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People with cardiac pacemakers require multidisciplinary care

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Echocardiographic screening during routine pacemaker checkups identifies pacing-induced cardiomyopathy in more than one-third of patients, requiring multidisciplinary, guideline-directed follow-up care.

Permanent cardiac pacing is an effective and life-saving therapy for patients with symptomatic bradycardia (slow heart rate). The endocardial right ventricle has become the conventional pacing site, given the simplicity and reliability of device implantation. However, over time, frequent right ventricular pacing (RVP) causes a dyssynchronous ventricular activation[1], which results in adverse cardiac remodeling known as as pacing-induced cardiomyopathy (PICM) and heart failure (HF), in about 20% of patients[2]. Alternative strategies, including cardiac biventricular pacing (also known as cardiac resynchronization therapy, CRT) and conduction system pacing can preserve ventricular synchrony better, but are recommended for patients with the highest risk of PICM.

RVP therefore remains the recommended pacing site in the current guidelines in patients with (near-) normal left ventricular ejection fraction (LVEF > 50%)[3]; but there is a lack of evidence and no clear recommendations on when and who to screen for PICM. In this issue of *Nature Medicine*, Paton et al.[4] present results of the OPT-PACE study, which is the first randomized controlled trial to address this evidence gap. Specifically, the trial evaluated the effect of echocardiographic screening for LV dysfunction on clinical outcome in patients with standard pacemakers implanted for bradycardia.

The study randomized 1,201 patients attending routine pacemaker follow-up to either echocardiographic screening or usual care. After a median of 31 months and a minimum follow-up for all patients of 12 months, 34% of patients were identified as having LV dysfunction (LVEF < 50%). Two care pathways were available to these patients, depending on the trial site protocol — either referral back to their primary care provider, or referral to a specialized, multidisciplinary HF and device clinic. The primary outcome, a composite of the time to first HF hospitalization or death, was observed in 18% of patients randomized to the screening arm and in 19% in the usual-care group (hazard ratio (HR) 0.89; 95% confidence interval (CI) 0.69–1.17). Patients randomized to screening and who were subsequently managed in a specialized clinic were almost three times more likely to initiate guideline-directed medical therapy than those referred to primary care.

The fact that more than one-third of patients screened in this trial had LV dysfunction indicates the substantial burden of PICM in those patients undergoing frequent RVP. Although the absence of a clear difference in clinical outcome between the two study groups is unexpected, the explanation may be simple. First, reductions in LVEF below 50% were modest, allowing for the absence of clinical HF symptoms in these patients. It is important to note that any patient presenting with overt HF symptoms would have probably been excluded from this study as they would have come to attention earlier. Second, as noted by the authors[4], the medical treatment initiated in the multidisciplinary HF clinic, even though substantially more than in the usual-care arm, was not as aggressive as might have been expected. Although it is well known that upgrading to CRT in these chronically paced patients enables further medical optimization (that would have previously been limited by low blood pressure), a mere 1.2% of the patients with PICM were upgraded to CRT. The absence of clinical HF symptoms may have curbed the tendency to increase medical therapy and/or upgrade to a more physiological pacing method, given the accompanying associated risks.

Others have shown improvements in clinical outcome after treatment in individuals with PICM. The BUDAPEST-CRT trial demonstrated a significant reduction in all-cause mortality, HF hospitalization and LV end-systolic volumes with upgrade to CRT in patients with chronic RVP and evidence of HF[5]. Upgrading to CRT, as well as guideline-directed medical therapy for HF, has proven effective in individuals with HF

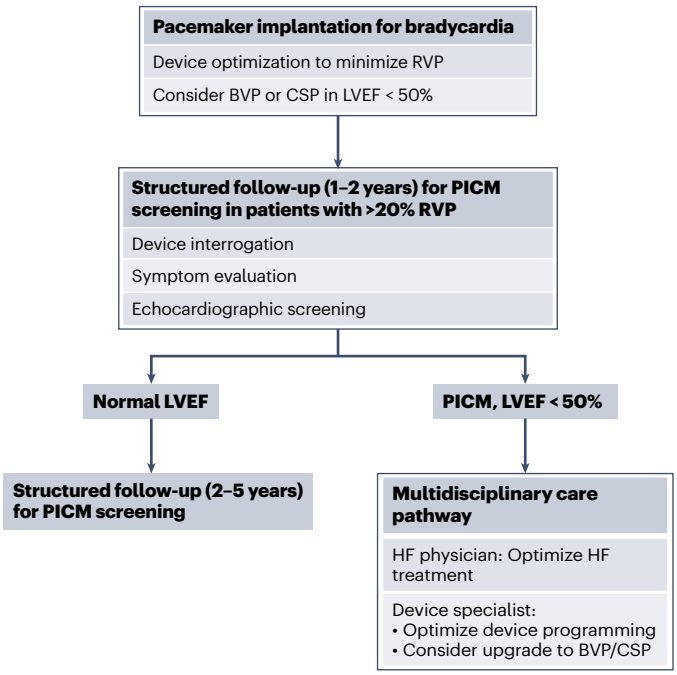

Fig. 1 | Care pathway to screen for pacing-induced cardiomyopathy. The figure illustrates a proposed screening and multidisciplinary follow-up pathway for patients with standard cardiac pacemaker implantation for bradycardia. BVP, biventricular pacing; CSP, conduction system pacing; HF, heart failure; LVEF, left ventricular ejection fraction, PICM, pacing induced cardiomyopathy.

symptoms, but the evidence — and hence the recommendations — are not so clear for asymptomatic individuals with a mildly reduced LVEF[3,6].

Nevertheless, the OPT-PACE study showed a clear difference in the PICM treatment that was received in the multidisciplinary HF clinic as compared to the primary-care clinic. Moreover, a trend towards improved clinical outcome was found for those referred to the multidisciplinary HF clinic. This may reflect the fact that PICM defined by a decrease in LVEF below 50% represents the same pathology as overt clinical HF, and strengthens the recommendation for guideline-directed medical therapy and upgrading to CRT in patients with PICM. A more aggressive treatment strategy in patients with PICM, whether referred to a specialized center or not, may have produced larger differences in clinical outcomes in the OPT-PACE trial.

The authors suggest that screening for PICM should be part of an integrated clinical care pathway, incorporating aggressive medical treatment up to current standard guideline-directed medical care for symptomatic HF and timely decision-making to upgrade to CRT. Such a strategy would necessitate a multidisciplinary pathway, incorporating access to clinical expertise in HF medical treatment and device therapy. First, a HF specialist should be involved in the evaluation of HF symptoms and additional diagnostic testing, and to initiate and optimize medical therapy. Although most clinical trials investigating medical HF therapy excluded patients with PICM, it seems reasonable to follow the same strategy in these patients as described in the current HF guidelines. Specialist knowledge of the cardiac pacing devices and their programming, and knowledge of the possibilities for reducing RVP and timing of CRT upgrade is also essential, requiring involvement of an electrophysiologist or device specialist. A proposal for a care pathway to screen for PICM in patients with cardiac pacing for bradycardia a provided in Fig. 1.

In support of such a strategy, observational studies show that in patients with HF who underwent CRT device implantation, a multidisciplinary care pathway improves clinical outcomes. For example, implementation of an optimized multidisciplinary CRT care pathway known as the Mullens checklist[7] resulted in a significant reduction in the combination of all-cause mortality and HF hospitalizations, and reduced cardiovascular-related hospital costs[8]. These results were in line with a previous observational study in which a multidisciplinary follow-up, consisting of HF, electrophysiology and echocardiography/imaging services, led to an improved two-year event-free survival in patients receiving CRT[9].

The OPT-PACE study highlights the importance of screening for PICM in patients undergoing standard RVP for bradycardia. But what happens after screening is crucial; the results from Paton et al.[4] underscore the need for treatment within a well-implemented, guideline-directed protocol — preferably in a multidisciplinary HF and device clinic — to improve outcomes for patients at risk of progressive HF.

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Competing interests

The authors declare no competing interests.