Commentary

Should all patients receive dual chamber pacing ICDs? The rationale for the DAVID trial

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Published online: 18 September 2001
Curr Control Trials Cardiovasc Med 2001, **2**:215-217

Abstract

All of the prospective multicenter trials that support the use of implantable defibrillators have used single chamber pacemakers/implantable cardiovertor defibrillators (ICDs). Despite the significantly increased cost of dual chamber pacemaker/ICD devices and the lack of outcome data, these devices accounted for approximately two-thirds of the ICDs implanted in the United States during the 12 months ending April 2001. Dual chamber pacemaker trials have not provided data that would support this trend, but the high incidence of atrial fibrillation, bradycardia, and congestive heart failure, as comorbid conditions, suggest that the situation could be different in the defibrillator patient population. The DAVID (Dual Chamber and VVI Implantable Defibrillator) trial is designed to measure the incremental benefit of dual chamber pacemaker/ICDs.

Keywords clinical trial, implantable cardiovertor defibrillator, pacemaker

Dual chamber pacemaker/defibrillators combine pacemaker and implantable defibrillator technology. Despite the lack of randomized or prospectively collected data to support this practice, 66% of implantable cardiovertor defibrillators (ICDs) implanted in the USA, during the 12 months ending April 30 2001, were dual chamber devices [C Gennaro, personal communication]. The additional cost to the system for the dual chamber ICDs ranges from US$2500 to US$5175 per patient.

The results of multicenter, randomized clinical trials of atrial or dual chamber pacemakers compared to ventricular pacemakers have been particularly sobering [1–3]. These trials suggest that there is a role for dual chamber pacemakers, but their impact is not nearly as dramatic as would be expected from the groundswell of support from experts in the field and its common usage particularly in Europe and in the USA. Are there reasons to believe that the addition of the atrial lead, rate responsive sensor, and dual chamber pacing modes, will help patients more than a single chamber ventricular pacemaker (VVI)/ICD? Perhaps there are, but with the modest improvements observed in the pacemaker realm, it is incumbent on the electrophysiology community to measure the incremental benefit of the dual chamber rate-adaptive pacemaker (DDDR)/ICDs. The DAVID (Dual Chamber and VVI Implantable Defibrillator) trial is designed to measure this benefit.

DAVID trial protocol design

The DAVID trial is a US, multicenter, randomized comparison of dual chamber rate responsive pacemaker ICD therapy to ventricular pacing ICD therapy. It is administered by the Department of Biostatistics, University of Washington, WA, and is funded by a research grant from St Jude Medical (Sylmar, CA). The inclusion criteria require that the patients have a left ventricular ejection fraction (LVEF) of 40% or less, and one of the following conditions:

1. Survived a ventricular fibrillation (VF) arrest.
2. Documented spontaneous ventricular tachycardia (VT) with, or without, syncope.

AVID = Antiarrhythmics Vs Implantable Defibrillators; DAVID = Dual Chamber and VVI Implantable Defibrillator.
DDDR = dual chamber rate adaptive pacemaker; EPS = electrophysiology study; ICD = implantable cardiovertor defibrillator; LVEF = left ventricular ejection fraction; VF = ventricular fibrillation; VT = ventricular tachycardia; VVI = single chamber ventricular pacemaker.

3. Electrophysiology study (EPS)-induced VT and a history of syncope.
4. Spontaneous, non-sustained VT, with sustained monomorphic VT induced during EPS.

Patients are excluded if they:
1. Have reversible causes of the VT/VF event.
2. Have permanent pacemakers.
3. Have second degree, third degree, or advanced, atrioventricular block.
4. Have symptomatic bradycardia.
5. Have pre-existing endocardial pacing leads.
6. Have permanent atrial fibrillation.
7. Are waiting for a cardiac transplantation.
8. Have a life expectancy of less than 1 year.

Eligible patients must have an indication for ICD therapy but have no indication for pacemaker therapy. All patients, however, receive a DDDR/ICD system, and the device is randomly programmed either to VVI pacing or to DDDR pacing. Although the patients randomly allotted to the VVI arm of the study have the atrial lead electrogram recording activated, the atrial signal is not used to aid in the diagnosis of arrhythmias. The investigators hypothesized that the atrial lead and the associated pacing modes and diagnostic capabilities in the DDDR mode will improve prognosis, quality of life and cost of care for patients with defibrillators.

All patients are treated aggressively for associated cardiovascular comorbidities. The primary endpoint is either mortality or hospitalization for congestive heart failure. Data from the AVID (Antiarrhythmics Vs Implantable Defibrillators) trial demonstrated that in a very similar patient population there was a 50% mortality rate within 2 years after a hospitalization for congestive heart failure. The primary comorbidity that affects mortality is congestive heart failure, so only patients with LVEF of 40% or less are included, and all patients are to be treated with beta-blockers, angiotensin-converting-enzyme inhibitors and other appropriate heart failure therapies.

Contrasting pacemaker and ICD patients

The patients treated with pacemakers are quite different to those treated with ICDs. Overall, the ICD population is sicker than the pacemaker population [4–7]. In every ICD study, the average LVEF, ventricular size, New York Heart Association Functional Class and quality of life scores are worse. In addition, the prevalence of congestive heart failure is lower in the pacemaker outcome studies than in the ICD outcome studies. Possibly the healthier nature of the patients in the pacemaker outcome trials is responsible for the benefit of the dual chamber mode becoming manifest only after prolonged follow up. If this is true, then patients with more advanced cardiac dysfunction, such as ICD patients, are more likely to demonstrate the benefit of dual chamber pacing.

In addition, there are significant differences in the programming and pacing therapy that is given to pacemaker patients and ICD patients. Pacemaker outcome studies compare patients programmed to the VVI(R) (VVI with rate response) or DDD(R) (dual chamber pacemaker with rate response) mode with the base rate and rate response designed to provide pacing for a significant portion of each day. Patients in most ICD outcome studies, however, were specifically screened to exclude the need for bradycardia support. In these studies, the ICD was programmed to the VVI mode, usually at the rate of 30–40 bpm, in an attempt to avoid pacing except during episodes of severe bradycardia. Use of VVI/ICDs to increase heart rate was considered ill advised because it often caused sensing problems due to interactions with the autogain algorithms and accelerated battery depletion, and it had the potential to produce pacemaker syndrome. Therefore the comparison of VVI/ICDs to DDDR/ICDs is, in fact, the comparison of intrinsic rhythm to DDDR-paced or possibly atrial-paced rhythms.

Biventricular pacing

Right ventricular pacing, intrinsic to DDDR/ICDs, may be detrimental to patients with significant ventricular dysfunction. The current multicenter trials evaluating biventricular pacing in both pacemaker and ICD patients suggest that prolonged ventricular electrical activation time, particularly due to complete left bundle branch block, causes an inefficient left ventricular contraction pattern. This may have a negative impact on LV function and produce more significant congestive heart failure symptoms. This pattern is precisely what occurs with right ventricular pacing. Thus the use of a DDDR/ICD with a right ventricular lead may reduce ventricular function and produce more congestive heart failure.

Comorbidities

ICD patients exist in a complicated cardiovascular milieu. In addition to the VT/VF required for entry into the AVID trial, patients had a mean LVEF of 32%. Forty six per cent of patients had a history of congestive heart failure, and 33% had a history of atrial fibrillation [4]. Most interestingly, if patients were admitted to the hospital for a diagnosis of congestive heart failure during the trial, their mortality rate over the subsequent two years was 50%, and this was no different in both the drug therapy and ICD arms of the trial [A Hallstrom, personal communication of unpublished observations from the AVID database]. By preventing death from VF in ICD patients, atrial fibrillation, bradycardia, and congestive heart failure will have a proportionally greater negative influence on mortality. Thus, if DDDR/ICDs are to reduce cardiovascular mortality or improve symptoms then they must significantly impact these comorbid conditions.

It is logical to expect DDDR/ICDs to impact on these conditions through several mechanisms. First, there are increasing data that support the use of atrial pacing to prevent atrial fibrillation. The clearest result of the Danish and

Canadian experience was that atrial pacing reduced the incidence of atrial fibrillation [1,3]. Second, atrial and ventricular tachyarrhythmias are often treated with negative chronotropic medications such as sotalol and amiodarone, and the lack of dual chamber pacing limits the ability to use these medications. Finally, the major comorbidity, responsible for most of the nonarrhythmic mortality in ICD patients, is congestive heart failure. The use of beta-blockers for patients with congestive heart failure has been shown to improve survival. When a VVI/ICD is implanted the use of beta-blockers is frequently limited by the potential for VVI pacing and significant bradycardia.

Endpoints

What is the incremental benefit of DDDR/ICDs over single chamber devices? There are three significant endpoints that should be considered. Do these devices improve prognosis, improve quality of life, or reduce the cost of treating these patients? Prognosis could be improved by reducing arrhythmic mortality, heart failure mortality, and stroke mortality. Quality of life could be improved by reducing the number of appropriate and inappropriate ICD shocks, reducing hospitalization due to ICD shocks or heart failure, and improving the tolerance of antiarrhythmic and heart failure medications, which result in improved heart failure status. Finally, it is possible that dual chamber devices will reduce costs to the medical system by reducing inpatient and outpatient visits, reduce reoperations for upgrades from a single chamber ICD, and reduce the need to use other diagnostic tests for rhythm diagnosis, since atrial sensing improves the ability to diagnose an arrhythmia. The DAVID trial is designed to answer these questions.

Conclusion

The major move towards biventricular pacing will come, when biventricular pacing and defibrillator therapy is combined with all of the features of conventional DDDR/ICDs. It is conceivable that, in certain situations, it will be better to place a VVI/ICD instead of a DDDR/ICD, or a DDDR/ICD instead of a biventricular pacing DDDR/ICD. Just as the impact of left ventricular stimulation is not yet established, neither has the incremental value of DDDR/ICDs over VVI/ICDs been determined. In the end, it is crucial that we understand the implications of these changes in technology.

Competing interests

None declared.

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