

Physiologic and ventricular pacing had similar rates of combined stroke and cardiovascular mortality

Connolly SJ, Kerr CR, Gent M, et al., for the Canadian Trial of Physiologic Pacing Investigators. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. *N Engl J Med.* 2000 May 11;342:1385-91.

QUESTION

In patients with symptomatic bradycardia who are scheduled for pacemaker implantation, is physiologic (dual-chamber or atrial) pacing as effective as ventricular (single-chamber) pacing for reducing stroke and cardiovascular (CV) mortality?

DESIGN

Randomized {allocation concealed*}†, blinded (patients and outcome assessors)*, controlled trial with a planned mean follow-up of 3.5 years.

SETTING

32 Canadian hospitals.

PATIENTS

7734 patients who were scheduled for a first pacemaker were screened, and 2586 (mean age 73 y, 59% men) were enrolled. Inclusion criteria were need for a pacemaker to correct symptomatic bradycardia and age > 18 years. Exclusion criteria were chronic atrial fibrillation (AF), atrioventricular nodal ablation, or decreased life expectancy. Follow-up was > 99%.

INTERVENTION

1094 patients were allocated to physiologic pacing (atrial or dual-chamber pacing depending on atrioventricular conduction), and 1474 were allocated to ventricular pacing. Rate-adaptive pacemakers

were required for patients with specified conditions in the physiologic-pacing group and for all patients in the ventricular-pacing group.

MAIN OUTCOME MEASURES

A combined end point of first occurrence of stroke or CV death. Secondary outcomes were all-cause mortality, documented AF, or hospitalization for congestive heart failure.

MAIN RESULTS

Some patients did not remain in their assigned group: At 5 years, 4.3% of patients in the ventricular-pacing group had their device programmed for physiologic mode, and 17% of patients in the physiologic-pacing group were programmed for ventricular pacing. Analysis was by intention to treat. The groups did not differ for any outcome except for the

occurrence of less AF in the physiologic-pacing group ($P = 0.05$) (Table). Survival analysis showed that this difference occurred only after 2 years; {the 4-year number needed to treat* was 18 (95% CI 11 to 50)}†.

CONCLUSION

Physiologic pacing was no more effective than ventricular pacing for reducing stroke and cardiovascular mortality.

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*See Glossary.

†Information provided by author.

Physiologic vs ventricular pacing for symptomatic bradycardia (annual incidence rates)‡

Outcome	Physiologic pacing	Ventricular pacing	RRR (95% CI)	NNT (CI)
Stroke or CV death	4.9%	5.5%	9.4% (-11 to 26)	Not significant
All-cause mortality	6.3%	6.6%	0.9% (-18 to 17)	Not significant
Atrial fibrillation	5.3%	6.6%	18% (0.3 to 33)	80 (43 to 784)
Hospitalization for CHF	3.1%	3.5%	7.9% (-19 to 28)	Not significant

‡CV = cardiovascular; CHF = congestive heart failure. Other abbreviations defined in Glossary; NNT and its CI provided by author.

COMMENTARY

The choice of pacemaker type remains a concern. The study by Connolly and colleagues is important but has several limitations. As acknowledged by the authors, follow-up was short (mean 3 y), and the cause of thromboembolic events is unclear. More events may have occurred in the ventricular pacing group because of its higher rate of AF. However, the difference in the rate of AF did not occur until after 2 years. If follow-up had been longer, the difference in underlying rhythm might have been associated with differences in stroke or CV mortality.

A longer follow-up period is critical to making valid assessments, which has been shown in similar studies (1, 2). In the first study, which had a mean 40-month follow-up, fewer occurrences of AF and stroke were seen with atrial pacing at all follow-up times after 3 months, but the decrease in heart failure and CV death was not seen until 8 years. Multivariate analysis found that only the presence of the ventricular lead itself was related to embolic events in the study by Connolly and colleagues. The second study by Andersen and colleagues (2) included patients with the sick-sinus syndrome, whereas most of the patients in the study by Connolly and colleagues had

atrioventricular node disease. This finding could have affected long-term outcomes.

Connolly and colleagues switched few patients from ventricular to physiologic pacing, which suggested that the pacemaker syndrome occurred infrequently. These switches were unblinded, which may have introduced bias. No explanation is offered as to why the rate of crossovers was so much lower than another large study that had a 26% crossover to physiologic pacing to combat the pacemaker syndrome (3).

The issue of whether to choose physiologic or ventricular pacing is still not resolved.

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References

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3. Lamas GA, Orav EJ, Stambler BS, et al. *N Engl J Med.* 1998;338:1097-104.