EDITORIAL COMMENT

The Heart Does Not Have Alzheimer’s Disease

Electrical and Mechanical Cardiac Memory After Ventricular Pacing*

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It has been known for some time that an altered sequence of ventricular activation with a left bundle-branch conduction disturbance or right ventricular pacing is associated with a reduction in systolic and diastolic function manifested by lower ejection fraction and higher filling pressures. Furthermore, a variety of studies have shown that for a period of time following cessation of the conduction disturbance (resolution of left bundle branch block or discontinuance of ventricular pacing), the heart manifests electrical and mechanical cardiac memory—persistent secondary repolarization changes and diastolic dysfunction.

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The concept of cardiac memory was first introduced in 1982 by Rosenbaum et al. (1), who applied the term “pseudoprimary T-wave changes” to alterations in ventricular repolarization that persist for days to weeks after the provoking stimulus (the change in activation sequence) is discontinued. We now know that alteration in conduction can modify synthesis of a variety of ion-channel proteins involved in electrical repolarization and that these protein changes can take time to resolve (2). Similar pacing-related changes have been reported with channel proteins involved in calcium currents, so it is reasonable to explain the sustained diastolic dysfunction following termination of ventricular pacing by this mechanism as well (3).

Nahlawi and colleagues have been investigating cardiac memory for some time. In this issue of the Journal, this group of investigators (4) has focused its attention on changes in systolic function following cessation of ventricular pacing in patients with normal ventricular function who received dual-chamber pacemakers for sinus node dysfunction. In brief, they showed that right ventricular pacing is associated with significant although modest reduction in left ventricular ejection fraction, and this decrease in left ventricular systolic function remains depressed for at least 24 h after cessation of ventricular pacing. We could refer to this effect as adverse cardiac memory.

These findings are extremely timely and take on added relevance in view of the increased frequency of heart failure that was reported in patients who received dual-chamber pacing with an implanted cardioverter-defibrillator (ICD) in the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial (5). The patients had pre-existing left ventricular dysfunction, and ventricular pacing clearly contributed to increased heart failure and mortality when compared with similar patients whose back-up pacemaker was set at 40 bpm and who received virtually no ventricular pacing. In the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II, patients randomized to ICD therapy had improved survival but a trend toward increased hospitalization for heart failure (6). In retrospective, post-hoc analysis of the MADIT-II database, approximately 40% of the ICD-treated patients had dual-chamber units (mostly set at DDD 60 to 70 beats/min) and 60% had single-chamber units (mostly set at VVI 60 beats/min). Patients with dual-chamber units paced the ventricle about 85% of the time, whereas those with single-chamber units paced the ventricle only 15% of the time. The slightly increased occurrence of heart failure was clearly associated with dual-chamber ICD units having a higher frequency of ventricular pacing.

The aforementioned findings indicate that the normal sequence of ventricular activation is preferred when a conduction disturbance does not exist. Right ventricular pacing contributes to left ventricular dysfunction in patients with normal as well as impaired cardiac function. In the presence of altered intrinsic conduction with a wide QRS complex, can left ventricular systolic and diastolic function be improved by changing the conduction pattern with left ventricular pacing? During the last few years, we have seen that cardiac resynchronization therapy with left ventricular pacing can improve cardiac function and survival in at-risk cardiac patients. In the recent Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial, cardiac resynchronization therapy with left ventricular pacing decreased the combined risk of death from any cause or first hospitalization in patients with advanced heart failure and prolonged QRS interval (7).

In contrast to right ventricular pacing that causes dyssynchronous contraction, appropriate left ventricular pacing seems to resynchronize the pattern of contraction when an intrinsic conduction disturbance is present, with the favorable pacing effect dependent, in part, on the site of left ventricular pacing. What is the mechanism by which this pacing-related benefit is achieved? Because hemodynamic improvement follows within a few beats after initiation of left ventricular pacing, it is reasonable to conclude that the direction of electrical depolarization originating from a left ventricular pacing site produces a more synchronous contraction than what exists with the intrinsic intraventricular conduction disturbance. An important question is whether this benefit from cardiac resynchronization therapy persists for some period of time after cessation of left ventricular pacing.
pacing. Does left ventricular pacing induce favorable changes in the structure, orientation, and/or function of the contractile cardiac proteins that persist when pacing is stopped? This is an important question, for it may be that positive changes in protein expression occur with appropriate left ventricular pacing, and this could be considered a manifestation of favorable cardiac memory.

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REFERENCES