Supplementary Table S1. Summary of the characteristics and outcomes of pharmacotherapy trials conducted in patients who were at risk for or who have established PICM.

Trial	Study Type	n	Study Population	Study Methods	PICM Definition	Outcome
Schwerg, 2015 [48]	Retrospective cohort Screening	20	*Inclusion:* Patients presenting for annual, routine pacemaker interrogation with ≥90% right ventricular pacing 3 months of optimal medical therapy vs CRT for patients with PICM *Exclusion:* Patients with single-chamber pacemaker Patients with other etiologies of impaired LVEF Age: 73.1±12.4 years Women: 47%	Screened patients with ≥90% right ventricular pacing PICM patients received 3 months of optimal medical therapy CRT upgrade if symptomatic left ventricular dysfunction Follow-up: 3, 6, 12 months	Preserved left ventricular function at first pacemaker implantation and LVEF <45% unexplained by other cardiac disease with right ventricular pacing ≥90%	LVEF improved significantly from 33.3±5.2% pre-upgrade to 47.6±9.3% within 6 months post-upgrade ($p<0.001$) Optimal medical therapy did not affect LVEF
Barbieri, 2002 [49]	Prospective Post hoc analysis	54	*Inclusion:* Symptomatic heart failure with LVEF <40% despite optimal	Transthoracic echocardiography performed prior to implantation and 3-5	Symptomatic heart failure with LVEF <40% despite optimal medical therapy and	Previous treatment with heart failure medications did not

			medical therapy and right ventricular pacing >40% Adjusted device programming to minimize right ventricular pacing prior to enrollment PICM patients who received CRT	months after CRT activation Evaluated effect of heart failure medication (BB, ACEi/ARB, MRA) on CRT	right ventricular pacing >40%	reduce CRT upgrade incidence CRT response (↓ LVESV by >15%) achieved in 30 patients (55.6%)
Lin, 2022 [51]	Single center Retrospective cohort	1717 Statin: 240 Nonstatin: 1477	*Inclusion:* Mobitz type II or complete atrioventricular block with pacemaker implantation *Exclusion:* Patients with alternative etiologies of heart failure or taking statin > 6 months Age: Statin - 73.9±10.5 years Nonstatin - 73.8±5.0 years Women:	Randomized to statin or nonstatin Primary outcome: (cardiovascular death or heart failure hospitalization) Secondary outcomes: Heart failure hospitalization All-cause mortality Cardiovascular death Follow-up: Statin - 5.1±3.3 years Nonstatin - 5.3±3.5 years	↓ LVEF ≥10% LVEF <50% post pacemaker implantation CRT upgrade after exclusion of other etiologies of cardiomyopathy	Statin was associated with ↓ cardiovascular death or heart hospitalization (HR 0.69 [95% CI 0.56-0.84], p<0.001) Statin was associated with ↓ heart hospitalization (HR 0.45 [95% CI 0.30-0.67], p<0.001) Statin was associated with ↓ all-cause mortality (HR 0.52 [95% CI 0.45-0.61], p<0.001) Statin was associated with ↓ cardiovascular

			Statin: 55% Nonstatin: 54%			death (HR 0.65 [95% CI 0.49-0.86], p=0.003)
Kerley, 2023 [50]	Single center Retrospective cohort	43	*Inclusion:* PICM patients who had CRT upgrade from a single- or dual-chamber pacemaker from 2011-2021 *Exclusion:* Patients with alternative etiologies of cardiomyopathy Age: 77±10.8 years Women: 30.2%	Measured LVEF pre- and post-upgrade at 3 to 6 months Identified LVEF improvement using multivariate linear regression Follow-up: 24 months	↓ LVEF ≥10% with >20% right ventricular pacing burden and with prior LVEF ≥50% prior to or immediately after pacemaker implantation Severe PICM: LVEF <35%	LVEF significantly improved from 28.7% pre- upgrade to 44.3% post-CRT upgrade (p<0.01) CRT response (↑LVEF >5%) observed in 88.4% of patients Trend of ACEi/ARB use with LVEF improvement (↑ by 7.21%, p=0.05)
Agha, 2025 [45]	Single center Retrospective cohort	642	*Inclusion:* Adult patients with normal LVEF and complete heart block who had single- or dual-chamber pacemaker with right ventricular lead implantation *Exclusion:* Patients who received epicardial, coronary sinus, or His bundle area leads	Comparison of medical therapy group (ACEI/ARB, BB, or both) vs control group Fine-Gray subdistribution hazard models (treated death as a competing risk) Follow-up: maximum 10 years	Upgrade to a biventricular device or reduction in↓ LVEF to ≤40% without another cause	Risk of PICM: significantly lower in medical therapy group (HR 0.59 [95% CI, 0.45-0.77]) vs control group Lowest risk in patients on combination therapy (ACEI/ARB and BB) (HR 0.46 [95% CI 0.31-0.69])

			Pre-existing cardiomyopathy or reduced LVEF before implantation Ischemic cardiomyopathy during follow-up Age: 71±14 years Women: 51%			

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor block; BB = β-blocker; CI = confidence interval; CRT = cardiac resynchronization therapy; HR = hazard ratio; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; PICM = pacing-induced cardiomyopathy