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Conduction System Pacing vs. Biventricular Pacing for Cardiac Resynchronization Therapy: An Updated Systematic Review and Meta-Analysis

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Article

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Abstract

Background

Conduction system pacing (CSP) has emerged as a potential alternative to biventricular pacing (BiVP) for cardiac resynchronization therapy (CRT). However, the relative efficacy and safety of different CSP techniques remain unclear.

Methods

We searched PubMed, Embase, Cochrane Library, and Web of Science for randomized controlled trials (RCTs) comparing CSP with BiVP. Primary outcome: composite of all-cause death or heart failure hospitalization. Secondary outcomes: change in left ventricular ejection fraction (LVEF), change in left ventricular end-systolic volume (LVESV), echocardiographic response (structural: LVESV reduction ≥ 15%; functional: LVEF increase ≥ 5%), QRS duration shortening, NYHA functional class improvement, and complication rate. Random-effects meta-analysis was used, with four pre-specified subgroups: CSP with optimization, strict left bundle branch pacing (LBBP), His-CRT, and left ventricular septal pacing (LVSP)-dominant.

Results

Ten independent RCTs (Vinther 2021/Frandsen 2026 counted as one trial) were included, CSP significantly reduced the risk of all-cause death or heart failure hospitalization (risk ratio RR 0.47, 95% CI 0.32–0.69, $P < 0.0001$; no subgroup interaction, $P = 0.35$), Overall LVEF change did not differ (MD 2.03%, 95% CI − 0.34% to 4.39%, $P = 0.09$, $I^2 = 80\%$), but subgroup differences were significant ($P = 0.03$): strict LBBP (MD 5.55%) and His-CRT (MD 3.12%) favored CSP. Overall LVESV change showed a non-significant trend (MD − 6.97 mL, 95% CI − 14.30 to 0.36 mL, $P = 0.06$, $I^2 = 64\%$); strict LBBP significantly reduced LVESV (MD − 23.98 mL). Functional response favored CSP (RR 1.10, 95% CI 1.00–1.20, $P = 0.05$, $I^2 = 0\%$), but structural response did not (RR 1.04, 95% CI 0.90–1.20, $P = 0.57$). CSP significantly shortened QRS duration (MD − 8.88 ms, 95% CI − 15.32 to − 2.45 ms, $P = 0.007$, $I^2 = 87\%$), driven by the CSP-with-optimization subgroup ($I^2 = 0\%$). NYHA class improvement favored CSP (MD − 0.21, 95% CI − 0.33 to − 0.09, $P = 0.0007$). Overall complication rates did not differ (RR 0.93, 95% CI 0.55–1.58, $P = 0.79$), but the His-CRT subgroup had a higher risk in the long-term Frandsen 2026 study (RR 4.00). Meta-regression showed that each 10-ms increase in baseline QRS duration was associated with a 4.09% reduction in LVEF benefit of CSP over BiVP ($P = 0.04$). CSP technique significantly explained heterogeneity in LVEF ($P = 0.004$) and LVESV ($P = 0.0003$), with strict LBBP reducing LVESV by 23.98 mL more than His-CRT.

Conclusions

CSP significantly reduces all-cause death or heart failure hospitalization, improves electrical synchrony and functional class, but LVEF and LVESV improvements are seen only in specific subgroups. Significant differences in efficacy and safety exist among CSP techniques, supporting individualized CRT strategies based on technical characteristics and patient condition.

Introduction

Cardiac resynchronization therapy is a key treatment for heart failure patients with ventricular electromechanical dyssynchrony. Traditional biventricular pacing (BiVP) combines right ventricular endocardial and left ventricular epicardial pacing, shortening QRS and improving synchrony. Large randomized trials have proven that BiVP reduces mortality and heart failure hospitalizations [1, 2]. However, BiVP has inherent limitations, with a clinical response rate of only 70% [3, 4]. Variations in coronary venous anatomy, phrenic nerve stimulation, high pacing thresholds, and non-physiological epicardial activation all limit its efficacy.

Conduction system pacing (CSP) has emerged as a more physiological alternative. His bundle pacing (HBP) activates the proximal conduction system, completely corrects left bundle branch block (LBBB), and restores normal ventricular activation [5, 6]. Left bundle branch pacing (LBBP) penetrates the interventricular septum, bypasses distal conduction block, and offers more stable pacing parameters [7, 8]. Optimized CRT strategies, such as left bundle branch-optimized CRT (LOT-CRT), allow a coronary sinus lead to be added when CSP alone does not achieve adequate resynchronization [9].

Results from RCTs comparing CSP and BiVP are inconsistent. Some show CSP superiority in QRS narrowing and LVEF improvement [10-12], while others find no significant difference or even favor BiVP [13, 14]. These discrepancies likely reflect differences in CSP technique, patient selection (e.g., stringency of LBBB definition, proportion of ischemic vs. non-ischemic cardiomyopathy), operator experience, and follow-up duration. Traditional meta-analyses that lump all CSP techniques together may obscure true differences.

Therefore, this systematic review and meta-analysis classifies CSP into four subgroups based on technical characteristics and electrophysiological criteria for confirming conduction system capture: CSP with optimization (allowing addition of a coronary sinus lead), strict LBBP (electrophysiologically confirmed left bundle capture), His-CRT (pure His bundle pacing), and LVSP-dominant (left ventricular septal pacing without confirmed LBB capture). We aimed to evaluate each subgroup's effects on the composite endpoint of all-cause death or heart failure hospitalization, left ventricular reverse remodeling, electrical synchrony, and safety, to provide more targeted evidence for clinical decision-making.

Methods

Search Strategy and Study Selection

We systematically searched PubMed, Embase, Cochrane Library, and Web of Science from inception to April 2026. Search terms included “conduction system pacing,” “His bundle pacing,” “left bundle branch pacing,” “left bundle branch area pacing,” “biventricular pacing,” “cardiac resynchronization therapy,” and “randomized controlled trial.” Reference lists of included articles were also manually screened(Supplementary Table 1).

Inclusion criteria were: (1) RCTs; (2) comparing any form of CSP (HBP, LBBP, LBBAP, or CSP with optimization) versus BiVP; (3) enrolling patients aged ≥18 years with symptomatic heart failure, LVEF ≤40%, and a guideline-based indication for CRT; (4) reporting at least one of the pre-specified outcomes. Exclusion criteria were: non-randomized studies, crossover trials without a parallel initial period, studies primarily enrolling patients with permanent atrial fibrillation or atrioventricular node ablation, and studies using CSP only as a bailout strategy without a randomized comparison.

Data Extraction and Outcomes

Two investigators independently extracted data: first author, publication year, sample size, baseline characteristics, CSP technique, intervention details, crossover rates, follow-up duration, and outcome data. The primary outcome was the composite of all-cause death or hospitalization for heart failure. Secondary outcomes included: (1) absolute change in LVEF (%); (2) absolute change in LVESV (mL); (3) echocardiographic response: structural response defined as LVESV reduction ≥15%, functional response defined as absolute LVEF increase ≥5%; (4) QRS duration shortening (ms); (5) NYHA functional class improvement; and (6) complication rate (lead dislodgement, infection, perforation, phrenic nerve stimulation, need for re-intervention, or procedure-related death).

Subgroup Definitions

To explore sources of heterogeneity and assess the effect of different CSP techniques, we pre-specified four mutually exclusive subgroups based on the delivered pacing strategy and electrophysiological criteria for confirming conduction system capture.

CSP with optimization: Studies that allowed adjunctive placement of a coronary sinus left ventricular lead when CSP alone achieved incomplete electrical resynchronization (e.g., LOT-CRT or His-Purkinje CSP-guided CRT with optional CS lead). This strategy aims to maximize QRS narrowing by fusing CSP with conventional LV pacing.

Strict LBBP: Studies that explicitly required electrophysiological confirmation of left bundle branch capture, including at least one of the following: (a) transition from non-selective to selective LBBP or from non-selective LBBP to LV septal pacing during threshold testing; (b) stimulus-to-peak R-wave time in lead V6 ≤90 ms; (c) V6-V1 interpeak interval ≥44 ms; or (d) recording of a left bundle branch potential. Studies that accepted LV septal pacing without proven LBB capture were not included in this subgroup.

His-CRT: Studies that intended to deliver CRT exclusively via His bundle pacing using a dedicated His lead, with correction of LBBB or QRS narrowing as the procedural target.

LVSP-dominant: Studies in which the majority of patients received LV septal pacing without meeting pre-defined criteria for LBB capture, i.e., the primary pacing modality was LVSP rather than true LBB capture.

When a study allowed more than one CSP technique but did not report outcomes separately by technique, it was assigned to the subgroup best reflecting the predominant strategy.

Risk of Bias Assessment

The Cochrane Risk of Bias 2 (RoB 2) tool was used to assess the risk of bias in five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result.

Statistical Analysis

Random-effects models (DerSimonian-Laird method) were used to pool effect sizes. Continuous outcomes were expressed as mean difference (MD) with 95% confidence interval (CI); binary outcomes as risk ratio (RR) with 95% CI; time-to-event outcomes were pooled using the generic inverse-variance method after log-transformation of hazard ratios. Heterogeneity was assessed using I^2 statistic and Cochran’s Q test (I^2 >50% indicating substantial heterogeneity). Subgroup differences were tested using meta-regression (categorical covariate). Univariate random-effects meta-regression was performed for LVEF change, LVESV change, and QRS shortening to explore potential sources of heterogeneity, including proportion of non-ischemic cardiomyopathy (per 10%), crossover rate (per 10%), follow-up duration (per 10 months), baseline QRS duration (per 10 ms), CSP technique (categorical), and for QRS shortening also the method of QRS measurement (stimulus vs. earliest deflection). Sensitivity analyses included leave-one-out analysis, fixed-effect model, and restriction to studies using strict Strauss LBBB criteria. Publication bias was assessed by funnel plots and Egger’s test when ≥10 studies were available. All analyses were performed using R version 4.3.2 (meta and metafor packages). The study followed the PRISMA 2020 statement and was registered with PROSPERO (CRD420261376094).

Results

Study Characteristics

Ten independent RCTs were included (Vinther 2021 and Frandsen 2026 represent short- and long-term follow-up of the same trial, counted as one trial) (Figure 2). Publication years ranged from 2019 to 2026, sample sizes from 40 to 200, and median follow-up from 6 to 36 months. Baseline characteristics,

subgroup assignments, and intervention details are summarized in Table 1.

Primary Outcome: All-Cause Death or Heart Failure Hospitalization

Eight studies (414 CSP, 416 BiVP) reported the composite endpoint. Random-effects meta-analysis showed that CSP significantly reduced the risk of all-cause death or heart failure hospitalization (RR 0.47, 95% CI 0.32–0.69, $P < 0.0001$), with no heterogeneity ($I^2 = 0\%$, $P = 0.58$) (Figure 3). Subgroup analysis: strict LBBP showed a significant benefit (RR 0.29, 95% CI 0.15–0.55, $P = 0.0002$, $I^2 = 0\%$); CSP with optimization showed a non-significant trend (RR 0.62, 95% CI 0.36–1.05, P=0.07, I^2=0%); the His-CRT subgroup consisted only of Frandsen 2026 [18] (HR 0.32, 95% CI 0.09–1.50); the LVSP-dominant subgroup consisted only of Cano 2026 [16] (RR 0.74, 95% CI 0.23–2.34). Subgroup differences were not statistically significant ($P = 0.27$).

Secondary Outcomes

Change in LVEF

Ten reports (512 CSP, 505 BiVP) showed no overall significant difference between CSP and BiVP (MD 2.03%, 95% CI −0.34% to 4.39%, $P = 0.09$, $I^2 = 80\%$) (Figure 4). Subgroup differences were significant ($P < 0.0001$). Strict LBBP significantly favored CSP (MD 5.55%, 95% CI 4.10–7.00%, $P < 0.0001$, I^2=0%); His-CRT also favored CSP (MD 3.12%, 95% CI 0.11–6.14%, $P = 0.04$, I^2=0%); CSP with optimization showed no difference (MD −0.24%, 95% CI −3.76 to 3.27%, $P = 0.89$, $I^2 = 73\%$); the LVSP-dominant subgroup alone showed no difference (MD −1.90%, 95% CI −5.26 to 1.46%).

Change in LVESV

Eight studies (324 CSP, 314 BiVP) showed a trend toward reduction with CSP but without statistical significance (MD −6.97 mL, 95% CI −14.30 to 0.36 mL, $P = 0.06$, I^2=64%) (Figure 5). Subgroup differences were significant ($P = 0.0003$). Strict LBBP significantly reduced LVESV (MD −23.98 mL, 95% CI −33.96 to −14.01 mL, $P < 0.0001$, I^2=0%); CSP with optimization showed no difference (MD −0.59 mL, 95% CI −9.03 to 7.84 mL, $P = 0.89$, I^2=0%); His-CRT showed no difference (MD −3.51 mL, 95% CI −14.76 to 7.75 mL, $P = 0.54$, I^2=0%); LVSP-dominant alone showed no difference (MD −1.40 mL, 95% CI −3.58 to 0.78 mL).

Echocardiographic Response

Nine studies (424 CSP, 414 BiVP) reported echocardiographic response. For structural response, no difference was observed (RR 1.04, 95% CI 0.90–1.20, $P = 0.57$, $I^2 = 47\%$) (Figure 6). For functional response CSP was superior to BiVP (RR 1.10, 95% CI 1.00–1.20, $P = 0.05$, $I^2 = 0\%$). When both response types were combined, no overall difference was observed (RR 1.07, 95% CI 0.99–1.16, $P = 0.11$, $I^2 = 29\%$), and the subgroup difference was not significant ($P = 0.56$).

QRS Duration Shortening

Ten studies (512 CSP, 505 BiVP) showed that CSP significantly shortened QRS duration compared with BiVP (MD −8.88 ms, 95% CI −15.32 to −2.45 ms, $P = 0.007$, $I^2 = 87\%$) (Figure 7). Subgroup differences were not significant ($P = 0.80$). However, substantial heterogeneity existed within subgroups. The CSP-with-optimization subgroup showed the most consistent effect with no heterogeneity (MD −5.14 ms, 95% CI −9.27 to −1.01 ms, $P = 0.01$, $I^2 = 0\%$), while the strict LBBP ($I^2 = 93\%$) and His-CRT ($I^2 = 97\%$) subgroups exhibited extremely high heterogeneity, partly attributable to the inconsistent methods of QRS measurement across studies (stimulus vs. earliest deflection). The LVSP-dominant subgroup alone showed a significant reduction (MD −6.70 ms, 95% CI −12.22 to −1.18 ms).

NYHA Functional Class Improvement

Five studies (247 CSP, 247 BiVP) showed that CSP significantly improved NYHA class compared with BiVP (MD −0.21, 95% CI −0.33 to −0.09, $P = 0.0007$, $I^2 = 11\%$) (Figure 8).

Complication Rate

Ten studies (524 CSP, 520 BiVP) showed no overall difference in complication rates (RR 0.93, 95% CI 0.55–1.58, $P = 0.79$, $I^2 = 28\%$) (Figure 9). Subgroup differences were not significant ($P = 0.81$). However, the His-CRT subgroup showed a non-significant pooled estimate (RR 1.75, 95% CI 0.24–12.90, $I^2 = 64\%$), and the single study Frandsen 2026 [18] reported a significantly higher risk of complications with His-CRT (RR 4.00, 95% CI 1.28–12.47).

Meta-Regression Analysis

Univariate random-effects meta-regression was performed for LVEF change, LVESV change, and QRS shortening (Table 2). For LVEF change, baseline QRS duration was significantly associated with the treatment effect (coefficient per 10 ms increase −4.09%, 95% CI −7.97 to −0.20, $P = 0.04$), and CSP technique overall was a significant moderator ($P = 0.004$). For LVESV change, CSP technique was also a significant moderator ($P = 0.0003$), with strict LBBP reducing LVESV by 23.98 mL more than His-CRT ($P = 0.008$). For QRS shortening, none of the examined covariates reached statistical significance.

Discussion

This systematic review and meta-analysis, based on ten independent RCTs and over 1000 patients, systematically compared the efficacy and safety of different types of conduction system pacing versus traditional biventricular pacing for CRT. Overall, CSP significantly reduced the composite endpoint of all-cause death or heart failure hospitalization, improved electrical synchrony and functional class, but did not show overall superiority in LVEF or LVESV improvement. More importantly, there were marked differences among CSP techniques: the His-CRT subgroup showed the most pronounced benefit for the hard clinical endpoint but at the cost of higher complication risk; strict LBBP showed inconsistent results for LV function improvement, with some studies

showing large benefits and others not; and the CSP-with-optimization strategy provided the most consistent QRS narrowing. These findings indicate that lumping all CSP techniques together under a single label may obscure their unique efficacy-risk profiles, and future clinical decision-making and guidelines should be more technique-specific.

Compared with previously published meta-analyses, this study has several important distinctions and extensions. The meta-analysis by Felix et al. (2024) included 7 RCTs and found that CSP significantly shortened QRS, improved NYHA class, and increased LVEF (MD 2.06%) but did not show a difference in hard endpoints [28]. Gin et al. (2023) included 15 studies (including observational studies) and reported larger QRS shortening (–20.3 ms) and LVEF improvement (5.2%), but was confounded by high risk of bias from non-randomized studies [29]. Menezes Junior et al. (2023) focused on His-CRT vs. BiVP and also found advantages for His-CRT [30]. None of these meta-analyses subdivided CSP into different technical subgroups, nor did they include several key RCTs published in 2024-2026. The present study updates and deepens the evidence in the following ways: first, it includes only RCTs with a large sample (505 CSP, 498 BiVP), excluding observational confounding; second, it is the first to classify CSP into four subgroups based on technical features and capture confirmation criteria, revealing efficacy differences between strict LBB capture and pure LV septal pacing; third, it incorporates the most recent large multicenter RCTs – including the negative PhysioSync-HF trial and the long-term hard-endpoint positive HeartSync-LBBP trial – thus providing the most complete picture of evidence to date.

Among all included trials, the PhysioSync-HF trial (Zimerman et al., 2026) stands out as the only large multicenter RCT demonstrating CSP to be inferior to BiVP. This discordance warrants careful examination. First, operator experience differed substantially: only 57% of procedures were performed by operators with ≥40 prior CSP cases, and the trial was conducted across 14 Brazilian centers with heterogeneous expertise, many in the early adoption phase. In contrast, positive trials like HeartSync-LBBP and HOT-CRT were conducted at experienced high-volume centers. Second, technical execution was suboptimal: nearly 20% of CSP patients received LVSP rather than confirmed LBB capture, a strategy that our subgroup analysis shows confers no LVEF benefit over BiVP. Third, patient selection differed: PhysioSync-HF enrolled patients with wider baseline QRS (median 180 ms) compared with positive trials (~168 ms), and our meta-regression confirmed that each 10-ms increase in baseline QRS was associated with a 4.09% reduction in LVEF benefit of CSP over BiVP. Thus, the PhysioSync-HF results do not refute the efficacy of CSP in experienced hands but serve as a critical caution: the benefits demonstrated in expert centers may not generalize to settings without structured training, quality assurance, and strict capture confirmation criteria.

The composite endpoint of all-cause death or heart failure hospitalization is the gold standard for evaluating CRT. Our analysis showed that CSP reduced the relative risk by 53% compared with BiVP (RR 0.47), an effect size that even exceeds that of early BiVP versus medical therapy trials (e.g., CARE-HF showed a 36% reduction in death or heart failure hospitalization [1]). However, subgroup analysis revealed that only the His-CRT subgroup showed a statistically significant benefit (RR 0.29), whereas the other subgroups did not reach significance. This finding needs cautious interpretation. On the one hand, His-CRT, as the most physiological pacing mode, directly activates the proximal conduction system and fully restores normal ventricular activation, so it is theoretically expected to confer the greatest clinical benefit. The on-treatment analysis of the His-SYNC trial showed a median LVEF improvement of 11.8% in patients with successful QRS correction [20]. Although the long-term His-Alternative trial did not reach statistical significance for the composite endpoint, the effect direction was consistent (HR 0.32 with CI crossing 1) [18]. On the other hand, the strict LBBP subgroup had a point estimate that also showed a high benefit (RR 0.27), but the CI was very wide (0.06–1.19), mainly because only Chen 2026 [17] contributed most of the events, while Žižek 2025 [12] and Wang 2022 [10] had short follow-up and very few events. Thus, the true clinical benefit of LBBP for hard endpoints still requires larger, longer-term RCTs. Notably, the PhysioSync-HF trial, a large multicenter RCT (173 patients, published 2026), gave a contradictory result: its composite endpoint (death, HF hospitalization, urgent HF visit, and LVEF change) showed CSP to be inferior to BiVP (OR 2.36) [13]. This negative result does not refute the value of CSP but rather highlights the decisive impact of operator experience, patient selection, and technical execution on CSP outcomes. In the 14 Brazilian centers, only 57% of operators had >40 CSP cases, and a stylet-driven lead was uniformly used, which may be less stable. This suggests that, during the early adoption of a new technology, randomization alone cannot eliminate learning-curve bias; future trials should stratify or restrict operator experience.

LVEF change is a core surrogate endpoint for CRT efficacy. Our overall analysis found no significant difference between CSP and BiVP, but with significant subgroup interaction ($P < 0.0001$). This apparently contradictory finding actually reflects the internal heterogeneity of CSP techniques. In the strict LBBP subgroup, Žižek 2025 [12] and Wang 2022 [10] both showed a clear advantage of LBBP over BiVP (MD 5.55%), whereas Zimerman 2026 [13] showed BiVP to be superior (MD –4.0%). This reversal cannot be explained by technical differences alone. Scrutiny of the study designs reveals that Zimerman 2026 [13] enrolled patients with a median LVEF of 26% and larger LVESV, making them sicker than those in other studies; moreover, the study allowed addition of a CS lead when LBBAP was suboptimal but still analyzed by intention-to-treat, which may have diluted the pure effect of LBBP. In addition, three procedure-related deaths occurred in the CSP arm in that study versus none in the BiVP arm, again signalling that the learning curve and patient selection critically affect outcomes during early adoption. In stark contrast, Chen 2026 [17] (median 36-month follow-up) was conducted at high-volume experienced centers with strict confirmation of LBB capture, and showed a 77% reduction in HF hospitalization risk with LBBP versus BiVP. These two studies together highlight a core message: the efficacy of CSP is highly dependent on operator skill and the stringency of capture confirmation. The reason previous meta-analyses concluded that CSP is superior to BiVP (e.g., Gin et al. reported a 5.2% greater LVEF improvement) is that they included mainly single-center, high-experience observational studies, while the “real-world” multicenter PhysioSync-HF trial revealed the challenges of early dissemination. Therefore, when interpreting CSP efficacy, it is essential to specify “under what operating conditions and for which patient population.”

The analysis of echocardiographic response revealed another important dimension. CSP showed a borderline statistically significant advantage for functional response (LVEF increase ≥5%, $P = 0.05$) with perfect homogeneity ($I^2 = 0\%$), a robust finding. In contrast, structural response (LVESV reduction ≥15%) did not differ between the two groups. This may reflect different pathophysiological mechanisms: early LVEF improvement depends mainly on restoration of contractile synchrony, whereas LV volume reverse remodeling requires longer electromechanical adaptation. Indeed, the 36-month follow-up of Chen 2026 [17] showed that LBBP reduced the risk of HF hospitalization by 77% compared with BiVP. Thus, short-term (6-month) volume response may not be the most sensitive marker for long-term CSP benefit. This observation is consistent with the “no difference in LVESV” reported by Felix et al. [28], but our long-term hard-endpoint data further supplement the evidence of clinical benefit.

QRS duration shortening is the most direct electrophysiological indicator of CRT. In our analysis, CSP overall significantly shortened QRS by nearly 10 ms, and all point estimates favored CSP. Notably, the CSP-with-optimization subgroup (which allowed adding a CS lead to CSP) showed a highly consistent effect (I^2=0%) with a mean reduction of about 5.1 ms, suggesting that a combined strategy may provide the most reliable QRS narrowing when maximum electrical resynchronization is desired. However, QRS narrowing and clinical benefit are not linearly correlated -- although Upadhyay 2019 [20] reported a dramatic QRS narrowing of 48 ms in the His-CRT subgroup, LVEF improvement was not significantly better than BiVP. This reminds us that electrical indexes alone cannot replace haemodynamic and clinical endpoints. Moreover, as noted in our results, the strict LBBP and His-CRT subgroups exhibited extremely high heterogeneity in QRS shortening (I^2 = 93% and 97%, respectively), which may be partly attributable to inconsistent methods of QRS measurement across studies (stimulus vs. earliest deflection) [14, 22]. Standardisation of QRS measurement methodology should be promoted in future research.

Regarding safety, overall complication rates were similar between CSP and BiVP. This is encouraging, because CSP techniques (especially LBBP) require deep septal screwing, theoretically carrying risks of perforation and thrombosis. Yet our analysis found no higher complication risk in the strict LBBP subgroup. However, the His-CRT subgroup in Frandsen 2026 [18] showed a significantly elevated risk (lead revision 37% vs. 3%, generator replacement 47% vs. 10%). This finding is consistent with the known technical limitations of HBP – higher pacing thresholds and late threshold rises leading to premature battery depletion and lead revision [6]. Nevertheless, it should be noted that the procedures in that study were performed in the early period (2018-2020), when acceptance of high thresholds (up to 5V/1ms) was more lenient, and operators were on the early part of the learning curve. With accumulated experience and more stringent implant criteria (e.g., threshold ≤1.5V/0.5ms), the long-term device survival of HBP has markedly improved. Thus, the safety of His-CRT should be re-evaluated in the context of modern, experienced centers.

Limitations

Several limitations should be considered. First, subgroup analyses were based on study-level rather than patient-level data, potentially introducing ecological bias. Second, most studies had short follow-up (6-12 months), and the number of hard-endpoint events was limited; only Chen 2026 [17] and Frandsen 2026 [18] provided follow-up >3 years. Third, the definition of LBB capture confirmation varied across studies, and despite our “strict” definition, differences remain, which may contribute to high heterogeneity within the strict LBBP subgroup for some outcomes. Fourth, the studies were mainly from high-volume centers, and operator experience was far above average clinical practice, limiting generalisability, especially to low- and middle-income countries. Fifth, some subgroups (e.g., His-CRT with only 2 studies) were small, resulting in low precision of pooled estimates. Sixth, although we included the negative PhysioSync-HF trial, publication bias may still exist – small negative studies might not have been published. Finally, the meta-regression analyses, though informative, had limited power because of the small number of studies, and should be considered exploratory.

Implications for clinical practice. For experienced CSP centers, His-CRT in well-selected patients (typical LBBB, non-ischaemic cardiomyopathy, high anticipated pacing burden) may provide the greatest hard-endpoint benefit, but close monitoring for threshold rises is needed. LBBP, because of its stable pacing parameters and lower technical difficulty, can be a first-line CSP strategy, especially when high pacing percentages are required or threshold rise is a concern. When CSP alone fails to achieve adequate electrical resynchronization (e.g., residual wide paced QRS), an optimisation strategy adding a CS lead can provide the most reliable QRS narrowing. However, in centres without high CSP expertise, conventional BiVP remains the safe and effective first choice – as the PhysioSync-HF trial clearly showed, premature dissemination of insufficiently trained technology can lead to worse outcomes [13]. Future large-scale RCTs with operator experience stratification, long-term follow-up (≥3 years), and hard endpoints are needed, along with standardisation of LBB capture confirmation (e.g., through a core laboratory), to define the optimal indications for each CSP technique.

Conclusion

In this meta-analysis of 10 RCTs, CSP significantly reduced all-cause death or heart failure hospitalization and improved NYHA class compared with BiVP. However, LVEF and LVESV benefits were technique-dependent: LVEF improvement was significant in both the strict LBBP and His-CRT subgroups, while LVESV reduction was significant only in the strict LBBP subgroup. His-CRT offered the greatest hard-endpoint benefit but at higher long-term reintervention risk. These findings support an individualized, technique-specific approach to CSP for cardiac resynchronization.

Declarations

Ethics approval and consent to participate

Human Ethic and Consent to Participate declarations: not applicable.

Consent for publication:

All authors approved the final version to be published. This article constitutes a reevaluation of previously published literature; hence, the declaration of patient consent is Not Applicable.

Data Availability Statement:

Data availability can be obtained from the authors upon reasonable request, without undue reservation.

Conflict of Interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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All authors made substantial contributions to the conception of the study. SS and QY contributed to the design of the study. QY, and HJP contributed to the acquisition and analysis of data. SS, QY contributed to the interpretation of data. HJP and QY contributed to the drafting of the manuscript. HJP contributed to the critical revision of the manuscript for important intellectual content. All authors approved the final version to be published.

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Table

Table 1. Baseline Characteristics, Subgroup Classification, Intervention Details, and Crossover Rates

Study	Subgroup	CSP Technique	Sample Size (CSP/BiVP)	Crossover Rate (CSP→BiVP / BiVP→CSP)	Age (years, CSP/BiVP)	Female (%)	Ischemic (%)	Baseline LVEF (%)	Baseline QRS (ms)	NYHA II/III (%)
Vinther 2021 / Frandsen 2026 (His-Alternative I)	His-CRT	HBP	19/31	28% / 4%	63.2 / 67.4	58 / 23	16 / 26	31 / 29	163 / 167	~100
Upadhyay 2019 (His-SYNC)	His-CRT	HBP	16 / 24 (as-treated)	48% / 26%	63.4 / 65.5	44 / 33	NA	28 / 28	174 / 165	~100
Wang 2022 (LBBP-RESYNC)	Strict LBBP	LBBP	20/20	10% / 20%	62.3 / 65.3	65 / 35	0 / 0	28.3 / 31.1	174 / 174	100
Vijayaraman 2023 (HOT-CRT)	CSP with optimization	HPcSP (HBP/LBBAP + optional CS lead)	50/50	4% / 18%	71.0 / 68.9	22 / 40	46 / 44	30.1 / 30.7	164 / 166	~100
Pujol-Lopez 2022 (LEVEL-AT)	CSP with optimization	CSP (HBP/LBBP)	35/35	23% / 6%	65.7 / 68.1	34 / 29	31 / 31	27 / 28	177 / 178	86
Pujol-Lopez 2025 (CONSYST-CRT)	CSP with optimization	CSP (HBP/LBBP)	67/67	27% / 8%	69 / 69	28 / 25	34 / 34	28 / 27	175 / 175	94
Žižek 2025 (CSP-SYNC)	Strict LBBP	LBBAP	31/31	3% / 0%	65 / 70	26 / 33	35 / 29	30 / 28	176 / 170	100
Zimerman 2026 (PhysioSync-HF)	CSP with optimization	LBBAP-first (stylet-driven, optional CS lead)	87/86	7% / 8%	61 / 63	52 / 48	15 / 11	26 / 27	180 / 180	99
Cano 2026 (LEFT-BUNDLE-CRT)	LVSP dominant	LBBAP (mostly LVSP)	92/83	10% / 21%	67 / 68	34 / 33	27 / 28	30 / 29	171 / 165	92
Chen 2026 (HeartSync-LBBP)	Strict LBBP	LBBP	100/100	2% / 6%	64.3 / 65.3	33 / 31	16 / 19	28.3 / 28.1	170 / 167	100

Study	Subgroup	CSP Technique	Sample Size (CSP/BiVP)	Crossover Rate (CSP→BiVP / BiVP→CSP)	Age (years, CSP/BiVP)	Female (%)	Ischemic (%)	Baseline LVEF (%)	Baseline QRS (ms)	NYHA II/III (%)

† Vinther 2021 reported 6-month outcomes; Frandsen 2026 reported long-term (median 64 months) outcomes from the same cohort. For the primary meta-analysis, 6-month data were used for QRS/LVEF, and long-term data for hard endpoints.

Crossover rate format: CSP→BiVP / BiVP→CSP (percentage crossing from assigned group to the alternative therapy). NYHA II/III% indicates the proportion of patients in NYHA class II or III at baseline (class I or IV excluded where reported). Subgroup definitions: His-CRT (pure His bundle pacing), Strict LBBP (electrophysiologically confirmed left bundle branch capture), CSP with optimization (CSP ± additional CS lead for maximal resynchronization), LVSP dominant (mostly left ventricular septal pacing without confirmed LBB capture). Ischemic %: proportion of patients with ischemic cardiomyopathy. Abbreviations: HBP = His bundle pacing; LBBP = left bundle branch pacing; LBBAP = left bundle branch area pacing; HPcSP = His-Purkinje conduction system pacing; CS = coronary sinus; LVSP = left ventricular septal pacing; FOI = fusion-optimized intervals; LOT-CRT = left bundle branch optimized CRT.

Figures

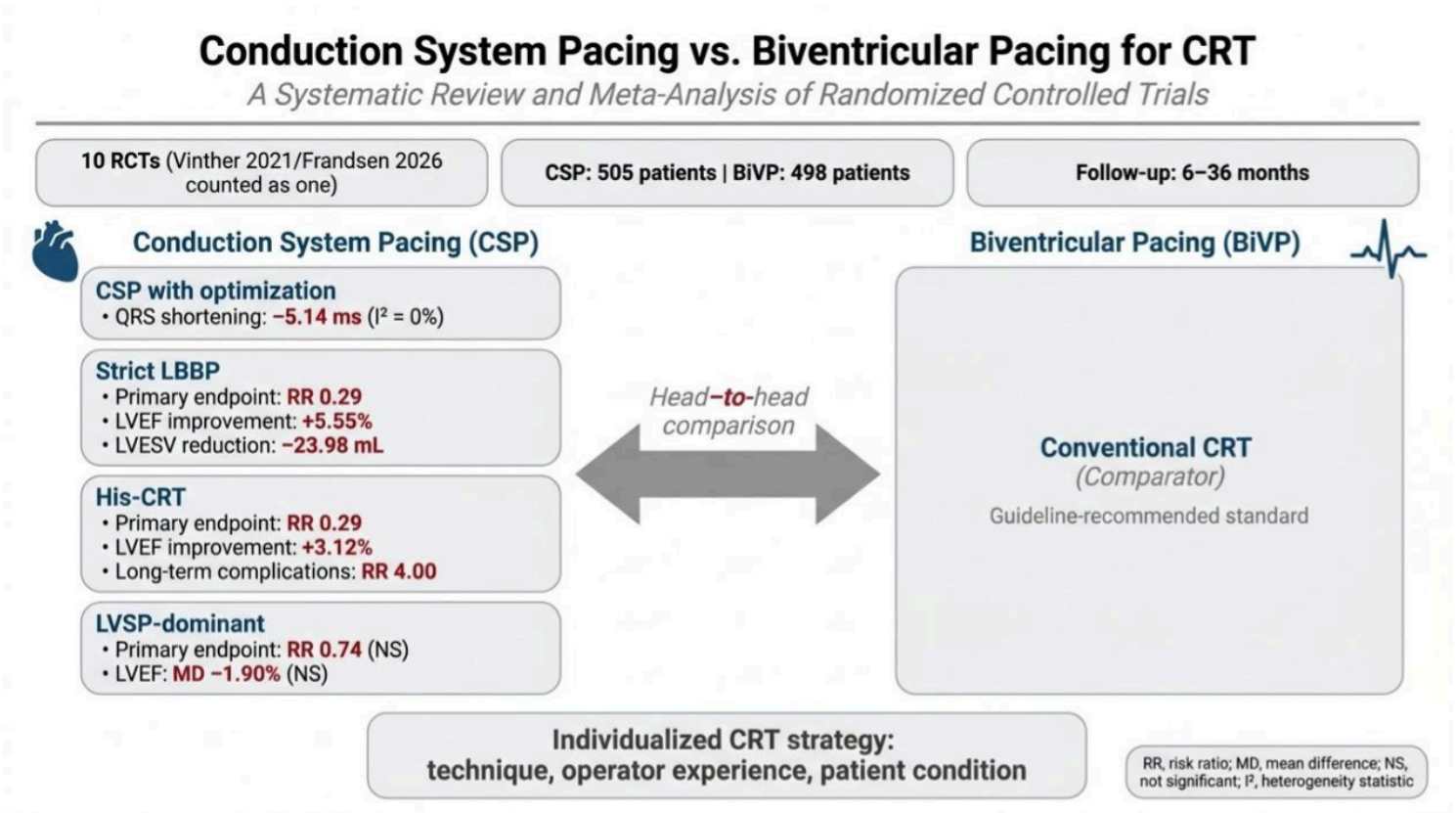


Figure 1

Schematic summary of the systematic review and meta-analysis comparing conduction system pacing (CSP) versus biventricular pacing (BiVP) for cardiac resynchronization therapy (CRT)

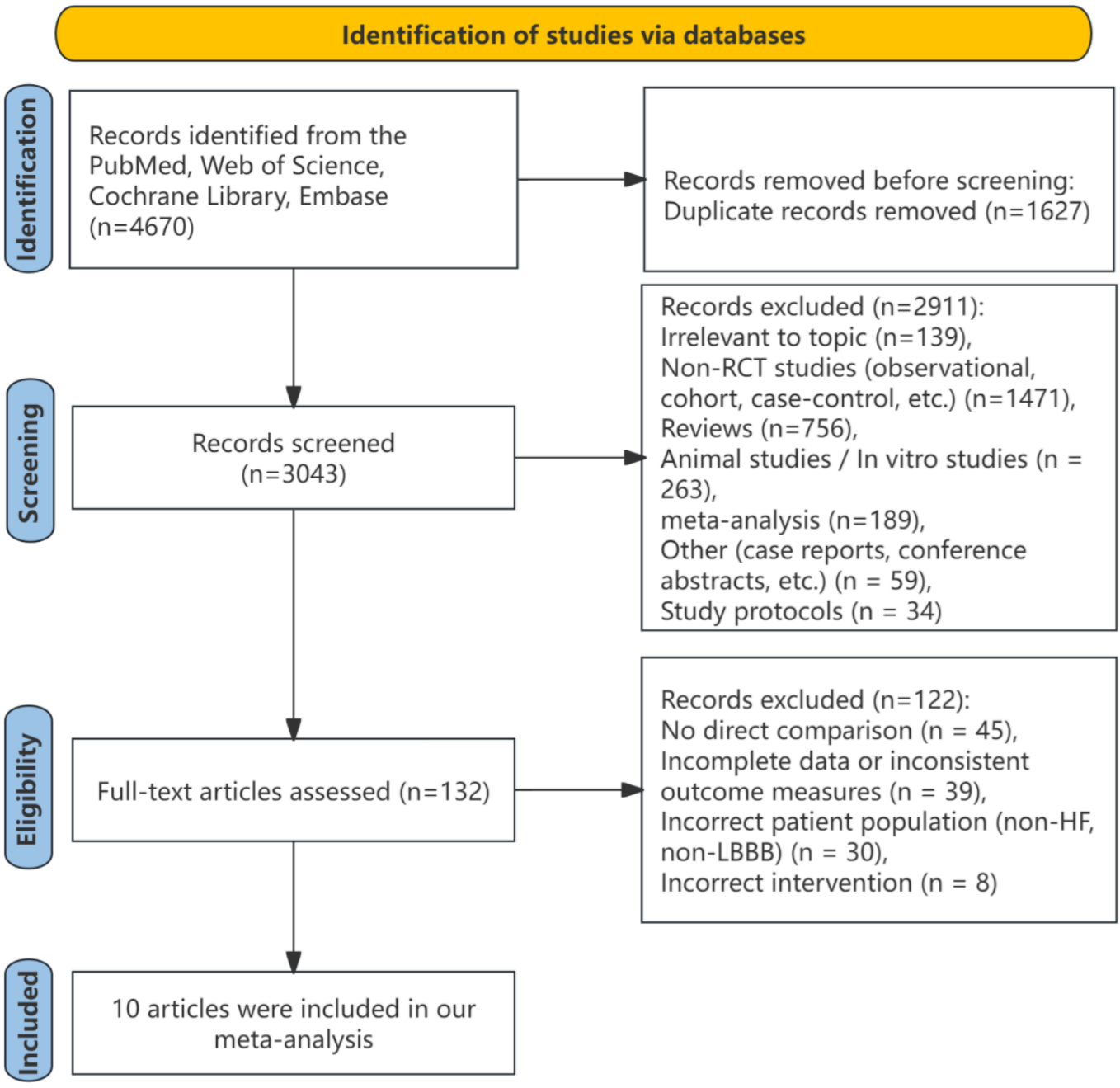


Figure 2

A PRISMA flow chart of study selection

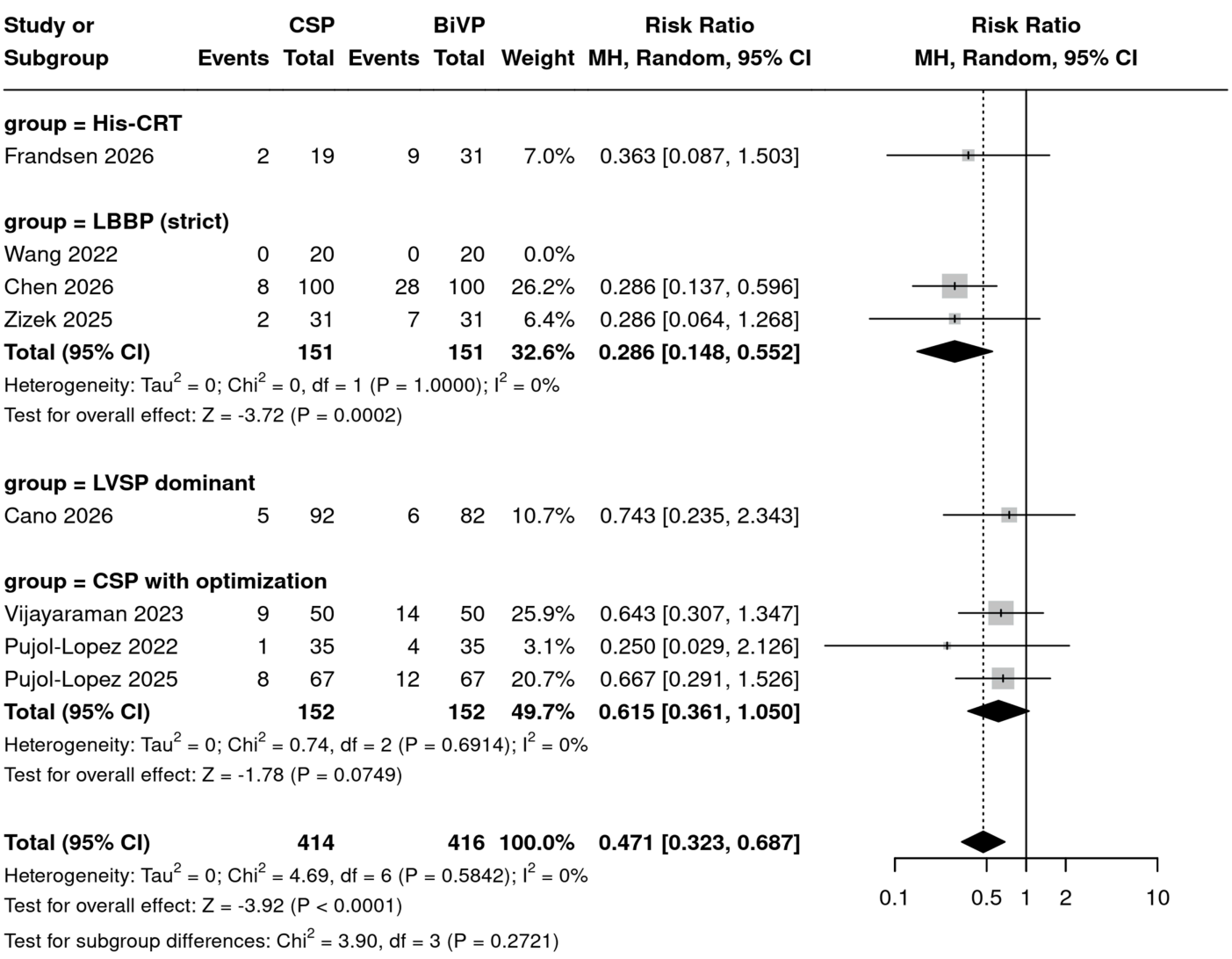


Figure 3

Risk of all-cause death or heart failure hospitalization with CSP versus BiVP. Risk ratios (RR) with 95% confidence intervals are shown. Diamonds represent pooled estimates.

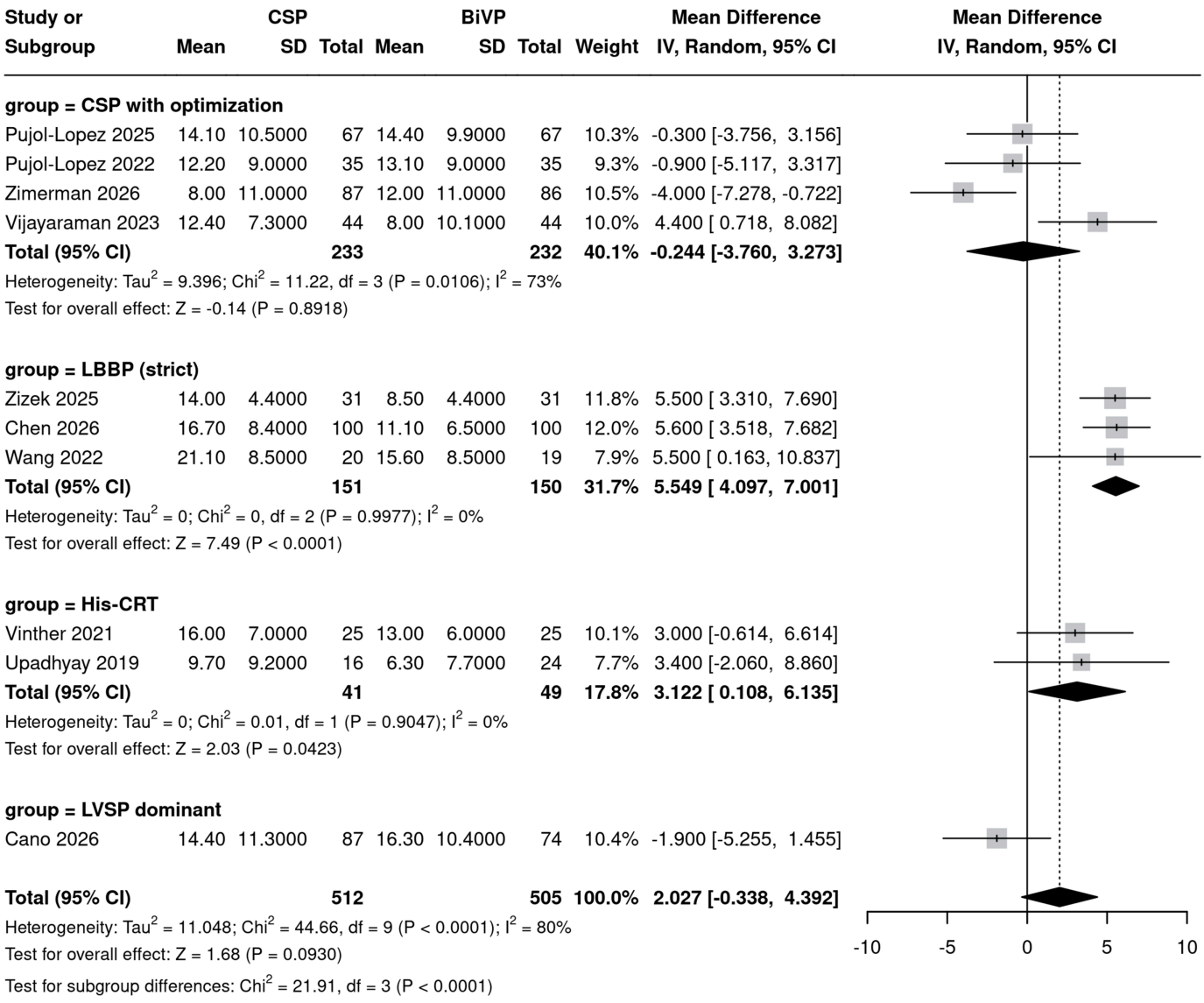


Figure 4

Mean difference in LVEF improvement (absolute percentage points) between CSP and BiVP. Positive values favor CSP.

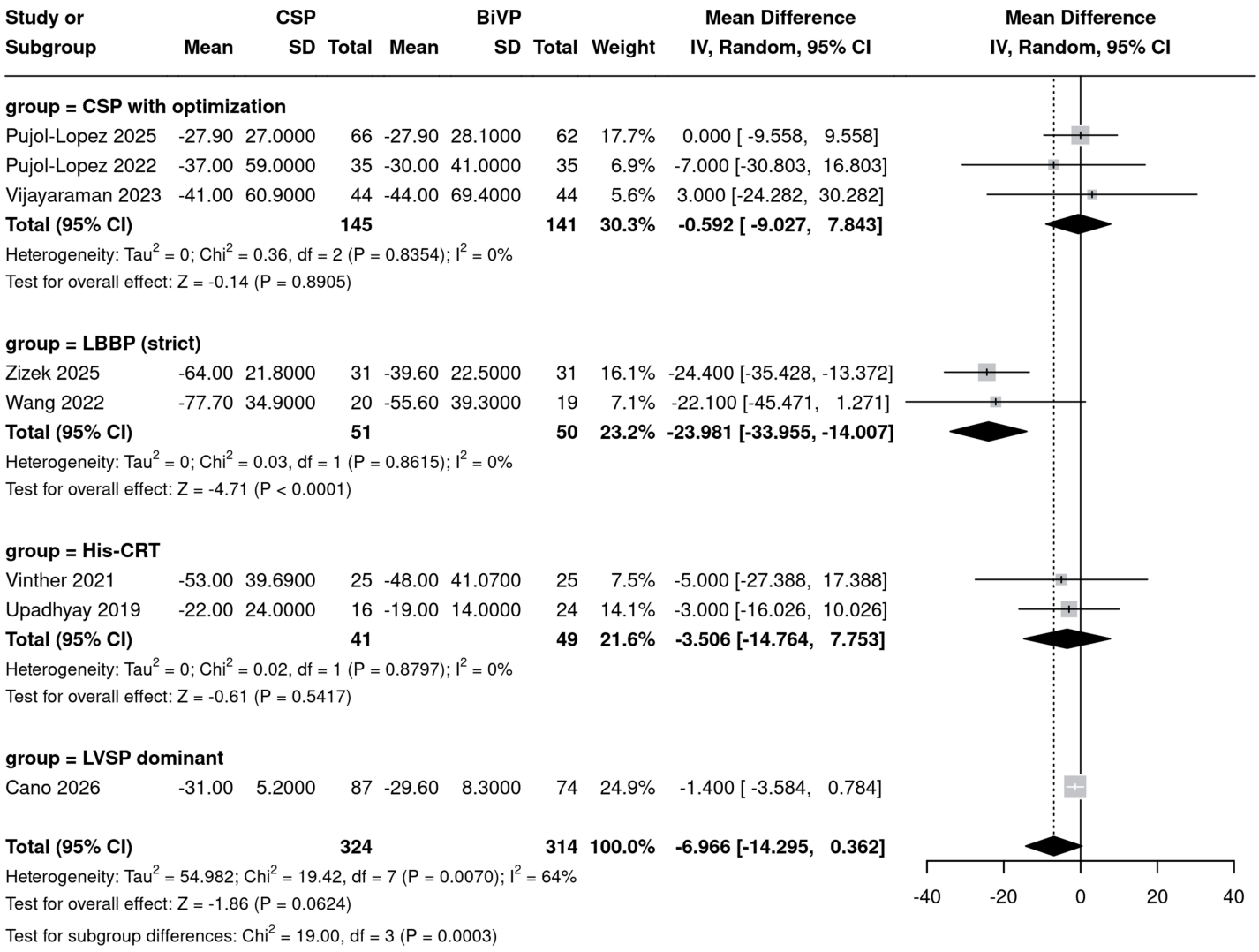


Figure 5

Mean difference in LVESV reduction (mL) between CSP and BiVP. Negative values favor CSP.

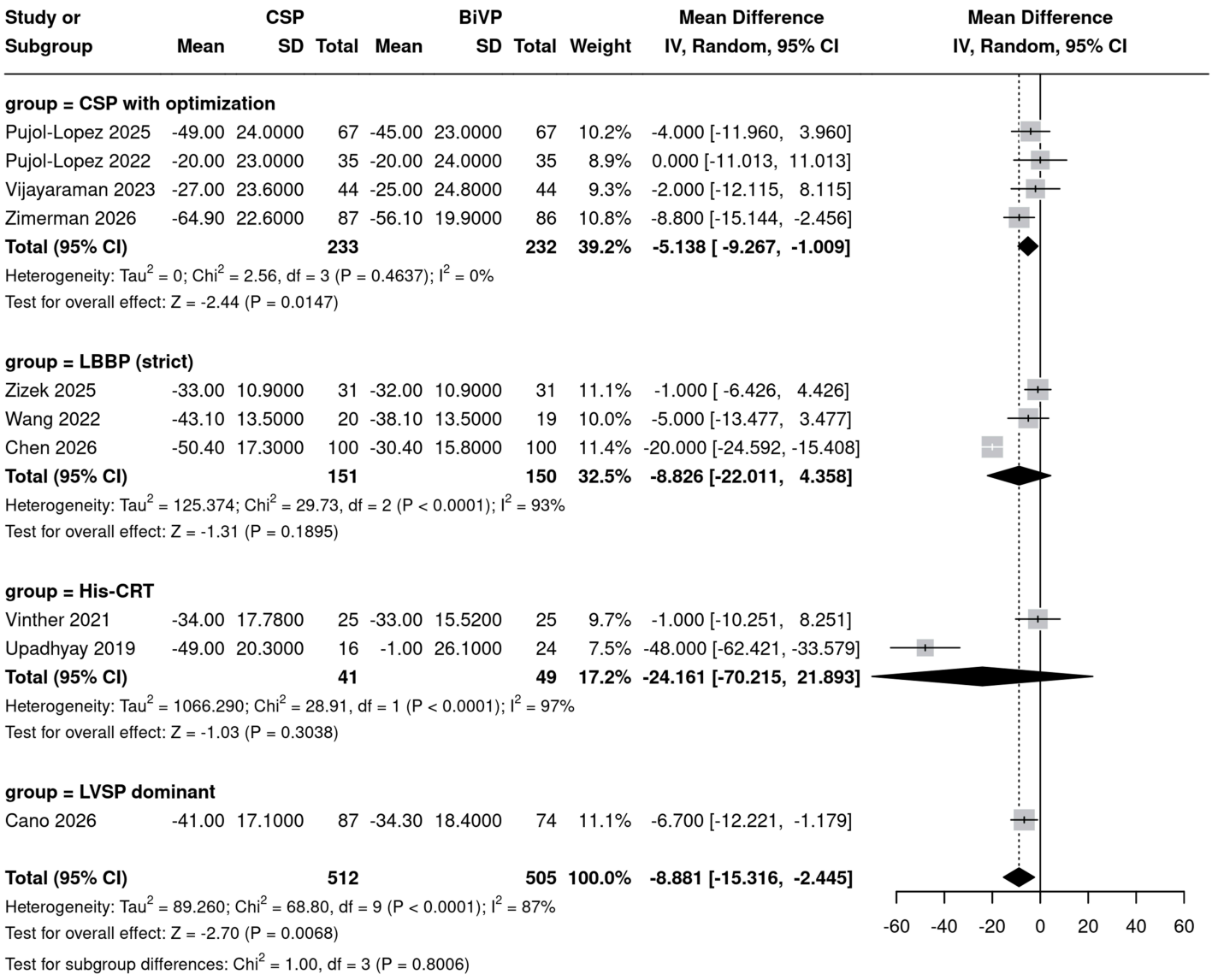


Figure 6

Mean difference in QRS duration shortening (ms) between CSP and BiVP. Negative values indicate greater QRS narrowing.

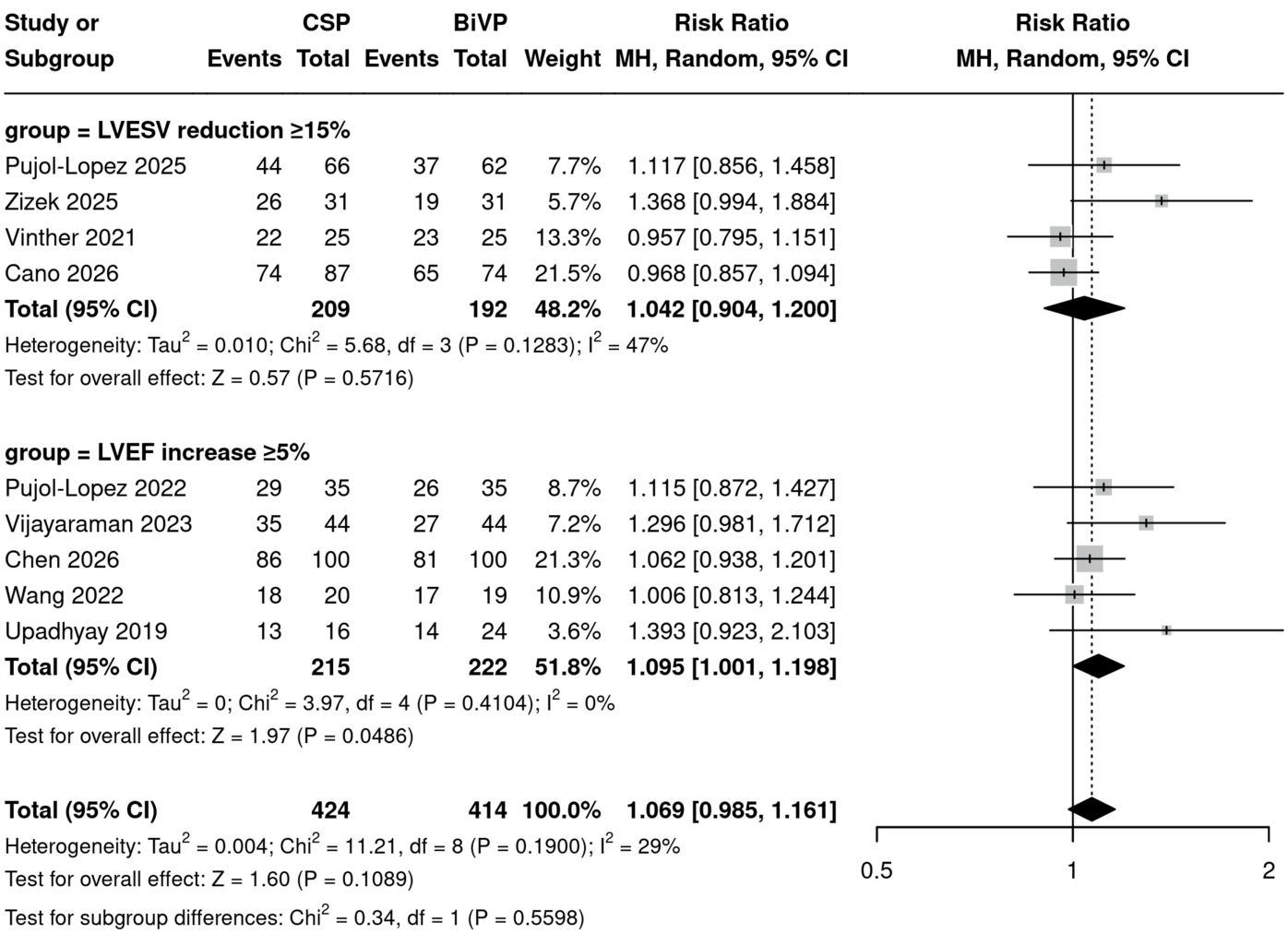


Figure 7

Echocardiographic response: structural (LVESV reduction ≥15%) and functional (LVEF increase ≥5%) response. Risk ratios with 95% CIs.

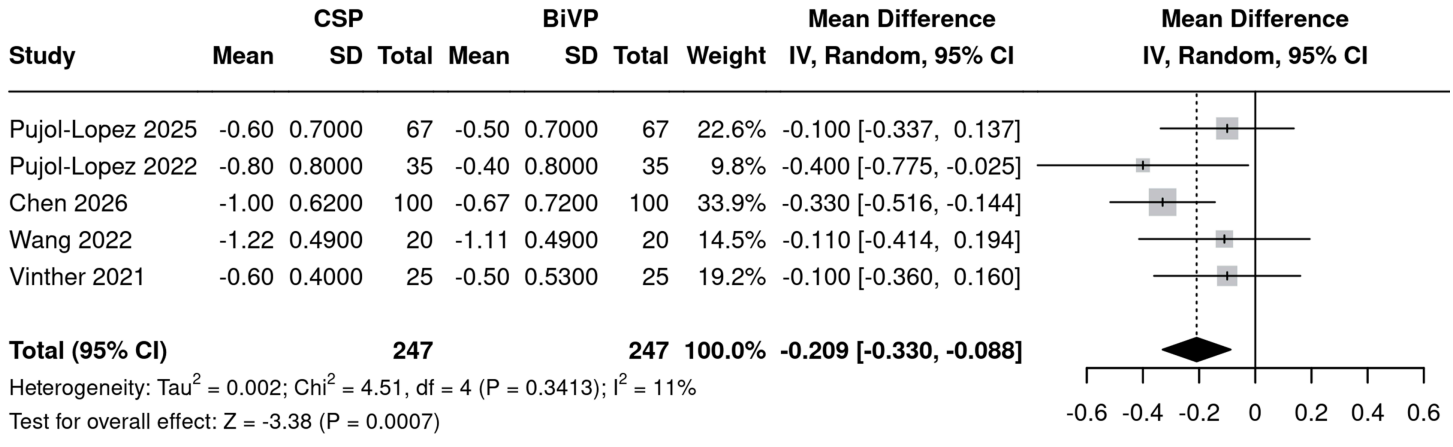


Figure 8

Mean difference in NYHA functional class improvement between CSP and BiVP. Negative values favor CSP.

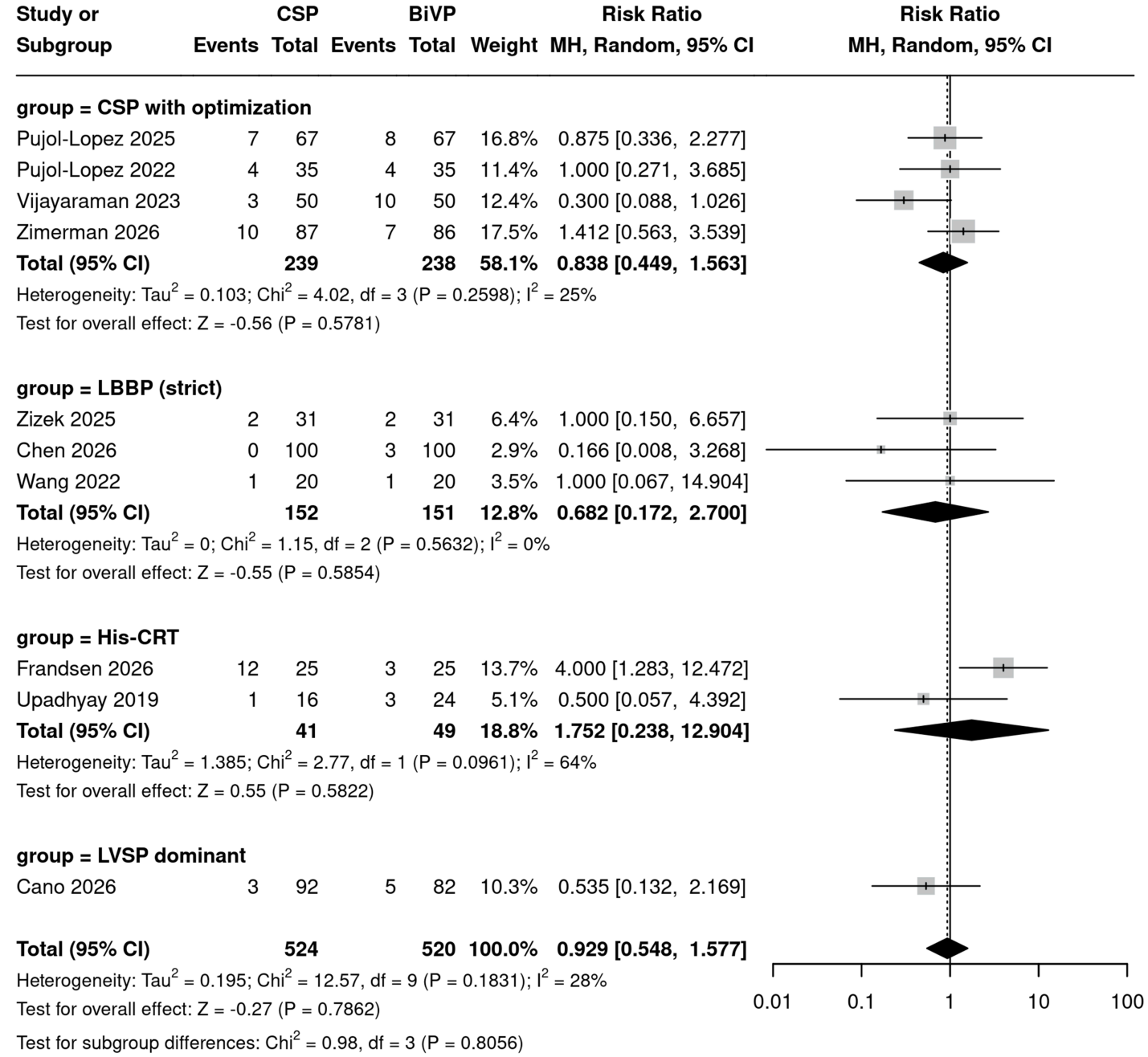


Figure 9

Risk of procedure-related or device-related complications with CSP versus BiVP.

Supplementary Files

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