Mini Review

Interventional Cardiology

Why is pacemaker-induced cardiomyopathy so fascinating?

Abstract

Today Cardiac Resynchronization Therapy (CRT) upgrade is the therapy of choice for Pacemaker-Induced Cardiomyopathy (PICM). Melzer et al., recently published the largest prospective study revealing the effectiveness of a CRT upgrade in patients suffering from PICM in an outpatient clinic. 55 patients received a CRT upgrade. 43.6% of patients were > 80 years (83.4 + 2.9 years). For the primary endpoint, Left Ventricular End Systolic Volume (LVESV) decreased from 101.6 + 48.2 ml to 75.9 + 35.8 ml (p< 0.001). For the secondary endpoints, LVEF increased from 31.5 + 5.4 % to 46.1 + 7.6 % (p < 0.001) the responder rate was 83.6%. The study shows, for the first time, that older patients (>80 years) benefit from upgrading CRT to the same extent as younger patients. In conclusion there are no reasonable arguments against the CRT upgrade in patients with PICM.

Keywords: Pacemaker; Pacemaker-induced cardiomyopathy; Cardiac resynchronization therapy

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Introduction

CRT upgrade is today the therapy of choice for Pacemaker-Induced Cardiomyopathy (PICM) [1]. Yet CRT upgrade is not always offered to elderly patients. In a typical pacemaker outpatient clinic, patients are quite advanced in age, with a mean age of 77.7 ± 10.8 years [2]. Therefore, when diagnosing PICM in such a setting, patient fragility and the potential complication rate make it more difficult to decide to upgrade CRT [3]. To address this, we initiated a prospective registry to investigate whether CRT upgrades are warranted for PICM in outpatient clinic patients. The results of this largest prospective PICM registry to date were recently published [4]. 55 patients with PICM received a CRT upgrade. The follow-up period was 6 months. The mean age was 75 ± 11.3 years. 43.6% of patients were>80 years (83.4+2.9 years). CRT upgrade was successful in 54 patients (98.1%). One patient underwent cardiac surgery to implant an epicardial lead. For the primary endpoint, Left Ventricular End Systolic Volume (LVESV) decreased from 101.6+48.2 ml to 75.9+35.8 ml (p<0.001). The LVEF increased from 31.5+5.4% to 46.1+7.6% (p<0.001). Even with an age>80 years CRT upgrade improves left ventricular function and functional capacity and is associated with an acceptable complication rate. Therefore, there are no reasonable arguments against a CRT upgrade at PICM.

Review Pacemaker-Induced Cardiomyopathy

Pacemaker-Induced Cardiomyopathy (PICM) is a common pacemaker complication [5]. However, awareness of PICM remains limited. PICM is not explicitly mentioned in the current 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Indeed, PICM is subsumed under all cardiac conditions that worsen under

RV pacing. Therefore, this review aims to raise awareness of these complication of pacemaker therapy and try to explain why PICM is so fascinating.

Incidence and predictors: The following facts are supported by sufficient evidence. Applying the usual PICM definition according to the Left Ventricular Ejection Fraction (LVEF) (drop in LVEF>10%, resulting in an LVEF<50%), its prevalence is 10%-20% [6]. Older age, male gender, Right Ventricular pacing (RV pacing)>40%, long QRS duration, and impaired LVEF are recognized predictors of PICM [7].

Pathophysiology

The pathophysiological substrate is an RV pacing induced electromechanical dyssynchrony [8]. While this concept appears logical, closer examination raises questions. Why do 80%-90% of patients with right ventricular pacing not develop PICM, especially in the patients with a very high pacing rate of>90%? The most plausible hypothesis suggests that varying degrees of ventricular asynchrony are responsible for this discrepancy. But the echocardiographic asynchrony measurement in the PICM does not have convincing scientific evidence after the disappointing results of the PROSPECT trail [9]. One reason could be that the current measurement methods of ventricular asynchrony are too inaccurate. I believe that we have not yet properly understood the pathophysiology of the disease. What factors must be present in addition to ventricular asynchrony so that a PICM can develop? In my opinion, this is the only reasonable way to explain why so few patients develop PICM under right ventricular pacing. So far, we have no answers or theories to this so exciting question.

Diagnostics

Diagnosis of PICM is time-consuming and costly due to it's a diagnosis of exclusion [10]. However, the right ventricular pacing percentage must be at least 40% [11]. All potential causes contributing to LV function deterioration must be ruled out, such as coronary artery disease, uncontrolled arterial hypertension, myocarditis etc. However, in clinical practice, there is also an overlap of different entities that have led to deterioration of LV function such as hypertension and PICM. This is why recruiting patients for PICM studies is so difficult. In our registry, we aimed to exclusively include pure PICM patients, excluding patients with other potential causes of LVEF decline. Despite intensive efforts and a high volume center, in 4 years our registry only successfully enrolled 66 patients with newly diagnosed PICM. Therefore, it is not surprising that the two largest studies to date on the effectiveness of CRT upgrade in PICM were retrospective and had a long inclusion interval [12,13].

Course of the Disease

On average, the time interval between the start of pacemaker therapy and the diagnosis of PICM is 4.3+3.9 years [14]. In our CRT registry, we examined the course of LVEF over the last 3 years before inclusion in the registry. The spectrum ranges from a sudden to continuous drop or a stabilized LVEF at a reduced level. Why do patients develop PICM within the first year of pacing and others after many years? Why is the course of LVEF before and during PICM in the patients very individual? Currently, these questions are still completely unanswered.

Until we better understand this variance, the only option is to proceed as other authors have suggested and perform echocardiography at least once a year after pacemaker implantation, especially for patients with symptoms of heart failure [15].

CRT Upgrade

Today CRT upgrade is the therapy of choice for PICM. His Bundle Pacing is not yet an alternative therapy supported by sufficient evidence [16]. After 3 months of optimal medical therapy, patients should receive a CRT device upgrade if LVEF remained<40% and functional status was NYHA class II or worse [17]. Probably because of the improved electrode technology and better tools for probing the coronary sinus side branch, as well as more implantation experience among surgeons, might explain why implantation failure and complication rates are low in recent publications. CRT Survey II data reporting a 97.1% success rate for CRT upgrades and the complication rate was only 5.2% [18]. Nowadays, CRT upgrade is considered as a safe therapeutic procedure.

From our perspective, there is only one situation in clinical practice in which the indication for CRT upgrade must be critically reconsidered, namely in cases of thrombosis of the ipsilateral subclavian vein. In our registry, in six patients (10.9%), the subclavian vein was so occluded on the pacemaker side, so that a new puncture, also more central puncture, was not possible. In our registry complete system was implanted on the contralateral side. This did not result in an elevated complication rate. There are well-founded concerns about this approach, which is common in non-tertiary centers. The general risk of complications increases, such as the risk of bilateral subclavian vein occlusion [19]. In addition to tunneling the electrodes, the literature describes various other venoplasty options, including laser techniques, to avoid contralateral reimplantation in patients with ipsilateral subclavian vein occlusion [20]. Another option is the cardiac surgical implantation of an epicardial left ventricular lead. In summary, the indication for CRT upgrade in subclavian vein thrombosis should be critically questioned and an individual decision for venous access should be made according to the risk/benefit.

To the best of our knowledge, our study represents the largest prospective study showing the effectiveness of a CRT upgrade in patients suffering from PICM. The responder rate in our registry

was 83.6%. Similarly high responder rates have also been reported in retrospective studies by Barra et al. (responder rate 77.4%) and Kurshid et al. (responder rate 86%). Overall, our responder rate accords with previous studies of CRT in PICM. Our study shows, for the first time, that older patients (>80 years) benefit from upgrading CRT to the same extent as younger patients. Although the comprehensive study data on CRT upgrade are quite convincing, this method is still rarely performed in clinical practice. Therefore, it is necessary to establish the CRT upgrade even more in clinical practice, as there are currently no reasonable arguments against this therapeutic option in cases of PICM.

Conclusion

CRT upgrade should be recommended for all patients with a correct diagnosis of PICM, irrespective of their age. In addition to the high responder rate and the associated frequent significant improvement of symptoms after CRT upgrade, the pathophysiology of the disease is fascinating, as many aspects of the pathophysiology of PICM are still not fully understood, because we have not yet understood many pathophysiological aspects of PICM. Our experience in the CRT registry shows that a single center cannot recruit the sufficient number of patients in a prospective design to be able to answer the so far open questions, especially on pathophysiology. We can only do this together in multicenter studies.

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