



Outcomes of conduction system and right ventricular pacing in bradyarrhythmia indications: A systematic review and meta-analysis of propensity-score matched and randomized studies

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A systematic review and meta-analysis of propensity-score matched and randomized studies

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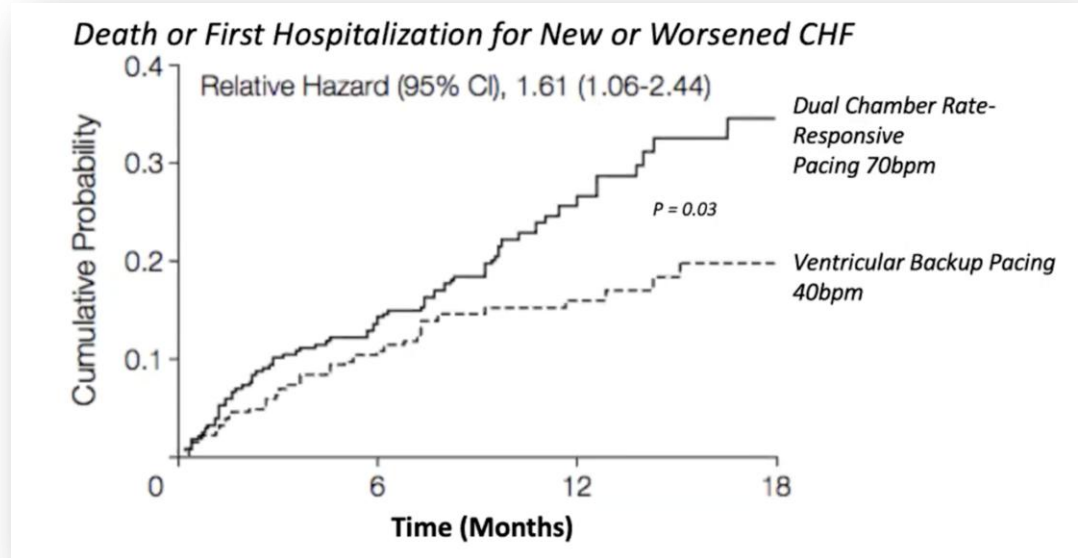
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Introduction

- RVP: standard therapy for bradyarrhythmias
- Non-physiological activation
 - (LBBB-like)
- Electrical and mechanical dyssynchrony of the left ventricle
- ↑ risk of heart failure and death



DAVID (The Dual Chamber and VVI ICD) Trial. Wilkoff B. JAMA 2002

Introduction

Conduction system pacing (CSP)

His bundle pacing or left bundle branch area pacing

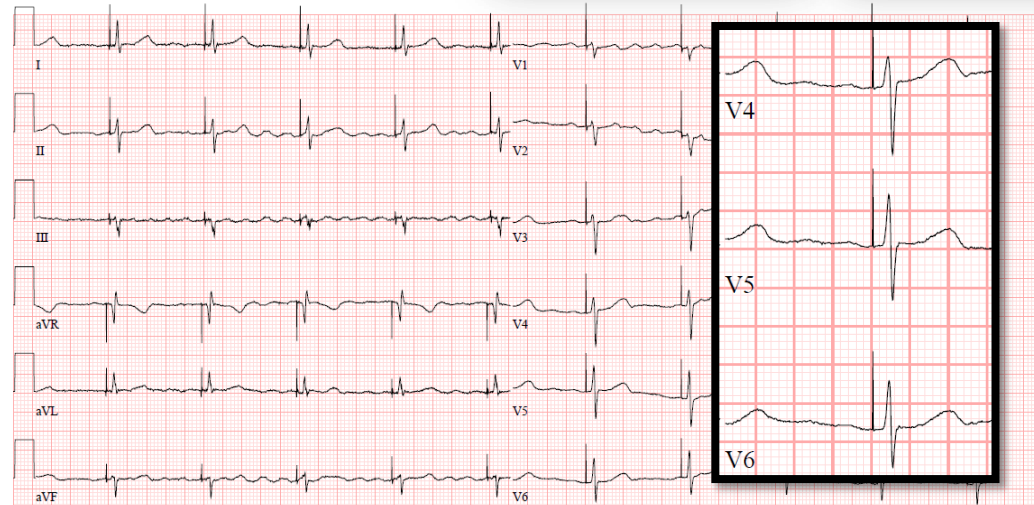
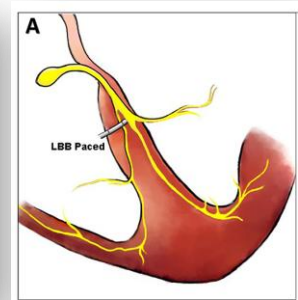
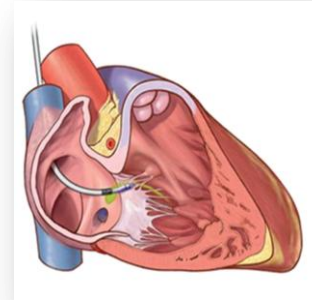
Physiological pacing

Goal: preservation or restoration of ventricular synchrony

Methods: CSP or CRT

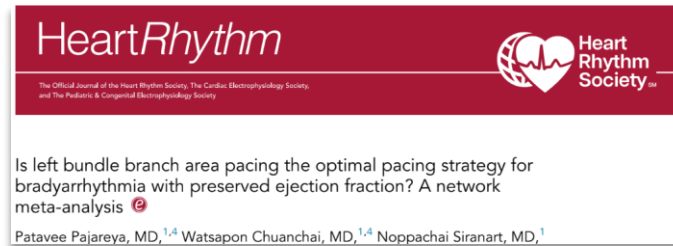
RVP: right ventricular pacing

PICM: pacing-induced cardiomyopathy



Introduction

- Observational studies in CSP vs. RVP:
 - ↓ HF events and mortality
- Previous meta-analyses lacked:
 - Relevant RCTs
 - Short follow-up
 - Focused on surrogate outcomes: QRS, echo, procedural and safety outcomes



Study objective

Systematic review and meta-analysis of recent **propensity-score matched** (PSM) studies and **randomized controlled trials** (RCTs) assessing the **clinical, procedural, and safety outcomes** of CSP and RVP in **bradyarrhythmia** indications.

Methods



- **Systematic literature search: September 2025**
- **Inclusion restricted to RCTs & PSM studies**
- **Minimum required follow-up:**
 - 12 months for key clinical outcomes.
 - 6 months for surrogate, procedural, and safety outcomes.

PROSPERO ID CRD420251160379

**Preferred Reporting Items for Systematic Reviews,
Meta-Analysis (PRISMA)**

**Cochrane Handbook for Systematic Reviews of
Interventions**

Methods



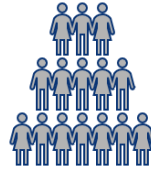
- Random effects meta-analysis.
- Main outcomes: all-cause mortality (**ACM**), cardiovascular mortality (**CVM**), heart failure (**HF**) hospitalizations, need for cardiac resynchronization therapy (**CRT**) upgrades, **LVEF**, QRS duration.
- Secondary outcomes: atrial fibrillation during follow-up, procedural complications, & procedural and fluoroscopy times.
- Risk ratios (**RRs**) and mean differences (**MDs**) with 95% confidence intervals (**CI**s) were pooled for binary and continuous outcomes respectively. Heterogeneity assessed with **I² statistics**.
- Subgroup analyses: **RCTs vs. PSM cohorts** for key outcomes; **AV block** as sole pacing indication.

Characteristics of included studies and their demographic parameters



- **15 studies** included: **9 RCTs** and **6 PSM cohorts**.

- **6,064 patients** in total.



- **CSP:** 3,010 (49.6%); **RVP:** 3,054 (50.4%); 40% females.

- Follow-up periods ranged from **6 to 60 months**, with an average of 3.5 years.



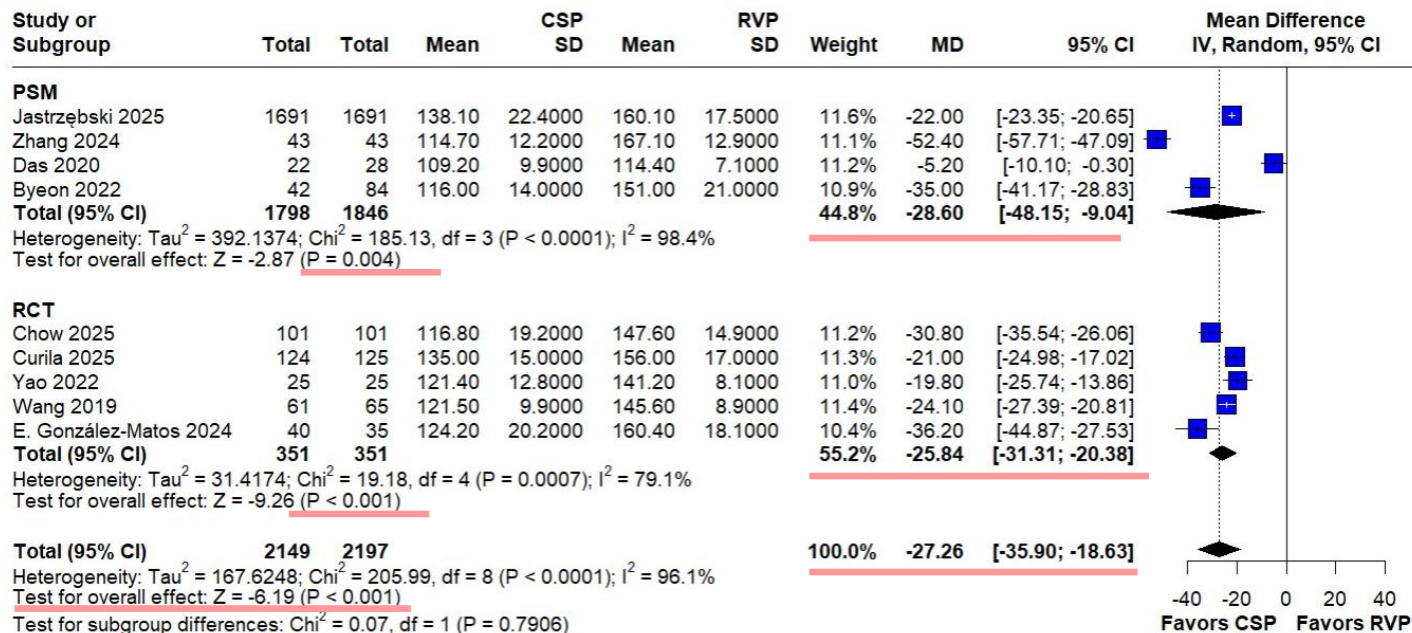
- Baseline LVEF: **50.8±8.4% to 63.3±5.2%**.



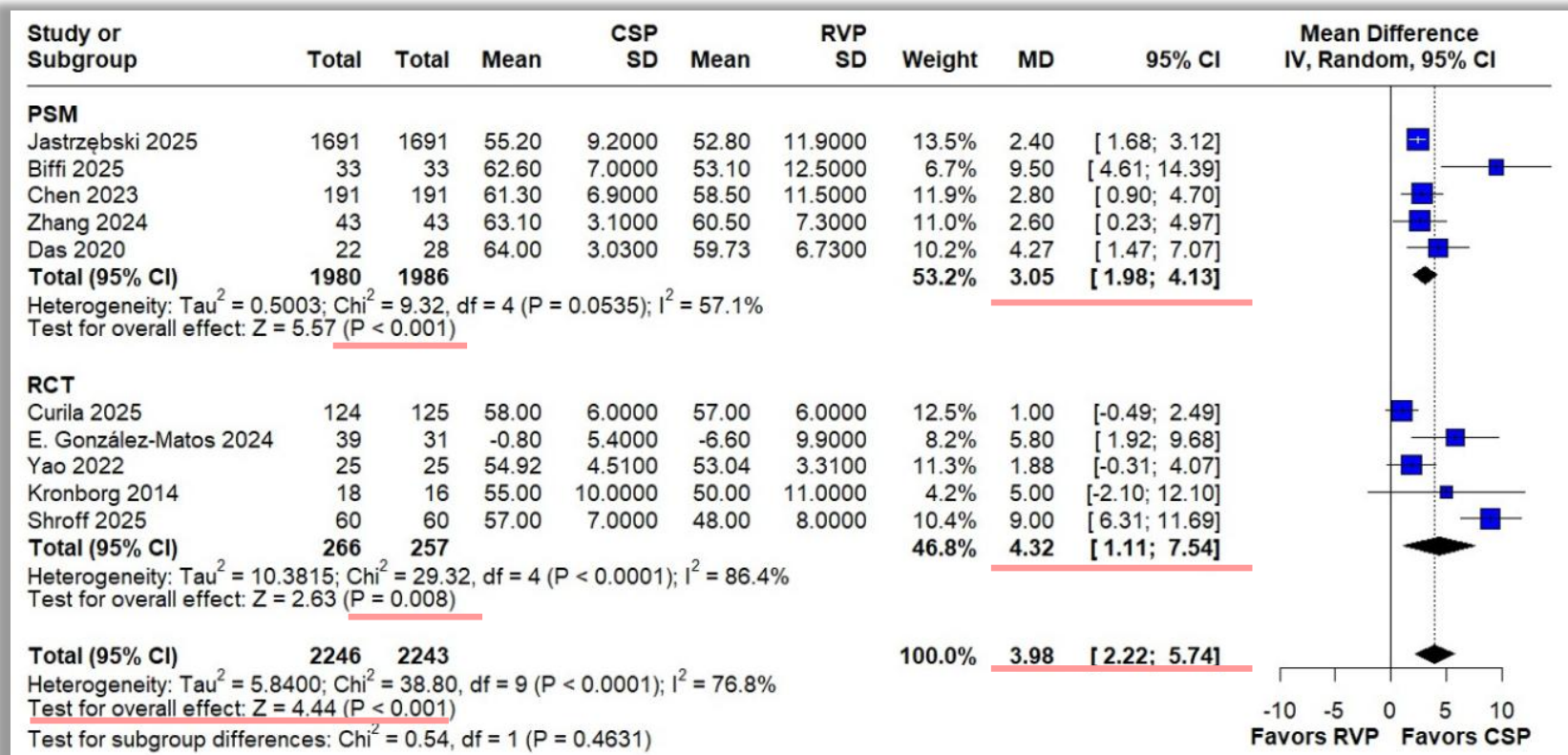
- **Pacing modalities:** LBBAP, LBBP, HBP vs. apical/septal RVP.

- **Primary pacing indication:** AV block.

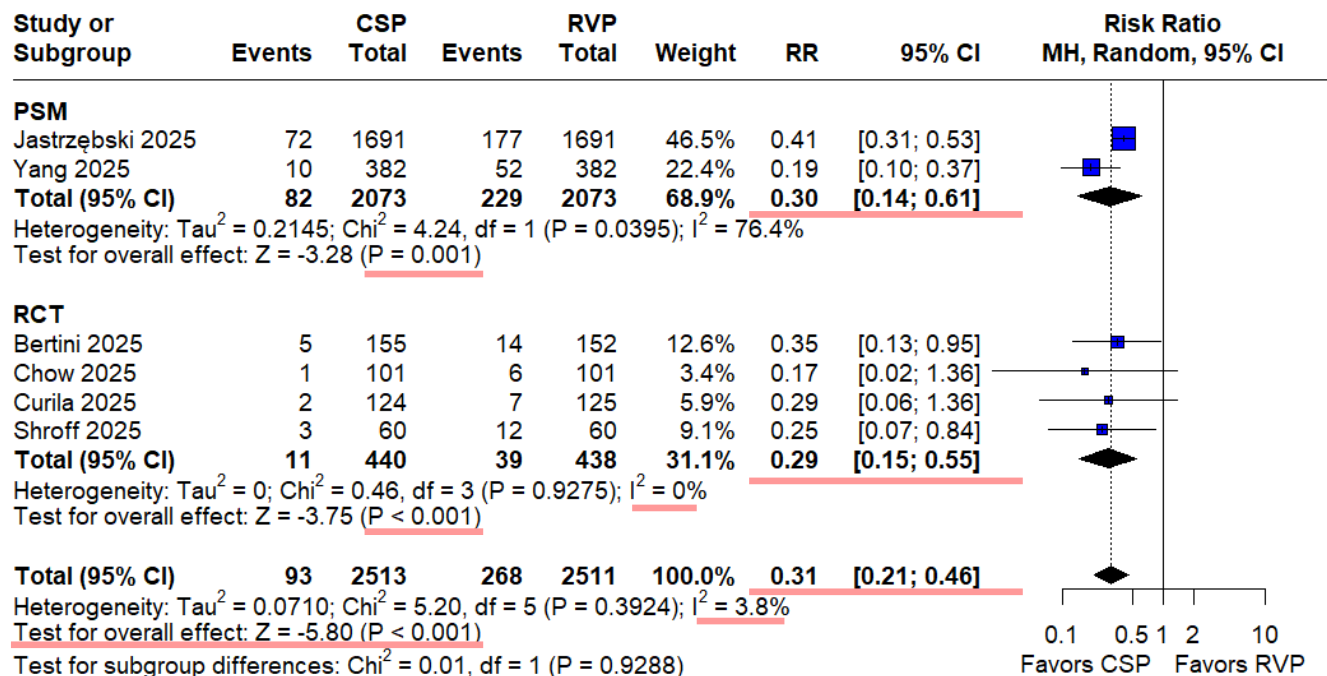
QRS duration



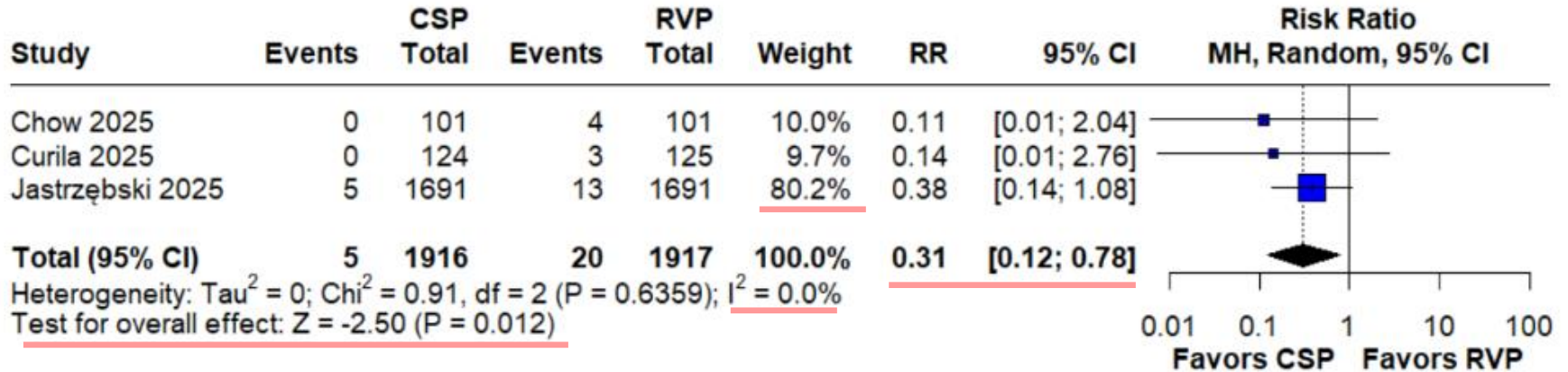
Left ventricular ejection fraction



Heart failure hospitalizations

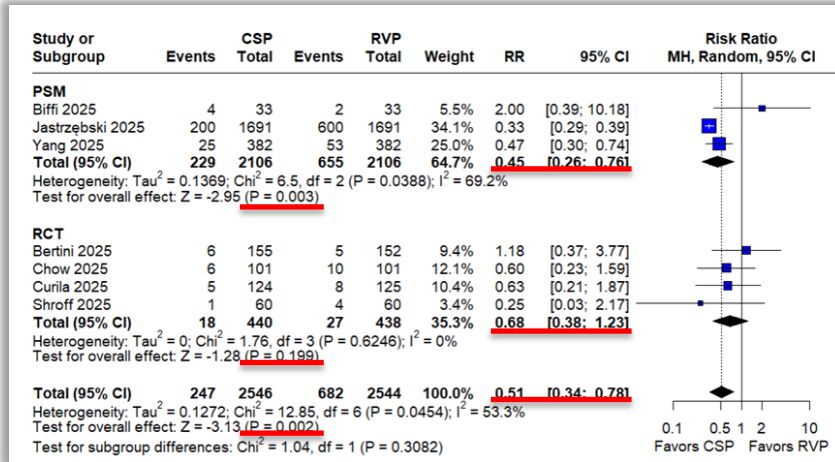


Need for CRT upgrades

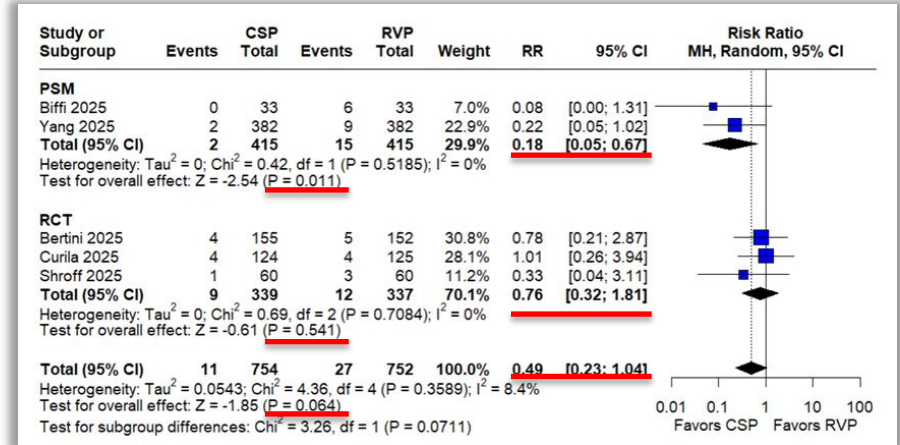


Mortality

All-cause mortality



Cardiovascular mortality

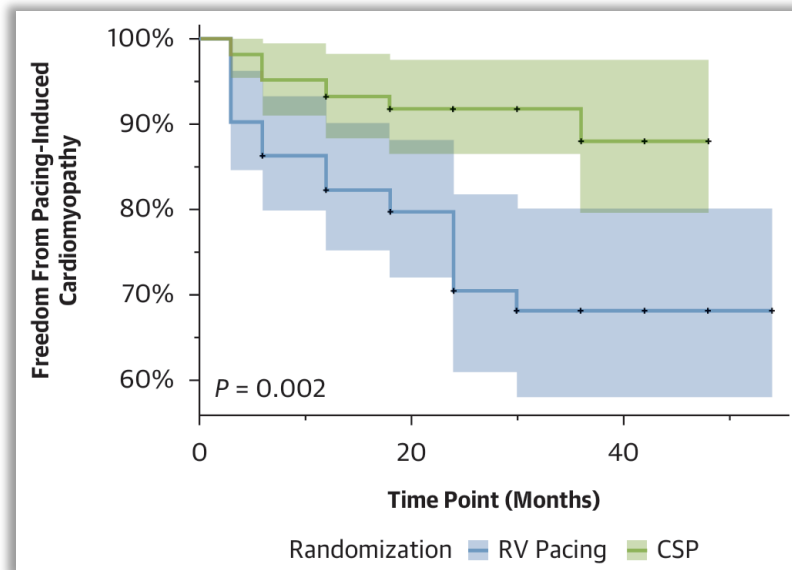


Discussion

Endpoint	CSP (PSM)	P value (PSM)	CSP (RCT)	P value (RCTs)
QRS duration (ms)	MD -29 ms	P = 0.004	MD -26 ms	P < 0.001
LVEF (%)	MD 3.0%	P < 0.001	MD 4.3%	P = 0.008
HF hospitalization	RRR 70%	P = 0.001	RRR 71%	P < 0.001
All-cause mortality	RRR 55%	P = 0.003	RRR 32%	P = 0.2
Cardiovascular mortality	RRR 82%	P = 0.01	RRR 64 %	P = 0.5

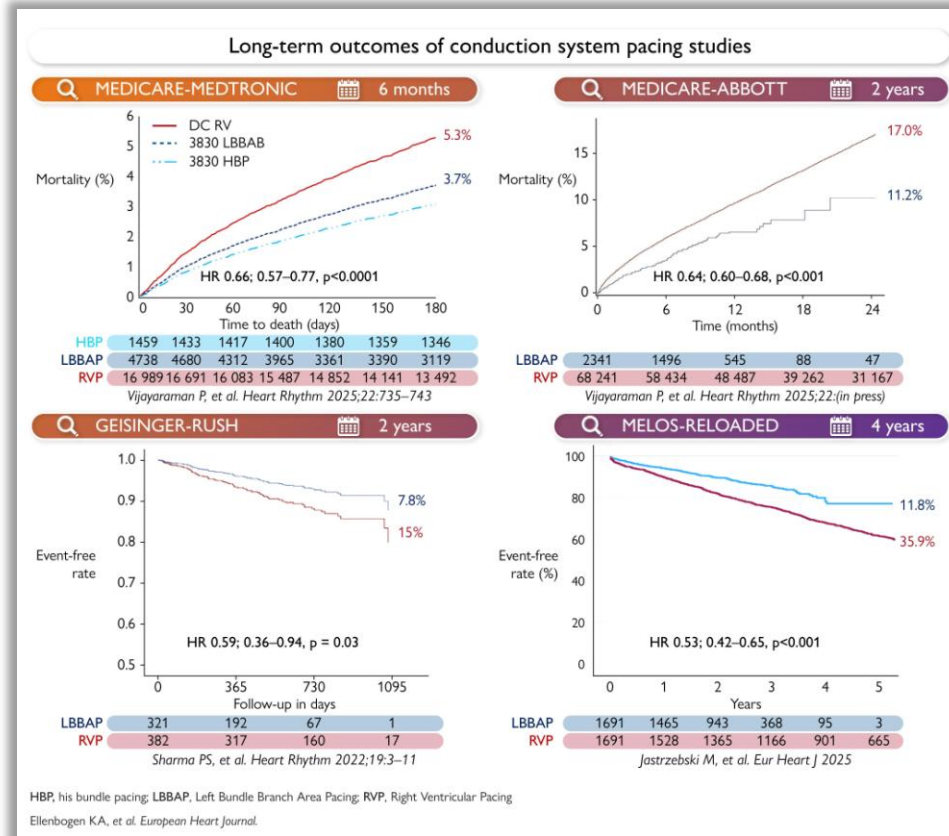
CSP mitigates PICM – CSPACE trial

- 202 patients enrolled; composite endpoint = PICM, CRT upgrade, HFH, and ACM.
- Primarily driven by significant reduction in PICM.
 - PICM: LVEF reduction of 10% resulting in an overall LVEF < 50%.
- (CSP 4.58 vs RVsP 14.69 events per 100-person-years; **HR: 0.31**; 95% CI: 0.15-0.67; $p = 0.002$).
- Current RCTs were not powered to detect a statistically significant difference in HF hospitalization individually (CSPACE, Prague CSP, PACE-HF).



CSPACE trial, Chow et al., JACC 2025

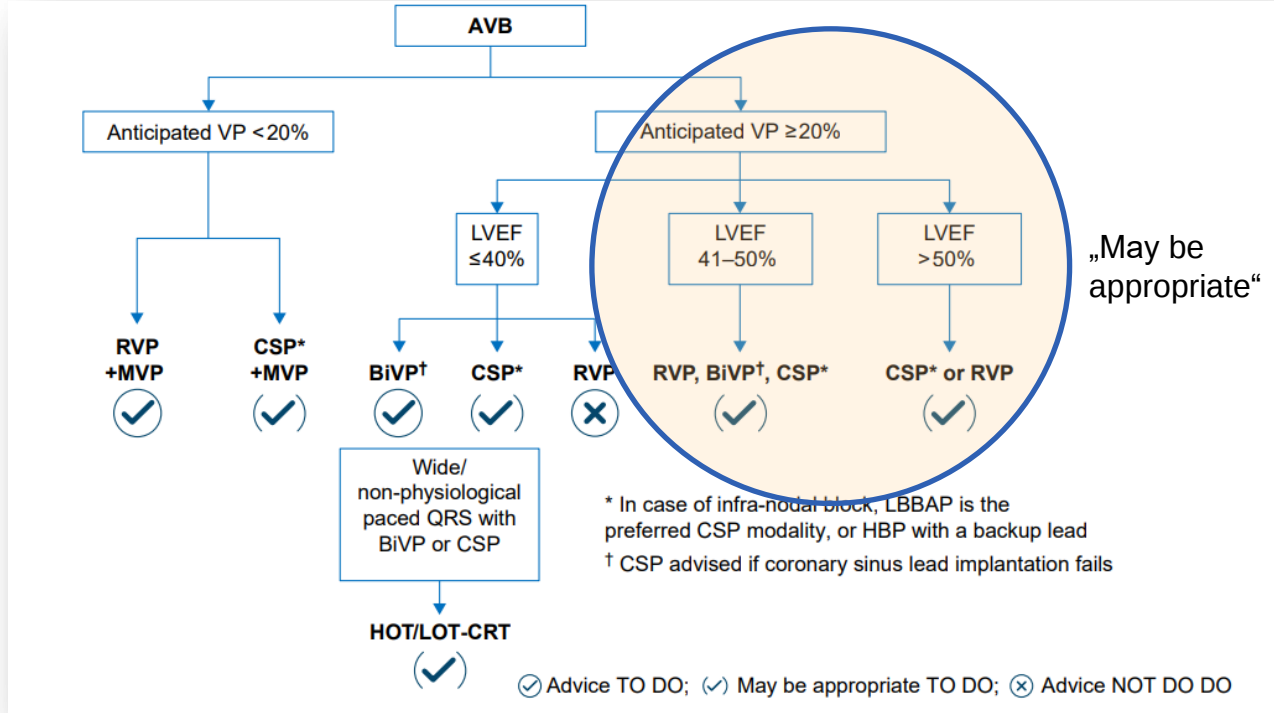
Mortality benefit in observational registries



Ongoing multicenter randomized trials (CSP vs. RVP)

- *Protect-HF (ICL)*: LVEF > 35%; PE: Mortality + HF; 6.5 yrs follow-up; 2600 patients; early 2030
- *LEFT-HF (Joza)*: 1300 patients; LVEF > 35%; composite primary endpoint – mortality, HF & PICM; 3 yrs follow-up; early 2030
- *LEAP-Block*: 486 patients; LVEF $\geq$ 50%; composite primary endpoint of mortality & HF; 2 yrs follow-up; completed (results pending)
- *OptimPacing*: 683 patients; composite primary endpoint of mortality; HF & PICM; 3 yrs follow-up; 2028

Current recommendations



Glikson M, Burri H, Abdin A, Cano O, Curila K, De Pooter J, et al. ESC clinical consensus statement on indications for conduction system pacing, with special contribution of the European Heart Rhythm Association of the ESC and endorsed by the APhRS, the CHRS, the HRS, and the LAHRS. EP Europace 2025; 27.

Conclusion

- CSP maintains electromechanical ventricular synchrony: significant reductions in paced QRSd (MD -27 ms) and improved LVEF (MD 4%).
- CSP significantly and consistently reduces the risk of PICM and HF hospitalizations.
- A reduction in mortality has not been demonstrated in available RCTs.
- No differences between groups for procedural and post-procedural complications.
- Ongoing large randomized trials (PROTECT-HF & LEFT-HF) are still needed to verify the long-term safety and potential mortality benefits of CSP.

References

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- **Chen Z**, *Cardiovasc Ther*, 2023; PMID: 37645544
- **Gonzalez-Matos CE**, *Circ Arrhythm Electrophysiol*, 2024; PMID: 38284238
- **Wang J**, *J Cardiovasc Electrophysiol*, 2020; PMID: 31778249

Limitations

Limitations:

- Statistical heterogeneity in analyses (ACM, LVEF, QRS duration).
- Variability in the definitions and criteria for CSP (LBBAP, HBP, LVsP).
- Important safety outcomes (lead durability/extractions) not assessed.
- Long-term follow-up still lacking (average follow-up duration: 3 years).
- Lack of individual patient data.
- Potential population overlap across Prague-CSP, MELOS-RELOADED, and TREEBEARD studies.



Risk of bias domains

	D1	D2	D3	D4	D5	Overall
Curila 2025	+	-	+	+	-	-
Bertini 2025	+	-	+	+	-	-
Kronborg 2014	+	-	+	+	-	-
Wang 2019	-	-	+	+	-	-
Yao 2022	-	-	+	+	-	-
Das 2020	-	-	+	+	-	-
González-Matos 2024	+	-	+	+	-	-
Chow 2025	+	-	+	+	-	-
Shroff 2025	-	-	+	+	+	-

Domains:

D1: Bias arising from the randomization process.
 D2: Bias due to deviations from intended intervention.
 D3: Bias due to missing outcome data.
 D4: Bias in measurement of the outcome.
 D5: Bias in selection of the reported result.

Judgement

- Some concerns
 + Low

Risk of bias domains

	D1	D2	D3	D4	D5	D6	D7	Overall
Biffi 2025	X	-	+	+	-	+	-	X
Chen 2023	X	-	+	+	+	+	-	X
Jastrzębski 2025	X	-	+	+	+	+	-	X
Yang 2025	X	-	+	+	-	+	-	X
Zhang 2024	X	-	+	+	+	+	-	X
Byeon 2022	X	-	+	+	+	+	-	X

Domains:

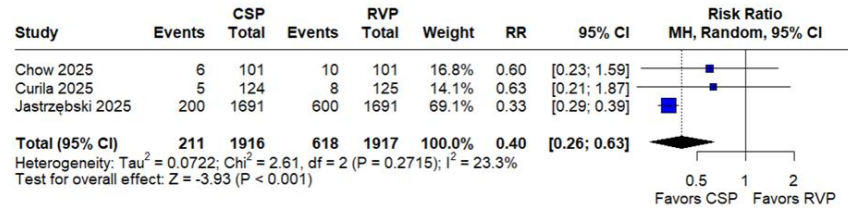
D1: Bias due to confounding.
 D2: Bias due to selection of participants.
 D3: Bias in classification of interventions.
 D4: Bias due to deviations from intended interventions.
 D5: Bias due to missing data.
 D6: Bias in measurement of outcomes.
 D7: Bias in selection of the reported result.

Judgement

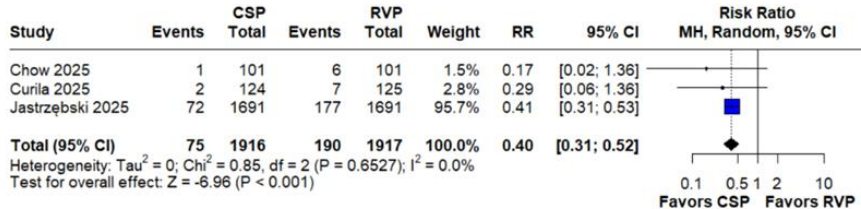
X Serious
 - Moderate
 + Low

AV block as the sole pacing indication

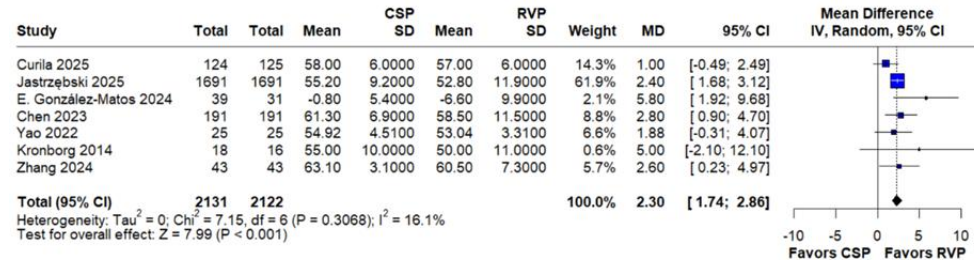
AV block: All-cause mortality (2 RCTs, 1 PSM)



AV block: HF hospitalizations (2 RCTs, 1 PSM)

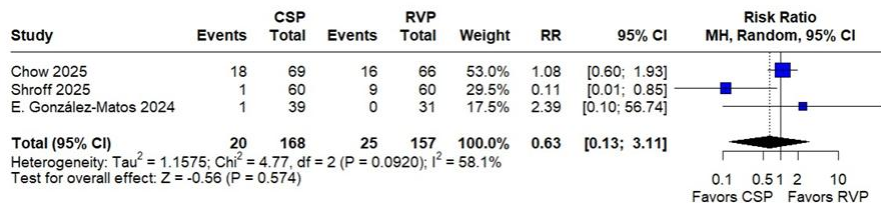


AV block: LVEF (4 RCTs, 3 PSM)

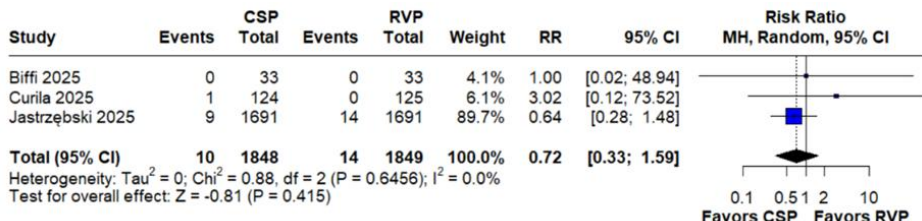


Secondary outcomes

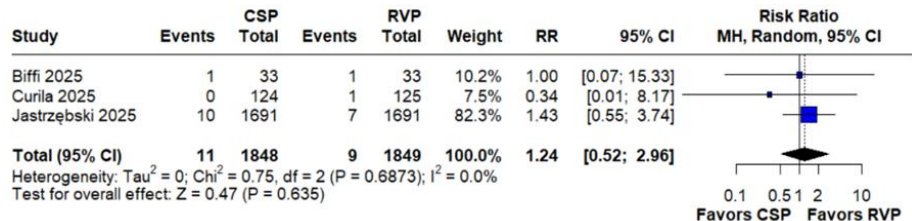
Atrial fibrillation during follow-up (3 RCTs)



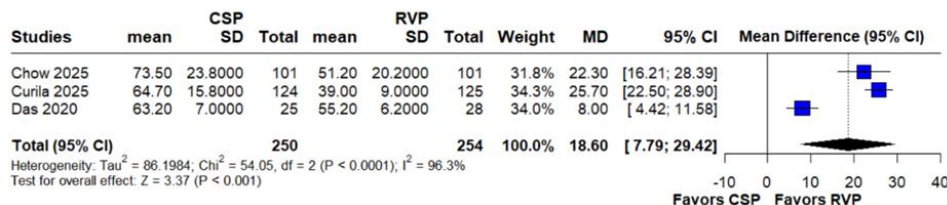
Pericardial effusion (1 RCT, 2 PSM)



Pneumothorax (1 RCT, 2 PSM)



Procedural duration (3 RCTs)



Time under fluoroscopy (3 RCTs)

