

Increased percentage of Atrial Pace Ventricular Pace was associated with increased cardiovascular mortality in patients with a DDD pacemaker

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Abstract

Background

Compared to single-chamber pacing system, dual chamber atrioventricular pacing system (DDD) was associated with reduced mortality and hospitalization for heart failure. High percentage of right ventricular pacing was reported to be associated with high cardiovascular events. However, another meta-analysis study showed ventricular pacing reduction modalities did not improve adverse clinical outcomes. Hence, the relationship between the pacing percentage and clinical outcomes is necessary to be further studied.

Methods

The present study was designed to evaluate the association of total and cardiovascular mortality with the percentages of atrial sense ventricular sense (ASVS), atrial sense ventricular pace (ASVP), atrial pace ventricular sense (APVS), and atrial pace ventricular pace (APVP) in patients with a DDD pacemaker. Study subjects were selected from patients arranged for permanent pacemaker follow-up at our special clinic. 177 patients with a DDD pacemaker were included. We collected their pacemaker follow-up data at their first visit for pacemaker follow-up after permanent pacemaker implantation.

Results

Among the 177 subjects, the mean follow-up to mortality was 2.44 ± 1.03 years. There were 22 and 10 patients documented as total and cardiovascular mortality. In the Cox proportional hazards regression analysis, old age ($P = 0.030$) and low hemoglobin ($P = 0.007$) were the predictors of increased total mortality and increased creatinine ($P = 0.023$) and high percentage of APVP (hazard ratio [HR], 1.030; 95% confidence interval [CI], 1.012–1.049; $P = 0.001$) were the predictors of increased cardiovascular mortality after multivariable analysis.

Conclusion

In patients with a DDD pacemaker, old age and low hemoglobin were associated with increased total mortality and high creatinine and high percentage of APVP were associated with increased cardiovascular mortality after multivariable analysis. Hence, reduction in unnecessary atrial and ventricular pacing in patients with a DDD pacemaker might be useful in improving cardiovascular prognosis.

Background

Cardiac pacing is the well-established treatment for patients with bradycardia. Pacemaker technology permits the use of either single-chamber ventricular pacemakers or dual-chamber pacemakers (DDD) for patients without permanent atrial fibrillation who require cardiac pacing. Compared to single-chamber pacing, dual-chamber pacing more closely resembles cardiac physiology by maintaining atrioventricular (AV) synchrony and thus reduces cardiovascular morbidity and mortality [1–3] and improves quality of life [4, 5].

Sakatani et al. found patients with a high percentage of ventricular pacing (> 90%) had a higher incidence of cardiac events than patients with a low percentage of ventricular pacing (< 10%) [6]. In contrast, Shurrab et al. concluded from a meta-analysis that reduction in unnecessary ventricular pacing failed to affect hard clinical outcomes in patients with preserved left ventricular function [7]. Hence, the relationship between the pacing percentage and clinical outcomes is necessary to be further studied. In the present study, we evaluated whether the pacing percentage in patients with DDD implantation was a useful parameter in prediction overall and cardiovascular mortality.

Methods

Study Protocols and Design

The patients with a DDD pacemaker implantation who visited the pacemaker follow-up clinic for a check-up in a regional hospital in southern Taiwan since April 2016. We consecutively enrolled all the patients at their first outpatient visit for regular pacemaker follow-up after their devices implantation. Exclusion were patients with malignancy. Finally, 177 patients were included in the present study. The study protocols were approved by the institutional review board committee of the Kaohsiung Medical University Hospital.

Measurements of devices parameters during follow-up visit

During the follow-up visit, we examined generator and leads status, including sensing, pacing threshold, impedance and percentage of sensing and pacing of atrial and ventricular leads. In particular, in order to decrease the percentage of ventricular pacing, we prolonged the PR interval to 20-30 ms longer than the intrinsic PR interval in patients with delayed AV conduction.

Collection of basic characteristics, medical, and laboratory profiles

Basic characteristics including age, gender, and comorbid conditions were acquired from medical records or interviews with our patients [8]. Blood samples were obtained within 3 month of enrollment. The diagnosis of diabetes mellitus and hypertension were defined by our previous study [8].

Collection of mortality data

Overall and cardiovascular mortality data were collected up to December 2019. All participants' mortality data were released from the Collaboration Center of Health Information Application, Ministry of Health and Welfare, Executive Yuan, Taiwan.

Statistical analysis

Result data were presented as mean \pm standard deviation or percentage. Time to mortality events were modeled using the Cox proportional forward hazards models. All tests were 2-sided and their significance was defined as $P < 0.05$. All statistical analyses were performed by SPSS 22.0 software (SPSS, Chicago, IL, USA).

Results

Baseline characteristics among study patients

The baseline characteristics of 177 study subjects are shown in Table 1. The mean age was 72 ± 14 years. The most common indication for pacemaker implantation was sick sinus syndrome, regarding 48% of the patients (81 cases). Advanced AV block, including Mobitz type II 2nd degree AV block, high-degree AV block, and 3rd degree AV block was the next in frequency, regarding 44% of the patients (78 cases). During pacemaker follow-up, the percentages of atrial sense ventricular sense (ASVS), atrial sense ventricular pace (ASVP), atrial pace ventricular sense (APVS), and atrial pace ventricular pace (APVP) were $32 \pm 37\%$, $33 \pm 40\%$, $24 \pm 33\%$, and $11 \pm 20\%$, respectively.

Major predictors of overall and cardiovascular mortality in study patients

The follow-up period to mortality was 2.4 ± 1.0 years in all patients. Mortality events were documented during the follow-up period, including total mortality ($n = 22$) and cardiovascular mortality ($n = 10$).

Table 2 shows the predictors of total mortality using Cox proportional hazards model. In the univariable analysis, increased total mortality was associated with increased age and decreased hemoglobin. After multivariable analysis, old age (hazard ratio [HR], 1.057; 95% confidence interval [CI], 1.006–1.112; $P = 0.030$) and low hemoglobin (HR, 0.753; 95% CI, 0.612–0.927; $P = 0.007$) were still the predictors of increased total mortality. All of sensing and pacing percentages were not correlated to increased total mortality. In addition, the percentage of total right ventricular pacing (ASVP + APVP) was also not correlated to total mortality ($P = 0.429$).

Table 3 shows the predictors of cardiovascular mortality using Cox proportional hazards model. In the univariable analysis, increased cardiovascular mortality was associated with increased creatinine and high percentage of APVP. However, the percentage of total right ventricular pacing (ASVP + APVP) was not correlated to cardiovascular mortality ($P = 0.182$). After multivariable analysis, increased creatinine (HR, 1.385; 95% CI, 1.045–1.835; $P = 0.023$) and high percentage of APVP (HR, 1.030; 95% CI, 1.012–1.049; $P = 0.001$) were still the predictors of increased cardiovascular mortality.

Discussion

This study aimed to evaluate pacing percentage in predicting total and cardiovascular mortality in patients with a DDD pacemaker implantation. We found old age and low hemoglobin were associated with increased total mortality, but all of sensing and pacing percentages were not associated with total mortality. In contrast, in addition to high creatinine, high percentage of APVP was significantly associated with increased cardiovascular mortality after multivariable analysis.

Compared to single-chamber ventricular pacemaker, DDD pacemaker has an important advantage because it more closely resembles cardiac physiology by maintaining AV synchrony. Hence, it might decrease cardiovascular morbidity and mortality, and may prolong survival and improve quality of life [4, 5]. Hence, in recent real-world practice, DDD pacemaker is a favor one unless patients have permanent atrial fibrillation. In patients with a DDD pacemaker, excessive right ventricular pacing may have a negative impact on cardiac function. Thus, it is necessary to optimize pacing parameters to minimize right ventricular pacing and maintain the cardiac function after pacemaker implant. In the study included patients with a DDD pacemaker by Zheng et al., subjects with a cumulative right ventricular percentage > 40% would have a more deterioration of cardiac function than those with a cumulative right ventricular percentage \leq 40% [8]. In the study of Sakatani et al. included 268 consecutive patients with permanent pacemakers, they also found patients with a high percentage of ventricular pacing (> 90%) had a higher incidence of cardiac events than patients with a low percentage of ventricular pacing (< 10%) [6]. In contrast, Shurrab et al. demonstrated ventricular pacing reduction modalities did not improve clinical outcomes and were not superior to standard DDD programming in reducing incidence of permanent atrial fibrillation, all-cause hospitalization, or all-cause mortality [7]. In the present study, we similarly found the percentage of total right ventricular pacing (ASVP + APVP) was not correlated to total and cardiovascular mortality.

APVP pacing mode has been considered inadequate in patients with a high degree of AV block and concomitant ischaemic heart disease. The possible explanation for this view was a fear of aggravating angina pectoris by a rate-dependent increase in myocardial oxygen consumption [9]. In addition, during ASVP pacing mode, both atria are activated via the intrinsic conduction system, but during APVP pacing mode, pacing of right atrial appendage resulted in a delayed electrical and mechanical activation of left atrium [10]. Hence, in the study of Bernheim et al., they found compared to ASVP pacing mode, APVP pacing mode could significantly worsen the myocardial performance index of left ventricle [11]. In the present study, although the percentage of total right ventricular pacing was not a predictor of total and cardiovascular mortality, the increased percentage of APVP was correlated to increased cardiovascular mortality. This finding implied that compared to ASVP pacing mode, APVP pacing mode might have a more deleterious impact on cardiovascular mortality. Therefore, reduction in unnecessary atrial and ventricular pacing in patients with a DDD pacemaker might be useful in improving cardiovascular prognosis.

Study limitation

There were several limitations in this study. First, the study generality was limited because our study patients were only included from one pacemaker follow-up clinic in a regional hospital in southern Taiwan. Second, our study was designed to assess the mortality events, so non-fatal events were not studied. Finally, the sample size of our study was relatively small, so the possibility of chance finding and the restricted power should be considered.

Conclusions

In patients with a DDD pacemaker, we found old age and low hemoglobin were associated with increased total mortality, but all of sensing and pacing percentages were not associated with total mortality. Besides, in addition to high creatinine, high percentage of APVP was significantly associated with increased cardiovascular mortality after multivariable analysis. Hence, reduction in unnecessary atrial and ventricular pacing in patients with a DDD pacemaker might be useful in improving cardiovascular prognosis.

Abbreviations

APVP, atrial pace ventricular pace; APVS, atrial pace ventricular sense; ASVP, atrial sense ventricular pace; ASVS, atrial sense ventricular sense; AV, atrioventricular; DDD, dual chamber atrioventricular pacing system; CI, confidence interval; HR, hazard ratio.

Declarations

Ethics approval and consent to participate

The study protocols were approved by the institutional review board committee of the Kaohsiung Medical University Hospital. Written informed consent was obtained from all subjects.

Consent for publication

Not applicable

Availability of data and material

All data that support the present findings are included in our study. The datasets in the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have declared no competing interest exists

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Tables

Table 1. Baseline characteristics in our study patients

Characteristics	All patients (n = 177)
Age (year)	72 ± 14
Male gender (%)	47
Diabetes mellitus (%)	29
Hypertension (%)	60
Hemoglobin (g/dl)	12.9 ± 1.9
Creatinine (mg/dl)	1.31 ± 1.16
Total cholesterol (mg/dl)	171 ± 40
Triglyceride (mg/dl)	109 ± 55
Indication for PM implantation	
Advance AV block (%)	44
Sick sinus syndrome (%)	46
Others (%)	10
Sensing and pacing percentage	
ASVS (%)	32 ± 37
ASVP (%)	33 ± 40
APVS (%)	24 ± 33
APVP (%)	11 ± 20

APVP: atrial pace ventricular pace; APVS: atrial pace ventricular sense; ASVP: atrial sense ventricular pace; ASVS: atrial sense ventricular sense; AV: atrioventricular; PM: pacemaker

Table 2. Predictors of total mortality using Cox proportional hazards model

Parameter	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age (year)	1.067 (1.017-1.119)	0.008	1.057 (1.006-1.112)	0.030
Male gender	1.318 (0.559-3.105)	0.527		
Diabetes mellitus	1.330 (0.509-3.479)	0.560		
Hypertension	0.849 (0.365-1.970)	0.393		
Hemoglobin (g/dl)	0.717 (0.584-0.880)	0.001	0.753 (0.612-0.927)	0.007
Creatinine (mg/dl)	1.236 (0.995-1.536)	0.055		
Total cholesterol (mg/dl)	1.001 (0.988-1.014)	0.917		
Triglyceride (mg/dl)	0.992 (0.980-1.004)	0.178		
Indication for PM implantation				
Advance AV block	0.759 (0.314-1.832)	0.540		
Sick sinus syndrome	0.542 (0.208-1.412)	0.210		
Sensing and pacing percentage				
ASVS (%)	0.991 (0.978-1.005)	0.194		
ASVP (%)	1.001 (0.991-1.011)	0.825		
APVS (%)	1.005 (0.993-1.018)	0.373		
APVP (%)	1.014 (0.996-1.031)	0.126		

HR, hazard ratio; CI, confidence interval; other abbreviations as in Table 1.

Table 3. Predictors of cardiovascular mortality using Cox proportional hazards model

meter	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
(year)	1.049 (0.984-1.119)	0.146		
gender	0.980 (0.263-3.653)	0.976		
diabetes mellitus	1.423 (0.364-5.566)	0.610		
hypertension	0.669 (0.1925-2.330)	0.525		
hemoglobin (g/dl)	0.800 (0.590-1.086)	0.149		
creatinine (mg/dl)	1.352 (1.047-1.745)	0.021	1.385 (1.045-1.835)	0.023
total cholesterol (mg/dl)	1.000 (0.981-1.018)	0.964		
triglyceride (mg/dl)	0.990 (0.973-1.006)	0.229		
Indication for PM implantation				
advance AV block	0.620 (0.155-2.483)	0.500		
bradycardic sinus syndrome	0.360 (0.075-1.736)	0.203		
Programming and pacing percentage				
ventricular S (%)	0.996 (0.978-1.014)	0.633		
ventricular P (%)	0.999 (0.984-1.015)	0.942		
ventricular S (%)	0.986 (0.960-1.012)	0.282		
ventricular P (%)	1.032 (1.012-1.052)	<0.001	1.030 (1.012-1.049)	0.001

HR, hazard ratio; CI, confidence interval; other abbreviations as in Table 1.