

# Pacemaker-ICD/Drug Interaction

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When a drug is prescribed for a patient with a permanent pacemaker or an implantable cardioverter defibrillator (ICD), consideration must be given to the potential interactions. Drug effect on pacemaker performance is usually thought to cause an increase or decrease in pacing threshold. From a practical view, Class IC drugs must be used cautiously in pacemaker patients, especially in those who are pacemaker-dependent. The possibility of a rise in threshold should always be considered in these patients, and the pacemaker output should be programmed to allow an adequate pacing margin of safety. In such patients, automatic output regulation would be particularly useful. Two-third of ICD recipients are treated with antiarrhythmic drugs to reduce the frequency of ventricular tachycardia/ventricular fibrillation (VT/VF) recurrences and enhance quality of life. However, antiarrhythmic drugs may alter ventricular defibrillation threshold (DFT). Class I agents that work primarily by slowing ventricular conduction velocity increase DFT. Class III agents that work primarily by prolonging ventricular action potential duration decrease DFT. Antiarrhythmic drugs with a balance of class I and class III actions (such as amiodarone) may increase or decrease DFT. Besides affecting DFT, antiarrhythmic drugs may also alter arrhythmia cycle length and frequency, pacing thresholds, and post-shock excitability. Finally, interactions between the ICD and the pacemaker may result in sensing problems, leading to multiple counting and inappropriate shocks, VF nondetection, sensing or capture failure post defibrillation, and pacemaker reprogramming induced by defibrillator discharge.

**Key Words:** Antiarrhythmic drug • ICD • Pacemaker

## EFFECT OF DRUGS ON PACEMAKERS

Drug effect on pacemaker performance is usually thought to cause an increase or decrease in pacing threshold. Numerous drugs have been reported in pacemaker malfunction, especially as an increase in pacing threshold.<sup>1-3</sup> Although there are many instances where a specific drug has complicated pacing therapy, there are few drugs that consistently result in pacing problems.

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## Agents increasing the pacing threshold

### Class I agents

Class IA agents, such as quinidine and procainamide, have been shown to have adverse effects on pacing thresholds.<sup>1-3</sup> Procainamide has resulted in failure to capture in patients with toxic levels,<sup>4</sup> but has not been shown in humans to increase pacing threshold at therapeutic levels. Similarly, quinidine-induced increases in pacing thresholds have not been demonstrated in humans.

Class IB agents, such as lidocaine and mexilitence, are not thought to have a clinically significant effect on pacing thresholds.<sup>1-3</sup> Although there are individual studies describing an effect of each of these agents in humans and/or animals, the use of these drugs in paced patients is safe.

Flecainide, encainide, and propafenone (Class IC agents)<sup>5-8</sup> have been shown to raise pacing threshold. These

drugs are probably best avoided in pacemaker-dependent patients. For such patients, automatic output regulation would be useful if there is no alternative drug therapy. When this option, automatic output regulation, is available, intermittent automatic pacing threshold determinations will detect a rise in pacing threshold and automatically increase the pacemaker output to avoid loss of capture. From a practical view, Class IC drugs must be used cautiously in pacemaker patients, especially in those who are pacemaker-dependent. The possibility of a rise in threshold should always be considered in pacemaker-dependent patients, and the pacemaker output should be programmed to allow an adequate pacing margin of safety.

### Other agents

It has been well documented that sympathetic stimulation usually lowers pacing threshold. Although it has been suggested that beta-blockers would raise pacing threshold, study results have been inconsistent. Clinically, this class of drugs did not show any significant rise in pacing threshold.<sup>1-3</sup> Similarly, calcium channel blockers have not been reported to have any significant effect on chronic pacing thresholds in humans.<sup>1-3</sup> Amiodarone has been shown to affect defibrillation thresholds (DFTs), but there is no convincing evidence that it significantly affects pacing thresholds.

### Agents lowering the pacing threshold

It is also important to consider drugs that may lower the pacing threshold. Corticosteroids are the most important of these. Human study has shown that the steroid-eluting lead prevents the usual rise in pacing threshold after pacemaker implantation.<sup>9</sup> Sympathomimetic agents, such as epinephrine, ephedrine, and isoproterenol, also have been reported to decrease pacing threshold.<sup>10</sup>

Sensing thresholds are much less commonly recognized to be affected by cardioactive drugs. Significant clinical sensing problems have not been found with any of the drugs discussed in relation to pacing threshold.

## EFFECT OF DRUGS ON IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS)

Two-third of ICD recipients are treated with antiarrhythmic drugs.<sup>11-14</sup> The uses for antiarrhythmic drug

therapy for ventricular tachycardia/ventricular fibrillation (VT/VF) patients who have received an ICD include: 1) drug therapy designed to prevent VT/VF recurrences; 2) drug therapy designed to render VT more amenable to ICD pace-termination; 3) drug therapy designed to prevent supraventricular tachyarrhythmias that are confusing the ICD; and 4) drug therapy designed to lower the ventricular DFT.<sup>11</sup>

Potential interactions between antiarrhythmic drugs and ICD include: 1) alternations in DFT; 2) increase in latency, PR interval, or conduction leading to double counting; 3) change in QRS morphology resulting in satisfaction of criteria for VT; 4) increase or decrease in VT cycle length; 5) change from sustained to nonsustained VT, resulting in inappropriate shock during nonsustained VT; 6) alternation in post-shock excitability, and 7) increase in pacing threshold.<sup>15</sup>

Regarding the alternations in DFT, ancillary antiarrhythmic drug therapy may have clinically significant effects in patients received an ICD. Antiarrhythmic drugs that work primarily by slowing ventricular conduction velocity are considered to be class I agents, and they increase DFTs.<sup>16-20</sup> Figure 1 shows an example. Antiarrhythmic drugs that work primarily by prolonging ventricular action potential duration are considered to be class III agents, and they decrease DFTs.<sup>21-23</sup> Antiarrhythmic drugs with a balance of class I and class III actions (e.g., amiodarone) may increase or decrease DFTs.<sup>24-27</sup> Clinically, antiarrhythmic drugs with predominant class III action (such as sotalol) may be useful to decrease defibrillation energy requirements in patients with high VF defibrillation energy requirements.<sup>28</sup>

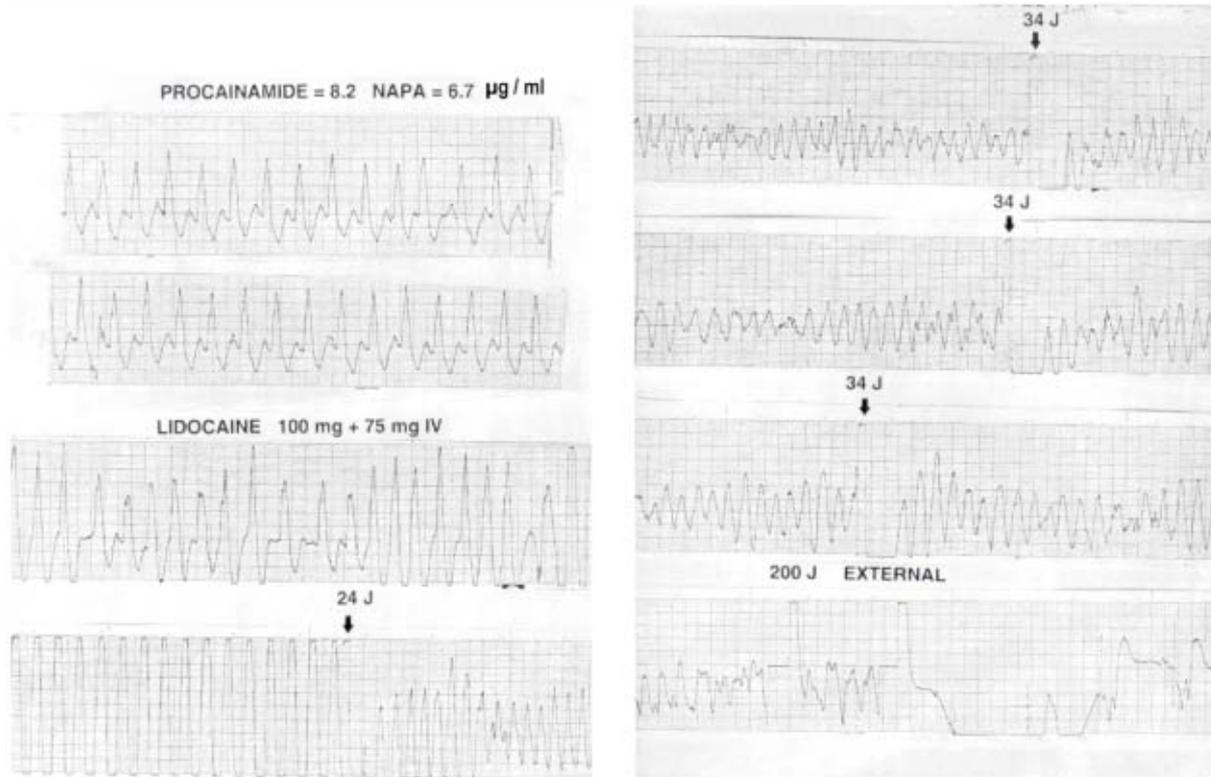
## INTERACTIONS BETWEEN PACEMAKER AND ICD

The interactions between pacemaker and ICD have been classified into four groups: 1) transient pacemaker dysfunction with failure to sense or capture immediately after ICD discharge (*pacemaker influenced by ICD*); 2) pacemaker reprogramming after ICD discharge (*pacemaker influenced by ICD*); 3) oversensing of the pacemaker stimulus by the ICD, leading to double counting and trouble shooting (*ICD influenced by*

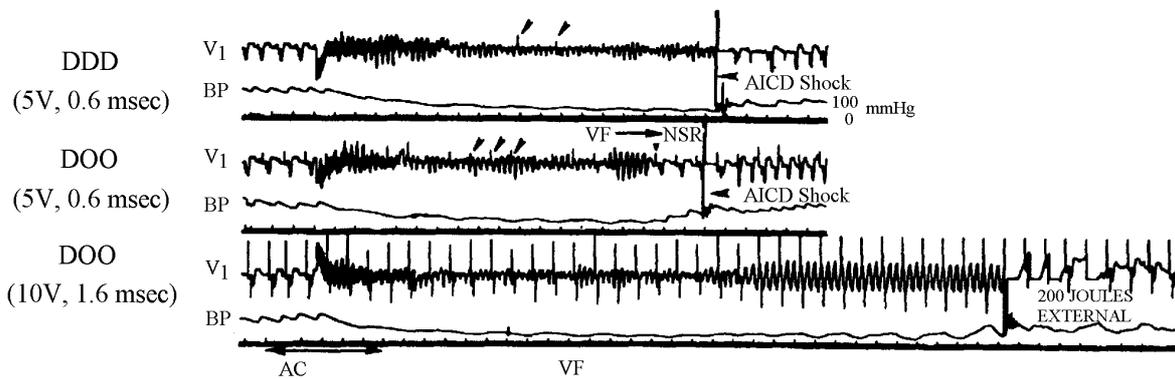
pacemaker); and 4) ICD failure to sense VF resulting from pacemaker stimulus oversensing (ICD influenced by pacemaker) (Figure 2).<sup>15,29</sup>

**ICD-induced pacemaker malfunction**

Clinically, insignificant pacemaker system malfunction may occur in patients (23%) after an ICD discharge,<sup>29</sup>



**Figure 1.** Increase of DFT probably due to the combined use of procainamide and lidocaine (data from a 58-Y/O male, with the ICD implantation due to CAD-related VT/VF). Spontaneous sustained VT occurred even with long-term use of procainamide. The serum levels of procainamide and N-acetylprocainamide (NAPA) were within the therapeutic limits. Lidocaine with a total dose of 175 mg failed to terminate VT. In contrast, VT degenerated to VF minutes later. With 4 shocks (24, 34, 34, and 34 joules, respectively), the ICD failed to restore sinus rhythm. VF was finally terminated by external defibrillation (200 joules). Without using lidocaine for 12 hrs, the ICD shocks with the energy of 24 joules consistently terminated induced VF twice during ICD testing. CAD = coronary artery disease.



**Figure 2.** ICD failure to sense VF resulting from pacemaker stimulus oversensing. Lead V<sub>1</sub> electrocardiogram and femoral blood pressure (BP) during ICD testing were demonstrated. As the three tests show, the patient's bipolar dual-chamber pacemaker was programmed in the DDD mode (5 V at 0.6 ms), DOO (5 V at 0.6 ms), and DOO (10 V at 1.6 ms), respectively. Incomplete suppression of pacemaker output is seen while in the DDD mode. Failure of ICD detection of VF is seen only with the pacemaker programmed at DOO (10 V at 1.6 ms). AC = alternating current; NSR = normal sinus rhythm (from reference 29, with permission from American College of Cardiology Foundation).

including failure to capture, transient pacemaker inhibition, and transient failure to sense after ICD discharges. However, as reported by Cohen et al,<sup>30</sup> the duration of pacemaker system malfunction was always less than one minute. No patient showed clinical symptoms at the time of testing or at long-term clinical follow-up. The most likely mechanism for the above phenomena is a local change in excitability at the electrode-myocardial interface.<sup>29</sup>

### **Pacemaker reprogramming by the ICD**

Reprogramming of pacemakers after an ICD discharge may also occur in patients (10%) after an ICD discharge,<sup>29</sup> shifting the pacemaker setting to a backup mode of ventricular pacing. Although optimal pacemaker function will be temporarily lost, marked bradycardia is prevented. Because reprogramming may occur with an unexpectedly high frequency, the potential for pacemaker reprogramming by an ICD discharge should be screened for in every patient.

### **Pacemaker spike oversensing by the ICD**

Oversensing of pacemaker stimuli by the ICD may lead to double or triple counting, caused by sensing of the atrial or ventricular pacer stimulus, or the evoked ventricular depolarization, or both.<sup>30,31</sup> This double or triple counting may in turn exceed the cutoff rate of the ICD, resulting in inappropriate discharge. Although oversensing of pacemaker stimuli occurs infrequently with bipolar pacemakers, it may still occur intermittently and lead to false firing of an ICD.

### **Mechanical interference**

Mechanical interaction between leads of the pacemaker and the ICD is another possible mechanism, leading to oversensing and trouble shooting by the ICD. Liao et al.<sup>32</sup> have recently reported an example. Intermittent mechanical contact between the ventricular lead of the pacemaker and the ICD lead was identified as the source of the artifacts recorded from the ICD lead. Removing the pacemaker and its leads eliminated inappropriate shocks.

### **Failure to detect ventricular fibrillation**

Pacemaker-induced failure to sense ventricular tachyarrhythmias has been reported clinically only with unipolar pacemakers.<sup>31</sup> Although failure to sense VF was not a clinical important factor with bipolar pacemakers at

standard output, it may occur with concomitant use of antiarrhythmic drugs that may increase pacing threshold and therefore be associated with higher programmed pacing outputs.<sup>29</sup> Pacemaker stimulus oversensing and the ICD function of auto-adjustment of sensing may then result in failure to detect VF. Thus, even though it is uncommon, this potentially lethal interaction should be screened for at the time of placement of the second device and at the time a higher pacing output is programmed.

### **Recommendations**

For the above potential problems, several recommendations can be made to minimize interactions between pacing systems and ICDs: 1) where possible, the pacemaker pacing lead and the ICD sensing lead should be placed as far apart as possible and perpendicular to each other. If the ICD is placed as the second procedure, it is advisable to minimize the pacemaker spike amplitude on the ICD sensing lead recording (i.e. low spike/electrogram ratio); 2) to screen for pacemaker reprogramming or prolonged pacemaker system malfunction after a defibrillator discharge, every patient should have the ICD tested during pacing in the clinically relevant mode at a rate higher than the patient's native heart rate. Clinically, post-shock screen of pacemaker function is important; 3) to screen for double counting and ICD inhibition, programming the pacemaker to the asynchronous mode (VOO or DOO mode) with maximal outputs and AV delay (in dual-chamber pacemakers) is recommended.

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