

Pacing induced cardiomyopathy; epidemiology, pathophysiology and clinical implication

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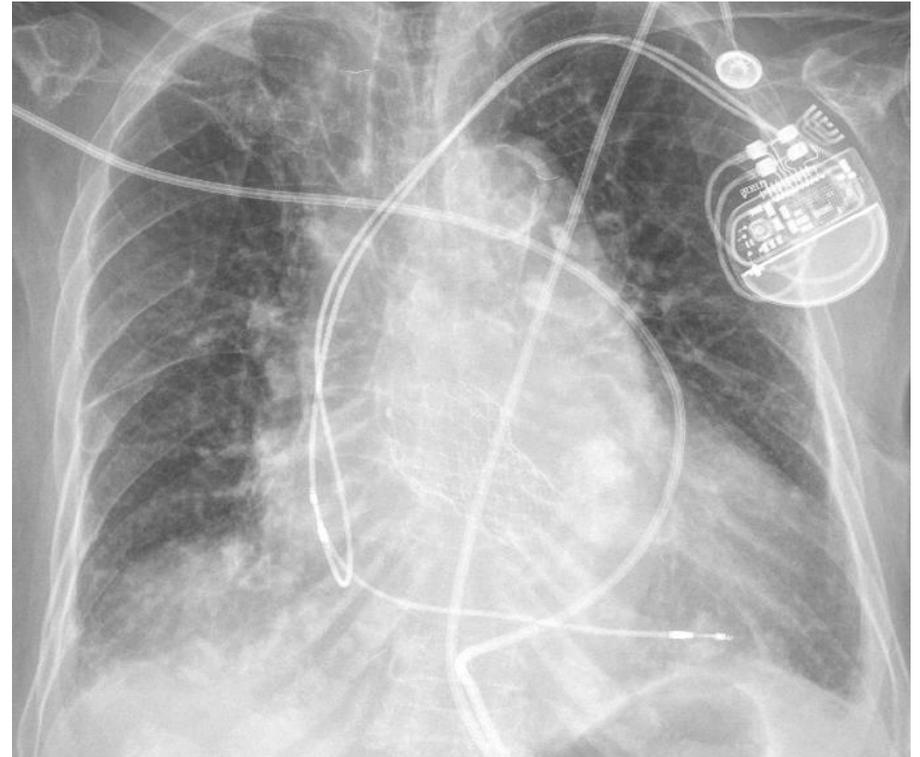
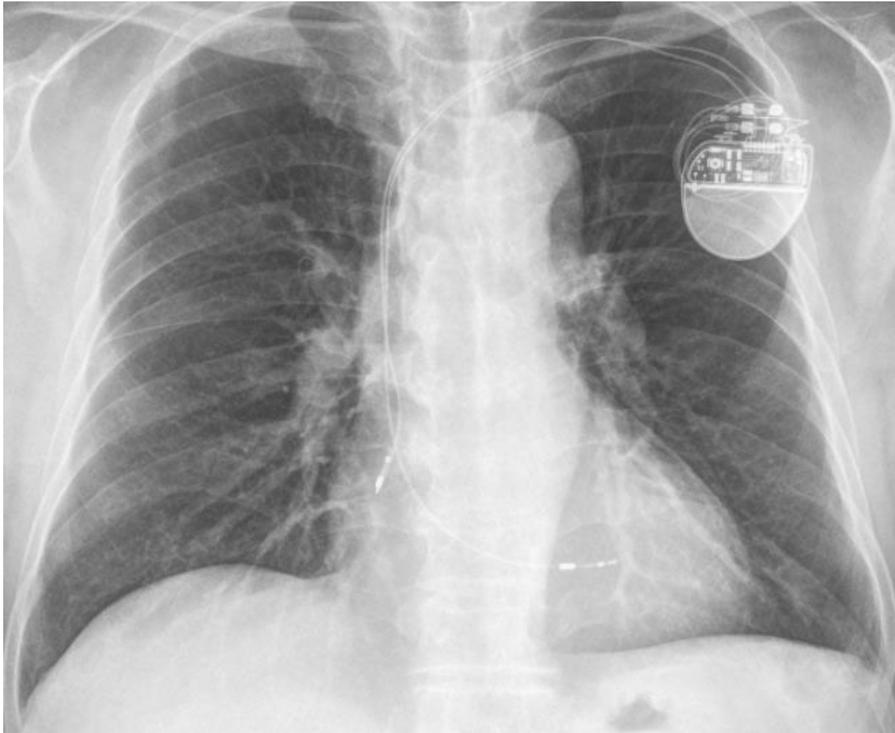
COI Disclosure

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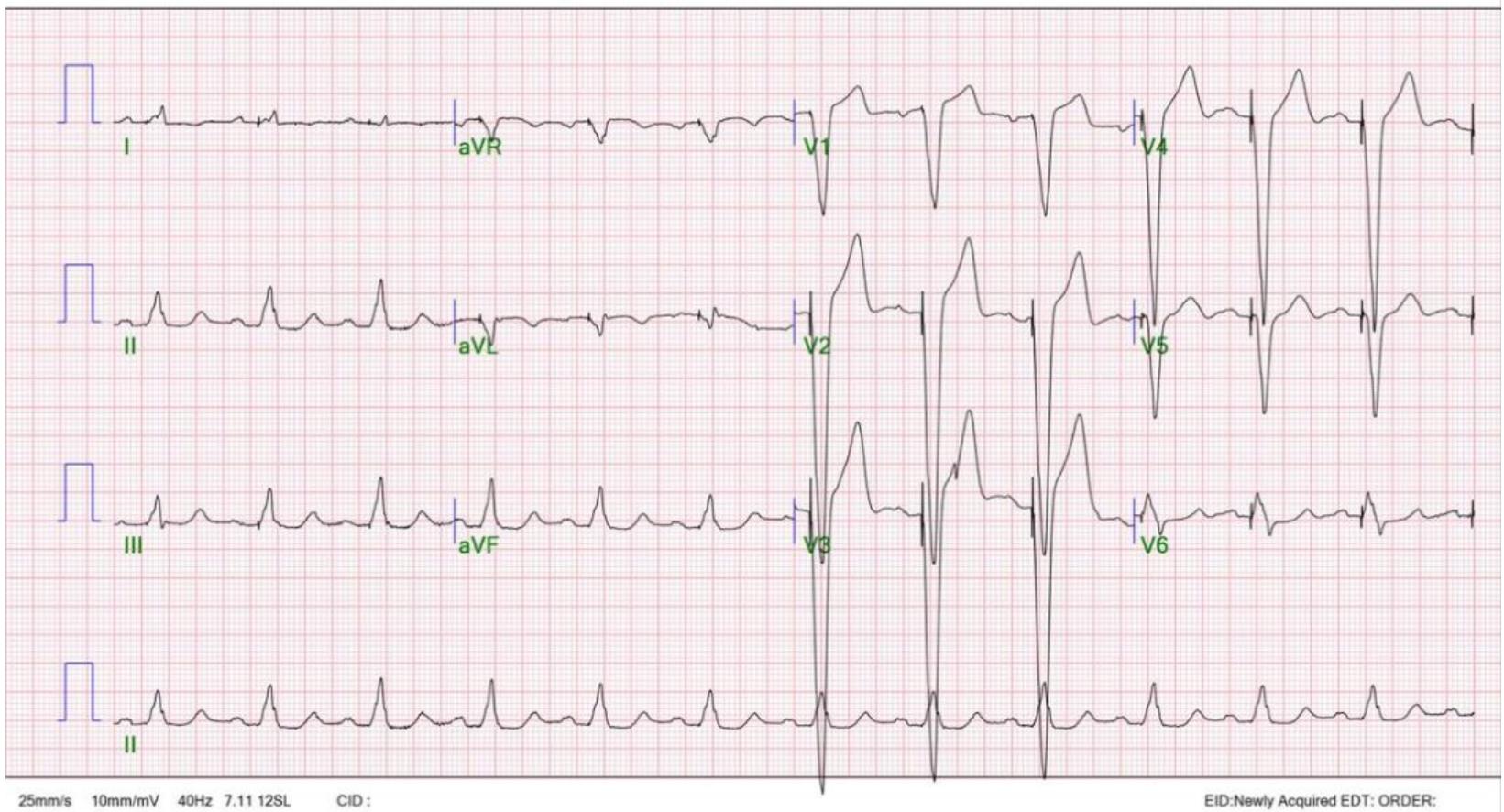
The authors have no financial conflicts of interest
to disclose concerning the presentation



Standard cardiac pacing



Sinus rhythm -> Pacing rhythm



Sinus rhythm -> Pacing rhythm



Pacing induced cardiomyopathy (PICM)

- ◆ Standard cardiac pacing means fixing a pacing lead into the muscle of the right ventricle
- ◆ From that spot, conduction spreads via slower muscle to muscle conduction,
 - which leads to a wide QRS complex
 - and the right ventricle contracts before the left ventricle (dyssynchrony)

Heart, Lung and Circulation (2019) 20
1443-9506/04/\$36.00
<https://doi.org/10.1016/j.hlc.2018.0>

The Prevalence of Cardiomyopathy in Long Term it a Matter of

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1. Retrospective analysis of patients with long term RV pacing
2. Echocardiography within 12 months of device implantation and at least one follow-up echocardiogram
3. 118 patients, the mean time was 3.5 + 1.4 years
4. Definition 1; follow-up LVEF of $\leq 40\%$ if baseline LVEF was $\geq 50\%$, or an absolute reduction in LVEF $\geq 5\%$ if baseline LVEF was $< 50\%$
5. Definition 2; follow-up LVEF of $\leq 40\%$ if baseline LVEF was $\geq 50\%$, or an absolute reduction in LVEF $\geq 10\%$ if baseline LVEF was $\leq 50\%$
6. Definition 3; an absolute reduction in LVEF $\geq 10\%$ irrespective of baseline LVEF

The prevalence ranged from 5.9 to 39% depending on PICM definition

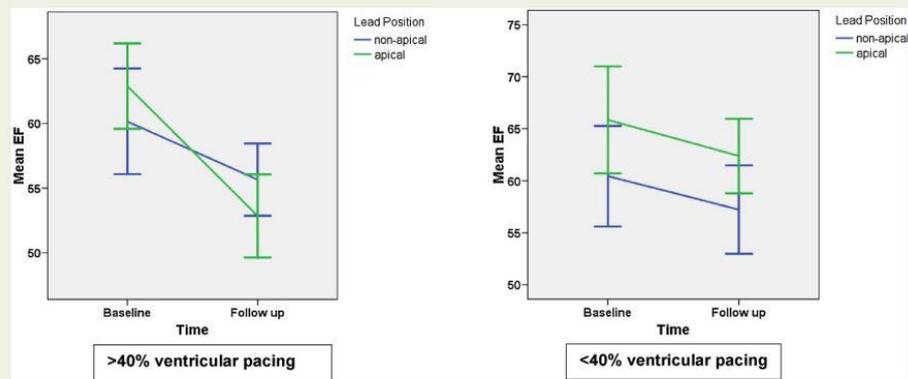


Figure 1 In patients with ventricular pacing burden >40% (left panel), there was a trend towards greater decline in LVEF on follow-up with RVA pacing compared to RVNA pacing (change in LVEF 10.0 ± 14.2 vs. $4.5 \pm 12.6\%$, $p = 0.075$). In patients with ventricular pacing burden <40% (right panel), there was no difference in the change in LVEF between RVA versus RVNA pacing (3.5 ± 10.1 vs. $3.2 \pm 8.8\%$, $p = 0.93$). Abbreviations: LVEF, left ventricular ejection fraction; RVA, right ventricular apex; RVNA, right ventricular non-apical.

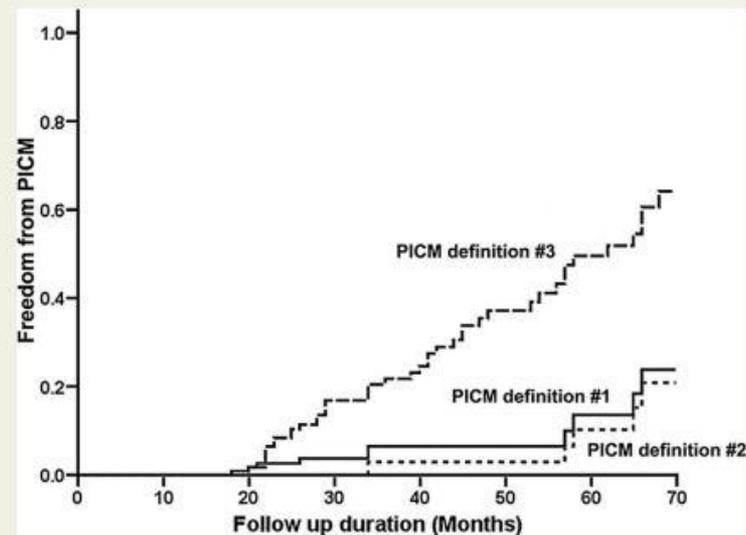


Figure 2 Freedom from pacing-induced cardiomyopathy (PICM) over time, in months. The solid line is PICM definition 1, dotted line is definition 2 and dashed line is definition 3.

CONTEMPORARY REVIEW

Pacing-induced and meta-analysis factors, and ma

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Pacing-induced cardiomyopathy (PiCM) is a complication of long-term right ventricular pacing. Definition varies between studies and the optimal management approach is uncertain. We aimed to characterize definition, prevalence, risk factors, and treatment strategies of pacing-induced cardiomyopathy (PiCM). We performed a systematic review and meta-analysis of studies that evaluated PiCM after pacemaker implantation identified through a literature search of PubMed and EMBASE up to March 2022. We collected data on the study definition of PiCM and calculated pooled prevalence across studies. Meta-analysis with random effects modeling was used to assess the association between potential risk factors and PiCM, reported as odds ratio with 95% confidence interval. Twenty-six studies (6 prospective studies) with a total of 57,993 patients (mean/median age range was 51–78 years; female 45%) were included in the final analysis. Fifteen unique definitions of PiCM were reported. The pooled prevalence of PiCM was 12% (95% confidence interval 11%–14%). In meta-analysis, risk factors included male sex, history of myocardial infarction, chronic kidney disease,

1. 26 studies (6 prospective studies) with a total of 57,993 patients were included in the final analysis
2. 15 unique definitions of PiCM were reported
3. Risk factors;
4. Managements; heart failure medications, biventricular CRT, conduction system pacing

QRS duration, right ventricular pacing percentage, and paced QRS duration. Treatment strategies identified included biventricular cardiac resynchronization therapy (6 studies) and His-bundle pacing (3 studies). Definition of PiCM varied significantly between studies. More than 1 in 10 patients with chronic right ventricular pacing developed PiCM. Key risk factors included baseline left ventricular ejection fraction, native QRS duration, RV pacing percentage, and paced QRS duration. The optimal management strategy has yet to be defined. Further research is needed to define and treat this understated complication.

KEYWORDS Pacemaker syndrome; Cardiac resynchronization therapy; Cardiomyopathy; His-bundle pacing; Right ventricular pacing

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Epidemiology

- ◆ The overall pooled prevalence of PICM was 12% (95% CI 11~14%)
- ◆ The individual study prevalence ranged from 6 to 25%
- ◆ Six studies reported time from implantation to PICM
 - The shortest onset time was 1 month
 - The longest was 16.9 years
 - The median time ranged from 13 months to 5.2 years

Table 1 Meta-analysis of potential risk factors for PiCM

Variable	Number of included studies	Total patients	Overall OR (95% CI)	<i>P</i>	Heterogeneity, <i>I</i> ² (%)
Age	7	2,762	1.01 (0.99–1.02)	.09	61
Male sex	9	3,129	1.23 (1.12–1.35)	<.001	36
History of MI	3	28,525	1.81 (1.54–2.12)	<.001	0
T2DM	3	28,301	0.86 (0.69–1.06)	.14	0
CKD	2	28,322	1.66 (1.32–2.01)	<.001	0
AF	2	21,405	1.32 (1.23–1.42)	<.001	0
Baseline LVEF (per 1% increase)	7	2,847	0.95 (0.93–0.97)	<.001	61
Native QRS duration (per ms increase)	3	1,005	1.02 (1.01–1.03)	<.01	36
RV pacing percentage (per 1% increase)	6	1,983	1.02 (1.01–1.02)	<.001	95
Paced QRS duration (per ms increase)	10	3,858	1.02 (1.01–1.03)	<.001	97

Forest plot of meta-analysis for each variable is included in the Online Supplement.

AF = atrial fibrillation; CI = confidence interval; CKD = chronic kidney disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OR = odds ratio; PiCM = pacing-induced cardiomyopathy; RV = right ventricular; T2DM = type 2 diabetes mellitus.

Pathophysiology

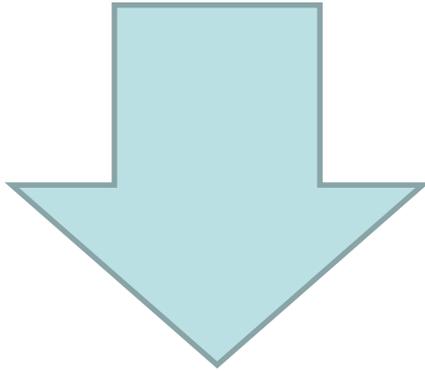
- ◆ Not fully understood,
- ◆ but it is thought to be related to the deleterious effects of chronic RV pacing on LV function
- ◆ Chronic RV pacing can lead to LV dyssynchrony, which can cause LV remodeling and dysfunction
- ◆ Other proposed mechanisms include
 - mechanical stress on the LV due to RV pacing-induced septal motion abnormalities,
 - neurohormonal activation
 - inflammation

Clinical implications

- ◆ PICM can lead to heart failure symptoms and reduced quality of life
- ◆ Patients with PICM may require additional medical therapy, such as diuretics and beta-blockers, to manage heart failure symptoms
- ◆ Biventricular CRT and conduction system pacing have been shown to improve echocardiographic and clinical outcomes in patients with PICM
- ◆ Early recognition and management of PICM is important to prevent irreversible LV dysfunction and heart failure

Case 1

- ◆ PPM d/t CAVB (June 27,2005)
- ◆ LVEF 30% (November 23,2011)
- ◆ LVEF 29% (May 29, 2013)



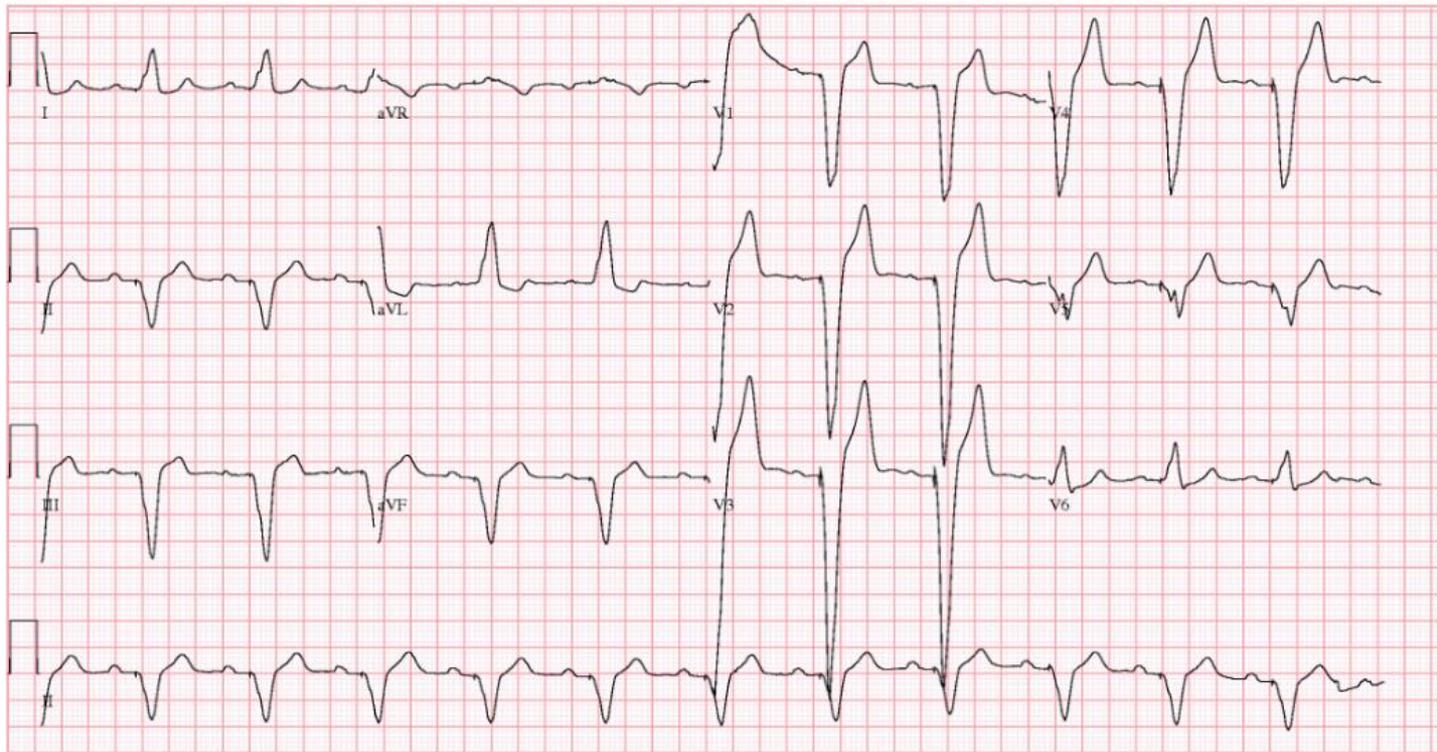
I have no idea
I don't know the reason
why...

- ◆ ICD upgrade (Aug 16,2013)

July 25, 2012

Referred by:

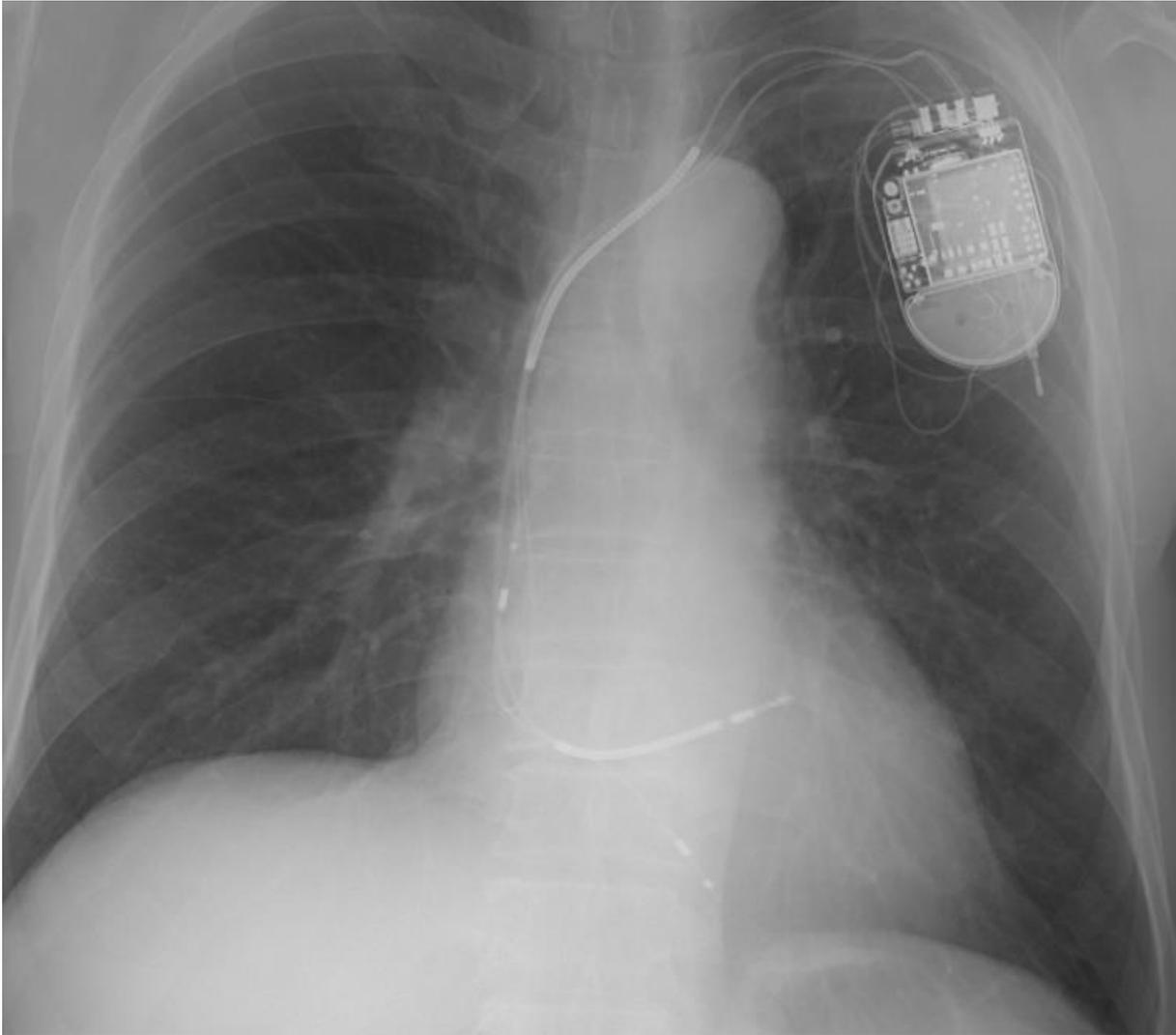
Newly Acquired



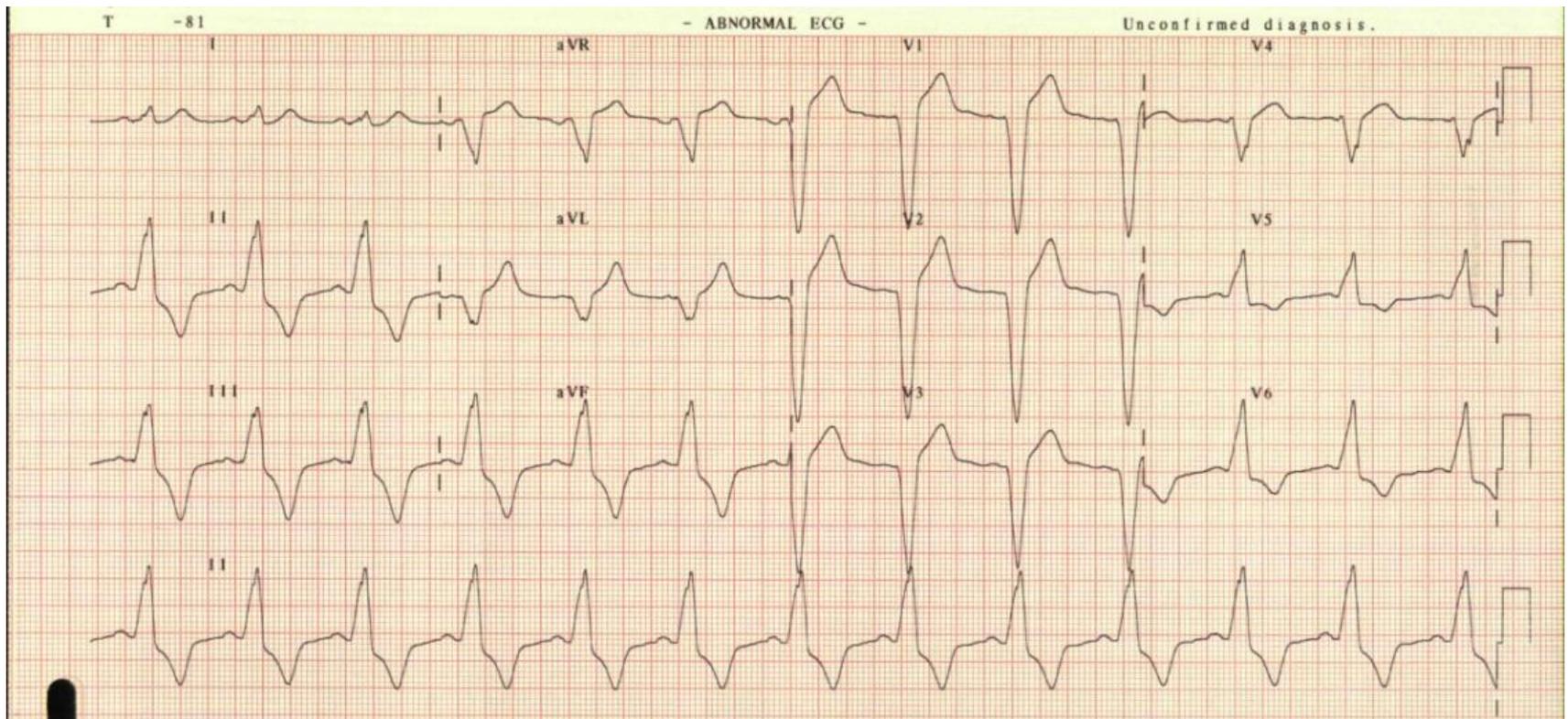


November 23, 2011, TTE



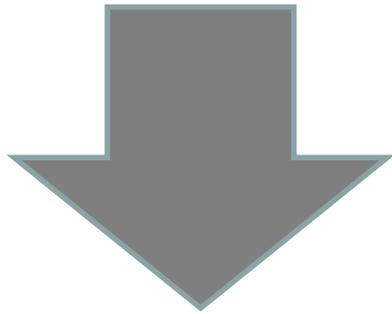


August 17, 2013



I have consistently prescribed HF medications for years

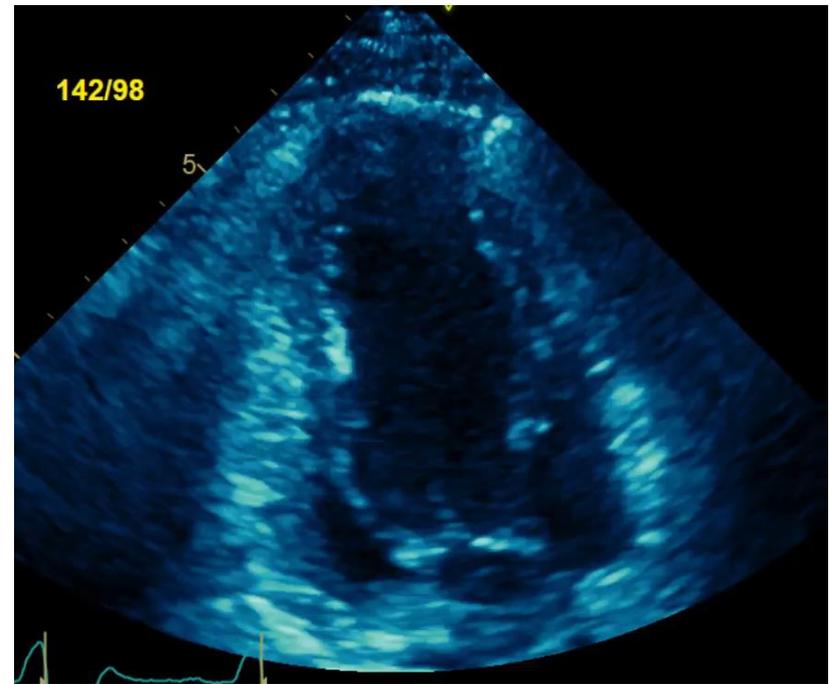
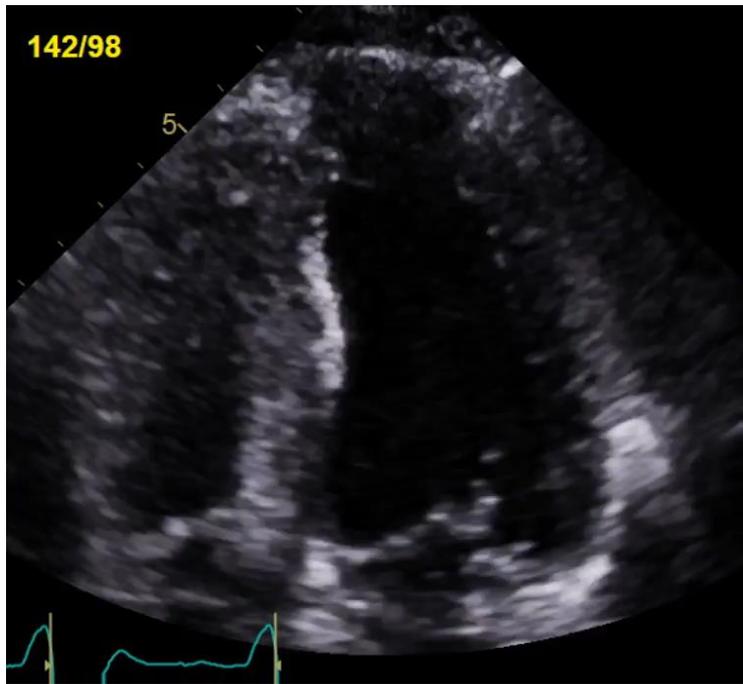
- ◆ LVEF 37 (May 5, 2016)
- ◆ LVEF 40% (May 13, 2020)



Add
sacubitril/valsartan 50mg bid

- ◆ LVEF 50% (December 26, 2022)

December 26, 2022

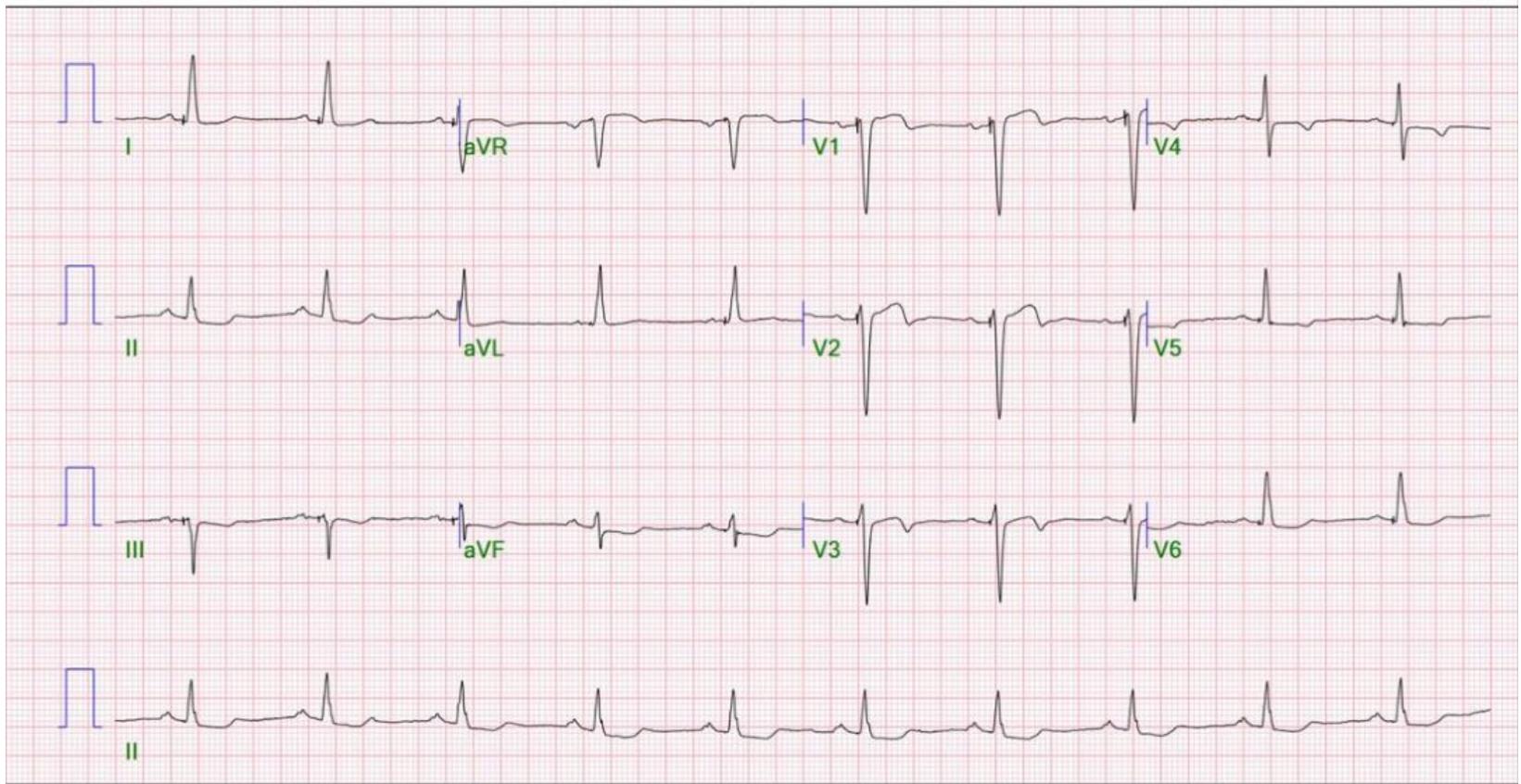


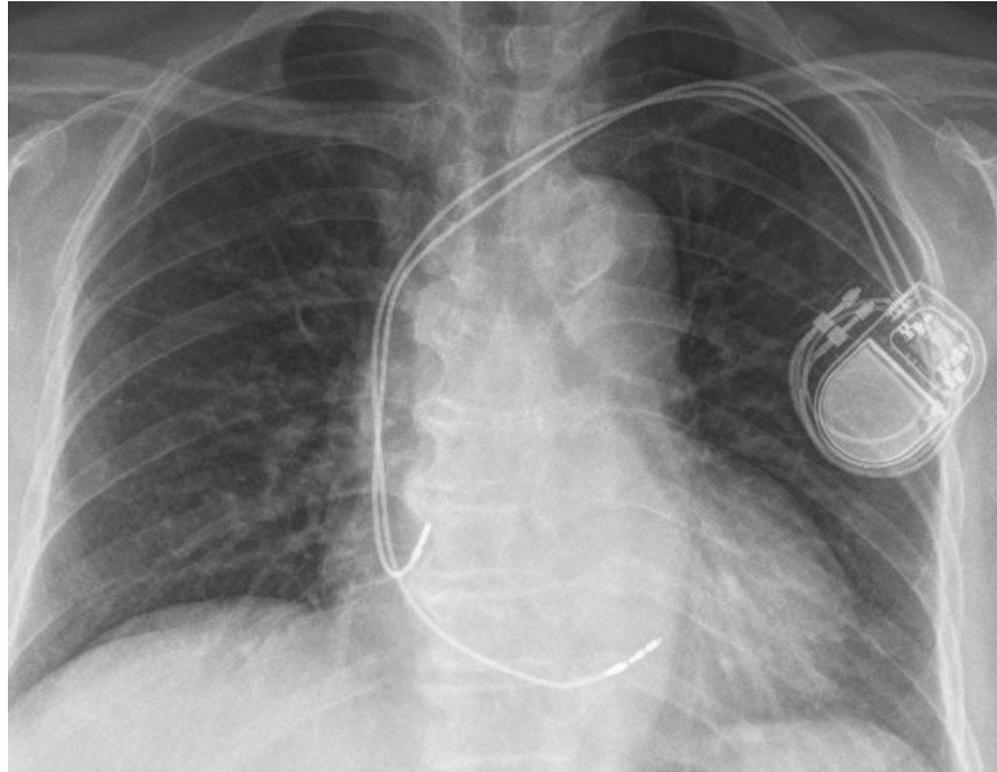
Case 2

- ◆ F/68
- ◆ 2:1 AV block
- ◆ LVEF 39%
- ◆ Normal CAG

- ◆ Conduction system pacing

ECG after implantation





Summary

◆ The epidemiology of PICM

- The prevalence ranged from 5.9 to 39% depending on PICM definition
- There is no one internationally accepted definition of PICM
- The overall pooled prevalence of PICM was 12% (95% CI 11~14%)

◆ The pathophysiology

- Standard RV pacing makes paced QRS duration wider and RV contracts before the LV
- Patient's substrate
 - male sex, h/o MI, CKD, AF, baseline LVEF, native QRS duration
- PPM itself problems
 - RV pacing percentage, paced QRS duration

◆ Clinical implications

- Early recognition and management, including HF medications and biventricular CRT or conduction system pacing, could reverse LVEF

Thank you for your attention

The therapeutic benefit of upgrade to cardiac resynchronization therapy in patients with pacing-induced cardiomyopathy



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BACKGROUND Pacing-induced cardiomyopathy (PICM) is an important cause of heart failure in patients with a right ventricular pacing burden. Recent evidence suggests that an upgrade to cardiac resynchronization therapy (CRT) may confer benefit in PICM.

OBJECTIVE To assess the extent and identify predictors of improvement following upgrade to CRT in patients with PICM.

METHODS We retrospectively analyzed 43 patients undergoing CRT upgrade for PICM over the 10-year period of 2011 to 2021 at our center. All patients with PICM who underwent device upgrade from a dual- or single-chamber ventricular pacemaker to CRT were included. PICM was defined as a decrease of $\geq 10\%$ in left ventricular ejection fraction (LVEF), resulting in an LVEF $< 50\%$ among patients with $\geq 20\%$ Right ventricular pacing burden without an alternative cause for cardiomyopathy.

RESULTS LVEF significantly improved from 28.7% preupgrade to 44.3% post-CRT upgrade ($P < .01$). Of 37 patients with severe LV

dysfunction, 34 (91.9%) improved to an LVEF $> 35\%$ and 13 (35.1%) improved to an LVEF $> 50\%$. The LV end-diastolic diameter decreased from 5.9 cm preupgrade to 5.4 cm postupgrade ($P < .01$). Using linear regression, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use was associated with significant LVEF improvement ($+7.21\%$, $P = .05$). We observed a low rate of complications, and 1 in 4 CRT upgrades required venoplasty ($n = 10$ of 43, 23.3%).

CONCLUSION We provide further evidence for the benefit of CRT upgrade in the management of patients with PICM.

KEYWORDS Pacing-induced cardiomyopathy; Cardiac resynchronization therapy; Heart failure; Pacing complications

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Introduction

Conventional right ventricular pacing (RVP) is the most widely used method to treat symptomatic bradycardia and high-degree atrioventricular block.^{1–3} RVP causes electromechanical ventricular dyssynchrony, which in some patients may eventually result in left ventricular systolic dysfunction (LVSD).^{3–5} Definitions have varied across the literature but the most common criteria for pacing-induced cardiomyopathy (PICM) are (1) LV ejection fraction (LVEF) $\geq 50\%$ before pacemaker implantation, (2) new onset of LVSD in patients with an RVP percentage $\geq 20\%$ with an LVEF $\leq 50\%$, and (3) absence of alternative causes of LVSD.^{6–8} PICM is an important and increasingly recognized cause of heart failure in patients exposed to frequent RVP.⁶ Placement of an LV lead for biventricular pacing or cardiac resynchronization therapy (CRT) has

been empirically recommended in international guidelines for the treatment of PICM despite limited clinical outcome data.⁹ A recent meta-analysis of patients with PICM treated with upgrade to CRT demonstrated an increase in LVEF of 10.9% and reduction in symptoms by 1 New York Heart Association (NYHA) functional class.²

In this study, we analyzed a large single-center cohort of consecutive CRT upgrades for patients with PICM over 10 years and sought to characterize the time course and degree of improvement in LVEF.

Methods

Study population

We performed a retrospective analysis of patients who underwent CRT upgrade for patients who developed a PICM at Cork University Hospital from January 2011 to December 2021. PICM was defined as a $\geq 10\%$ decrease in LVEF with $> 20\%$ RVP burden with a prior documented LVEF $\geq 50\%$ either prior to or shortly after pacemaker implantation. The onset of PICM was considered the date of the first

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- ◆ PiCM is a condition where chronic RV pacing can lead to HF
 - Electromechanical dyssynchrony, which means that the electrical and mechanical functions of the heart rate are not coordinated properly.
 - This can lead to a decrease in LVEF and overall heart function
- ◆ Upgrading to CRT can improve heart function in pts with PiCM by attenuating electromechanical dyssynchrony.
- ◆ CRT devices deliver electrical impulses to both ventricles of the heart, which can synchronize the electrical and mechanical functions of the heart and improve LVEF.
- ◆ The study found that upgrading to CRT can lead to near-complete resolution of RV PiCM in 9 of 10 cases of severe PiCM