The Impact of the Distance between the Atrial Electrode and the Atrial Wall on Atrial Undersensing in Patients with VDD Pacemakers: Long-Term Follow-Up

Timucin Altin, M.D., Muharrem Guldal, M.D., Basar Candemir, M.D., Cegerhun Polat, M.D., Aydan O. Ozdemir, M.D., Cansin Tulunay, M.D., Cagdas Ozdol, M.D., Omer Akyurek, M.D., Remzi Karaoguz, M.D., and Cetin Erol, M.D.

From the Ankara University School of Medicine, Department of Cardiology, Ankara, Turkey

Aim: Atrial undersensing (AUS) in single-lead VDD pacemakers may be due to diminished P-wave amplitude secondary to local inflammation beneath the electrodes closer to atrial wall. The aim of this study was to assess the potential effect of distance between atrial electrode and atrial wall on immediate and long-term atrial sensing stability in VDD systems.

Methods: A total of 275 patients with normal sinus node function who received VDD pacemakers were enrolled into the study and were followed up for a median duration of 33 months. During each control visit, a standard 12-lead electrocardiogram (ECG) was obtained and standard pacemaker function assessment was performed including testing for pacing threshold and atrioventricular synchrony. The distance between atrial electrode and atrial wall was measured from chest X-ray.

Results: Of the 275 patients, AUS was detected in 59 patients. Univariate predictors of AUS were use of closely spaced bipolar ring atrial electrode (CSBR) ($P = 0.01$), wider atrial ring-spacing ($P = 0.03$), and atrial sensitivity programmed to a higher level ($P = 0.001$). Use of CSBR ($P = 0.04$) and atrial sensitivity ≥ 0.3 mV ($P = 0.02$) were observed to be the independent predictors for AUS. When the distance between atrial electrode and atrial wall was < 7 mm, AUS was less with diagonally arranged bipolar ring electrodes (DABR) than it was with CSBRs ($P = 0.02$).

Conclusions: The distance between atrial electrode and atrial wall does not appear to affect AUS incidence in VDD pacemakers. For VDD electrodes closer to atrial wall, AUS was significantly less likely in DABR-type electrodes.

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VDD pacemakers; atrial undersensing; atrial electrode; atrial wall

The single-lead VDD system for atrial synchronous ventricular pacing could be an acceptable alternative to DDD systems in patients with normal sinus node function, owing to the advantages of reduced implantation time, decreased complication rate, and lower procedural cost.¹ However, due to high variability of the atrial signal amplitudes received by floating atrial electrodes, intermittent atrial undersensing may constitute a significant problem in single-lead VDD pacemakers.² The atrial electrode configuration of the pacemaker lead and the distance between the atrial electrode and the atrial wall have been demonstrated to be associated with P-wave amplitude (PWA).^{3,4} Sensing

of PWA in VDD systems usually diminishes soon after the implantation and remains stable afterward,⁵ but the underlying mechanism has not been established yet. In an experimental animal study, Higashi et al. suggested a possible mechanism that proposed a local inflammatory process with development of edema, hypertrophy, and fibrosis in the atrial wall just beneath the atrial electrode, as evidenced by macroscopical and histological examination.⁶

In this study, we aimed to investigate the possible relationship between the incidence of atrial undersensing (AUS) and distance between atrial electrode and atrial wall in patients with VDD pacemakers.

Table 1. Characteristics of the 275 Patients Followed

Age at Implantation, Years	62 ± 16
Male, %	44
Indication for cardiac pacing, %	
Third-degree AV block	74
Second-degree AV block	21
Trifascicular AV block	4
HCM	1
Coronary artery disease, %	24
Hypertension, %	56
Diabetes mellitus, %	17
Rheumatic heart disease, %	7
Congenital heart disease, %	2
LV wall motion abnormality, %	23
Follow-up time, months*	33 (6–66)

*Median (25–75th percentile).

AV = atrioventricular; HCM = hypertrophic cardiomyopathy; LV = left ventricle.

MATERIALS AND METHODS

Study Population

Three hundred twenty-six patients experiencing high-degree atrioventricular block or symptomatic hypertrophic cardiomyopathy with documented normal sinus node function received VDD pacemakers between June 1995 and October 2006. Preimplantation sinus node function was interpreted using 12-lead resting electrocardiograms (ECG) or ECG monitors. Exclusion criteria were history of chronic or intermittent atrial arrhythmia and age <18 years. Follow-up data were obtained from 275 patients (121 males, mean age: 62 ± 16 years) who regularly visited outpatient pacemaker follow-up unit. The follow-up duration of patients who experienced chronic atrial arrhythmia were presumed to be the time period until atrial arrhythmia development.

Patients were grouped according to the presence or absence of AUS, and groups were then compared

with respect to baseline and follow-up characteristics. Baseline characteristics of the study groups are summarized in Table 1.

Implantation and Devices

Pacemaker implantations were performed by a team consisting of one experienced electrophysiologist and a trainee in cardiology. Implanted pacemakers were Intermedics (Angleton, TX) 292–06, 292–07 Unity, Virtus; Medtronic (Minneapolis, MN, USA) 7944, 8948, 8968 Thera, 8168 Prodigy, Sigma 303, Kappa 701; St Jude Medical (Sylmar, CA, USA) Affinity 5430, Identity 5480, Verity 5456; Guidant (St Paul, MN, USA) Insignia; Ela (Le Plessis-Robinson, France) Talent 3, Symphony; Vitatron (Arnhem, the Netherlands), Sapphire 3 and the leads were Intermedics 425–04, 425–06, 425–13, 425–33, 425–36; Medtronic 5032, 5038; St Jude Medical 1368, and Guidant 4341. Characteristics of the leads are summarized in Table 2. Only Intermedics VDD leads had atrial electrodes designed as diagonally arranged bipolar ring (DABR), whereas the rest had closely spaced bipolar atrial ring (CSBR). DABR leads had the smallest atrial ring spacing (Table 2). DABR leads had three different configurations in terms of the distance between atrial and ventricular electrodes; 11 cm (n = 50), 13 cm (n = 103), and 16 cm (n = 4). The leads were inserted preferably via right or left cephalic vein cut-down in 58% of the patients under fluoroscopic guidance. If cephalic cut-down approach was unsuccessful, a route via subclavian vein puncture (42%) was selected. The site of lead insertion, the length of VDD lead, and the distance between atrial and ventricular electrodes were left to the discretion of the operator according to the fluoroscopic dimensions of the heart and the patient size. Final lead position was optimized according to maximal atrial and ventricular signal amplitudes and the

Table 2. Characteristics of the VDD Leads

	Intermedics N = 157	Medtronic N = 67	St. Jude Medical N = 18	Guidant N = 33
Model	425–04, 06, 13, 33, 36	5032, 5038	1368	4341
Distance between atrial and ventricular electrodes, cm	11 (n = 50) 13 (n = 103) 16 (n = 4)	13	13	13
Atrial ring spacing, mm	5	8.6	11.9	10.0
Atrial electrode configuration	Diagonal/bipolar	Ring/bipolar	Ring/bipolar	Ring/bipolar

lowest ventricular pacing threshold. A minimum PWA of 1 mV during deep breathing, coughing, and Valsalva maneuver was accepted as suitable. Initial programming was VDD mode with a minimum rate of 47 ± 8 bpm and with an atrial sensitivity level at least three times more sensitive than intraoperative PWA. These settings were not modified unless an AUS was detected or it was deemed as necessary.

Follow-Up and Measurements

Follow-up visits were scheduled at first month postoperatively, and every 4–6 months afterward. At each control visit a 12-lead ECG was obtained, and a detailed pacemaker function assessment was performed including testing of pacing threshold, atrial sensing performance, and atrioventricular synchrony. AUS was defined as a definite, clearly seen P wave not sensed by the pacemaker on the routine ECG, during deep breathing in supine and upright position as evidenced by ECG, and/or 24-hour Holter monitoring. In patients with AUS, atrial sensitivity was reprogrammed to the highest sensitive level.

Atrial sensing threshold was defined as the least sensitive level with a reliable P wave detected during forced maneuvers. Atrial sensing threshold measurements were available in 127 (46%) patients at a median duration of 5 months (25–75th percentile, 1–31 months).

Telecardiography (CXR) was obtained from 180 cm during inspiration while standing, as standard technique, at a median duration of 2 months (25–75th percentile, 1–11 months). The distance between atrial electrode and atrial wall was defined as the distance between the center of the atrial dipole and the right atrial wall on the CXR (Fig. 1). The data regarding the atrial sensing threshold and the distance between atrial electrode and atrial wall were obtained from concurrent measurements. Right atrium was divided into three equal portions (high, mid, and low) to determine the effect of vertical position of the atrial dipole.

Statistical Analysis

All of the analyses were performed using a commercially available statistical software package (SPSS version 10.0 for Windows, SPSS Inc.,

Figure 1. A telecardiogram showing the position of the VDD atrial electrode. Dotted lines show the margins between the high (H), mid (M), and low (L) right atrium. *The distance between the atrial electrode and the right atrial wall.

Chicago, IL, USA). Data were expressed as numbers and percentages for discrete variables, means $\pm$ SD for normally distributed continuous variables, and median and 25–75th percentile for other continuous variables. The chi-square analysis was performed to assess the significance of difference between dichotomous variables. Continuous variables were compared using Student's *t*-test, Mann-Whitney *U* test, or one-way ANOVA. The receiver operating characteristics (ROC) curves were created to define the optimal cutoff value for the prediction of AUS level for intraoperatively programmed atrial sensitivity, which was determined as the value with the highest possible sensitivity and specificity. A multivariable logistic regression analysis was used to investigate the independent predictors for the development of AUS that were previously found to be significant correlates in the univariate analysis. A *P* value <0.05 was considered as statistically significant. Freedom from AUS for all patients was calculated by Kaplan-Meier analysis and lifetables. Freedom from AUS between DABR and CSBR electrode configurations were compared by Kaplan-Meier and Cox regression analysis.

RESULTS

Median duration of follow-up for 275 patients was 33 months (25–75th percentile; 6–66 months). In 59 (22%) patients, AUS was detected at a median duration of 2 months (25–75th percentile 1–20 months). The probability of freedom from AUS was 63% by Kaplan-Meier analysis and lifetables (Fig. 2). Forty-one percent and 70% of all the AUSs were observed at the end of the first and 12th month, respectively. In case of AUS, atrial sensitivity level was reprogrammed (from 0.34 ± 0.14 mV to 0.15 ± 0.06 mV). Programming the atrial sensitivity to the highest value completely resolved the problem in 47 (80%) of those patients. After reprogramming the atrial sensitivity, 96% of the 275 pacemakers had proper VDD function at a median duration of 33 months and no atrial oversensing (e.g., far-field R-wave sensing) was observed during follow-up. In the remaining 12 patients in whom reprogramming could not solve the problem, lead repositioning ($n = 2$) or adding an atrial lead ($n = 6$) was needed to overcome atrial undersensing. In three patients with infrequent AUS without clear symptoms, pacemakers were left in VDD mode. In one patient with symptomatic AUS and accompa-

Figure 2. Kaplan-Meier analysis showing freedom from atrial undersensing by time.

nying sinus bradycardia, the pacemaker was programmed to VVI mode as the patient refused the upgrading of the system.

Characteristics of the patients with and without AUS were outlined in Table 3. In patients with AUS, atrial electrodes with CSBR configuration were observed to have been more frequently implanted (58% vs 39%; $P = 0.01$) and atrial ring spacing was larger (7.5 ± 2.3 mm vs 6.8 ± 2.4 mm; $P = 0.03$). The distance between the atrial and ventricular electrodes of VDD leads were similar between the two groups ($P = 0.5$). Intraoperative PWAs were similar in both groups (2.9 ± 1.3 mV vs 2.8 ± 1.4 mV; $P = 0.6$). Of 127 patients who had reliable atrial sensing threshold measurements, atrial signal amplitudes were observed to diminish from 3.0 ± 1.3 mV intraoperatively to 1.9 ± 1.2 mV during follow-up ($P < 0.001$). The atrial sensing thresholds ($P = 0.9$) and the mean change in PWAs ($P = 0.5$) during follow-up were similar in groups with and without AUS. In patients with AUS, programmed atrial sensitivity was significantly lower (numerically higher) than those with regular sensing (0.34 ± 0.14 mV vs 0.27 ± 0.11 mV; $P = 0.001$). Vertical position of atrial electrode (high, mid, low) and lead insertion sites (right or left venous access) did not differ between the two groups ($P = 0.2$ and $P = 0.7$, respectively). When the distance between atrial electrode and atrial wall was divided

Table 3. Comparison of Patients with and without Atrial Undersensing

	Regular Sensing N = 216	Atrial Undersensing N = 59	P Value
Age, years	63 ± 16	61 ± 16	0.5
Male, %	46	36	0.1
Hypertension, %	57	56	0.9
Diabetes mellitus, %	17	19	0.8
Coronary artery disease, %	26	19	0.3
Rheumatic heart disease, %	6	9	0.4
LV dysfunction, %	23	20	0.7
Atrial electrode configuration, %			
DABR	61	42	0.01
CSBR	39	58	
Atrial ring spacing, mm	6.8 ± 2.4	7.5 ± 2.3	0.03
Distance between atrial and ventricular electrodes, cm	12.7 ± 0.9	12.8 ± 0.8	0.5
Minimum PWA, mV ^a	2.8 ± 1.4	2.9 ± 1.3	0.6
Atrial sensing threshold at follow-up, mV ^b	1.9 ± 1.3	1.8 ± 1.0	0.9
Δ PWA, mV ^b	-1.1 ± 1.5	-1.3 ± 1.3	0.5
Programmed atrial sensitivity ^a , mV	0.27 ± 0.11	0.34 ± 0.14	0.001
Distance between atrial electrode and atrial wall, %			
<7 mm	35	31	0.8
7–11 mm	33	33	
>11 mm	32	37	
Vertical atrial electrode position, %			
High	61	68	0.2
Mid	32	20	
Low	6	12	
Insertion site, %			
Right	59	62	0.7
Left	41	38	

CSBR = closely spaced bipolar ring; DABR = diagonally arranged bipolar ring; LV = left ventricular; PWA = P-wave amplitude; Δ PWA = change in PWA during follow-up.

^aIntraoperative.

^bOnly confined to 127 patients with atrial sensing threshold measurement at follow-up.

into tertiles (<7 mm, 7–11 mm, and >11 mm), no difference was found between the tertiles with respect to AUS (P = 0.8).

An ROC curve, which was created to determine a cutoff value of programmed atrial sensitivity for the prediction of AUS (area under the ROC curve of 0.64 ± 0.04 , P = 0.001), revealed an atrial sensitivity value of ≥ 0.3 mV with a sensitivity of 58% and a specificity of 60%. Multivariate logistic regression analysis demonstrated that the implantation of a lead with atrial CSBR electrode configuration (OR 6.14, 95% CI 1.11–33.92; P = 0.04) and a programmed atrial sensitivity value of ≥ 0.3 mV (OR 2.06, 95% CI 1.14–3.74, P = 0.02) were independent predictors for development of AUS. As shown in the Figure 3, when the atrial electrode was closer to the atrial wall (<7 mm), AUS was less likely with leads with DABR configuration than the leads with CSBR. The incidence of AUS was not different

among tertiles of distance between atrial electrode and atrial wall for any specific atrial electrode configuration (for DABR, P = 0.4 and for CSBR, P = 0.9). Intraoperative and follow-up parameters that were presumed to effect atrial sensing performance were compared among tertiles of distance between atrial electrode and atrial wall and it revealed no statistically significant difference (Table 4).

Kaplan-Meier and Cox regression analysis revealed that the probability of development of AUS was less with DABR than CSBR electrodes (OR 0.415, 95% CI 0.246–0.699, P = 0.001) (Fig. 4).

DISCUSSION

Our study investigated a probable relationship between the proximity of atrial electrode to atrial wall and AUS in a large population who received single-lead VDD pacemakers in a single center.

Figure 3. Incidence of atrial undersensing in relation to the distance between atrial dipole and right atrial wall. Atrial undersensing was observed less with the use of atrial electrodes with DABR configuration only in close position (<7 mm) to the atrial wall. CSBR = closely spaced bipolar ring; DABR = diagonally arranged bipolar ring.

In spite of some methodological differences and vigorousness in the assessment of AUS, our results are comparable to previous reports.^{5,7-9} Overall incidence of AUS was 22%. Most of the patients with AUS were asymptomatic, and reprogramming to the most sensitive setting resolved the problem in the majority (80%). In eight of the remaining patients, lead repositioning and adding an atrial lead was performed because of related symptoms. Although Campen et al.¹⁰ reported that undersensing of atrial beats <10% would not effect the quality of life, maximal proper AV synchrony is still a desirable goal for most of the clinicians.

The distance between atrial electrode and atrial wall was demonstrated to be associated with PWA obtained by the VDD pacemaker.³ PWA usually

decreases in the postoperative period, but the underlying mechanisms still remain to be identified. Higashi et al. proposed that this decrease could be due to the inflammation in the atrial wall just beneath atrial electrode that adhered to it.⁶ We tested this hypothesis by investigating a potential relationship between the distance of atrial electrode to the atrium and the incidence of AUS in a large group of patients with long-term follow-up. In the end, our results did not support this hypothesis as the distance between atrial electrode and atrial wall did not show any significant relationship with neither the incidence of AUS nor intraoperative PWAs and follow-up atrial sensing thresholds.

The observation that 41% and 70% of AUSs were detected at the end of the first month and

Table 4. Comparison of Pacemaker Parameters among Tertiles According to Distance between Atrial Electrode and Atrial Wall

	Distance between Atrial Electrode and Atrial Wall			P Value
	<7 mm	7-11 mm	>11 mm	
Programmed atrial sensitivity, mV ^a	0.29 ± 0.1	0.28 ± 0.1	0.31 ± 0.1	0.5
DABR atrial electrode configuration, %	58	59	60	0.9
PWA, mV ^a	2.8 ± 1.4	2.6 ± 1.1	3.1 ± 1.5	0.1
Follow-up atrial sensing threshold, mV ^b	2.1 ± 1.3	1.8 ± 0.7	1.7 ± 1.3	0.5

DABR = diagonally arranged bipolar ring; PWA = P-wave amplitude.

^aIntraoperative.

^bOnly confined to 127 patients with atrial sensing threshold measurement at follow-up.

Figure 4. Analysis of comparison of freedom from atrial undersensing between patients with DABR and CSBR atrial electrode configurations by Kaplan-Meier analysis. CSBR = closely spaced bipolar ring; DABR = diagonally arranged bipolar ring.

12th month, respectively, is supported by the previous studies that reported that most of the AUS occurred early after the implantation due to diminished PWA.^{5,6} In concordance, follow-up atrial sensing thresholds were lower than intraoperative PWAs in our patients. However, AUS mechanism could not solely be explained by a decrease in PWA in this study, because intraoperative PWAs and follow-up atrial sensing thresholds were similar in patients with and without AUS.

There might be other mechanisms responsible for AUS, such as atrial electrode configuration. In our study, use of CSBR electrode was an independent predictor for AUS. There are some differences in the specifications of DABR and CSBR electrodes. First, the DABR electrodes have the narrowest ring spacing. Our results demonstrated that narrower ring spacing is associated with better sensing performance, as previously reported.¹¹ Especially, in a close position to the atrium, electrodes with wide ring spacing detect less clear-cut signals than electrodes with narrow ring spacing.^{12,13} Indeed, in this study, as electrodes moved closer to atrial wall (<7 mm), AUS was less likely with DABR configuration. Second, DABR leads were available in three different forms in terms of the distance between atrial and ventricular electrodes, whereas all the

CSBR leads had the same distance. The operators have to push the leads with longer distance more vigorously in order to place the atrial ring closer to atrium. Higashi et al.⁶ recommended not to press the lead hard against atrial wall in order not to aggravate inflammatory response. Therefore, the leads with longer distance may provoke more inflammation at atrial wall and may lead to AUS.⁶ However, this could not be the case in our study, as the distance between atrial and ventricular electrodes were similar in patients with and without AUS. Third, the DABR electrodes come from only one manufacturer (Intermedics).

In contrast to our findings, Lau et al.⁸ reported comparable clinical performances between DABR and CSBR electrodes in a smaller population. But this study differs from ours in various aspects. First, they compared only two different pacemaker systems (Intermedics and Medtronic). Our leads with DABR configuration were all Intermedics, but CSBR leads were connected to various pacemakers that belonged to different manufacturers, in a manner reflecting general clinical practice. Second, they used an investigational software allowing to program atrial sensitivity levels to as low as 0.18 mV for Medtronic Thera VDD pacemakers. In one-fifth of our patients, CSBR electrodes were connected to

Medtronic Thera pacemakers with the most sensitive level of 0.25 mV. Therefore, programming to a more sensitive level might have underestimated the AUS incidence in CSBR group in their study.

Another independent predictor of AUS in this article was found to be selecting a lower atrial sensitivity. This was not surprising as it has been well known that the higher the programmed atrial sensitivity, the higher the atrial sensing capability.^{8,12} In a study in which all the atrial sensitivities were programmed to the most sensitive levels, Hunziker et al. reported that maximum programmable atrial sensitivity was a predictor of loss of AV synchrony.¹⁴ One might speculate that, if atrial sensitivity had been set to the most sensitive level, less patients would have experienced AUS. However, in the earlier periods of VDD implantation practice, operators might have been worrisome of possible oversensing at more sensitive levels. Although, setting the atrial sensitivity to the most sensitive level was reported to be safe in terms of oversensing,¹⁵ we could not change our practice due to retrospective nature of the study. Indeed, none of our patients experienced oversensing after reprogramming.

LIMITATIONS

Our study has some limitations. First, posteroanterior CXR gives information about only the position of atrial electrode relative to the lateral atrial wall. However, it has been well known that floating atrial electrode changes position with body movements in the right atrium, which is a three-dimensional structure. The pacemaker lead is inserted in supine position, whereas CXR is performed while standing. In a recent study, 80% of atrial electrodes in VDD leads came closer to the atrial wall while standing.¹⁶ On the other hand, other studies reported that atrial signal amplitudes varied significantly and unpredictably in different postures or maneuvers, even in the same individual.^{2,17} So, it is quite difficult to determine at which position the AUS will occur more frequently. In this study, atrial sensing performances were evaluated by ECGs obtained in supine and upright positions and/or Holter recordings during pacemaker control visits. Unfortunately, the data regarding what percentage of the AUSs were observed during routine ECG, at different postures or Holter recordings were not recorded. Second, all the CXRs were performed only during inspiration. So, the effect

of breathing (inspiration vs expiration) on the distance of atrial electrode to the atrial wall could not be evaluated as the CXRs were performed only during inspiration. Third, it was not possible to define precisely the position of the atrial endocardium and possible variations in the anatomy, and to identify the exact cardiac cycle phase when the measurement was being performed. However, CXR is an easy but indirect measure of intraoperative fluoroscopic views. Fourth, measurements of atrial sensing thresholds were not available in all patients. But in approximately half of the population with follow-up measurements, atrial sensing thresholds were significantly lower than intraoperative PWAs, as expected.^{5,8} In these patients, the decrease in atrial signal amplitudes was similar between patients with and without AUS. This may reflect general population. In fact in a given individual, high variability of atrial sensing thresholds at the time of measurement is probably a transient phenomenon due to changes in the position and respiratory or cardiac cycle phase which could not be further clarified at this time. Finally, this study included more than one type of pacemaker systems, especially for the leads with CSBR configuration, so our results might have reflected various atrial electrode designs. But, because these systems are widely used and most VDD leads with CSBR configuration show similar designs, we believe that our results represent routine clinical practice.

CONCLUSION

The distance between atrial electrode and atrial wall does not appear to effect the incidence of AUS in patients with VDD pacemakers. However, when atrial electrode is closer than 7 mm to atrial wall, AUS was less with DABR electrodes. Use of DABR electrodes and programming atrial sensitivity to the most sensitive level were associated with decreased incidence of AUS. However, in general, leads with CSBR configuration also have good performance. Further research is warranted to state that DABR configuration is superior to CSBR configuration.

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