Predictors of inappropriate atrial sensing in long-term VDD-pacing systems

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Aims
The efficacy and stability of the atrial electrode sensing function is essential for maintaining atrioventricular (AV) synchrony. This study aimed to explore the long-term reliability and causes of the long-term sensing failure of VDD systems.

Methods and results
We enrolled all the patients with complete or high-degree AV block who received VDD pacemakers between August 1994 to January 2006 and who were followed up for more than 12 months. The interrogation parameters, including the atrial potentials (APs) and AV-synchrony ratio were acquired immediately post-implantation and at 3–6 month intervals thereafter. An inappropriate atrial sensing efficacy was defined as an AV-synchrony ratio of < 90%. Totally 157 patients (70 ± 12 years, 103 males) were enrolled into the study with a follow-up for 4.9 ± 2.5 years. Twenty-six patients (16.6%) suffered from inappropriate atrial sensing. According to a Kaplan–Meier analysis, the incidence of inappropriate atrial sensing was higher in the patients with an age ≥ 72 years old (P = 0.047), mean AP during the implantation of <3.0 mV (P = 0.015), concomitant use of non-dihydropyridine calcium channel blockers (CCBs) (P = 0.003), and atrial fibrillation (AF) (P < 0.001). A Cox regression analysis showed that non-dihydropyridine CCBs (hazard ratio, 3.255; 95% confidence interval, 1.148–9.227, P = 0.026) and AF (hazard ratio, 6.507; 95% confidence interval, 2.478–17.104, P < 0.001) predicted inappropriate atrial sensing.

Conclusion
VDD pacing is a reliable pacing modality. However, we should monitor the pacemaker sensing function in the patients with the concomitant use of non-dihydropyridine CCBs and AF.

Keywords
Atrial fibrillation • Calcium channel blocker • Inappropriate atrial sensing • Pacing • VDD

Introduction
Permanent cardiac pacemaker implantations are a well-accepted therapeutic procedure for the treatment of various types of symptomatic bradyarrhythmias. Single-lead VDD pacing provides the physiological benefit of atrioventricular (AV) synchrony with the convenience of a single-lead system.¹,² The lower cost,³,⁴ lower incidence of complications,⁵,⁶ reduced implantation time,⁷,⁸ and lower incidence of atrial fibrillation (AF)⁹ compared with dual-chamber pacing systems make this system a suitable pacing mode when appropriately indicated.² Therefore, VDD pacemakers have become an alternative to DDD pacemakers and are suggested in patients with AV block and normal sinus node function in the current ACC/AHA/NASPE guidelines.¹⁰

One of the limitations of VDD-pacing systems is inappropriate atrial sensing. That has been estimated to range from 2 to 11% in patients undergoing VDD pacing.¹¹–¹³ Inappropriate atrial sensing of more than 10% in patients with single-lead VDD pacing was associated with a decrease in the exercise duration and increase in the subjective severity score, in addition to a decrease in the quality-of-life.¹⁴ Because inappropriate atrial sensing is an important issue for the efficacy of the VDD-pacing system, this study aimed to report that rate over a long-term follow-up in a single centre in Taiwan and to investigate the possible causes.
Methods

Study population
All patients who had a VDD pacemaker implanted at Taipei Veterans General Hospital between 1994 and 2006 were analysed if they were followed up for more than 12 months. A retrospective review was conducted using the detailed records of all the consecutive patients. The demographic information was recorded, including the patient age, sex, indication for pacing, underlying disease, and drug history. In general, the indication for the implantation of a VDD pacemaker was based on the history of symptomatic AV block. Intact sinus node function was determined by the patient’s history, stress tests, 24-h-Holter ECG monitoring, and/or an electrophysiological study. The study protocol was approved by the ethics committee of Taipei Veterans General Hospital.

Implantation technique and devices
A single-pass lead with a ventricular tip to atrial ring-pair distance (AV distance) of 13.5 cm was inserted by a cephalic vein cut-down. If the cephalic vein could not be found, or the lead could not pass through the access, the subclavian vein was punctured. The tip of the lead was positioned in the apex of the right ventricle. Measurement of the atrial potentials (APs) was performed during normal and deep breathing with the atrial electrode positioned in different accessible right atrial positions. The position of the atrial electrode was then adjusted to obtain the maximal APs on the pacing system analyser. The programmable atrial sensitivity threshold was set to a value of 0.25 or 0.18 mV (the highest sensitivity level) in all patients.

Three major companies were chosen: (i) St. Jude Medical Inc. (St. Paul, MN, USA)—two different models including the Affinity VDR 5430 and Identity Adx VDR 5480 with a 1368 AV plus lead; (ii) Medtronic Inc. (Minneapolis, MN, USA)—six different models including the Thera VDD 7964i, Thera D 7966i, Thera VDD 8968i, Sigma SVDD 303, Kappa KVDD 901, and Kappa KSR 903 with a 5032 or 5038 lead; and (iii) Intermedics Inc. (Angleton, TX, USA)—the Unity 292-07 with a 425-04 or 426-33 lead.

Follow-up
The post-procedural follow-up visits were arranged at the pacemaker follow-up clinics 2 weeks after the implantation and at 3- to 6-month intervals thereafter. A history review and thorough physical examination were performed. The routine assessment included a free-run ECG, retrieval of the pacing parameter settings, AP recordings, and ratio of the AV synchrony. The sensing efficacy of the atrial electrode was evaluated according to the stored AV-synchrony ratio. A poor atrial sensing efficacy in our study denoted an AV-synchrony ratio of <90%.12 The amplitudes of the APs were measured automatically in the sitting position.

Statistical analysis
A statistical analysis was performed utilizing SPSS software (Version 15.0, SPSS Inc., Chicago, IL, USA). All data were expressed as the frequency (percentage) or mean ± standard deviation (SD), or median with interquartile ranges. The parametric continuous data measured between the different response groups were compared by an unpaired Student’s t-test and non-parametric data by a Mann–Whitney test. The categorical data between the patients with inappropriate or normal atrial sensing were compared with a χ2 test and Yates’ correction or Fisher’s exact test as appropriate. A survival analysis was assessed using a Kaplan–Meier analysis with the significance based on the log-rank test. The survival time was calculated from the date of the implantation to the date of inappropriate atrial sensing in the patient. A multiple regression analysis was carried out using a Cox proportional hazard regression analysis. Statistical significance was inferred at a two-sided P-value of <0.05.

Results

Patient population
From August 1994 to January 2006, there were 192 patients who received VDD pacemaker implantations at our centre. Thirty-five patients who were followed up for <12 months were excluded. Thus, a total of 157 patients (age at implantation, 70 ± 12 years, 103 males and 54 females) were enrolled in the study. The mean follow-up duration was 4.9 ± 2.5 years. The indications for a pacemaker implantation were third-degree AV block (55.4%), infrahisian AV block (31.8%), and intermittent AV block (8.9%). A miscellaneous group of electrocardiographic patterns determined the remaining indications (3.8%), among which were biventricular or triphasic block, as well as symptomatic first-degree AV block.

Implantation and follow-up
During the entire follow-up period, three patients (1.9%) underwent a revision of their VDD lead for different reasons: one for a lead dislocation and two for lead fractures. Overall, a symptomatic failure of the VDD-pacing mode was determined in seven patients (4.5%) due to inappropriate atrial sensing. Five patients had a history of paroxysmal AF. Those patients were permanently programmed to the VVI mode.

Among the 157 patients, 26 patients (16.6%) suffered from inappropriate atrial sensing despite the atrial sensitivity threshold programmed to the highest sensitivity level during the follow-up period. The mean duration of the inappropriate atrial sensing was 2.9 ± 2.5 years after the pacemaker implantation. The patients with inappropriate atrial sensing were older, had a longer follow-up duration, and higher percentage of concomitant non-dihydropyridine calcium channel blocker (CCB) usage when compared with the patients with normal atrial sensing (Table 1). The APs during the implantation, comorbidity, and use of other concomitant anti-arrhythmic drugs were similar in the patients with inappropriate and normal atrial sensing. In total 13 patients received non-dihydropyridine CCBs in the current study. Five of them suffered from inappropriate atrial sensing, including two with diltiazem (180 mg per day) and three with verapamil (120–240 mg per day). The other eight patients did not suffer from inappropriate atrial sensing; all of them took diltiazem (one with 30 mg twice per day; six patients with 90 mg per day; one patient with 180 mg per day). The time period over which the CCBs had been used was from 0.54 to 7.50 years. There were six patients with a history of paroxysmal AF before the pacemaker implantation, and all of them met the criteria of AV-synchrony ratio <90% after the follow-up.

According to the Kaplan–Meier analysis, there was no significant difference in the incidence of inappropriate atrial sensing between the female and male patients (P = 0.063). However, the incidence of inappropriate atrial sensing was higher in the patients with an age ≥72 years old (P = 0.047), mean AP during the implantation
of < 3.0 mV (P = 0.015), concomitant use of non-dihydropyridine CCBs (P = 0.003; Figure 1), and AF (P < 0.001; Figure 2). Multivariate analyses using the Cox proportional-hazards regression model showed that non-dihydropyridine CCBs (hazard ratio, 3.255; 95% confidence interval, 1.148–9.227, P = 0.026) and AF (hazard ratio, 6.507; 95% confidence interval, 2.476–17.104, P < 0.001) predicted inappropriate atrial sensing (Table 2).

**Discussion**

The main finding of this study was that inappropriate atrial sensing was not related to the age, sex, comorbidity, or APs. However, the concomitant use of non-dihydropyridine CCBs and AF predicted the occurrence of inappropriate atrial sensing.

Kistler et al. found that aging was associated with both global and regional reductions in the atrial voltage with an increase in the
reported a 95% maintenance rate in 150 patients with an implant AP of $2.01 \pm 0.94$ mV after a mean follow-up of $24 \pm 11$ months. In the Saphir Multicenter Follow-Up Study, the minimal AP ($<0.6$ mV), range of the APs ($>3.3$ mV), and atrial dipole position influenced the atrial sensing performance in single-lead VDD-pacing systems. However, Hunziker et al. found that only the dipole position, and not the implant AP, could predict the outcome of the single-lead VDD-pacing systems. Furthermore, VDD pacing was found not to be inferior to DDD pacing despite the lower implant AP ($2.91 \pm 1.48$ vs. $4.0 \pm 1.7$ mV, $P < 0.0001$). One possible reason may be the influence of the body position on the measurement. In our current study, the mean AP was not a predictor for inappropriate atrial sensing. Further studies should be conducted to clarify the role of the implant AP in inappropriate atrial sensing in the future.

To the best of the authors’ knowledge, the effects of anti-arrhythmic drugs on the atrial sensing function of the VDD pacemakers had not been previously reported. In the current study, the concomitant use of non-dihydropyridine CCBs was a predictor of inappropriate atrial sensing. One possibility is that the CCBs could affect the calcium-induced calcium release and increase the threshold. Another possibility is mechanoelectrical feedback. Mechanoelectrical feedback can affect both the inward and outward ionic currents and result in shortening of the AP duration and increase the automaticity. It is possible that CCBs may reduce the tissue tension and decrease the sensitivity. The use of concomitant non-dihydropyridine CCBs should be done with care in the patients who receive VDD pacemakers.

Some retrospective studies have shown a lower incidence of AF in patients with VDD pacemakers than in those with DDD devices in the patients with isolated AV block. That result was further confirmed by our previous study. In the study by Pakarinen et al., a strong predictor of the discontinuation of VDD pacing was a combination of a history of AF and cardiac enlargement. In the current study, patients with paroxysmal AF were stratified at the time of the implantation. We found that AF was a predictor for inappropriate atrial sensing. Further, five of the six patients with paroxysmal AF had the pacemaker downgraded to the VVI or VVIR mode. AF may result in anatomic and electric remodelling, which may result in the development of inappropriate atrial sensing in the follow-up. In our current study, we relied on the pacemaker’s auto-recorded AV-synchrony ratio to evaluate atrial sensing efficacy. The definition of inappropriate atrial sensing was according to previous studies. It had been noted that inappropriate atrial sensing of more than 10% in patients with single-lead VDD pacing was associated with a decrease in the exercise duration and increase in the subjective severity score, in addition to a decrease in the quality-of-life. Although it is possible that patients with paroxysmal AF may have perfect atrial sensing function during sinus rhythm, the AV-synchrony could not be maintained during the episodes of AF. That finding supported the previous studies that VDD pacing should be used more carefully in patients with paroxysmal AF.

There were some limitations to the current study. First, this study was a retrospective study with a small sample size. However, the follow-up periods in the current study were long, and the significant predictors could be found. Second, there were heterogeneity of the voltage. Although the cause of the loss of the voltage amplitude was unknown, that potentially represented the development of interstitial fibrosis. Concern had been raised about the sensing function of the VDD pacemakers in the elderly. Wiegand et al. found an inverse relationship between the patient age and APs perceived via floating leads. However, even in old patients with VDD pacemakers, the maintenance of the AV synchrony was comparable to that of DDD pacemaker follow-up studies. The results were further strengthened by our current study that age was not a predictor for inappropriate atrial sensing.

One important issue during single-lead implantations of VDD-pacing systems is the minimal acceptable AP. Rey et al. have perfect atrial sensing function during sinus rhythm, the AV-synchrony could not be maintained during the episodes of AF. That finding supported the previous studies that VDD pacing should be used more carefully in patients with paroxysmal AF.

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different VDD devices and leads used in this study. There may be concern about the different atrial sensing performances of the different VDD systems. However, a previous study\(^7\) showed that the measured APs did not differ among the different VDD-pacing systems. Furthermore, the atrial sensitivity threshold was set to the highest level in all patients. Third, we relied on the pacemaker’s auto-recorded AV-synchrony ratio to evaluate the atrial sensing efficacy, which may not be the true atrial sensing function. However, it was commonly used and was the most practical parameter in daily practice.\(^12\),\(^14\),\(^31\)

In conclusion, VDD pacing is a reliable pacing modality after the long-term follow-up. The concomitant use of non-dihydropyridine CCBs and AF were predictors of inappropriate atrial sensing. The pacemaker sensing function should be monitored in the patients with the concomitant use of non-dihydropyridine CCBs and AF.

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**References**