

Ten-year Survival and Its Associated Factors in the Patients Undergoing Pacemaker Implantation in Hospitals Affiliated to Shiraz University of Medical Sciences During 2002 - 2012

Abdolreza Rajaeefard,^{1,*} Mohammad Ghorbani,¹ Mohammad Ali Babaee Baigi,² and Hamidreza Tabatabaei¹

¹Department of Epidemiology, School of Health, Shiraz University of Medical Sciences, Shiraz, IR Iran

²Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran

*Corresponding Author: Abdolreza Rajaeefard, Department of Epidemiology, School of Health, Shiraz University of Medical Sciences, Shiraz, IR Iran, Tel: +98-7137251001, Fax: +98-7137260225, E-mail: sovalde2006@yahoo.com

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Background: Heart failure is a prevalent disease affecting about 4.9 million people in the U.S. and more than 22 million individuals worldwide. Using electric pacemaker is the most common treatment for the patients with heart conduction problems. The present study aimed to determine the factors affecting survival in the patients undergoing pacemaker implantation in the hospitals affiliated to Shiraz University of Medical Sciences.

Objectives: The aim of the present study was to identify the factors affecting the survival of the patients suffering from arrhythmia.

Patients and Methods: This retrospective survival analysis was conducted on all 1207 patients with heart failure who had undergone permanent pacemaker implantation in the hospitals affiliated to Shiraz University of Medical Sciences from 2002 to 2012. The data were analyzed using non-parametric methods such as Kaplan-Meier method, life table, and Cox regression model. The risk factors of mortality were determined using multivariate Cox proportional hazards method.

Results: Survival data were available for 1030 (80%) patients (median age = 71 years [5th to 95th percentile range: 26 - 86 years]) and follow-up was completed for 84.28% of them. According to the results, 56% of the patients had received dual-chamber systems, while 44% had been implanted by single-chamber ventricular systems. Moreover, sick sinus syndrome and pacemaker mode were independent predictors of increased mortality.

Conclusions: In this study, sick sinus syndrome and pacemaker mode followed by syncope were independently associated with increased mortality.

Keywords: Survival Analysis, Risk Factors, Pacemaker, Artificial

1. Background

Cardiovascular diseases are the first cause of mortality in the world and their prevalence is increasing worldwide, especially in low- and middle-income countries (1). According to the international mortality reports, cardiovascular diseases will be 1 of the 3 main causes of the global burden of disease by 2030 (2). Heart failure is a high prevalent disease all around the world, so that about 4.9 million people in the U.S. and more than 22 million people worldwide are suffering from this disease. Also, these figures are annually increasing by about 550,000 in the U.S. and 2 million individuals in the world (3). In the U.S., approximately 56,000 deaths occur annually because of heart failure, with the mortality rate of 20.2 per 100,000 (4). According to the report by Iran's Ministry of Health, 1% - 2% of the health budget of the country is spent on treating heart failure and its associated complications. Yet, 50,000 patients lose their lives because of congestive heart failure and its complications every year (5). In 1910,

only 10% of worldwide deaths was due to cardiovascular diseases. However, this figure increased to 50% in 2000 and it has been predicted to reach about 75% by 2020 (6). Overall, around 50% of the deaths resulting from heart attacks are caused by arrhythmias. Nonpharmacological treatments, such as heart transplant and using an artificial pacemaker, are applicable in the later stages of the disease (5). One of the most important therapies for patients with cardiac conduction problems is using an electrical pacemaker (7-13). Implantation of a cardiac pacemaker is one of the treatments for severe and/or symptomatic bradycardia (14-19). Currently, more than 55 years after the first pacemaker implantation, the worldwide annual implantation rate has exceeded 400,000. Owing to its widespread utilization, pacemaker technology has greatly evolved and highly sophisticated devices have become available (20). In 1997, more than 153,000 pacemakers were implanted in patients in the U.S. (21).

Despite the therapies with antiarrhythmic drugs, studies have shown the recurrence rate of 50%-60% during the first or second year after implantation. In the patients with severe symptoms and failure of drug therapy, ablation of the atrioventricular node and permanent pacing are effective in controlling the ventricular rate. However, no evidence is available regarding the effectiveness of this treatment in improving the symptoms and long-term survival in the patients with severe symptoms and failure of drug therapy (22). The results of the study conducted by Brunner et al. (20) in 2004 showed that the median survival time was 8.5 years. Besides, 44.8% and 21.4% of the patients were alive for 10 and 20 years, respectively. Another study performed by Pyatt et al. (23) on 803 patients in England demonstrated the median survival time of 5 years in the patients who had implanted their first pacemakers. In the recent years, most of the studies which have been conducted by the clinicians in Iran have focused on the impact of pacemakers on the clinical symptoms and less attention has been paid to survival rate analysis (5, 7). Because of the medical advances and increase in life expectancy, one of the most important factors in choosing the type of the pacemaker is its survival rate (24-28). In fact, clinicians are faced with the question "how much time do I have to live?" The study findings will help clinicians select the most appropriate type of pacemaker.

2. Objectives

The present study aimed to identify the factors affecting the survival of the patients suffering from arrhythmia.

3. Patients and Methods

This retrospective survival analysis was conducted on all 1207 patients who had undergone permanent pacemaker implantation in the Hospital Departments of Cardiovascular Surgery and Angiography of Shiraz University of Medical Sciences (Nemazi, Shahid Faghihi, and Al-Zahra hospitals) from 2002 to 2012.

3.1. Data Collection and Follow-up

The data were collected from the patients' medical records. The patients' survival status was obtained through phone contacts as well as using Shiraz Department of Health mortality database. This project was approved by the Ethics Committee of Vice-Chancellor for Research Affairs of Shiraz University of Medical Sciences, Shiraz, Iran (Code: 91-6082).

3.2. Statistical Analysis

The study data were entered into SPSS software (V.19) and analyzed using non-parametric survival analyses, including Kaplan-Meier, life table, and Cox regression models. In Kaplan-Meier and life table methods, the cumulative survival rate was calculated univariately based on different variables and the log rank test was used to compare different groups. The variables with P less than 0.25 in the univariate analysis were entered into the Cox model, pro-

viding the basis for computation of the death hazard ratio. The starting point of the survival analysis was the date of pacemaker implantation, while its end point was either death or the end of the 10 years period (2002 to 2012).

4. Results

Among the study patients, 53% were female and 47% were male. In addition, the patients' mean age at the time of pacemaker implantation was 66.32 ± 17.9 years (65.01 ± 19.98 years in males vs. 67.42 ± 15.77 years in females). The patients were followed up for 4231 person-years and the survival data were available for 1030 patients. Accordingly, 312 patients (30%) died during the follow-up, while 718 patients (70%) were alive at the end of the study. The mean age of the dead patients was 68.1 ± 17.38 years, while that of the live ones was 65.8 ± 18.04 years. Moreover, atrioventricular node block, sick sinus syndrome, and atrial fibrillation were detected in 108 (10%), 680 (66%), and 27(3%) patients, respectively.

The mean cumulative survival after pacemaker implantation was 99.4 months (about 8.3 years). Besides, the 1, 3, 5, and 10 years cumulative survival rates were 86%, 78%, 70%, and 60%, respectively. The means and SDs of blood glucose, serum creatinine, systolic blood pressure, and diastolic blood pressure were 64.1 ± 133.24 mg/dL, 0.76 ± 1.3 mg/dL, 133.05 ± 27.5 mmHg, and 79.24 ± 14.4 mmHg, respectively. According to the results, single chamber pacemakers were implanted in 44% of the cases and 56% received two chamber pacemakers. Furthermore, 58.2% of the pacemakers were inserted by cardiology specialists, 18.5% were implanted by interventional cardiology fellowships, and 23.3% were inserted by electrophysiology fellowships. Univariate variables are presented in Table 1.

4.1. Kaplan-Meier Estimates of the Survival Function

In this study, log-rank test was used to determine the differences between the survival curves (Tables 2 and 3). According to the results, the mean survival time was 99.4 months (95% CI: 96 - 103) (Figure 1).

Moreover, the results of univariate analysis using the log-rank test indicated that sick sinus syndrome and pacemaker mode significantly affected the survival rate after pacemaker implantation (Figures 2 and 3).

4.2. Cox Regression Model

Multivariate analysis was performed through forward stepwise (LR) method. Following the application of this method, diabetes mellitus and ischemic heart disease were excluded from the model.

This model showed that syncope, pacemaker mode, and sick sinus syndrome affected the period of survival after pacemaker implantation (Table 4).

According to Figure 3, the overall cumulative survival rate was significantly lower in the patients who had implanted single chamber pacemakers compared to those who had received two chamber pacemakers ($P < 0.014$).

Table 1. Distribution of the Patients Undergoing Permanent Pacemaker Implantation In Terms Of Univariate Variables ^a

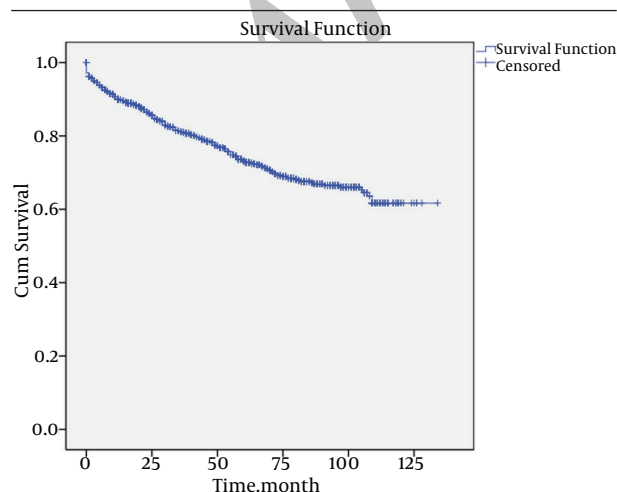
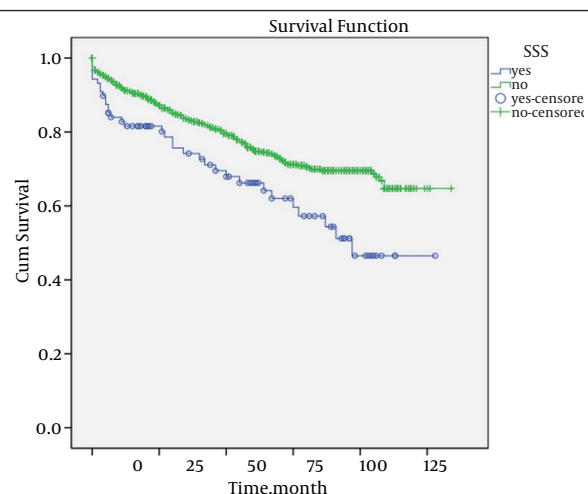
Univariate Variables	Frequency of the Patients ^b		P Value
	Yes	No	
Diabetes mellitus	138 (11.4)	1069 (88.6)	0.001
CVA	47 (3.9)	1160 (96.1)	0.001
Cardiomegaly	5 (0.4)	1202 (99.6)	0.001
Smoking	147 (12.2)	1060 (87.8)	0.001
Hypertension	445 (36.9)	762 (63.1)	0.001
Ischemic heart disease	361 (29.9)	846 (70.1)	0.001
Congenital heart disease	16 (1.3)	1191 (98.7)	0.001
Valvular heart disease	237 (19.6)	970 (80.4)	0.001
Cardiomyopathy	14 (1.2)	1193 (98.8)	0.001
Syncope	120 (9.9)	1087 (90.1)	0.001

^a Data are presented as No. (%).^b n = 1207.**Table 2.** Estimated 10 Years Survival Rate and Mean Survival Time Considering Suffering From Sick Sinus Syndrome Using Kaplan-Meier Method

Sick Sinus Syndrome	Cumulative Survival Rate ^a				Survival Time, Mo ^b	CI 95% (Lower Limit - Upper Limit)
	1 year	3 years	5 years	10 years		
Suffering	0.816	0.742	0.662	0.465	82.50 ± 5.98	70.79 - 94.22
Not-Suffering	0.919	0.836	0.759	0.647	102.51 ± 1.90	98.79 - 106.23

^a P value (Log rank test) = 0.003.^b Values are presented as Mean ± SD.**Table 3.** Estimated 10 Years Survival Rate and Mean Survival Time Considering the Type of Pacemakers Using Kaplan-Meier Method

Pacemaker Mode	Cumulative Survival Rate ^a			
	1 year	3 years	5 years	10 years
Single chamber	0.903	0.804	0.725	0.603
Two chamber	0.927	0.853	0.783	0.747

^a P value (Log rank test) = 0.014.**Figure 1.** 10 Years Survival Curves in the Patients Undergoing Pacemaker Implantation Using Kaplan-Meier Method**Figure 2.** 10 Years Survival Curves in the Patients Undergoing Pacemaker Implantation Based on Sick Sinus Syndrome Using Kaplan-Meier Method

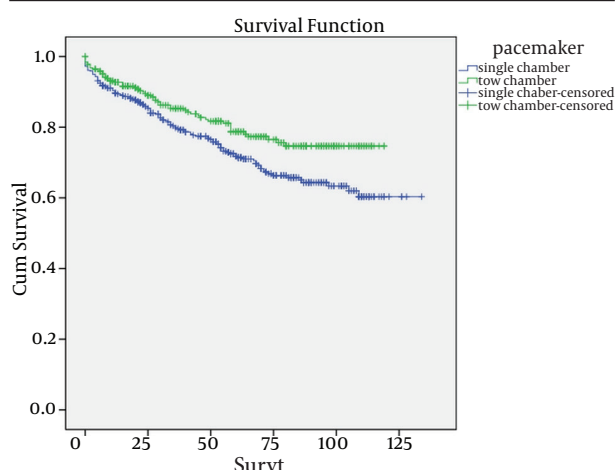


Figure 3. 10 Years Survival Curves in the Patients Undergoing Pacemaker Implantation Based on the Type of Pacemaker Using Kaplan-Meier Method

Table 4. Multivariate Results Using Cox Regression Model

Variables Affecting Survival	Hazard Ratio	95% CI for HR		P Value
		Lower limit	Upper limit	
Age	1.011	1.00	1.021	0.055
Gender	1.058	0.787	1.423	0.708
Syncope	0.577	0.346	0.962	0.035
Sick Sinus syndrome	1.850	1.217	2.812	0.004
Pacemaker mode	1.470	1.066	2.027	0.019

5. Discussion

This study was performed based on the patients' medical records in the hospitals affiliated to Shiraz University of Medical Sciences during 2002 - 2012. Among the study subjects, 53% were female and 47% were male. In the study conducted by Brunner et al. (20) in Germany, 52.7% of the patients were male and 47.3% were female. The study conducted by Ozcan et al. (22) in the U.S. also showed that 52.8% of the patients were male and 47.2% were female.

In the present study, the mean age of the male patients was significantly lower (on average, 2.4 years) than that of the females at the time of pacemaker implantation ($P < 0.02$). Other studies, such as the one conducted by Brunner et al. (20), also reported that the male patients' mean age at the time of pacemaker implantation was significantly lower compared to the females (71 vs. 72.3 years). Thus, the mean age of the patients in Iran was 6 years lower than that of the German patients at the time of pacemaker implantation.

The results of the present study showed that the 5 years survival rate was 0.70. This figure was 0.66 in Germany,

0.67 in the U.S. Ozcan et al. (22), 0.55 in England, 0.41 in the U.S. Shen et al. (29), and 0.89 in South Africa (20, 23, 30).

To compare the survival rates, many points should be taken into account. Age at time of pacemaker implantation is an important factor affecting survival rate. In this study, the mean age of the patients was 66.3 years. In addition, the starting point of this study was the date the patients underwent pacemaker implantation and, consequently, the patients who died in the hospital after surgery were taken into consideration in the survival analysis. In some studies, on the other hand, time of discharge from the intensive care unit after surgery was considered as the starting point of survival analysis and the patients who died after surgery were considered as hospital mortality.

In the current study, the mean survival time after pacemaker implantation was 82.50 months (range 70.79 - 94.22 months) for the patients with sick sinus syndrome and 102.51 months (range 98.79-106.23 months) for others ($P < 0.003$). This result is similar to the findings of Brunner et al. (20). Moreover, the mean survival time after pacemaker implantation was lower in the patients who had implanted single chamber pacemakers compared to those with two chamber pacemakers ($P < 0.014$). Similar results were also obtained by Pyatt et al. (23).

The findings of the present study revealed no significant relationship between survival time and variables of sex, diabetes mellitus, cerebrovascular attack (CVA), cardiomegaly, smoking, hypertension, ischemic heart disease, congenital heart disease, valvular heart disease, cardiomyopathy, syncope, atrioventricular block, and atrial fibrillation. However, sick sinus syndrome and pacemaker mode were found to affect the survival rate.

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Authors' Contributions

Study concept and design: Mohammad Ghorbani and Abdolreza Rajaefard; Analysis and interpretation of data: Mohammad Ghorbani, Abdolreza Rajaefard, Hamidreza Tabatabae, and Mohammad Ali Babaee Baigi; Drafting of the manuscript: Mohammad Ghorbani; Critical revision of the manuscript for important intellectual content: Hamidreza Tabatabae, Abdolreza Rajaefard, and Mohammad Ali Babaee Baigi; and Statistical analysis: Mohammad Ghorbani.

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