Journal of Cardiology Cases xxx (2019) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

Strategy for estimating optimal heart rate in refractory heart failure with relative sinus bradycardia: A case report

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ARTICLE INFO

Article history:
Received 3 June 2019
Received in revised form 22 November 2019
Accepted 29 November 2019

Keywords:
Optimal heart rate
Relative sinus bradycardia
Pacing study

ABSTRACT

Relative bradycardia (mild sinus bradycardia) is one of the major barriers for the effective treatment of hemodynamically unstable patients with heart failure and reduced cardiac output. We report a case of a man aged 58 years with an old broad anterior myocardial infarction and relative bradycardia (about 60 bpm) suffering from symptoms of congestive heart failure at rest in spite of optimal medical therapy, including the use of the inotropes. Transvenous atrial pacing during right heart catheterization indicated that an increase in heart rate (up to 80 bpm) improved hemodynamics immediately. Implantation of a pacemaker (atrial pacing of 80 bpm) was effective for stabilizing the heart failure symptoms. Transvenous atrial pacing during right heart catheterization is effective for estimating the optimal heart rate in patients with heart failure and relative bradycardia.

<**Learning objective:** Temporary atrial pacing during right heart catheterization is effective for estimating the optimal heart rate in patients with refractory heart failure and relative bradycardia. We present a case of inotrope-dependent heart failure. Our findings, obtained through echocardiography and right heart catheterization, showed dramatic improvements in hemodynamic parameters following an increase in heart rate via a cardiac pacemaker. This case assesses the impact of optimal heart rate in severe heart failure with relative bradycardia.>

Introduction

Bradycardia is one of the exacerbating factors of heart failure, especially in patients with underlying heart disease [1]. Severe bradycardia that is clearly adversely influencing a patient's hemodynamic status is an absolute indication for insertion of a permanent cardiac pacemaker. However, this is not necessarily true for heart failure patients with relative bradycardia. There are several reasons for this. Firstly, patients have no symptoms of bradycardia itself. Secondly, it is unclear whether augmentation of cardiac output by increasing heart rate is a sufficient indication for implantation of a pacemaker. Furthermore, the optimal dose of beta-blockers is also uncertain in such cases. Here we report a patient with severe heart failure and relative bradycardia in whom increasing the heart rate by atrial pacing (from 60 to 80 bpm) greatly improved his hemodynamics and symptoms.

Case report

A 58-year-old male was transferred to our hospital for additional treatment of refractory heart failure (HF) after acute broad anterior myocardial infarction (MI). MI occurred 3 months before transfer, which was caused by an ostial lesion of the left anterior descending artery for which primary percutaneous coronary intervention was performed. Peak creatine phosphokinase was 12,840 IU/L. The patient required intra-aortic balloon pumping and continuous hemodiafiltration in the acute phase, and noninvasive positive pressure ventilation for respiratory support. Atrial flutter (AFL) had developed after the onset of MI. He had never been discharged after the onset of MI, and when he was transferred, he had symptoms of dyspnea and general fatigue with slight exertion while on intravenous inotropes and optimal medical therapy. Myocardial perfusion imaging with thallium-201 performed after transfer showed severely reduced perfusion in a broad region of the anterior left ventricle (LV). The LV ejection fraction (LVEF) was 18%, and LV end-diastolic volume was 251 ml. Echocardiography showed that there were no

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https://doi.org/10.1016/j.jccase.2019.12.003
1878-5409/

significant valvular diseases. He declined offers of LV assist devices and heart transplantation, and we aimed to treat the patient so he could be discharged home. The clinical course in chronological order from transfer is shown in Fig. 1. Adaptive servo ventilation was introduced after transfer, and this led to a decrease in heart rate (HR) from around 100 bpm to 80 bpm while he remained in AFL. Other medical adjustments did not improve his condition. Six months after transfer (9 months after the onset of MI), AFL converted to sinus rhythm with a resting HR of 60 bpm. Soon afterwards, HF had further deteriorated. He complained of dyspnea at rest, and echocardiography showed that the pulse-wave Doppler of trans-mitral flow had a restrictive pattern suggesting elevated LV end-diastolic pressure. Furthermore, the tricuspid regurgitation pressure gradient had risen to around 70 mmHg and mitral regurgitation had slightly worsened. The inotropes did not improve any of the hemodynamic parameters. We suspected that relative bradycardia (mild sinus bradycardia of 60 bpm) was the exacerbating factor; therefore, we reduced the dose of beta-blocker (carvedilol 15 mg to 7.5 mg), but the HR did not change and the hemodynamics did not improve. The patient did not take any other negative chronotropic agents, and we refrained from a further reduction in the dose of carvedilol because of the expectation of long-term LV reverse remodeling. We were indecisive about the optimal HR or dose of beta-blocker. We hypothesized that chronotropic incompetence should be the target treatment for improving hemodynamic status because further exacerbation of HF occurred after conversion of the cardiac rhythm. Therefore, we performed temporary atrial pacing during right heart catheterization (RHC) to investigate how hemodynamics were affected by HR (Fig. 2). We found that increasing HR by right atrial pacing drastically improved hemodynamics. Comparisons between sinus rhythm (HR 57 bpm) and atrial pacing (HR 70, 80, and 90 bpm) led us to decide that atrial pacing with a HR of 80 bpm was optimal. Cardiac index (CI) and mixed venous oxygen saturation increased (2.2–2.9 l/min/m^2 and 59% to 67%, respectively), and pulmonary artery systolic pressure and mean pulmonary capillary wedge (PCW) pressure decreased (74–42 mmHg and 30–18 mmHg, respectively). These RHC parameters improved in spite of a slight decrease in stroke volume (69–65 ml). Based on the results of the pacing study with RHC, we implanted a dual chamber permanent cardiac pacemaker and selected an atrial pacing (AAI mode) rate of 80 bpm. We did not choose cardiac resynchronization therapy because atrioventricular conduction and QRS duration were normal, and the patient would not give consent for an implantable cardiac defibrillator. Soon after implantation of the pacemaker, systemic blood pressure increased slightly (82–90 mmHg systolic), and serum creatinine and brain natriuretic peptide (BNP) decreased (2.2–1.9 mg/dl and 820–302 pg/ml, respectively). Echocardiography showed that the A wave of the trans-mitral flow increased gradually and the restrictive pattern improved, indicating a decrease of LV end-diastolic pressure (Fig. 3). The tricuspid regurgitation pressure gradient also decreased (73–31 mmHg, Fig. 3). Additionally, peak oxygen uptake during cardiopulmonary exercise (CPX) testing improved from 9.6 to 12.5 l/min. The improvement in peak VO_2 may have been dependent on atrial systolic function because the first CPX (peak VO_2; 9.6 ml/kg/min) was performed prior to the conversion to sinus rhythm. However, other clinical parameters indicated that an increase in HR had a bigger contribution to hemodynamic improvement. These hemodynamic improvements led us to increase the dosage of angiotensin-converting enzyme inhibitor and β-blocker (Fig. 1). His symptoms improved and he was finally discharged. To date, more than three years after being discharged, the patient has been stable in spite of low cardiac function.

Discussion

The present case has two important clinical implications in relation to refractory HF patients with mild sinus bradycardia and reduced cardiac output. First, temporal atrial pacing during right heart catheterization is effective for the evaluation of optimal HR. Second, augmentation of cardiac output by increasing HR with a cardiac pacemaker may be a good option for improving hemodynamics. HR is a major adaptive cardiac mechanism, along

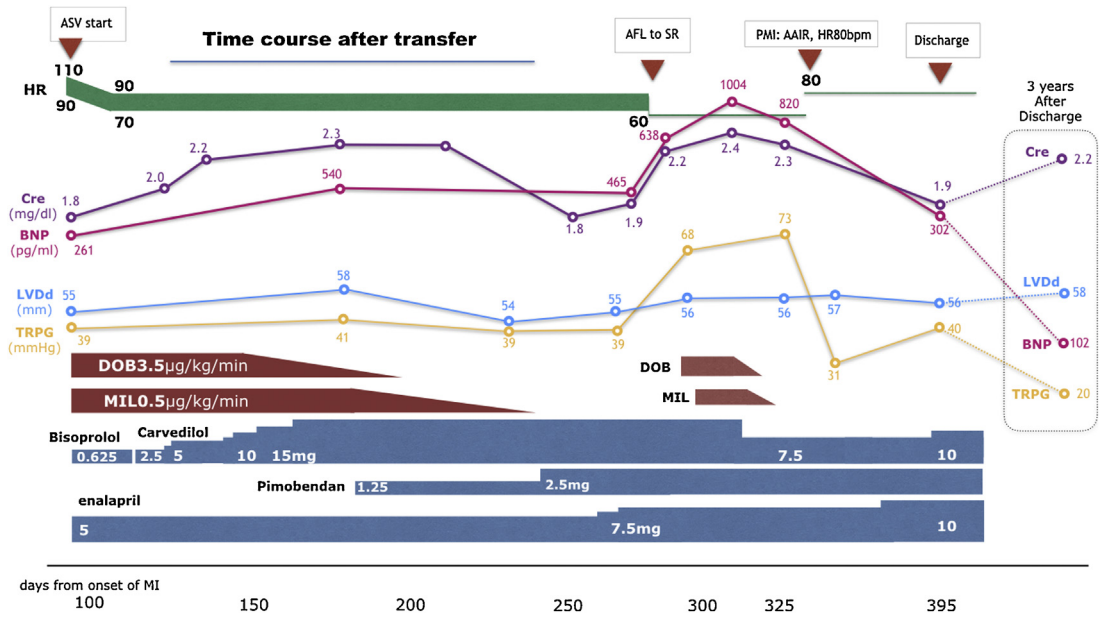

Fig. 1. The clinical course in chronological order following transfer.
ASV: adaptive servo ventilator, AFL: atrial flutter, SR: sinus rhythm, PMI: pacemaker implantation, LVDd: left ventricular diastolic diameter, TRPG: tricuspid regurgitation pressure gradient, DOB: dobutamine, MIL: milrinone.

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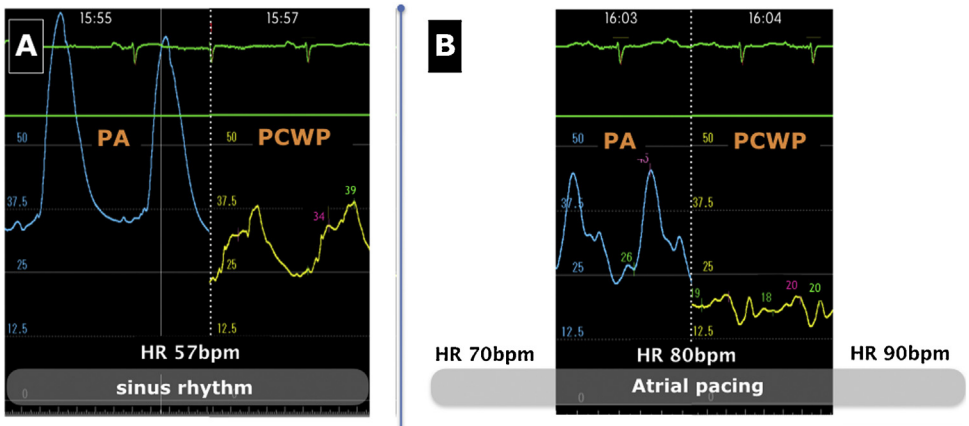
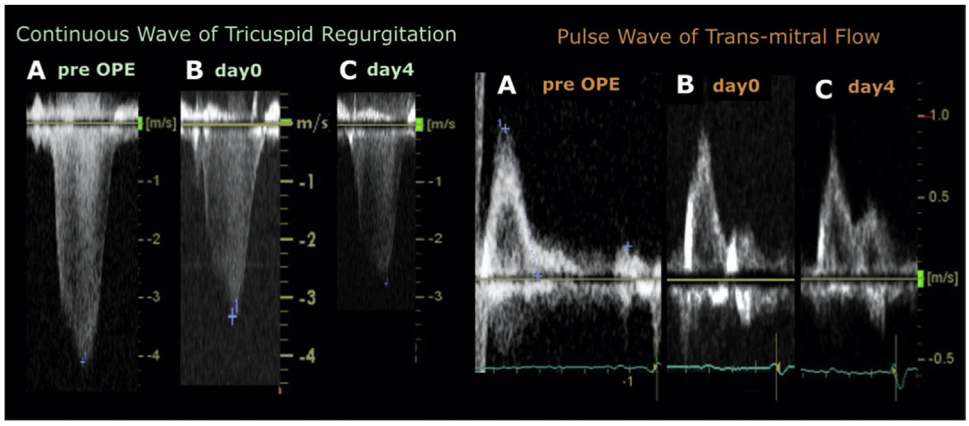


PA 74/34(48) mmHg	59/30(41)	42/24(30)	40/22(28)
PCWP 34 mmHg	26	18	17
SV 69ml		65	
CI 2.2 l/min/m²		2.9	2.7
SvO₂ 59%		67	

Fig. 2. Drastic acute improvements in hemodynamic parameters in temporal pacing.
A little less than 10 min after increasing heart rate (HR) by atrial pacing, pulmonary artery (PA) pressure and pulmonary capillary wedge pressure (PCWP) dramatically decreased and mixed venous oxygen saturation (SvO_2) increased. Cardiac Index (CI) was also slightly improved in spite of a reduction of stroke volume (SV).



A: pre operation	B: day 0	C: day4
HR 61 bpm	HR 80	HR 80
E/A 4.59	E/A 2.85	E/A 1.72
DcT 131 msec	DcT 123	DcT 152
TRPG 73 mmHg	TRPG 45	TRPG 31

Fig. 3. Changes in echocardiographic parameters after pacemaker implantation.
Echocardiography revealed that trans-mitral flow was of the restrictive pattern in sinus rhythm with a heart rate (HR) of 61 bpm (A). The A wave was augmented and the tricuspid regurgitant pressure gradient (TRPG) decreased soon after implantation of a cardiac pacemaker (B). These findings were improved and the deceleration time of the E wave was prolonged four days after the operation (C). These findings indicated that left ventricular end-diastolic pressure had decreased.
DcT: deceleration time.

with ventricular dilatation and myocardial hypertrophy. These adaptive and compensatory mechanisms always complement each other. In the present case, symptoms of low output syndrome were not improved with a dilated LV, which indicated that the Frank-Starling mechanism was fully activated. So in this situation, increasing the HR was effective for stabilizing hemodynamics rapidly.

In patients with stable HF, sinus bradycardia is one of the factors that can precipitate overt HF [1]. In the THEOPACE study, increasing HR by means of a permanent pacemaker or oral theophylline was

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associated with a lower incidence of overt HF in elderly patients who had symptomatic sick sinus syndrome (HR < 50 bpm) [2]. However, this study has not shown that increasing HR can improve hemodynamics acutely in unstable HF patients. Estimating optimal HR is difficult in congestive HF patients with relative bradycardia especially in those with vulnerable hemodynamics. Such patients need just a small improvement in cardiac output. Certainly, an increase in HR can augment cardiac output, but is it enough to improve the hemodynamics? We need reasonable grounds for implanting a permanent cardiac pacemaker in those without symptoms of bradycardia. Although there are several reports in which similar symptomatic and hemodynamic responses to permanent pacemaker implantation [3–5] were shown in severe bradycardia cases (HR < 50 bpm), there has been no report on the effectiveness of increasing HR for relative sinus bradycardia.

Temporary atrial pacing during right heart catheterization can provide valuable information about this clinical problem. By estimating not only the cardiac output but also the pressure of the pulmonary and right heart circulatory systems, we can evaluate whether an increase in HR by atrial pacing contributes to improvement of the patients' status.

There is another hemodynamic advantage after implantation of a pacemaker. Augmentation of cardiac output by increasing the HR elevates systemic blood pressure. Thereby, the greater dose of a vasodilator such as an angiotensin-converting enzyme inhibitor that can be administered, the more cardiac output can increase. In addition, beta-blockers can be increased after implantation of a pacemaker, which may improve the long-term prognosis.

The question remains as to whether atrial pacing at HR 80 bpm is advantageous in the long-term. Some clinical trials have suggested that a low resting sinus rate may be protective in stable HF patients. The subgroup analysis of the SHIFT trial revealed that the lower the resting HR, the lower was the risk of cardiovascular death or admission for worsening HF [6]. Moreover, patients with HR of 70 bpm or greater had an increased risk of cardiovascular death or events in the subgroup analysis of the BEAUTIFUL trial [7]. However, in the present case, RHC performed one year after pacemaker implantation showed that several hemodynamic parameters with atrial pacing of 80 bpm surpassed those with pacing at 60 bpm: PCW pressure of 15 and 20 mmHg, respectively; mean pulmonary artery pressure of 24 and 34 mmHg; and CI of 2.13 and 2.02 ml/min/m^2. From these results, we concluded that the optimal pacing rate was 80 bpm for this patient. Even in the setting of a high HR, echocardiography at 3 years of follow-up showed that LV remodeling did not progress (Fig. 1) in spite of severe LV systolic dysfunction.

Disclosures

There are no conflicts of interest and no author has any relation with industry.

Acknowledgment

None.

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