

Supplementary Material

Supplementary Material 1: Search Strategy Details

("Cardiac Pacing, Artificial"[Mesh] OR "right ventricular pacing"[Title/Abstract] OR "Artificial Cardiac Pacing"[Title/Abstract] OR "Cardiac Pacing"[Title/Abstract])

AND ("RV function"[Title/Abstract] OR "right ventricular function"[Title/Abstract] OR "pulmonary hypertension"[Title/Abstract] OR "RV infarction"[Title/Abstract] OR "RV MI"[Title/Abstract] OR "right ventricular MI"[Title/Abstract])

(('cardiac pacing'/exp OR 'cardiac pacing') OR ('right ventricular pacing':ab,ti OR 'artificial cardiac pacing':ab,ti OR 'cardiac pacing':ab,ti)) AND (('RV function':ab,ti OR 'right ventricular function':ab,ti) OR 'pulmonary hypertension':ab,ti OR ('RV infarction':ab,ti OR 'RV MI':ab,ti OR 'right ventricular MI':ab,ti))

(TITLE-ABS-KEY("cardiac pacing" OR "artificial cardiac pacing" OR "right ventricular pacing")) AND (TITLE-ABS-KEY("RV function" OR "right ventricular function" OR "pulmonary hypertension" OR "RV infarction" OR "RV MI" OR "right ventricular MI"))

Supplementary Table 1: Reference standards for the echocardiographic assessment of the right ventricle adapted from the American Society of Echocardiography guidelines

MEASUREMENT	UNIT	ABNORMAL
TAPSE	cm	<1.6
RIMP	*	>55**
2D-FAC	%	<35
2D RVEF	%	<44
S'	cm/s	<10
SPAP	mmHg	>30
RV DP/DT	mmHg/s	<400
RV BASAL	mm	>33
RV MID CAVITY	mm	>28
RV LONGITUDINAL	mm	>71
TR VENA CONTRACTA WIDTH	cm	>0.3
ERO	cm ²	>0.2
REGURGITANT VOLUME	mL	>30

TAPSE: tricuspid annular plane systolic excursion; RIMP: RV index of myocardial performance; FAC: Fractional area change; RVEF: RV ejection fraction; S': Tissue Doppler-derived tricuspid lateral annular systolic velocity; sPAP: systolic pulmonary artery pressure; RV dP/dt: Derivative pressure / time; ERO: Effective regurgitant orifice.

*Unitless measurement.

**Measured by tissue Doppler.

Supplementary Table 2: Baseline characteristics of included studies

Study	Type of study	Indication for PPM	Measurement of RV function	Follow up (months)	N/female	Age (years)	Baseline LV EF >50% (n)	Mean pacing >40% (n)	Baseline TR (n)	Baseline pulmonary hypertension (n)	Baseline sinus rhythm (n)	Using anti-arrhythmic (n)	Pacing Location
Dwivedi et al 2006 ¹	Prospective, non-randomized	SSS CHB	2D echocardiography **	6	48;18	65.6	41	NA	NA	NA	NA	NA	NA
Ichiki et al 2006 ²	Prospective, non-randomized	SSS AV block	2D and pulsed wave Doppler	45	76;43	63	46	46	NA	NA	NA	NA	NA
Kindermann et al 2006 ³	RCT	Standard indication for PPM	2D and pulsed wave Doppler	3	30;7	69.6	0	NA	NA	NA	19	10	NA
Nunes et al 2011 ⁴	Prospective, non-randomized	CHB	2D and tissue Doppler imaging	6	85;46	62	85	NA	78	85	NA	0	NA
Domenichini et al 2012 ⁵ (a)	Prospective, randomized	Bradyarrhythmia	Multigated equilibrium blood pool planar scintigram	52.8	59;13	77.5	23	28	NA	NA	20	3	RV apex
Domenichini et al 2012 ⁵ (b)	Prospective, randomized	Bradyarrhythmia	Multigated equilibrium blood pool planar scintigram	52.8	59;13	77.5	22	31	NA	NA	18	7	RV Septum
Porapakkham et al 2012 ⁶	Retrospective	CHB SSS	2D and tissue Doppler imaging	76.8	96;53	67.7	96	53	96	NA	0	NA	NA
Chen et al 2015 ⁷ (a)	Prospective, non-randomized	SSS High degree AV block	2D and pulsed wave Doppler	62	50;20	72	14	14	NA	NA	2	4	RV apex
Chen et al 2015 ⁷ (b)	Prospective, non-randomized	SSS High degree AV block	2D and pulsed wave Doppler	20	50;20	72	36	36	NA	NA	0	7	RV Septum
Saito et al 2015 ⁸	Sub-group analysis of RCT	High grade - AV block	2D and pulsed wave Doppler	24	145;48	75	145	0	109	NA	116	NA	NA
Salaun et al 2018 ⁹	Prospective, non-randomized	Bradyarrhythmia Unexplained syncope	2D and tissue Doppler imaging	2	23;12	85	23	NA	23	23	8	3	Leadless
Beurskens et al 2019 ¹⁰	Retrospective & Prospective, non-randomized	SSS Sinus node dysfunction Atrioventricular block	2D and pulsed wave Doppler	12	53;16	80	53	NA	47	53	0	NA	Leadless
Nadar et al 2020 ¹¹	Retrospective	SSS CHB asystole	2D echocardiography **	12	65;34	70	NA	65	29	NA	4	NA	RV Apex
Soliman et al 2020 ¹²	Case-control	CHB	2D speckle tracking echocardiography **	6	30;18	63	NA	NA	NA	NA	0	NA	RV Apex
Majos-Karwaka et al 2021 ¹³	Case-control	HFrEF and permanent A-fib	2D echocardiography **	36	69;10	73	0	NA	NA	NA	0	NA	RV Apex

Sinkar et al 2021 ¹⁴	Prospective, non-randomized	CHB High grade - AV block	3D and tissue Doppler imaging	6	60;29	68	60	NA	1	0	60	NA	RV Septum
Huang et al 2022 ¹⁵ (a)	Prospective, non-randomized	SSS	2D and tissue Doppler imaging	0.1	84;29	67	42	NA	42	NA	0	NA	LBBP
Huang et al 2022 ¹⁵ (b)	Prospective, non-randomized	SSS	2D and tissue Doppler imaging	0.1	84;29	67	42	NA	42	NA	0	NA	RV Septum
Youssef et al 2022 ¹⁶ (a)	Retrospective & Prospective, non-randomized	SSS CHB	2D echocardiography**	24	60;25	71.5	21	21	NA	NA	21	NA	RV Apex
Youssef et al 2022 ¹⁶ (b)	Retrospective & Prospective, non-randomized	SSS CHB	2D echocardiography**	24	60;25	71.5	39	0	NA	NA	39	NA	RV Apex
Bednarek et al 2024 ¹⁷	Prospective, non-randomized	SSS AVB CRT	2D and tissue Doppler imaging	21	122;60	76.5	122	122	122	NA	93	NA	LBBP
Tian et al 2024 ¹⁸ (a)	Prospective, non-randomized	CRT	3D echocardiography**	6	65;32	64	0	NA	NA	30	NA	NA	LBBP
Tian et al 2024 ¹⁸ (b)	Prospective, non-randomized	CRT	3D echocardiography**	6	65;32	64	0	NA	NA	35	NA	NA	LBBP

**Doppler modality not specified.

Supplementary Table 3: Baseline comorbidities of patients in the included studies

Comorbidities (number of patients/number of studies)

Smoking: 33/3

HTN: 626/15

CAD: 182/9

DM2: 298/15

Stroke: 11/3

Dyslipidaemia: 45/3

CKD: 47/4

COPD: 11/3

Supplementary Table 4: Right ventricular pacing characteristics and associated right ventricular parameters

Study	RV Parameters
Dwivedi et al 2006 ¹	<p><u>RV EF:</u> RV dP/dt (mmHg/s): 300 -> 420 (p<0.0001)*</p> <p><u>RV dimension:</u> RV internal diameter: 1.26 -> 1.77 (p<0.001)*</p>
Ichiki et al 2006 ²	<p><u>RIMP:</u> >50%: 0.34* <50%: 0.25*</p> <p><u>TR:</u> Peak flow velocity TR (m/S) 2.1 vs 2.0</p>
Kindermann et al 2006 ³	<p><u>RIMP:</u> RVP: 0.85->0.55* p<0.001 BVP: 0.85->0.49* p<0.001</p>
Nunes et al 2011 ⁴	<p><u>RIMP:</u> RVP vs control: 0.34 vs 0.28 p=0.27</p> <p><u>S':</u> 12.1 vs 12.7 p=0.601</p>
Domenichini et al 2012 ⁵ (a)	<p><u>2D RV EF:</u> Apex (44->46)</p>
Domenichini et al 2012 ⁵ (b)	<p><u>2D RV EF:</u> Septum (44->47)*</p>
Porapakkham et al 2012 ⁶	<p><u>TR:</u> 50% vs 21% p=0.16</p>
Chen et al 2015 ⁷ (a)	<p><u>S':</u> Apex (13->11)*</p>
Chen et al 2015 ⁷ (b)	<p><u>S':</u> Septal (13->12)</p>
Saito et al 2015 ⁸	<p><u>TAPSE:</u> RV septum: 2.1 -> 1.9 p=0.06 RV apex: 2.0 -> 2.0 p=0.61</p> <p><u>TR gradient (mmHg):</u> Overall: 12->15 p=0.04* RV septum: 8 -> 15 p=0.06 RV apex: 13->16 p=0.09</p>
Saulan et al 2018 ⁹	<p><u>S':</u> 13.0 -> 13.0 (p=0.82)</p> <p><u>TAPSE:</u> 20.9 -> 20.1 (p=0.051)</p> <p><u>SPAP:</u> 38.2 -> 42.9 (p=0.026)*</p> <p><u>FAC%:</u> 48.6 -> 48.2 (p=0.57)</p>

Beurskens et al 2019 ¹⁰	<p><u>RIMP:</u> 0.40 -> 0.50 (p=0.04) *</p> <p><u>S':</u> 11.8 -> 10.9 (p=0.02) *</p> <p><u>TAPSE:</u> 1.9 -> 1.6 (p=0.003) *</p> <p><u>SPAP:</u> 32.3 -> 32.0 (p=0.21)</p> <p><u>TR:</u> More severe in 34% of patients (p<0.001) *</p>
Nadar et al 2020 ¹¹	<p><u>TAPSE:</u> Pre-pacemaker vs post: 1.9 -> 1.7*</p> <p><u>RV dimension:</u> RV mid-level: 2.9 vs 3.3*</p> <p><u>SPAP:</u> 10 vs 30*</p> <p><u>TR:</u> 29 patients vs 51 patients*</p>
Soliman et al 2020 ¹²	<p><u>TAPSE:</u> 2.3->2.0 (p<0.001)*</p> <p><u>RV dimension:</u> RV basal: 3.2 -> 3.5 (p=0.067)</p>
Majos-Karwaka et al 2021 ¹³	<p><u>3D RV EF:</u> CRT 38.3 vs RVp 37.1*</p> <p><u>S':</u> 9.3 vs 9.3</p> <p><u>TAPSE:</u> 1.9 vs 2.0</p> <p><u>RV dimension:</u> RV longitudinal: 7.5 vs 7.5</p> <p><u>FAC%:</u> 39.2 vs 37.4</p>
Sinkar et al 2021 ¹⁴	<p><u>3D RV EF:</u> 3D RVEF pre vs post PPM 47.7 vs 44.9 p<0.001*</p> <p><u>RIMP:</u> 0.66 vs 0.61 p=0.03*</p> <p><u>S':</u> 13.6 vs 10.7 p<0.001*</p> <p><u>TAPSE:</u> 1.8 vs 1.6 p<0.001*</p> <p><u>RV dimension:</u> RVmid 2.6 vs 2.5 p=0.096</p> <p><u>SPAP:</u> 20 vs 26 p<0.001*</p> <p><u>FAC%:</u> 42.6 vs 39.4 p<0.001*</p> <p><u>TR:</u> TR Jet area (cm2) 0.03 vs 0.55 p<0.001*</p>

Huang et al 2022 ¹⁵ (a)	<p><u>RV dimension:</u> LBBB: EDDbase: 3.3->3.4 EDDmid: 2.5->2.6</p> <p>RVSP: EDDbase: 3.4->3.4 EDDmid: 2.7->2.7</p> <p><u>FAC%:</u> LBBP: (47.1->48.6) RVSP: (52.1->45.1)*</p> <p><u>TR:</u> LBBP: VCW: 0.33->0.32 RVSP: VCW: 0.3->0.37*</p>
Huang et al 2022 ¹⁵ (b)	
Youssef et al 2022 ¹⁶ (a)	<p><u>TAPSE:</u> Baseline vs 12 months: >40% pacing 26.0 vs 23.3 p=0.78 <40% pacing 23.7 vs 23.4 p=0.91</p>
Youssef et al 2022 ¹⁶ (b)	
Bednarek et al 2024 ¹⁷	<p><u>S':</u> 13->13 (p=0.16)</p> <p><u>TAPSE:</u> 2.2->2.3 (p=0.06)</p> <p><u>RV dimension:</u> RV basal diameter: 37.1->37.4 (p=0.44)</p> <p><u>FAC%:</u> 41.1->41.2 (p=0.96)</p>
Tian et al 2024 ¹⁸ (a)	<p><u>3D RV EF:</u> No baseline RV dysfunction: 51.3->52.5 (p=0.54) Baseline RV dysfunction: 38.8 -> 47.1 (p<0.001)*</p> <p><u>TAPSE:</u> No baseline RV dysfunction: 16.7 -> 17.9 (p=0.096) Baseline RV dysfunction: 14.4->17.4 (P=0.001)*</p> <p><u>SPAP:</u> No baseline RV dysfunction: 36.8 -> 33.6 (p=0.758) Baseline RV dysfunction: 43.6->34.4 (p=0.001)*</p> <p><u>FAC%:</u> No baseline RV dysfunction: 46.2 -> 49.5 (p=0.183) Baseline RV dysfunction: 37.4->42.6 (P=0.023)*</p> <p><u>TR:</u> Severe TR: No baseline RV dysfunction: 6.7% -> 0% (p=0.492) Baseline RV dysfunction: 29%->17% (P=0.255)</p>
Tian et al 2024 ¹⁸ (b)	

TR: Tricuspid regurgitation; RIMP: RV index of myocardial performance; S': Systolic velocity (cm/s); RV dimension (cm); TAPSE: Tricuspid annular plane systolic excursion (cm); RV dimension: SPAP: systolic pulmonary artery pressure (mm Hg); FAC%: fractional area change percentage

*Denotes significant difference.

(Green) Significant improvement in an RV parameter.

(Red) Significant worsening in an RV parameter.

Supplementary Table 5: Results of meta-regression of differential effects of length of treatment and site of pacing on variability across studies

	RVEF	TAPSE	RIMP	S'	FAC%	sPAP
Length of treatment	Coefficient = 0.1362, p=0.2082	Coefficient = 0.0056, p=0.5304	Coefficient = 0.0380, p=0.0106	Coefficient = 0.0273, p=0.2209	Coefficient = -0.0678, p=0.6765	Coefficient = 0.0910, p=0.9160
Site of pacing	Coefficient = 3.3500, p=0.1083	Coefficient = 0.1073, p=0.0198	Insufficient data	Coefficient = 1.0250, p=0.0124	Coefficient = 3.8720, p=0.0014	Coefficient = -7.9763, p=0.0006
Residual Heterogeneity (I²)	87.89%	88.18%	73.83%	76.65%	83.03%	84.01%

Supplementary Table 6: Tabular presentation for QUADAS-2 results

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Chen et al. 2015 ⁷	✓	✓	✓	✓	✓	✓	✓
Domenchini et al. 2012 ⁵	✓	✓	✓	✓	✓	✓	✓
Huang et al. 2022 ¹⁵	✓	✓	✓	✗	✓	✓	✓
Ichiki et al. 2006 ²	✓	✓	✓	✓	✓	✓	✓
Kindermann et al. 2006 ³	✓	✓	✓	✓	✓	✓	✓
Majos-Karwaka et al. 2021 ¹³	✓	✓	✓	✓	✓	✓	✓
Nadar et al. 2020 ¹¹	✓	✓	✓	✓	✓	✓	✓
Nunes et al. 2011 ⁴	✓	✓	✓	✓	✗	✓	✓
Saito et al. 2015 ⁸	✓	✓	✓	✓	✓	✓	✓
Sinkar et al. 2021 ¹⁴	✓	✓	✓	✓	✓	✓	✓
Youssef et al. 2022 ¹⁶	✓	✓	✓	✓	✓	✓	✓
Porapakkham et al. 2012 ⁶	✓	✓	✓	✓	✓	✓	✓
Tian et al. 2024 ¹⁸	✓	✓	✓	✓	✓	✓	✓
Bednarek et al. 2024 ¹⁷	✓	✓	✓	✓	✓	✓	✓
Dwivedi et al. 2006 ¹	✓	✓	✓	✓	✓	✓	✓
Soliman et al. 2020 ¹²	✓	✓	✓	✓	✓	✓	✓
Saulan et al. 2018 ⁹	✓	✓	✓	✓	✓	✓	✓
Beurskens et al. 2019 ¹⁰	✓	✓	✓	✓	✓	✓	✓

✓Low Risk ✗High Risk ? Unclear Risk

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