Pacemaker therapy did not reduce recurrent vasovagal syncope

Connolly SJ, Sheldon R, Thorpe KE, et al. **Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial.** JAMA. 2003;289:2224-9.

QUESTION

In patients with vasovagal syncope, does pacemaker therapy reduce the risk for recurrent syncope?

DESIGN

Randomized (allocation concealed*), blinded {patients, data collectors, outcome assessors, monitoring committee, manuscript writers, and data analysts/statisticians}†,* controlled trial with follow-up to time of first episode of recurrent syncope or 6 months.

SETTING

15 centers in Canada, United States, Australia, and Colombia.

PATIENTS

100 patients > 19 years of age (mean age 49 y, 60% women) who had a history of recurrent vasovagal syncope with ≥ 6 episodes of syncope ever or ≥ 3 episodes in the past 2 years, and a positive result on the head-up tilt table test (TTT) with a heart rate × blood pressure product < 6000/min × mm Hg. Exclusion criteria were other obvious causes of syncope; important valvular, coronary artery, or myocardial disease; abnormal result on electrocardiography; or major noncardiovascular disease. Follow-up was complete.

INTERVENTION

All patients received implantation of a dual-chamber pacemaker (Medtronic Kappa, Medtronic Inc, Minneapolis, Minnesota, USA) and were allocated to dual-chamber pacing (DDD) (n = 52) or sensing without pacing (ODO) (n = 48).

MAIN OUTCOME MEASURE

Recurrent syncope.

MAIN RESULTS

Analysis was by intention to treat. Fewer patients in the DDD group than the ODO group had syncope during follow-up, but the difference did not reach statistical significance (Table). Compared with ODO, the relative risk reduction in time to syncope with DDD was 30% (95% CI −33% to 63%). The study had 80% power to detect a 50% relative reduction in risk for recurrent syncope. The number of pacemaker complications was similar between the DDD and ODO groups (10 vs 9 complications).

CONCLUSION

In patients with vasovagal syncope, pacemaker therapy did not prevent recurrent syncope.

Sources of funding: Canadian Institutes for Health Research and Medtronic Inc.

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*See Glossary.

†Information provided by author.

Pacemaker therapy with dual-chamber pacing (DDD) vs sensing without pacing (ODO) for vasovagal syncope at 6 months‡

Outcome	DDD	ODO	RRR (95% CI)	NNT
Recurrent syncope	33%	42%	21% (−30 to 53)	Not significant

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

In this well-designed study, Connolly and colleagues address whether DDD with a rate-drop function decreases the incidence of recurrent syncope in patients with severe vasovagal syncope. This study is unique because all patients received a dual-chamber pacemaker before randomization, both the patients and the investigators were blinded to treatment assignment, and the study had the largest sample size to date improving the power to detect a treatment difference. Furthermore, unlike previous studies, the study was not terminated prematurely because of a favorable effect of pacing. However, the event rate in the ODO group was lower than in some studies, suggesting that only highly symptomatic patients may have been included in earlier studies. Interestingly, the first Vasovagal Pacemaker Study (1) did not show a beneficial effect of pacing in the incidence of presyncope, despite a significant reduction in recurrent syncope.

A positive TTT result was required for inclusion in the study. Although the TTT is widely used for assessment of patients with syncope, it has a modest sensitivity of 60% to 85%, whereas the specificity is about 90% depending on how aggressively provocative interventions are performed. In most patients with syncope, a detailed history may obviate the need for a TTT and consultations from specialists.

A nonsignificant relative risk reduction of 30% with DDD pacing observed in this study may underscore the fact that vasovagal syncope has 2 components: cardioinhibitory (bradycardia) and vasodepressor (vasodilatation). Pacing prevents bradycardia, but it has no effect on vasodilatation. Although some patients with vasovagal syncope who have a predominant cardioinhibitory component may benefit from DDD, pacing should not be considered in patients with vasovagal syncope, or at least not as first-line therapy. Treatment of these patients depends on the severity and frequency of episodes and includes preventive measures as well as pharmacologic agents. Randomized studies are necessary to determine the most effective pharmacologic approach alone or in combination with pacing.

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Reference

1. **Connolly SJ, Sheldon R, Roberts RS, Gent M.** The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. J Am Coll Cardiol. 1999;33:16-20.