Bradycardia-dependent rise in the atrial capture threshold early after cardiac pacemaker implantation in patients with sick sinus syndrome

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Introduction

After the implantation of a cardiac implantable electronic device, a rise in the capture threshold is a common complication that requires early reintervention. Precise measurements of the sensing amplitude and capture threshold are important to estimate lead position and stability and to determine sensing and pacing settings. Although pacing rate is commonly thought not to significantly affect capture threshold, we encountered 3 patients undergoing pacemaker implantation for sick sinus syndrome (SSS) in whom the pacing rate was a critical determinant of successful capture of the atrial myocardium because of a bradycardia-dependent rise in the atrial capture threshold.

Case reports

Case 1

A 76-year-old woman was admitted to our hospital with presyncope. Holter electrocardiography (ECG) showed sinus pauses with a maximum R-R interval of 3.7 seconds associated with the symptoms and paroxysms of atrial fibrillation. She received a dual-chamber pacemaker with a passive fixation atrial lead (CapSure Sense, Medtronic, Minneapolis, MN) placed in the right atrial appendage. The initial atrial capture threshold (0.5-V amplitude at 0.4-millisecond pulse width) was measured at the pacing rate of 90 beats per minute (bpm), 20 bpm higher than her baseline heart rate. The sensing and impedance values were 1.4 mV and 551 Ω, respectively. The initial pacemaker mode was managed ventricular pacing (Medtronic) and 60 to 130 bpm. The next day, patient monitoring showed atrial pacing spikes without atrial depolarizations (P waves). Pacemaker interrogation revealed a marked rise in the atrial capture threshold, to 3.75 V at 0.4 milliseconds at 70 bpm. The sensing and impedance values were slightly decreased, to 0.9 mV and 475 Ω, respectively. No measurement of the capture threshold using different pacing rates was performed. Although chest radiographs showed no apparent dislodgement of the atrial lead, atrial lead replacement was performed with an active fixation lead (CapSureFix Novus, Medtronic). The initial atrial capture threshold of this lead was 1.25 V at 0.4 milliseconds at 90 bpm. Monitoring on the following day again showed failure of atrial pacing. This time, detailed measurement of the atrial capture threshold was performed. The threshold changed remarkably in accord with pacing rate: 1.0 V at 0.4 milliseconds at 100 bpm, 1.5 V at 0.4 milliseconds at 80 bpm, and >3.5 V at 0.4 milliseconds (noncapture) at 60 bpm. There was no significant change in the sensing or impedance value (1.4 mV and 475 Ω, respectively). Therefore, the lower rate increased temporarily to 75 bpm to avoid pacing failure.

Five days after implantation, a noninvasive electrophysiological study (EPS) was performed using the device's system. Programmed atrial stimulation at a basic cycle length of 600 milliseconds was performed with the pacing output fixed at 4.0 V at 0.5 milliseconds (default setting of the device's EPS system). One atrial extrastimulus (S2) was delivered after 15 paced atrial stimuli (S1). Because the device system does not allow the S1-S2 interval to be > 600 milliseconds, the EPS protocol was as follows (Figure 1):

KEYWORDS Bradycardia; Pacemaker; Phase 4 block; Sick sinus syndrome; Threshold

ABBREVIATIONS **bpm** = beats per minute; **ECG** = electrocardiography; **EPS** = electrophysiological study; **SSS** = sick sinus syndrome

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KEY TEACHING POINTS

- A bradycardia-dependent rise in the atrial capture threshold can occur in patients undergoing implantation of cardiac implantable electronic devices.
- Because this unfavorable phenomenon is expected to resolve within a few months, reintervention for lead revision may be avoidable.
- Electrocardiologists should measure the capture threshold by pacing at higher rates if a rise in the atrial capture threshold is observed early after implantation.

When the S1-S2 interval is > 600 milliseconds:

First, the basic setting of pacemaker was set as atrial pacing, atrial sensing, inhibited response (AAI) 30 bpm (2000 milliseconds). Next, 15 basic stimuli (S1-S1 interval, 600 milliseconds) were delivered using an EPS function. After S1 stimuli were stopped, the next stimulus was delivered 2000 milliseconds later as a function of AAI 30 bpm. This stimulus was substituted as the S2 stimulus. The basic setting of the pacemaker was changed from AAI 30 bpm (2000 milliseconds) to AAI 95 bpm (632 milliseconds) in increments of 5 bpm. Because the reset rate in this system is 65 bpm (923 milliseconds), the S1-S2 interval of 65 bpm cannot be assessed.

When the S1-S2 interval is ≤ 600 milliseconds:

The S1-S2 interval was set from 600 milliseconds until the atrial effective refractory period in decrements of 10 milliseconds.

The results of the EPS were as follows (Figure 1):

1. When the S1-S2 interval was 2000 milliseconds (30 bpm), a sinus beat appeared prior to S2.
2. When the S1-S2 interval was 1714 milliseconds (35 bpm), S2 was captured with reproducibility.
3. When the S1-S2 interval was from 1500 milliseconds (40 bpm) to 750 milliseconds (80 bpm), S2 was not captured.
4. When the S1-S2 interval was from 706 milliseconds (85 bpm) to 260 milliseconds, S2 was captured.
5. When the S1-S2 interval was ≤ 250 milliseconds, S2 was not captured, and 260 milliseconds was the atrial effective refractory period.

In summary, a unique bradycardia-dependent phenomenon with a noncapture range between 1500 milliseconds and 750 milliseconds was observed shortly after device implantation.

One month after implantation, the same EPS was repeated. The S2 stimulus did not capture the atrium only when the S1-S2 interval was 1000 milliseconds (60 bpm) (Figure 2). The noncapture range had clearly decreased in 1 month. Two months later, the noncapture range had disappeared, and the atrial capture threshold improved to 0.75 V at 0.4 milliseconds at 60 bpm. The sensing and impedance values were stable (1.4 mV and 361 Ω, respectively).

Case 2

A 74-year-old woman was hospitalized with presyncope due to SSS. A Holter ECG showed long pauses with a maximum R-R interval of 6.8 seconds. She received a dual-chamber pacemaker with an active fixation lead (Fineline II, Boston Scientific, Marlborough, MA) placed in the upper atrial septum. The initial atrial capture threshold was 0.8 V at 0.4 milliseconds at 80 bpm, 20 bpm higher than her baseline heart rate. The sensing and impedance values were 2.3 mV and 587 Ω, respectively. The initial pacemaker mode was dual-chamber pacing, dual-chamber sensing, dual response (DDD) and 60 to 110 bpm. Two days after implantation, patient monitoring showed ventricular pacing after the failure of atrial pacing. Pacemaker interrogation revealed that the atrial capture threshold was dependent on the pacing rate as follows: 1.4 V at 0.4 milliseconds at ≥70 bpm, 3.75 V at 0.4 milliseconds at 65 bpm, and 5 V at 0.4 milliseconds at 60 bpm. There were slight decreases in the sensing and impedance values to 1.9 mV and 409 Ω, respectively. Therefore, the lower rate rose to 70 bpm to avoid pacing failure. One month after implantation, the atrial capture threshold had improved to 0.6 V at 0.4 milliseconds at ≥70 bpm, 1.0 V at 0.4 milliseconds at 65 bpm, and 1.7 V at 0.4 milliseconds at 60 bpm. Seven months after implantation the atrial capture threshold had improved to 0.6 V at 0.4 milliseconds at all pacing rates. Although the sensing value was unavailable because of the lack of her own atrial activity, there was no change in the impedance value (429 Ω).

Case 3

An 86-year-old woman was hospitalized with syncope due to SSS. A Holter ECG showed sinus arrest with junctional escape beats at 30 bpm. She received a dual-chamber pacemaker with an active fixation lead (Fineline II, Boston Scientific) placed in the right atrial appendage. The initial atrial capture threshold was 0.6 V at 0.4 milliseconds at 60 bpm. The sensing and impedance values were 2.4 mV and 549 Ω, respectively. The pacemaker mode was DDD 60 to 130 bpm. One month after patient discharge, the ECG showed ventricular pacing after the failure of atrial pacing. Pacemaker interrogation revealed that the atrial capture threshold had changed according to the pacing rate as follows: 0.7 V at 0.4 milliseconds at 90 bpm, 1.1 V at 0.4 milliseconds at 80 bpm, and >5 V at 0.4 milliseconds at 60 bpm. The sensing and impedance values were decreased to 0.7 mV and 493 Ω, respectively. Therefore, the lower rate rose to 80 bpm to avoid pacing failure. At 1 year after implantation, the atrial capture threshold had improved to 0.4 V at 0.4 milliseconds at 90 bpm, 0.6 V at 0.4 milliseconds at

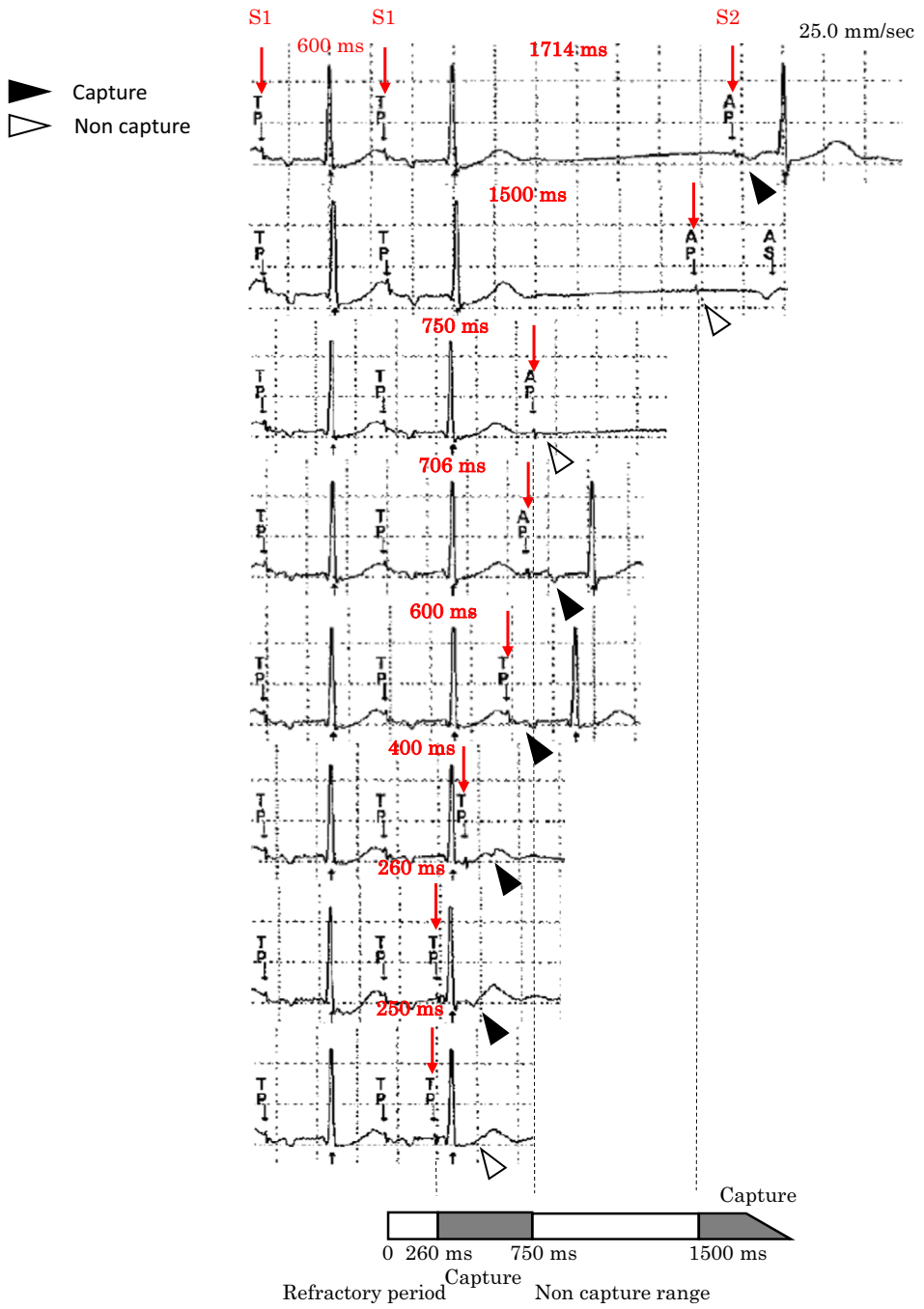

Figure 1 Programmed atrial stimulation was performed on the fifth day after implantation. The basic stimuli (S1) cycle length was 600 milliseconds, and one atrial extrastimulus (S2) was delivered 1714 milliseconds to 250 milliseconds after S1. When the S1-S2 interval was 1714 milliseconds (35 bpm), S2 was captured with reproducibility. When the S1-S2 interval ranged from 1500 milliseconds (40 bpm) to 750 milliseconds (80 bpm), S2 did not capture the atrium. When the S1-S2 interval ranged from 706 milliseconds (85 bpm) to 260 milliseconds, S2 captured the atrium. When the S1-S2 interval was $\leq$ 250 milliseconds, S2 did not capture the atrium (atrial effective refractory period = 260 milliseconds). The "noncapture range" lay between 1500 milliseconds and 750 milliseconds.

80 bpm, and 2 V at 0.4 milliseconds at 60 bpm. There was no significant change in the sensing or impedance value (1.0 mV and 580 Ω, respectively).

Discussion

The similarities in these 3 cases were that the patients were elderly women with SSS but with no structural heart disease. In cases 1 and 2, the bradycardia-dependent rise in the atrial capture threshold appeared within a few days after implantation and had improved several months later. In case 3, the manifestation of threshold rise was slower and remained slight over 1 year.

The myocardial threshold to electrical stimulation (capture threshold) is sensitive to a variety of physiological, pathologic, and pharmacologic changes. During the first 24

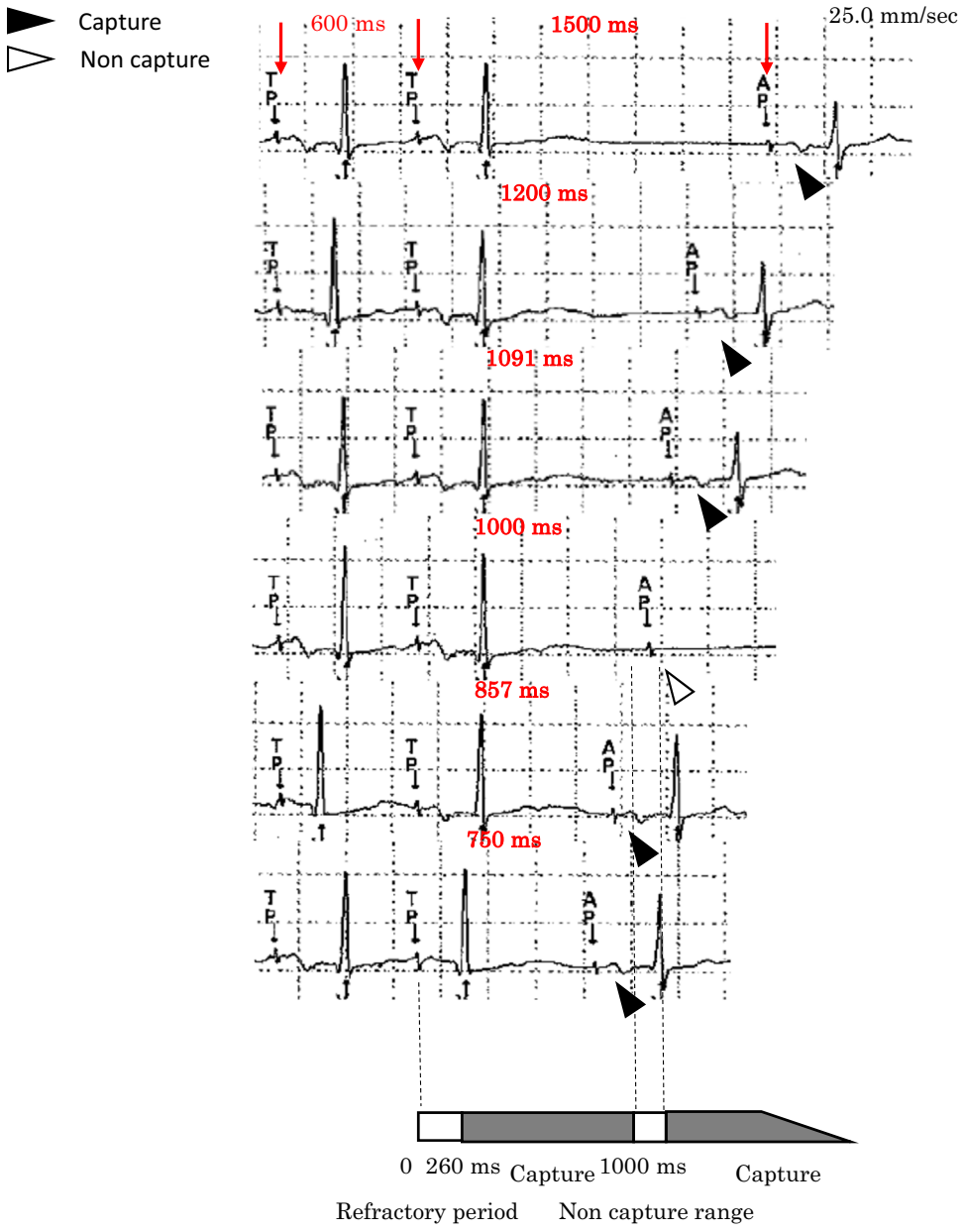

Figure 2 Programmed atrial stimulation was performed 1 month after implantation. The S2 stimulus failed to capture the atrium only when the S1-S2 interval was 1000 milliseconds. The "noncapture range" was clearly reduced.

hours after electrode implantation, the capture threshold appears to change very little. Over the next 7 to 10 days, the threshold rises acutely as a result of injury, necrosis, and subsequent fibrosis of the myocardium at the point of electrode contact. This early threshold increase after electrode implantation apparently stabilizes by 3 months.[1,2] To the best of our knowledge, only 1 previous report has referred to capture threshold changes dependent on pacing rate. Katsumoto et al[3] demonstrated rate-dependent threshold changes, with lower thresholds at higher pacing rates (2.91 ± 1.01 mA at 70 bpm vs. 2.32 ± 0.75 mA at 120 bpm, $P < 0.01$). Because higher pacing rates reduce atrial end-diastolic diameter, electrode contact with the endocardial surface improves. Therefore, they suggested that fluctuations in electrode contact with the endocardium appeared responsible for such threshold changes. However, their report was different from our cases in the degree of capture threshold rise dependent on lower pacing rates (20% vs. >300%). In addition, the capture threshold was normalized again at a remarkably low pacing rate (35 bpm) in case 1. Clearly, different electrophysiological mechanisms contributed to the phenomenon observed in our cases compared with those of the prior report.

The bradycardia-dependent rise in the atrial capture threshold observed in our cases may be explained by "phase 4 block." Phase 4 block is responsible for atrioventricular block, bundle branch block, and accessory pathway conduction block in some cases.[4–6] Singer et al[7] suggested that phase 4 depolarization in potentially automatic cells could explain the conduction abnormalities associated with

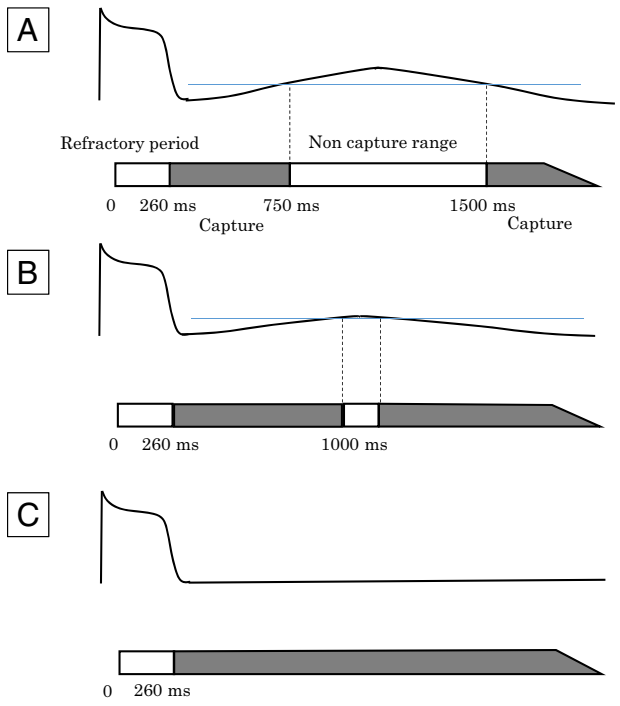

Figure 3 Our assumption as to the membrane potentials of atrial myocardium around the pacing lead according to the results from the electrophysiological study of Case 1. **A:** The greater diastolic (phase 4) depolarization caused by acute histologic changes creates a wide noncapture range on the fifth day after implantation. **B:** As diastolic depolarization gradually improves, the noncapture range is reduced at 1 month after implantation. **C:** Three months after implantation, the noncapture range has disappeared.

prolongation of the cycle length. Subsequently, Rosenbaum et al[8] proposed that phase 4 block results from spontaneous diastolic depolarization by reducing action potential amplitude and upstroke velocity in an attempt to activate the depolarized area.

Although the mechanism of the bradycardia-dependent rise in the atrial capture threshold is unclear, it is possible that pacemaker lead-induced inflammation, necrosis, and fibrosis of the atrial myocardium may cause spontaneous phase 4 depolarization. Our hypothesis is shown in detail in Figure 3. Time-dependent recovery from such myocardial injury (commonly within a few months) may account for the transient nature of bradycardia-dependent threshold rise. Moreover, atrial fibrosis associated with SSS, female sex, and aging that exists before the implantation may also contribute to phase 4 depolarization.[9]

Nowadays, reintervention is needed in 2.8% to 4.4% of patients who receive cardiac implantable electronic devices.[10,11] About 20% of the reinterventions are due to lead electrical malfunction, defined as an abrupt change in lead impedance, electrogram amplitude, or capture threshold.[11] We estimate that cases of transient bradycardia-dependent rise of atrial capture threshold might lead to reintervention. However, early reintervention is associated with a >10-fold increase in the risk of device infection.[12] From the present cases, we recommend that electrocardiologists measure capture threshold at higher rates if failure of atrial pacing appears early after implantation. Also, if atrial pacing can stabilize at a permissively high rate, it might be good to wait a few months using this setting. Further investigations are needed to clarify the precise mechanisms behind this phenomenon.

Conclusion

Bradycardia-dependent rise in the atrial capture threshold can occur in patients undergoing implantation of cardiac implantable electronic devices. Because this phenomenon can be easily recognized by pacing at a higher rate and is usually transient early after implantation, it is important to avoid unnecessary reintervention.

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