Misdiagnosis of pseudo-ineffective biventricular pacing using the automatic effective cardiac resynchronization therapy algorithm

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Introduction

After implantation of cardiac resynchronization therapy (CRT), a high percentage of biventricular pacing (%BiVp) is associated with response to CRT and the prognosis.[1–4] EffectivCRT (Medtronic, Minneapolis, MN) is a device-based automatic algorithm used to diagnose effective BiVp beats based on heartbeat.[5,6] The effective capture of the left ventricular (LV) cathode lead creates a negative waveform in the unipolar region. Pseudofusion, loss of capture, LV conduction latency anodal capture, and premature ventricular contraction can disturb effective BiVp.[5–8] We present a case of idiopathic dilated cardiomyopathy after CRT implantation that showed an effective BiVp waveform that was misdiagnosed by the EffectivCRT automatic algorithm because of decreased LV unipolar amplitude. Furthermore, the unipolar waveform amplitude increased after treatment for congestive heart failure (CHF). These findings demonstrate a drawback of the EffectivCRT algorithm.

Case report

An 83-year-old man with idiopathic dilated cardiomyopathy after CRT with defibrillator (CRT-D) implantation routinely visited our hospital with the symptom of dyspnea on effort. At age 79 years, he was first admitted to our hospital with CHF worsening, complete atrioventricular (AV) block, and sustained ventricular tachycardia. He was diagnosed with idiopathic dilated cardiomyopathy (left ventricular ejection fraction [LVEF] 27% and QRS duration 134 milliseconds under ventricular escape rhythm) and underwent CRT-D implantation (Claria MRI Quad CRTD; Medtronic, Minneapolis, MN). The LV lead was placed in the lateral vein and longitudinal mid portion (Supplemental Figure 1).

KEYWORDS Cardiac resynchronization therapy; EffectvCRT; Congestive heart failure; Biventricular pacing; Algorithm; Misdiagnosis
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KEY TEACHING POINTS

- The misdiagnosis of ineffective biventricular pacing (BiVp) by the EffectivCRT (Medtronic, Minneapolis, MN) algorithm could be a cause of the pseudodecrease in the percentage of effective BiVp.
- Congestive heart failure can lead to changes in the unipolar waveform amplitude.
- The electrogram morphology should be reviewed when the percentage of effective BiVp decreased.

At age 80 years, he underwent catheter ablation for new-onset persistent atrial fibrillation (AF) and atrial tachycardia. However, AF and atrial tachycardia recurred as a persistent form 3 months after the procedure. Because the percentage of ventricular pacing (%Vp) was maintained at 100% under VVI mode and 80 ppm, AV nodal ablation was not performed. He had not been hospitalized for CHF since the CRT-D implantation, although his LVEF and LV end-systolic volume did not change. As the pacing threshold of LV pacing (LVp) increased, he underwent the first generator exchange (Cobalt XT HF Quad; Medtronic) 3 years after the initial implantation. As the LVp threshold was 2.0–2.5 V at 0.8 milliseconds of pulse width (PW), the LVp output was set to 3.0 V at 0.8 milliseconds (polarity: LV1–3; VV delay: 0 milliseconds).

The patient's symptoms of dyspnea on effort started 2 weeks before the current visit. His home physician diagnosed worsening CHF, and 10 mg of furosemide and 2.5 mg of pimobendan daily were started. At the visit, he exhibited lung congestion and pretibial edema, and increased serum N-terminal pro–B-type natriuretic peptide level of 5771 pg/mL. A 12-lead electrocardiogram showed BiVp under AF rhythm (Figure 1A). The LVp threshold (LV1–3) was 2.5 V at 1.0 milliseconds of PW and the impedance was 304 ohms. The %Vp was maintained at 100%. Because we suspected the possibility of loss of BiVp capture, multiple configurations

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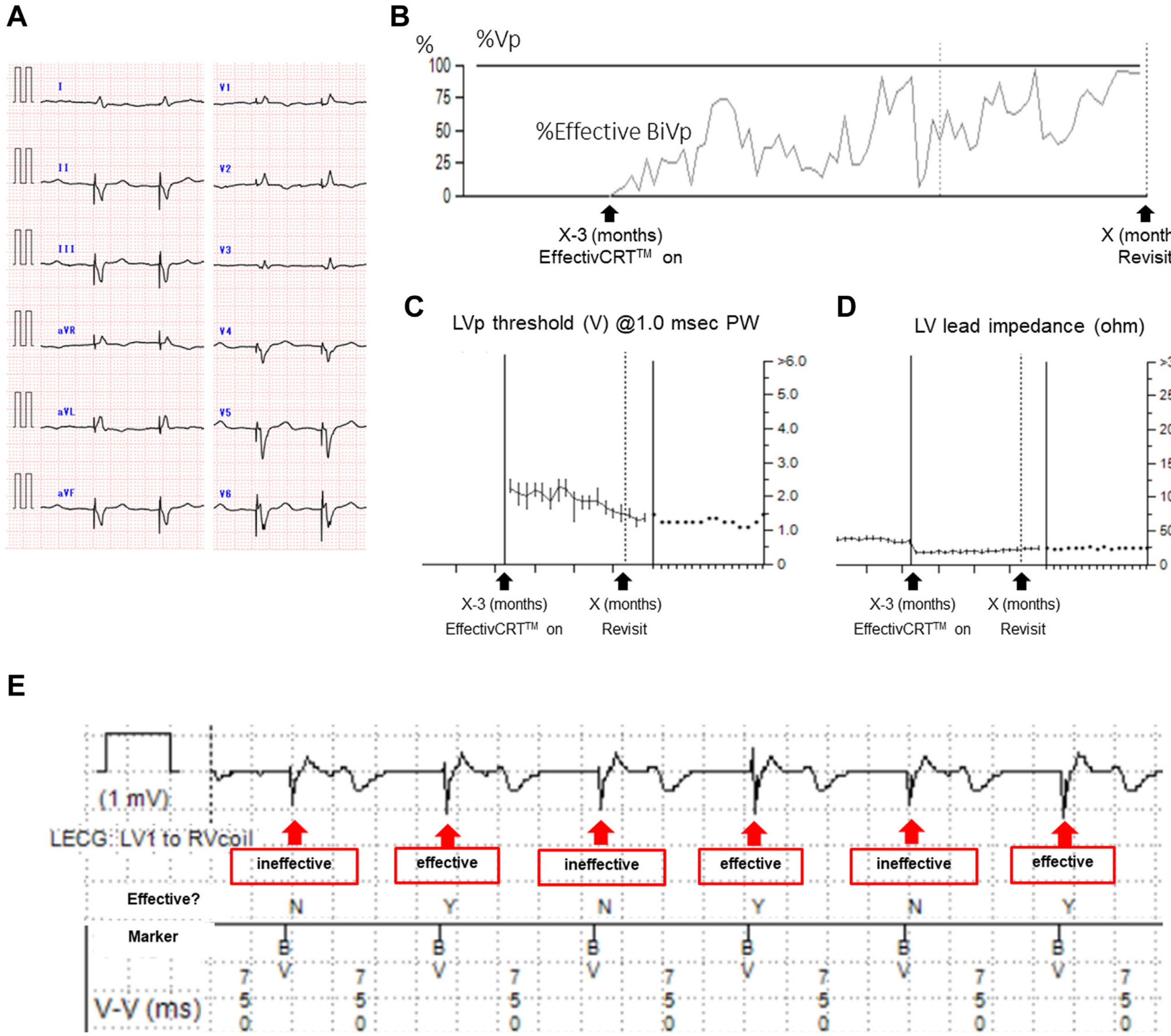

Figure 1 **A:** Twelve-lead electrocardiogram of biventricular pacing (BiVp) at the routine visit immediately before EffectivCRT (Medtronic, Minneapolis, MN) was turned on. **B:** Trends in the percentage of effective BiVp (%EBiVp) and ventricular pacing (%Vp) after EffectivCRT was turned on. **C:** Trends in the pacing threshold of left ventricular pacing (LVp) after EffectivCRT was turned on. **D:** Trends in LV lead impedance after EffectivCRT was turned on. **E:** Intracardiac electrogram when the %EBiVp was approximately 30% just after EffectivCRT was turned on. ms = milliseconds; PW = pulse width.

were changed. Because the LVp threshold (LV1 coil) was 2.0 V at 1.0 milliseconds of PW and the impedance was 190 ohms, the LVp polarity was changed from LV1–3 to LV1-coil, the pacing output was set to 3.0 V at 1.0 milliseconds, and the autocapture management was set from monitor to adaptive mode (maximum output 6.0 V). To monitor the percentage of effective biventricular pacing (%EBiVp), we set the pacing mode to VVIR 80 ppm and EffectivCRT on.

After 3 months, his CHF symptoms had improved. The %EBiVp was 99.3% around the visit; however, it was <30% immediately after EffectivCRT on (Figure 1B). The %EBiV had fluctuated but gradually increased over the 3 months. The %Vp was 100% and LVp threshold was <2.5 V at 1.0 milliseconds supported by autocapture management. The LVp threshold tended to decrease, and the impedance tended to increase gradually (Figure 1C and 1D). To assess the cause of the low %EBiVp 3 months earlier, the unipolar electogram (EGM) of LV1-right ventricular (RV) coil was reviewed (Figure 1E). In all beats, the negative wave preceded the positive wave, indicating effective BiVp. However, some of the beats were diagnosed as "ineffective." Pseudofusion, loss of capture (LOC), LV conduction latency, and anodal capture were considered as possible mechanisms. As the escape beat did not appear during BiVp off (Figure 2A) and the waveform under each pacing rate was unchanged (Supplemental Figure 2), pseudofusion was unlikely. When we created LOC manually, LV-coil EGM showed an apparent preceding positive wave, suggesting that LOC could be ruled out (Figure 3B). Regarding latency, we assessed the unipolar waveform of RVp only, LVp only, and BiVp for each VV delay (LV→RV: 60, 40, 20, 0 milliseconds and RV→LV: 20, 40, 60, 80 milliseconds). At a VV

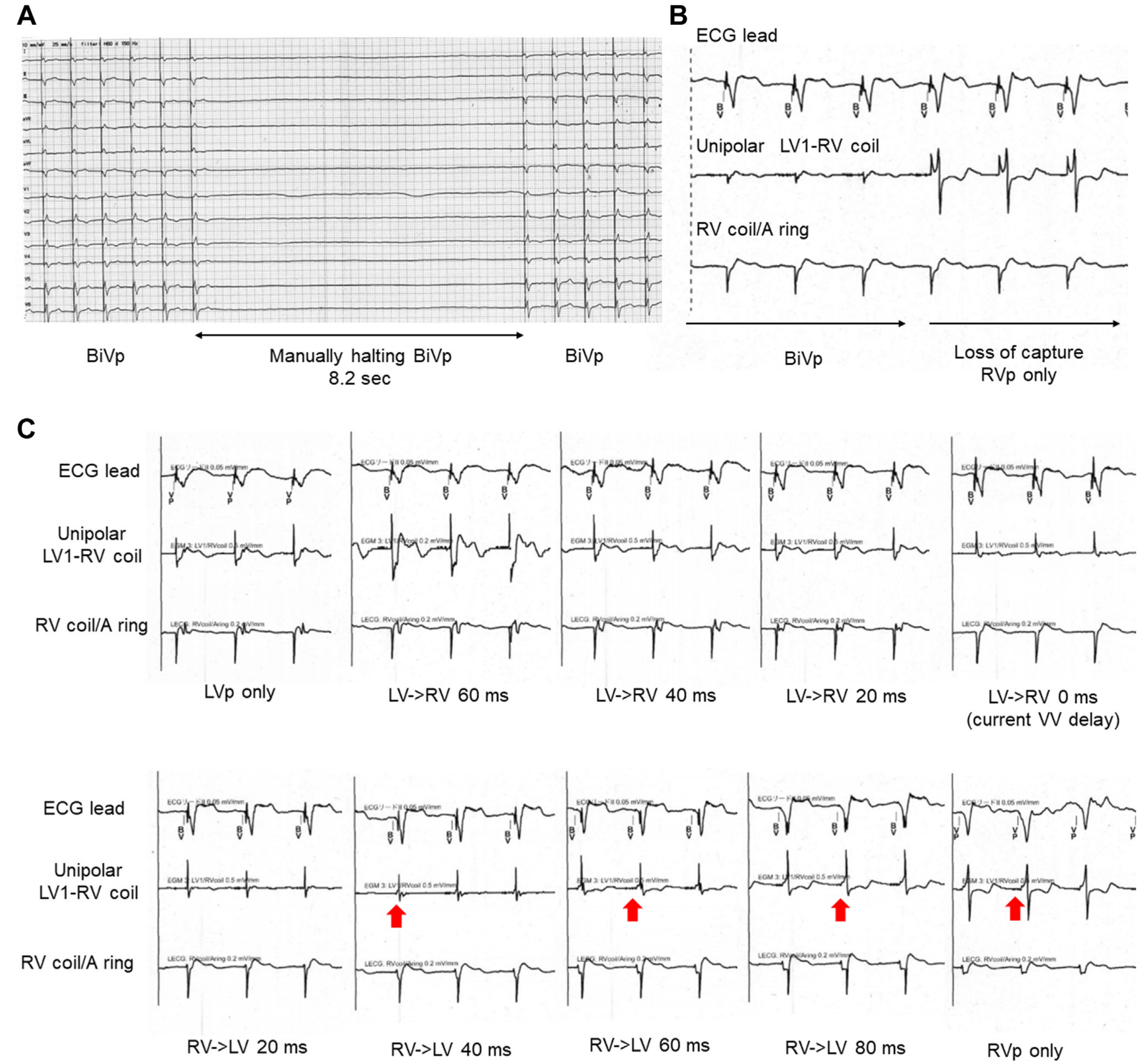

Figure 2 **A:** A 12-lead electrocardiogram (ECG) showing the absence of own beat under biventricular pacing (BiVp) off. **B:** Electrogram (EGM) during manually created loss of capture. **C:** EGMs under left ventricular pacing (LVp) only, BiVp (VV delay: left ventricle → right ventricle 60–0 milliseconds and RV → LV 0–80 milliseconds), and right ventricular pacing (RVp) only. *Red arrows* indicate positive wave preceding negative wave in unipolar LV. LV = left ventricle; ms = milliseconds; RV = right ventricle.

delay of RV → LV of 40 milliseconds, a positive wave started to appear (Figure 2C). The latency was 20 milliseconds after LVp and 23 milliseconds after RVp (Figure 3A). These results suggested the impact of latency could be ruled out. Although we failed to create anodal capture, the waveform under RVp demonstrated an apparent preceding positive wave. Next, we reviewed the diagnostic algorithm for EffectiveCRT (Figure 3B). This algorithm requires the sum of the negative peak amplitudes (|minimum|) and positive peak amplitude (|maximum|) to surpass 1.6 mV to diagnose effective BiVp. Two electrophysiologists manually measured the sum of the positive and negative wave amplitudes (|maximum| + |minimum|) (Figure 3B). The sum of the beats diagnosed as "ineffective" were <1.6 mV, which did not meet the criteria for effective BiVp regardless of preceding negative peak to positive peak. Thus, we concluded that the sum of the amplitudes was the border value between effective and ineffective pacing, and that the automatic algorithm had misdiagnosed true "effective" BiVp as "pseudo-ineffective." We also investigated why the %EBiVp fluctuated and improved over time. The unipolar amplitude of BiVp at the revisit was higher than that at 3 months before (Figure 3C). Most of the sums were >1.6 mV, which met the criteria for effective BiVp. We speculate that CHF treatment

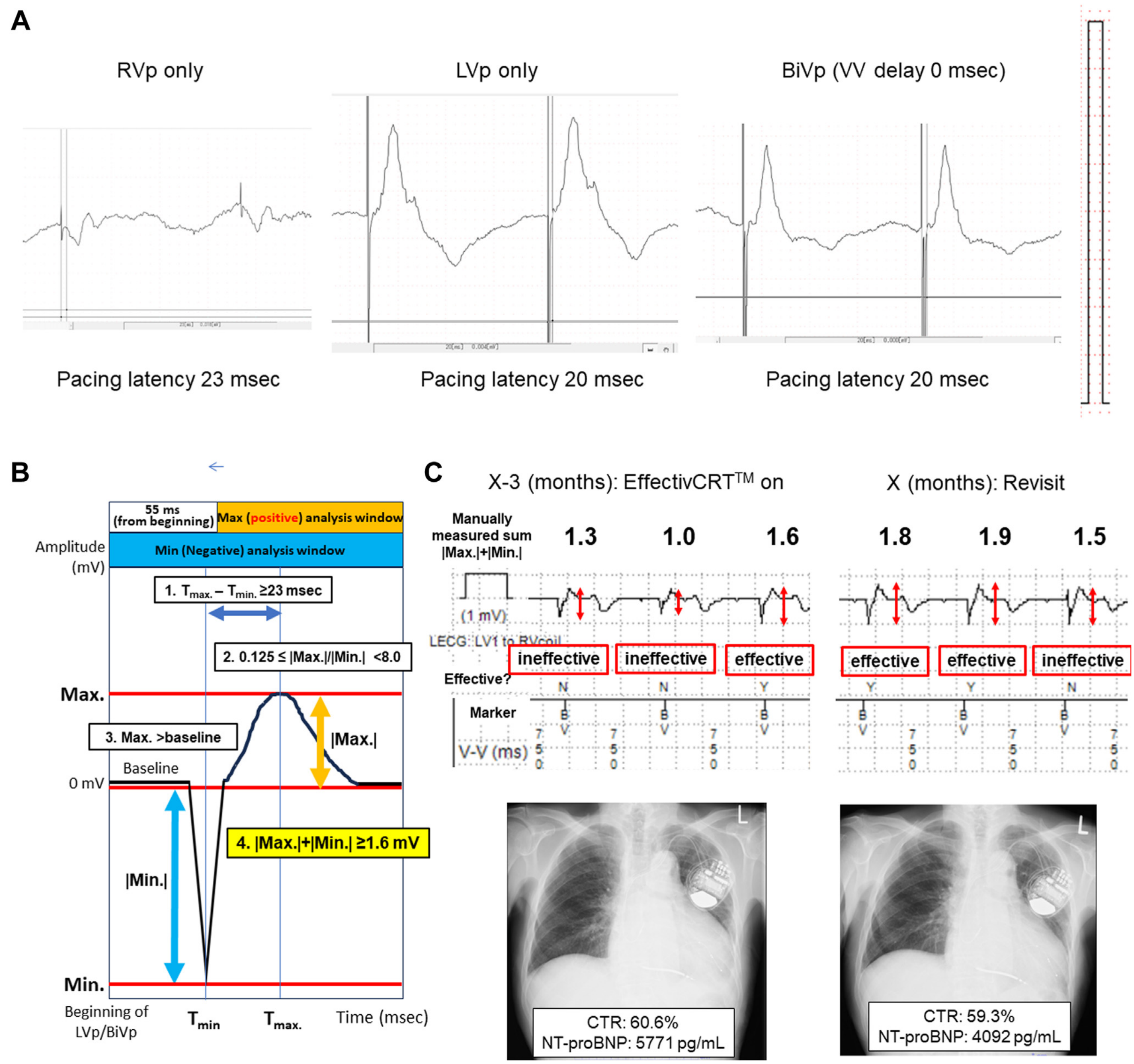

Figure 3 **A:** Conduction latency under right ventricular pacing (RVp) only (*left*), left ventricular pacing (LVp) only (*middle*), and biventricular pacing (BiVp) (*right*). Amplitude: 0.25 mV/10 mm. **B:** EffectivCRT algorithm. The 4 criteria (1–4) must be fulfilled for the diagnosis of effective BiVp. Criterion 4 (|Max.|+|Min.| ≥1.6 mV) was the key criterion in this case. **C:** Electrogram (EGM) (*upper*) immediately after turning on EffectivCRT (*left*) and at the revisit (*right*). The manually measured sums of the negative and positive peaks (|Max. |+|Min.|) are shown above the EGMs. Chest radiograph (*lower panel*). The cardiothoracic ratio (CTR) and serum N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels are also shown. Max. = maximum; Min. = minimum; msec = milliseconds.

might induce the change. The serum N-terminal pro–B-type natriuretic peptide level decreased from 5771 to 4092 pg/mL, and the chest radiograph findings improved after CHF treatment (Figure 3C). Not only did the BiVp amplitude decrease, but the LVp threshold as well, and impedance increased (Figure 1C and 1D), which suggests that LV anatomic change by decongestion might impact the lead parameter. We attempted to find a more appropriate LVp polarity to obtain a stable waveform for EffectivCRT, however, this was not possible because of a higher threshold or phrenic nerve stimulation. Therefore, we did not change the LVp polarity. We instead followed EGM with remote monitoring when the % EBiV decreased.

Discussion

CRT is an established therapeutic option for patients with HF and reduced EF.[9] Patient-related factors, such as QRS morphology and duration, sex, cardiomyopathy etiology, CHF stage, and cardiac rhythm, are associated with response to CRT. Furthermore, device-related factors, such as lead location, %Vp, and optimal AV/VV timing, are also important.[3] Although a higher %Vp is associated with LV reverse remodeling and better prognosis,[2,4] the true %BiVp is underestimated by the %Vp.[1] An investigation of 24-hour Holter electrocardiogram revealed that decreased %BiVp is often caused by pseudofusion, loss of capture, and LV conduction latency. EffectivCRT is an automatic algorithm used to diagnose effective or ineffective BiVp based on the waveform of a unipolar LV EGM during pacing.[5] The utility of the EGM-based algorithm was validated in the OLĚ CRT (Holder for Efficacy Analysis of CRT) study.[6] Patients with a high %EBiVp were recently reported to exhibit greater LV reverse remodeling and decreased HF hospitalization.[10] Thus, EffectivCRT can provide valuable information for the follow-up of patients undergoing CRT. In terms of echocardiographic CRT response, this patient was a nonresponder, but not a progressor, experiencing LVEF and LV end-systolic volume exacerbation even after CRT implantation.[11,12] The patient benefitted from CRT because CRT-D implantation prevented HF hospitalization. Therefore, the CRT effect should be maximized by maintaining a high %EBiVp.

We assessed the cause of decreased %EBiVp diagnosed by EffectivCRT algorithm. The plausible differential diagnoses included pseudofusion,[5] LOC,[8] LV conduction latency, premature ventricular contraction,[6] and anodal capture.[7] In patients with AF, own beat, or pseudofusion can decrease the %BiVp.[1,13] Additional AV nodal ablation is occasionally warranted to eliminate the influence of own beats.[14] In this case, however, we assumed that the effective BiVp might not be disturbed by pseudofusion, as %Vp remained at nearly 100% throughout the observation period. Furthermore, our assessment of the presence of own beat revealed complete Vp dependence. Next, we ruled out LOC, as the LVp threshold was relatively high (LV1–3, 2.5 V at 1.0 milliseconds of PW). To prevent LOC, we selected the polarity with the lowest threshold (LV1-coil) and used auto-capture management in the adaptive mode setting with a sufficient margin. The waveform during LOC demonstrated a preceding positive wave, suggesting that LOC could be ruled out. Regarding conduction latency, we measured latency under RVp, LVp, and BiVp, and assessed the unipolar waveform changing VV-delay. Latency did not cause ineffective BiVp under 0 milliseconds of VV-delay. Finally, a review of the EGM was helpful for the correct diagnosis. In the BiVp waveforms diagnosed with "ineffective," the negative wave preceded the positive wave. We investigated the EffectivCRT automatic algorithm, which includes 4 criteria (Figure 3B). When the sum of the amplitudes was on the boundary between effective and ineffective BiVp (approximately 1.6 mV), a misdiagnosis could be induced. Low unipolar amplitude may be a risk factor.

After CHF treatment, unipolar amplitude increased. As decongestion can induce LV anatomic changes, such as reduced LV volume and wall stretch, we speculate that these changes could affect LV lead contact, local myocardial voltage, and conduction properties. A previous study reported a significantly lower sensing threshold in patients with LVEF <40% than in those with LVEF >40%, suggesting that CHF severity might influence sensing properties.[15] Further investigation of the impact of CHF on lead parameters is warranted to improve the accuracy of the EffectivCRT algorithm. Troubleshooting to prevent a misdiagnosis was challenging in this case. Because the value of the EffectivCRT algorithm is not configurable, we attempted to find a stable LVp polarity to be correctly diagnosed by the algorithm, but failed because the high pacing threshold or phrenic nerve stimulation was disturbed in all other polarities. Therefore, this case might continue to experience "pseudo-ineffective" diagnoses. EGMs should be reviewed to ensure that the diagnosis of ineffective BiVp is true or false. Waveforms diagnosed as "ineffective" can be reviewed using remote monitoring or face-to-face device interrogations.

Conclusion

Our findings emphasize the pitfall of the use of EffectivCRT. Misdiagnosis by this automatic algorithm should be recognized as the cause of pseudo-ineffective BiVp. A review of EGM is basic and important for troubleshooting EffectivCRT.

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Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2024.08.023.

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