



## Original Article

## Dependency to Pacemaker in Patients with Normal Ejection Fraction, who is more at Chemical Risk

Faezeh Dehghani-Tafti<sup>1</sup> , Mina Nikvarz<sup>2</sup> , Mohammadtaghi Sarebanhassanabadi<sup>2</sup>   
 Mohammad Shafiee<sup>3</sup> , Mozhgan Modarresi<sup>4</sup> , Hossein Fallahzadeh<sup>5</sup> , Seyed Kazem Razavi Ratki<sup>6</sup> , Maryam Tavakkoli<sup>7</sup>, Seyed-Mostafa Seyed Hosseini<sup>8,\*</sup>

<sup>1</sup>Fellowship of Echocardiography, Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup>Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>3</sup>General Practitioner, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>4</sup>Diabetes Research Center, Sadoughi University of Medical Sciences and Health Services of Yazd, Iran

<sup>5</sup>Professor, Center for Healthcare Data Modeling, Departments of Biostatistics and Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>6</sup> Yazd Medical Science, Branch Islamic Azad University, Yazd, Iran

<sup>7</sup>Department of Radiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>8</sup>Assistant Professor of Cardiology, Yazd Cardiovascular Research Centre, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

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## ABSTRACT

**Background:** Although there is a clear clinical benefit from implantable pacemakers, part of patients is exposed to hazards associated with device implantation. One of the important issues among paced patients is pacemaker dependency, which is not an uncommon phenomenon and has a significant impact on the patient's outcomes. The purpose of the present study is to evaluate the incidence of pacemaker dependency and to determine its probable predictors.

**Methods:** This was a cross-sectional study among patients with permanent pacemaker implantation according to guideline-recommended indications, from March 2016 to March 2017 in Yazd province. During the interrogation of the device, an electrophysiologist recorded the percentage of ventricular pacing/all events according to stored data. Pacing dependency was categorized into three groups based on pacing percentage in the analysis (group 1: below 30%, group 2: between 30-70%, and group 3: above 70%).

**Results:** A total number of 123 patients with permanent cardiac pacemakers were enrolled in our study. The mean duration between the device implant and follow-up visit was 37.4±34.4 months. The majority of patients were female (61.8%). The mean age of participants was 69.9±15 years. None of the clinical variables including age, gender, and body mass index predicted pacing dependency percentage (P-value: 0.64, 0.88, and 0.18 respectively). However, patients with dual-chamber pacemakers were more frequently pace-dependent (>70%) than single chamber pacemakers (86.8% versus 59.4 %, P-value: 0.001).

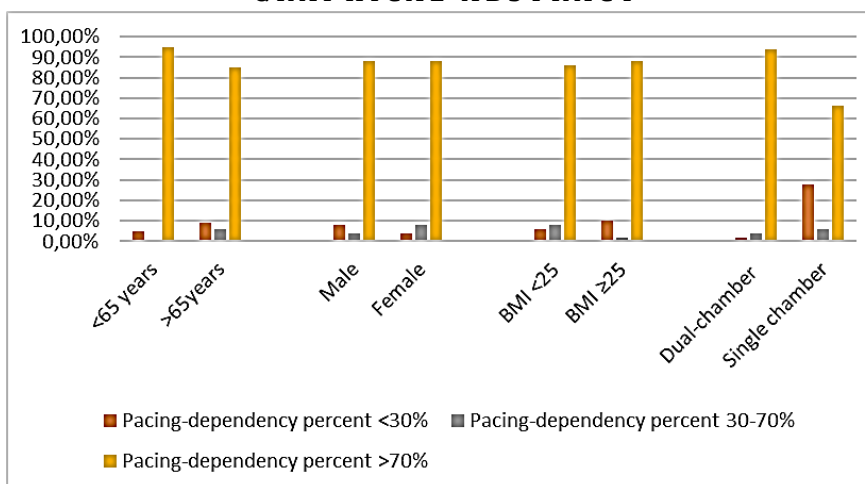
**Conclusion:** Pacing dependency after the permanent pacemaker is much more common in our community. In addition, pacing dependency is associated with pacemaker type, which highlights the importance of device settings.

\* Corresponding author: Seyed-Mostafa Seyed Hosseini

✉ E-mail: Email: [m.seydhossaini@gmail.com](mailto:m.seydhossaini@gmail.com)

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## GRAPHICAL ABSTRACT



## Introduction

Pacemaker is the recommended therapy for treating the conduction system disorders [1]. The primary purpose of a pacemaker is to maintain an adequate heart rate [2]. According to recently published research, the adjusted incidence rate of permanent pacemaker implantation increased 2.7-fold over 30 years [3]. The advances in technology, growing evidence-based indications, and the aging population are potentially attributable factors [4].

Although there is a clear clinical benefit from implantable pacemakers, part of patients is exposed to hazards associated with device implantation [5]. Permanent pacemakers have significantly increased survival and improved quality of life for many patients with Brady arrhythmia [6]; On the other, current day pacemakers are safe and mature; but there are complications, when enumerated are many [7]. cardiac pacemakers are limited by device-related complications, notably infection and problems related to pacemaker leads [8]. Also using pacemakers can cause anxiety in patients [9].

One of the important issues among paced patients is pacemaker dependency, which is not an uncommon phenomenon and has a significant impact on the patient's outcomes [10]. Generally, pacemaker dependent patients have inadequate intrinsic rhythm so they would exhibit remarkable symptoms or cardiac arrest after cessation of pacing [5]. According to the stored percentage of paced ventricular events during the interrogation of devices in these patients, there is ventricular

pacings most of the time [11]. Nevertheless, there is a great diversity in the definition among different kinds of literature [12].

Prevalence and predictors of pacemaker dependency have not well been studied and the impact of this phenomenon on survival is not well known [10]. These patients are at risk of untoward consequences such as pacing inhibition by electromagnetic interference or premature battery depletion [13].

heart failure is a complex pathophysiological disease that can occur due to variety of diseases [14]. Besides, a higher rate of ventricular pacing might be associated with an increased rate of heart failure hospitalization [15]; and reduce the quality of life in these patients [16]. The purpose of the present study is to evaluate the incidence of pacemaker dependency and to determine its probable predictors.

## Materials and Methods

### Study design

This was a cross-sectional study among patients who came to the pacemaker clinic for routine follow up, from March 2016 to March 2017 in Yazd province. Adults, who received permanent pacemaker according to guideline-recommended indications, were enrolled. Exclusion criteria are patients with heart failure (left ventricle ejection fraction under 50%), indication for CRT implantation, incomplete cooperation, and psychiatric problems.

### Groups

All patients filled the informed consent. Baseline information (age, gender, BMI, history of heart disease, drugs that affect AV conduction, indication for pacemaker implantation, pacemaker type, timing since pacemaker insertion) were taken by a questionnaire. Then patients underwent pacemaker analysis. During the interrogation of the device, an electrophysiologist recorded the percentage of ventricular pacing/all events according to stored data.

Pacing dependency was categorized into three groups based on pacing percentage in the analysis (group 1: below 30%, group 2: between 30-70%, and group 3: above 70%).

#### Ethical issues

The ethics committee reviewed and approved the study protocol. Statistical analysis results are expressed as mean  $\pm$  standard deviation (SD) for continuous variables. Continuous variables were compared between groups using a Student's t-test. Dichotomous variables are presented as percentages and were compared between groups via Fischer's exact test. Logistic regression analysis was used to generate a multivariate model including all potential predictors of pacing

dependency. A probability value of  $p < 0.05$  was considered to indicate statistical significance. Data were analyzed using SPSS for Windows (version 21, Chicago, Inc.)

#### Results and Discussions

A total number of 123 patients with permanent cardiac pacemakers were enrolled in our study. The mean BMI of the participant was  $26.1 \pm 6$  kg/m<sup>2</sup>. The mean duration between the device implant and follow-up visit was  $37.4 \pm 34.4$  months with a minimum implant duration of 7 months. The majority of patients were female (61.8%). The mean age of participants was  $69.9 \pm 15$  years. The average LV ejection fraction was  $51.1 \pm 1.0$  %.

Indication for pacemaker implantation were high degree AV block in 88 (71.5%) patients, intermittent AV block in 21 (17.1%) patients, sick sinus syndrome in 8 (6.5%) patients, unexplained syncope in 2 (1.6%) patients and congenital AV block in 4 (3.3%) patients.

Decision-making about single or dual-chamber pacemaker implantation was based on patient condition and physician opinion. 26.1% of patients had a single chamber pacemaker and 73.9% had a dual-chamber pacemaker. Detail clinical characteristics are summarized in table 1.

**Table 1:** Clinical characteristics of participants

Clinical characteristics	All patients N:123
Mean age (years)	69.9 $\pm$ 15
Gender, N (%)	
Male	47(38.2%)
Female	76(61.8%)
Body mass index [kg/m <sup>2</sup> ]	26.1 $\pm$ 6
Pacemaker indication, N (%)	
High degree AV block	88(71.5%)
Sick sinus syndrome	8(6.5%)
Unexplained Syncope	2(1.6%)
Intermittent AV block	21(17.1%)
Congenital AV block	4(3.3%)
Pacemaker type	
Dual-chamber	91(73.9%)
Single chamber	32(26.1%)
Pacemaker dependency	
< 30%	17(13.8%)
30-70%	8(6.5%)
> 70%	98(79.7%)
Follow up duration(months)	37.4 $\pm$ 34.4

Patients were divided into three groups according to their ventricular pacing percentage (group 1: <30%, group 2: 30-70%, and group 3: >70%). Nearly 80% of patients were found to be pacing more than 70%. None of the clinical variables including age, gender, and body mass index predicted pacing dependency percentage (P-value: 0.64, 0.88, and 0.18 respectively).

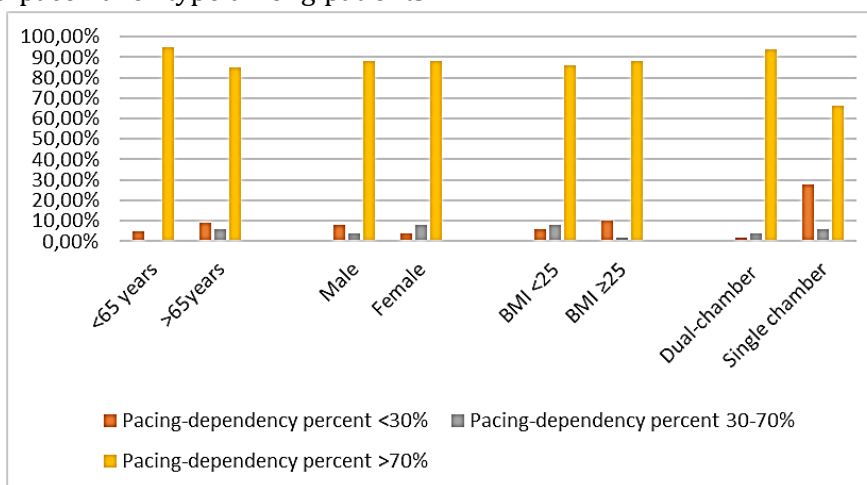
Multivariate logistic regression analysis revealed a significant association between pacing dependency and pacemaker type. Patients with dual-chamber pacemaker were more frequently pace dependent (>70%) than single chamber pacemaker (86.8% versus 59.4 %, P-value: 0.001) (Table 2).

**Table 8:** Comparison between patients with different percentage of pacing dependency

Clinical variable	All patients N:123	Pacing-dependency percent			P-value
		<30% n:17	30-70% n:8	>70% n:98	
Age					0.64
<65 years	34(27.6%)	4(23.5%)	1(12.5%)	29(29.6%)	
>65years	89(72.4%)	13(76.5%)	7(87.5%)	69(70.4%)	
Gender					0.88
Male	47(38.2%)	7(41.2%)	2(25.0%)	38(38.8%)	
Female	76(61.8%)	10(58.8%)	6(75.0%)	60(61.2%)	
Body mass index [kg/m2]					0.18
<25	58(47.2)	6(35.3%)	6(75.0%)	46(46.9%)	
≥25	65(52.8%)	11(64.7%)	2(25.0%)	52(63.1%)	
Pacemaker type					0.001
Dual-chamber	91(73.9%)	8(8.8%)	4(4.4%)	79(86.8%)	
Single chamber	32(26.1%)	9(28.1%)	4(12.5%)	19(59.4%)	

Most of our patients (71.5%) had a high degree AV block as an indication for pacemaker implantation, so we reevaluate our analysis in this particular group (figure 1). Multivariate analysis showed a significant correlation between pacing dependency and pacemaker type among patients

with high degree AV block (P-value: 0.001). Other clinical data such as age, gender, and BMI had no statistical relationship to pacing dependency percentage (P-value: 0.89, 0.71, and 0.41 respectively).



**Figure 1:** Comparison of clinical characteristics between patients with high degree AV block and different percentage of pacing dependency

Pacemaker implantation knowledge is improving through recent decades. Therefore, it is important to know probable unwanted consequences. One important consideration is the degree of pacemaker dependency among patients with a permanent pacemaker [17]. Individuals who are totally pace dependent are at increased risk of asystole when encountering electromagnetic interference or pacemaker system malfunction (battery depletion, lead fracture ...) [10]. Besides, the risk of heart failure is increased in continuous right ventricle pacing [18]. Although pacing dependency definition is still controversial, similar to some investigators we used the percentage of ventricle pacing during device interrogation and consider patients with >70% pacing percentage to be more at risk and need more attention.

The main finding of the present study is a 79.7% prevalence of pacing percentage above 70% at 36 months mean follow-up, which was associated with pacemaker type.

This high prevalence of pacing dependency is in controversy with some large trials like the Wolfram study (16%) [10]; and the Canadian Trial of Physiologic Pacing (22%) [19]. Notably, the prevalence of pacing dependency is highly variable in the literature between 2% in the study of Lekalowski [13] and 63% in the study of Merin [20]. This discrepancy is partly due to different definitions used for pacing dependency. Maybe the high pacing dependency rate in our study relates to selecting patients with permanent AV block. Besides, we need to keep in mind that the incidence of pacemaker dependency is based on the unique practices at each center or even country and insurance coverage and costs. This difference is somehow the reason for the higher pacing rate in our community compared to Europe or the United States. Apart from the reason, it indicated that these patients need more attention, closer follow up and precise drug or imaging selection to prevent probable interaction with pacemaker function.

Several previous studies found a relationship between pacing dependency and body mass index, age, and male gender [21-23]. Whereas none of these variables predicted pacing dependency in

the present investigation. The most important predictor of pacing dependency in our study was the pacemaker type. We found that patients with dual-chamber pacemakers had a higher pacing rate [24-26].

We think it is probably because first, we choose patients with the worse condition for dual-chamber pacing than a single chamber. In addition, several potential settings should be taken into accounts such as dual-chamber pacing with short atrioventricular (AV) delay, ventricular pacing with a high base rate, and no programming of features that promote intrinsic ventricular rhythm [27-29]. Therefore, these results indicate that implanting a dual-chamber pacemaker needs a more precise basal setting to prevent high pacing dependency.

### Conclusions

In conclusion, pacing dependency after the permanent pacemaker is much more common in our community and between patients with permanent high-degree AV-block. In addition, pacing dependency is associated with pacemaker type. Which highlights the importance of device setting for better function and lowering of pace dependency rate.

### Ethical issues

In this study, except for maintaining the secrets of the patient in accordance with the Helsinki Treaty, it is assured to patients that their information will be confidential and will be used only for the purposes of the research. In addition, no additional costs were imposed on patients. The proposal is approved by ethics committee of Yazd Shahid Sadoughi University of Medical Sciences.

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### Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

**Conflict of Interest**

We have no conflicts of interest to disclose.

**ORCID:**

Faezeh Dehghani-Tafti

<https://www.orcid.org/0000-0001-9266-8128>

Mina Nikvarz

<https://www.orcid.org/0000-0002-2612-4242>

Mohammadtaghi Sarebanhassanabadi (Phd)

<https://www.orcid.org/0000-0002-8867-4717>

Mohammad Shafiee

<https://www.orcid.org/0000-0001-5924-7583>

Mozhgan Modarresi

<https://www.orcid.org/0000-0003-2490-5448>

Hossein Fallahzadeh

<https://www.orcid.org/0000-0001-6518-366X>

Seyed Kazem Razavi Ratki

<https://www.orcid.org/0000-0002-7201-4511>

Seyed-Mostafa Seyed Hosseini

<https://www.orcid.org/0000-0001-7115-6596>

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