Gender			
Male	196(43.8%)	307(63.7%)	< 0.0001
Female	251(56.2%)	170(36.3%)	
Hypertension	117(26.2%)	171(35.5%)	0.003
Diabetes mellitus type-II	36(8.1%)	93(19%)	< 0.0001
Hypertension + Diabetes mellitus type-II	29(6.5%)	72(14.9%)	0.0001
Smoking	102(23%)	92(19%)	0.19
Obesity	7(1.6%)	7(1.5%)	0.9
Family history of CAD	89(20.1%)	72(15%)	0.06
Dyslipidemia	94(21%)	82(17%)	0.14

CAG-coronary angiography; CAD-coronary artery disease.

Table 2
Coronary angiographic profile of patients with bradyarrhythmia.

	Normal & Non-obstructive CAD N = 609		Obstructive CAD N = 320		
	Normal N = 447	Non-obstructive CAD = 162 (<50% stenosis)	SVD = 142(15.3%)	DVD = 95(10.2%)	TVD = 83(8.9%)
Complete heart block	335(74.94%)	110(67.9%)	108(76.06%)	15(15.79%)	54(65.06%)
Sick Sinus Syndrome	21(4.7%)	38(23.46%)	8(5.63%)	52(54.74%)	3(3.61%)
2° Atrio-ventricular Block/High grade AV block	44(9.85%)	6(3.7%)	13(9.15%)	18(18.95%)	10(12.05%)
Bifascicular and Trifascicular AV block	35(7.83%)	8(4.94%)	4(2.82%)	2(2.10%)	16(19.28%)
Junctional bradycardia	12(2.68%)	0	9(6.34%)	8(8.42%)	0

CAD-coronary artery disease; SVD-single vessel disease; DVD-double vessel disease; TVD-triple vessel disease; AV- atrioventricular.

Table 3
CAD Classification according to severity in patients with obstructive CAD.

	Mild (50–70%)N = 47	Moderate (70–90%) N = 122	Severe (≥90%) N = 151
Complete heart block	31(65.96%)	76(62.3%)	98(64.9%)
Sick Sinus Syndrome	1(2.13%)	16(13.11%)	21(13.9%)
2° Atrio-ventricular Block/High grade AV block	6(12.77%)	17(13.93%)	18(11.92%)
Bifascicular and Trifascicular AV block	9(19.14%)	7(5.74%)	7(4.64%)
Junctional bradycardia	0	6(4.92%)	7(4.64%)

CAD-coronary artery disease; AV- atrioventricular.

Table 4
Sub classification of coronary anatomy of all patients according to Mosseri's classification.

	Type-I N = 624	Type-II N = 85	Type-III N = 70	Type IV N = 150	P value
Complete heart block	427(68.43%)	59(69.41%)	45(64.29%)	91(60.67%)	0.29
Sick Sinus Syndrome	90(14.42%)	9(10.59%)	9(12.86%)	14(9.33%)	0.35
2° Atrio-ventricular Block/High grade AV block	52(8.33%)	6(7.06%)	11(15.71%)	22(14.67%)	0.03
Bifascicular and Trifascicular AV block	39(6.26%)	9(10.59%)	3(4.29%)	14(9.33%)	0.23
Junctional bradycardia	16(2.56%)	2(2.35%)	2(2.35%)	9(6)	0.18

AV- atrioventricular.

was advised in majority of cases (245 patients; 76.56%), while medical management was advised in 75 patients (23.43%).

Coronary anatomy of all patients (including normal and abnormal CAG) with symptomatic bradycardia was categorized according to Mosseri's classification (Table 4). 624 patients (67.17%) had type I coronary anatomy, 85 patients (9.14%) had type II anatomy, 70 patients (7.53%) had type III & 150 patients (16.15%) had type IV coronary anatomy. Out of 320 patients with obstructive coronary artery disease, type 4 coronary anatomy was the commonest type (46.88%) followed by type 2 (26.25%), type 3 (21.87%) and type 1 (5%).

Nodal conduction disease status was compared with disease of respective artery. SA nodal artery was found diseased among 16 patients (13.11%) of SSS out of 122 patients. This association was found significant with *P* value of 0.01. AV nodal artery was found diseased among 50 patients (6.43%) of AV conduction block out of 778 patients. Association was not found to be statistically significant (*P* = 0.2).

5. Discussion

A long list of diseases may cause transient or permanent conduction disturbances. Currently, there are no reliable predictors of associated coronary artery disease & its severity in patients undergoing PPI for symptomatic bradyarrhythmia.

The most common conduction disturbance in our study was CHB in 67% patients. Presence of CAD had no significant correlation with smoking, obesity, family history of coronary artery disease or dyslipidemia. Our study showed that age more than or equal to 50 years, male sex, hypertension & diabetes were significantly more prevalent coronary risk factors in patients with abnormal coronary angiography. These risk factors may be used as clinical markers in selecting patients for coronary evaluation prior to permanent pacemaker implantation.

Association of chronic CAD in patients with conduction disorders has been shown to be 15–70% in various studies depending on patient's characteristics & diagnostic modalities used to diagnose CAD.^{7–10} Our study results have revealed that 51.88% patients with symptomatic bradyarrhythmia had abnormal CAG including obstructive & non-obstructive CAD and 34.44% patients had significant obstructive coronary artery disease. Indian study by Mohammad S. Ali et al, an angiographic study of 100 patients requiring permanent pacemaker implantation and having at least one atherosclerotic risk factor found 29% incidence of significant obstructive CAD in such patients.² Similar study by Brueck et al showed 71% of incidence of CAD in 507 patients requiring permanent pacemaker implantation.⁸ Though we didn't select patients in reference to coronary risk factors in our study, more than one third of our patients (34.44%) were found to have significant obstructive CAD. Rubenstein et al found that 35.71% patients with sick sinus syndrome had coronary artery disease based on either histological or electrocardiographic evidence.³ Shaw et al reported 48% of

patients with sick sinus syndrome had abnormal postmortem coronaries.⁴ In our study also obstructive coronary artery disease was found in almost half (51%, 63 out of 122 patients) of the cases of sick sinus syndrome.

If we analyze the coronary anatomy of all patients undergoing PPI irrespective of their obstructive or non-obstructive coronary artery disease status according to Mosseri's classification, we found type-I coronary anatomy as the commonest (67.16%) coronary anatomy followed by type IV (16.14%), type II (9.14%) & type III (7.53%). This finding suggests that two third of patients (67.16%) did not have significant obstruction in coronaries supplying the conduction system. In patients with obstructive coronary artery disease, we found that type 4 coronary anatomy was the commonest type (46.88%) followed by type II (26.25%). In study by Mosseri et al, they found that type II & type IV pathological coronary anatomies were more frequently observed in patients undergoing permanent pacemaker implantation.¹² The similar findings were confirmed in studies by Tandogan et al, Yesil et al & Indian study of by Mohammad et al. Study by Jordan et al suggested pathological role of CAD in development of sinus nodal dysfunction.^{2,12–14} Study by Shaw et al. Showed 16% of patients with chronic sinoatrial disorder had significant obstruction of SA nodal artery.⁴ In our study 13.11% patients with sick sinus syndrome had diseased SAN artery. When we compared involvement of AV nodal artery in patients with AV conduction block & involvement of sinus nodal artery with symptomatic SSS; AV nodal artery involvement was not found significant with AV conduction block while relation between SA nodal artery involvement & SSS was statically significant (*p* = 0.01).

Revascularization study by Yesil et al showed that only small percentage of patients (27%) returned to sinus rhythm post revascularization & coronary revascularization has very little role impact on returning to normal AV conduction.¹² The limitation of our study is that we have not studied the effect of revascularization on reversibility of conduction disturbances.

One third of our patients had significant associated obstructive coronary artery disease, out of which majority (three fourth) were advised for revascularization due to critical coronary artery obstruction. Patients with bradyarrhythmia usually experience decline in exercise capacity and do not experience angina due to reduced myocardial oxygen demand even in presence of underlying obstructive coronary artery disease. After pacemaker placement with DDD mode application, the pacemaker tracking of the atrial P waves may raise ventricular rate to more than 100 beats/min from 40 beats/min. This sudden increase in heart rate leads to myocardial ischemia due to the increased oxygen demand and cause the patient to experience typical angina post PPI. In the majority of patients with permanent pacemakers with endocavitary stimulation on the right ventricle, a left bundle branch block pattern on the surface electrocardiogram that makes it difficult to identify myocardial ischemia. Obtaining a detailed history and coronary evaluation before permanent pacemaker implantation is crucial in selected patients. Though coronary artery disease may not have

causal association with severe conduction disturbances, its significant association with conduction disturbances has definitely a major prognostic impact on these patients. It will affect long term patient management in form of revascularization & will need appropriate pacemaker mode selection to prevent aggravation of baseline underlying myocardial ischemia.

5.1. The limitation of the study

Limitation of our study is that we have not studied the effect of revascularization on reversibility of conduction disturbances. We could have studied the effect of revascularization in stable bradyarrhythmia cases where PPI could have been safely delayed. This could have given better insight to understand cause– effect relationship between chronic conduction disturbances and chronic CAD.

6. Conclusion

Coexistent obstructive CAD was noted in one third (34.44%) of our patients requiring permanent pacemaker implantation for symptomatic bradyarrhythmia. Among the conventional risk factors, age more than or equal to 50 years, male sex, diabetes & hypertension were found significantly correlated with presence of coronary artery disease. Even patients with sinus node dysfunction were more likely to have coronary artery disease & SA nodal artery involvement was significant in patients with sick sinus syndrome. Though causal association between chronic CAD & conduction disturbances cannot be established from this data, significant association between obstructive CAD and conduction disturbances cannot be ignored. Though it is not a routine practice to do coronary evaluation in all patients undergoing PPI, we suggest coronary angiographic screening in selected patients before pacemaker implantation to improve long term prognosis of these patients.

Key message

Epidemiology of CAD in India is different from western population. Our study showed significant association between obstructive CAD and conduction disturbances which cannot be ignored and coronary evaluation in selected patients is suggested prior to PPI.

Declaration of competing interest

No Conflict of interest.

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References

1. Cohle SD. Histopathology of the cardiac conduction system in the investigation of sudden unexpected death. *Acad Forensic Pathol.* 2011 Sep;1(2):206–215.
2. Alai MS, Beig JR, Kumar S, et al. Prevalence and characterization of coronary artery disease in patients with symptomatic bradyarrhythmias requiring pacemaker implantation. *Indian Heart J.* 2016 Dec 1;68:S21–S25.
3. Rubenstein JJ, Schulman CL, Yurchak PM, Desanctis RW. Clinical spectrum of the sick sinus syndrome. *Circulation.* 1972 Jul;46(1):5–13.
4. Shaw DB, Linker NJ, Heaver PA, Evans R. Chronic sinoatrial disorder (sick sinus syndrome): a possible result of cardiac ischaemia. *Heart.* 1987 Dec 1;58(6):598–607.
5. Davies MJ. *Pathology of Conducting Tissue of the Heart.* New York: Appleton-Century-Crofts; 1971:26–27.
6. Jayaram AA, Nayak K, Rao S, et al. Lipid profile parameters and coronary artery disease in young patients undergoing diagnostic angiography. *Int J Cardiovasc Pract.* 2019 Jul;4(2).
7. Hsueh CW, Lee WL, Chen YT, Ting CT. The incidence of coronary artery disease in patients with symptomatic bradyarrhythmias. *Jpn Heart J.* 2001;42:417–423.
8. Brueck M, Bandorski D, Kramer W. Incidence of coronary artery disease and necessity of revascularization in symptomatic patients requiring permanent pacemaker implantation. *Med Klin Suppl.* 2008 Dec 1;103(12):827–830.
9. Ciaroni S, Bloch A, Albrecht L, Vanautryve B. Diagnosis of coronary artery disease in patients with permanent cardiac pacemaker by dobutamine stress echocardiography or exercise thallium-201 myocardial tomography. *Echocardiography.* 2000 Oct;17(7):675–679.
10. Hsueh CW, Lee WL, Chen YT, Ting CT. The incidence of coronary artery disease in patients with symptomatic bradyarrhythmias. *Jpn Heart J.* 2001;42(4):417–423.
11. Prabhakaran D, Singh K, Roth GA, Banerjee A, Pagidipati NJ, Huffman MD. Cardiovascular diseases in India compared with the United States. *J Am Coll Cardiol.* 2018 Jul 3;72(1):79–95.
12. Yesil M, Bayata S, Arikani E, Yilmaz R, Postaci N. Should we revascularize before implanting a pacemaker? *Clin Cardiol.* 2008;31:498–501.
13. Tandoğan I, Yetkin E, Güray Y, et al. Distribution of coronary artery lesions in patients with permanent pacemakers. *Anadolu Kardiyol Derg.* 2002 Dec;2(4):279–283.
14. Jordan J, Yamaguchi IW, Mandel WJ. Characteristics of sinoatrial conduction in patients with coronary artery disease. *Circulation.* 1977 Apr;55(4):569–574.