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Myocardial work parameters in left bundle branch area pacing versus other pacing techniques: a systematic review and aggregate comparative analysis

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ABSTRACT

Cardiac conduction disease often necessitates permanent pacemaker implantation. While right ventricular pacing (RVP) effectively treats bradycardia, it may lead to adverse cardiac remodeling and heart failure. Left bundle branch area pacing (LBBAP) has emerged as an alternative, potentially preserving myocardial function. Non-invasive myocardial work (MW) assessment provides valuable insights into left ventricular systolic function, energetics, and efficiency. This study systematically reviewed and analyzed MW parameters, comparing LBBAP to RVP and His bundle pacing (HBP). A meta-analysis of 241 patients across five studies examined four MW parameters—Global Work Index (GWI), Global Constructive Work (GCW), Global Wasted Work (GWW), and Global Work Efficiency (GWE)—at baseline, post-implantation, and last follow-up (median: 180 days, IQR: 7–360 days). At baseline, MW parameters were similar between LBBAP and RVP. Post-implantation, LBBAP preserved MW more effectively, showing significantly higher GWI than RVP (2250.0 ± 400.0 vs. 1600.0 ± 300.0 mmHg%, p = 0.027), a difference that remained significant at follow-up (p = 0.035). GWE was also significantly higher at follow-up (p = 0.011), while GCW and GWW showed no significant differences. MW parameters did not differ significantly between LBBAP and HBP (all p-values >0.05). These findings suggest that LBBAP provides superior MW preservation compared to RVP, with significant benefits in GWI and GWE, while demonstrating comparable performance to HBP.

1. Introduction

Cardiac conduction disease is a serious and potentially life-threatening condition. Permanent pacemaker implantation is the only effective treatment for non-reversible symptomatic bradycardia and conduction system dysfunction [1]. Right ventricular pacing (RVP) has been a reliable therapy for bradycardia for over half a century. However, long-term RVP can lead to iatrogenic electro-mechanical dyssynchrony [2], progressive cardiac remodeling [3], heart failure, and atrial fibrillation (AF) [4,5].

Recently, conduction system pacing has gained considerable attention and adoption in clinical practice. Initially, His Bundle Pacing (HBP) was pursued which, despite its benefits, still presents challenges in implantation technique and is not suitable for patients with distal conduction system damage [6]. Left bundle branch area pacing (LBBAP), which involves pacing of the left bundle branch or one of its fascicles along with the left ventricular (LV) septal myocardium via a *trans*-septal approach, has recently emerged as a promising alternative to HBP, addressing many of its limitations [7,8]. Several studies have demonstrated the mid-term and long-term feasibility and safety of LBBAP in patients with bradycardia, showing low capture thresholds and high success rates [9–11]. Compared to RVP, LBBAP better preserves electrical synchrony of the left ventricle, characterized by shorter paced QRS duration and LV activation time. However, the impact of LBBAP on LV

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global function compared to RVP and HBP remains unclear.

Myocardial work (MW) is a validated echocardiographic parameter for assessing LV systolic function, offering insights into myocardial energy consumption and efficiency. MW is calculated using non-invasive brachial cuff pressure and longitudinal strain of the left ventricle using speckle tracking echocardiography. It provides diagnostic information beyond LV ejection fraction and strain by incorporating afterload and offering a measure of myocardial efficiency [12,13].(Fig. 1) In patients with bradycardia indication, studies comparing changes in MW after the implantation of different devices are limited, heterogeneous, and often inconclusive. To consolidate the findings, we conducted a systematic review and comparative/aggregate analysis to compare MW parameters between LBBAP and (RVP and HBP).

2. Methods

2.1. Data sources and search strategy

This systematic review was conducted in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Review and Meta-Analysis). Pubmed, Embase, Web of Science and Scopus databases were searched for relevant articles using the following keywords: "left bundle branch area pacing" OR "LBBAP" OR "left bundle branch pacing" OR "left bundle pacing" OR "right ventricular pacing" OR "his bundle branch pacing" OR "HBP") AND ("myocardial work" OR " MW" OR "left ventricular strain" OR "myocardial contraction". No language restriction was applied. The study protocol was registered in PROSPERO (CRD42024533804).

2.2. Study selection, data extraction and quality assessment

Articles retrieved from the systematic search were screened for eligibility by two independent reviewers (R.M. and S.G.) based on title, abstract and study design. Disagreements were resolved by a third investigator (A.I.). Studies were included if they met the following criteria: (1) involved patients with bradycardia requiring pacemaker implantation; (2) compared LBBAP with RVP and/or HBP; (3) reported MW parameters or related echocardiographic measures; (4) were original research articles. We excluded the review articles, case reports, and studies lacking relevant outcome data. Two authors (R.M, S.G.) independently extracted data regarding study design, population characteristics, outcomes, and follow-up, using a standardized data extraction form Fig. 2.

The quality of the included studies was assessed using the ROBINS-I tool (Risk Of Bias In Non-randomized Studies – of Interventions), which evaluates the risk of bias in non-randomized studies across seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each domain was rated as low (++), moderate (+−), or high (−−) risk of bias. The results of the quality assessment are summarized in Table 1. Due to the significant heterogeneity between the studies and the limited number of patients, a rigorous meta-analysis was not feasible, leading to a comparative/aggregate analysis.

2.3. Outcome definition

The primary aim of this study was to evaluate whether LBBAP preserves global left ventricular (LV) function, as measured by MW, more effectively than both RVP and HBP. This aim focuses on comparing LBBAP separately to RVP and HBP, conducting two distinct analyses to assess its efficacy in preventing a decline in myocardial function post-implantation. This approach ensures a comprehensive evaluation while considering the distinct physiological effects of each pacing technique.

2.4. Statistical analysis

To evaluate the impact of LBBAP on MW parameters in comparison to RVP and HBP, an aggregate comparative analysis was conducted. The study examined four key myocardial work parameters—Global Work

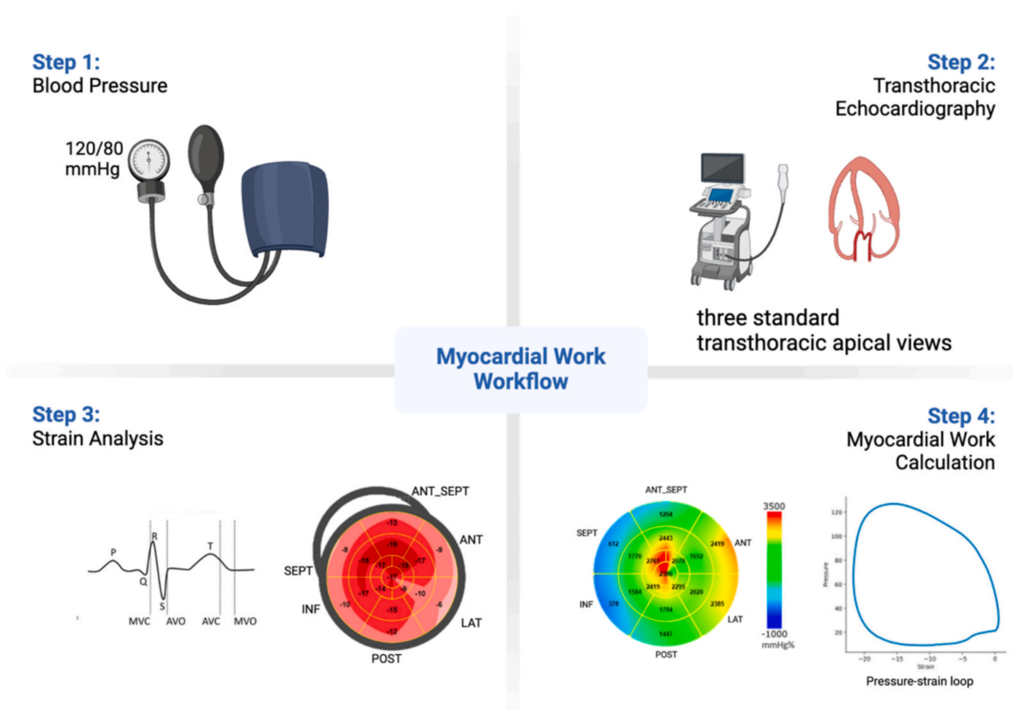

Fig. 1. Workflow for myocardial work assessment, integrating key measurements: (1) Blood pressure recording during echocardiography, ensuring positional consistency for accurate SBP estimation. (2) Acquisition of three standard transthoracic apical views with optimal frame rate. (3) Strain analysis with GLS and valve timing assessment. (4) Calculation of myocardial work indices, visualization of bull's-eye plots, and PSL generation for functional evaluation.

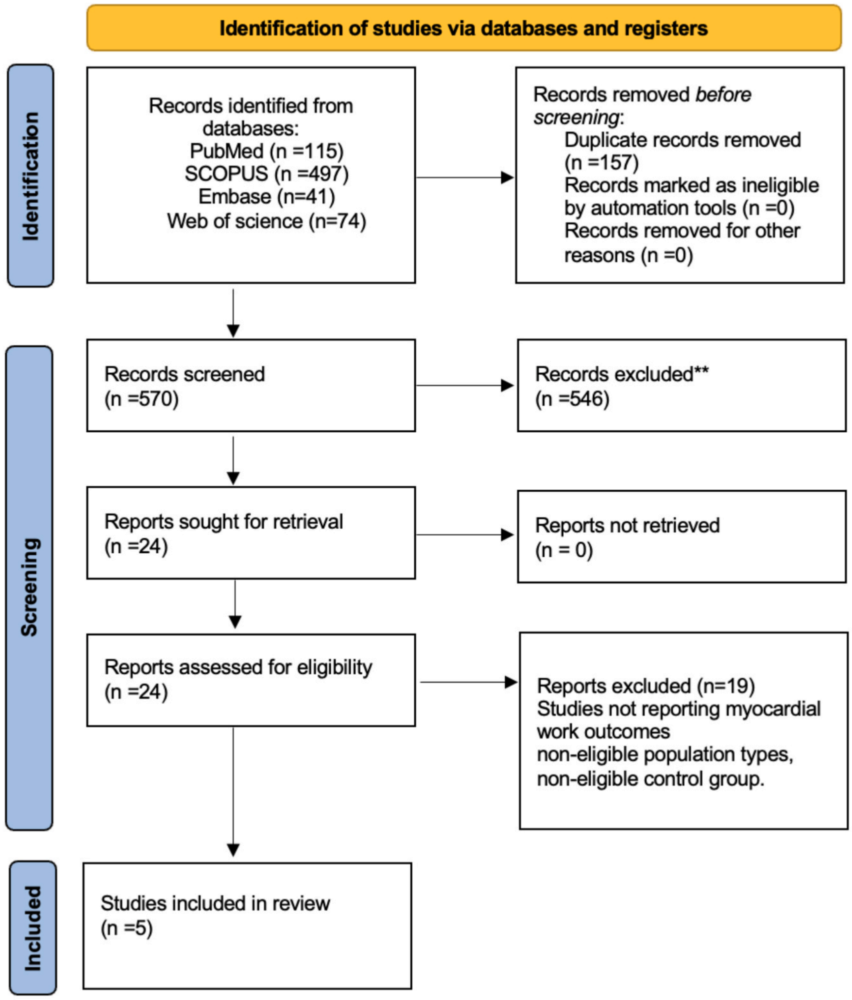

Fig. 2. PRISMA flow-chart.

Table 1
Quality assessment adapted from Cochrane's Collaboration Tool (ROBINS-I) for non-randomized trials.

Domains	Azzolini et al. [14].	PeiWei Wang et al. [15]	Huang-Chung Chen et al. [16]	Leventopoulos et al. [17]	Mao et al. [18]
Confounding	+−	+−	+−	+−	+−
Selection of Participants	++	++	++	++	++
Classification of Interventions	++	++	++	++	++
Deviations from Intended Interventions	++	++	++	++	++
Measurement of Outcomes	++	+−	++	++	+−
Incomplete Follow-up	++	+−	++	+−	+−
Selection of Reported Result	++	+−	++	+−	+−

Index (GWI), Global Constructive Work (GCW), Global Wasted Work (GWW), and Global Work Efficiency (GWE)—across Baseline, Post-Implantation, and Follow-Up (where applicable).

Given the distinct pacing mechanisms of RVP and HBP, separate statistical analyses were performed for each comparison, ensuring a precise evaluation of LBBAP's effects relative to both pacing techniques.

Baseline measurements were obtained before the implantation procedure. For some studies, this involved echocardiograms performed during spontaneous ventricular activation or using previous echocardiographic exams conducted within six months prior to the procedure.

Post-implantation measurements were recorded shortly after the implantation procedure, typically within 7 days and during pacing stimulation, to assess the immediate impact of the device on myocardial function. Follow-up measurements were taken to evaluate the long-term effects of the pacing technique. The timing of follow-up varied across studies, with measurements taken at 6 months, 12 months, and up to 15 months after implantation, depending on the study. However, for HBP, only Baseline and Post-Implantation phases were analyzed due to the limited availability of follow-up data from multiple studies.

For each study included in our analysis, we extracted the mean values and standard deviations (SD) for the MW parameters at each specified phase. In cases where standard deviations were not directly provided, they were derived from the reported confidence intervals.

We calculated the aggregated means and standard deviations for each MW parameter (GWI, GCW, GWW, GWE) across the studies, separately for LBBAP and other pacing techniques.

An independent samples *t*-test was performed to compare the means between LBBAP and other pacing techniques for each phase (Baseline, Post-Implantation, Follow-Up). This test was used to determine whether there were statistically significant differences in the MW parameters between groups. We evaluated the assumptions of normality and equal variance for each comparison to ensure the validity of the *t*-test results. We set the threshold for statistical significance at $p < 0.05$. To assess the consistency of the results across studies, we calculated the I^2 statistic for each parameter and phase. This provided a measure of the percentage of total variation across studies that is due to heterogeneity rather than chance. All analyses were conducted using Python and the SciPy and pandas libraries to ensure accurate and reliable comparisons between the pacing techniques across the specified phases.

3. Results

3.1. Study search and characteristics

Of the 727 studies, 547 studies were excluded at title and abstract level and 19 studies were excluded at full-text level. Finally, 5 studies provided data on MW in patients with LBBAP and were therefore included in the quantitative analysis. The search strategy is illustrated in Fig. 1.

The study population comprised a total of 241 patients from five prospective studies, providing a comprehensive overview of individuals who underwent different pacing techniques. The overall mean age of the patients was approximately 75 years, ranging from 53 to 85 years, with about 50 % of the cohort being male. Hypertension was a common comorbidity, present in about 70 % of the patients, while atrial fibrillation (AF) was reported in around 40 %. Coronary artery disease (CAD) was identified in 25 % of the patients, and diabetes mellitus affected approximately 30 % of the patients. Additionally, dyslipidemia was present in 55 % of the patients, chronic kidney disease in 20 %, and obesity, indicated by a body mass index (BMI) above normal, was found in about 25 %.

LV ejection fraction was preserved (59.4 ± 5.3 %) while Global Longitudinal Strain (GLS) was mildly impaired (−17.38 ± 2.0 %). The mean QRS duration before device implantation was 109.6 ms (±8.4) and after device implantation was 110.5 ms (±12.6).

All pacing devices, including LBBAP, RVP and HBP, were implanted primarily for bradycardia due to atrioventricular block, bundle branch block (BBB), or sinus node dysfunction (SND). LBBAP was also used as an alternative to HBP when the latter was not feasible.

The baseline characteristics of the studies included are presented in Table 2 and Table 3.

3.2. Main results

At baseline, both RVP and LBBAP groups showed similar MW values, as indicated by GWI averages of 2200.0 (SD = 150.0) for LBBAP and 2180.0 (SD = 200.0) for RVP, with no significant difference (T-value = 0.567, P-value = 0.573). Post-implantation, LBBAP had a mean GWI of 2250.0 (SD = 400.0) compared to 1600.0 (SD = 300.0) for RVP (T-value = 2.232, P-value = 0.027), indicating better preservation of myocardial work. At the last follow-up, LBBAP continued to show a significantly higher mean GWI of 2100.0 (SD = 300.0) compared to 1500.0 (SD = 250.0) for RVP (T-value = 2.312, P-value = 0.035), reinforcing its long-term benefits in preserving MW. For GCW, both groups had comparable values at baseline, with LBBAP at 2344.0 (SD = 361.9) and RVP at 2240.0 (SD = 520.3) (T-value = 0.405, P-value = 0.694). Post-implantation, LBBAP had a mean GCW of 2435.8 (SD = 368.3) versus 2043.8 (SD = 554.8) for RVP (T-value = 1.705, P-value = 0.108). At the last follow-up, GCW values were 2340.0 (SD = 365.0) for LBBAP and 2235.0 (SD = 510.0) for RVP (T-value = -0.045, P-value = 0.965).

For GWW, baseline values were 147.0 (SD = 14.1) for LBBAP and 174.0 (SD = 60.8) for RVP (T-value = -0.865, P-value = 0.453). Post-implantation, GWW was 280.5 (SD = 23.3) for LBBAP and 253.3 (SD = 166.1) for RVP (T-value = 0.366, P-value = 0.731). At the last follow-up, GWW for LBBAP was 197.9 (SD = 18.5) compared to 396.0 (SD = 93.3) for RVP (T-value = -2.118, P-value = 0.124).

For GWE, both groups had comparable values at baseline, with LBBAP at 93.25 (SD = 4.243) and RVP at 90.875 (SD = 3.750) (T-value = 0.792, P-value = 0.471). Post-implantation, LBBAP had a mean GWE of 91.1 (SD = 4.303) compared to 84.37 (SD = 2.850) for RVP (T-value = 2.444, P-value = 0.067). Notably, at the last follow-up, LBBAP exhibited a higher myocardial efficiency, with a mean GWE of 91.5 (SD = 4.0) compared to 85.0 (SD = 3.5) for RVP (T-value = 2.620, P-value = 0.011), highlighting its potential to sustain a more favorable cardiac function over time (Fig. 3).

For HBP, only baseline and post-implantation phases were considered in the comparative analysis. The last follow-up phase was excluded as data were available from a single study, limiting its statistical robustness and comparability. No significant differences were observed between LBBAP and HBP in MW parameters (all p-values > 0.05). (Fig. 4).

The comparison of EF values between the LBBAP group and the HBP and RVP techniques across different phases revealed no statistically significant differences, with all p-values greater than 0.05.

4. Discussion

The results of the present analysis can be summarized as follows: (1)

Table 2
Included studies characteristics. AF, atrial fibrillation; HBP; His Bundle Pacing; LBBAP, Left Bundle Branch Area Pacing; RVP, Right Ventricular Pacing.

Study (Author, type of study, year)		Patients, no	Age (y), mean, SD	Male, (%)	AF (%)	SpontaneousQRS (ms) Mean, SD	PacedQRS (ms) Mean, SD	Pacing Indication
Azzolini et al[14]	LBBAP	12	81 ± 3	17	42	115 ± 10,5	128 ± 3,5	Symptomatic bradycardia
Prospective, Single center, 2023	HBP	12	80,5 ± 3	17	58	106 ± 13	124 ± 10,5	(AV block, BBB, SND, slow AF)
PeiWei Wang et al[15]	LBBAP	20	66 ± 5	50	–	96 ± 12,9	98,5 ± 10,12	Symptomatic bradycardia
Prospective, Single center, 2022	RVP	29	68 ± 3	44,8	–	100 ± 6,75	–	(AV block, BBB, SND, slow AF)
Huang-Chung Chen et al[16]	LBBAP	46	73 ± 11	60.9	21,7	107 ± 33	114 ± 11	Symptomatic bradycardia
Prospective, Single center, 2023	HBP	24	79 ± 7	41,7	58,3	96 ± 24	116 ± 12	(AV block, BBB, SND, slow AF)
	RVP	16	76 ± 5	31,3	62,5	89 ± 12	145 ± 14	
Leventopoulos et al[17]	LBBAP	20	80,5 ± 2,5	60	–	–	121.8 ± 4	Symptomatic bradycardia
Prospective, Single center, 2024	RVP	18	81,5 ± 2,6	72	–	–	151.5 ± 4.3	(AV block, BBB, SND, slow AF)
Mao et al [18]	LBBAP	31	71 ± 10	58	16	107 ± 24	43 ± 6	Symptomatic bradycardia
Prospective, Multicenter, 2023	RVP	29	75 ± 9	79	35	114 ± 22	42 ± 6	(AV block, BBB, SND, slow AF)

Table 3
Baseline echocardiographic characteristics of included studies. GLS, global longitudinal strain; HBP; His Bundle Pacing; LA; left atrium; LBBAP, Left Bundle Branch Area Pacing; LVEDV; left ventricular end diastolic volume; LVEF; left ventricular ejection fraction; PSD; peak strain dispersion; RVP, Right Ventricular Pacing.

Study (Author, type of study, year)		LVEF (%)	GLS	PSD	LVEDV (ml)	LA size (mm)
Azzolini et al[14]	LBBAP	55 ± 1,25	−15 ± 2	–	–	–
Prospective, Single center, 2023	HBP	51 ± 5,25	−14 ± 2	–	–	–
PeiWei Wang et al[15]	LBBAP	61.1 ± 3.6	17,7 ± 3,5	51,7 ± 10,9	112.9 (88.9–135.3)	36.0 (34.0–40.0)
Prospective, Single center, 2022	RVP	61.7 ± 4,1	–	–	112.8 (93.7–144.4)	34.0 (32.0–38.0)
Huang-Chung Chen et al[16]	LBBAP	65 ± 7	19.4 ± 2,7	56 ± 13	101 ± 31	37 ± 5
Prospective, Single center, 2023	HBP	64 ± 8	20.2 ± 5.4	55 ± 21	108 ± 39	39 ± 5
	RVP	65 ± 7	19.6 ± 2.9	63 ± 16	99 ± 27	38 ± 8
Leventopoulos et al[17]	LBBAP	Only follow-up data	Only follow-up data	Only follow-up data	–	–
Prospective, Single center, 2024	RVP				–	–
Mao et al[18]	LBBAP	65 ± 6	20 ± 3	–	–	–
Prospective, Multicenter, 2023	RVP	65 ± 7	19 ± 4	–	–	–

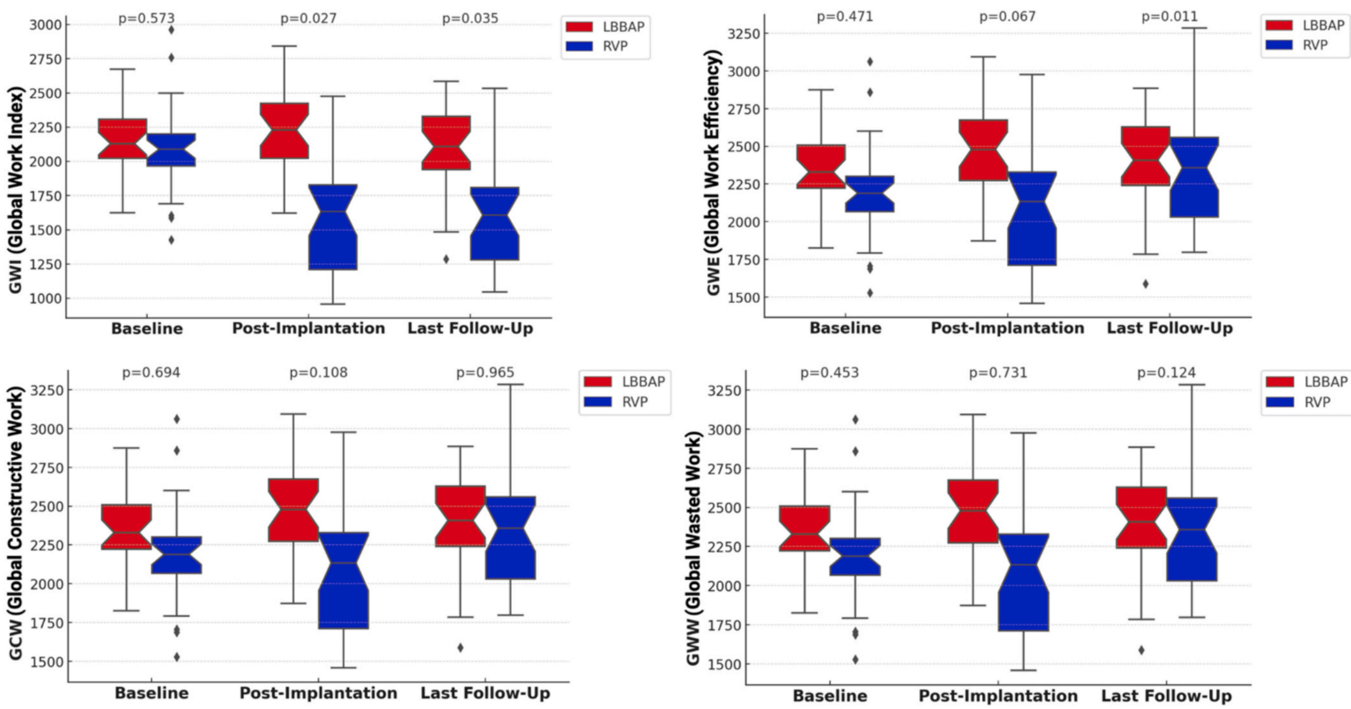

Fig. 3. Comparison of myocardial work parameters (GWI, GWE, GCW, and GWW) between LBBAP and RVP across Baseline, Post-Implantation, and Last Follow-Up. Box plots show data distribution, with notches indicating confidence intervals and p-values denoting statistical differences. Error bars represent standard deviation.

LBBAP demonstrated a significant advantage over RVP in preserving GWI, with statistically higher values both post-implantation and at follow-up. While RVP was associated with a progressive decline in GWI, LBBAP maintained more stable values over time, reinforcing its role in preserving myocardial work and LV contractile function; (2) In addition to GWI, LBBAP also showed a significant advantage over RVP in GWE at the last follow-up; 3)No significant differences were observed between LBBAP and RVP for GCW or GWW; 4)The comparison between LBBAP and HBP revealed no significant difference in MW parameters.

4.1. RV versus physiological pacing

Previous studies have demonstrated that abnormal electrical activation due to RVP leads to dyssynchronous ventricular contraction, especially between the anteroseptal wall (with early activation) and the posterolateral wall (with late activation), similar to typical activation patterns in left bundle branch block [19,20]. This dyssynchrony may lead to adverse cardiac remodeling, LV dysfunction and heart failure over time [4,5]. LBBAP and HBP are physiological pacing modes designed to stimulate the myocardium by recruiting its own conduction system [21]. Both pacing modes have demonstrated better preservation of LV ejection fraction, lower all-cause mortality, reduced hospitalizations for heart failure, and a lower likelihood of needing cardiac resynchronization therapy compared to RVP [22–24]. However, HBP presents several issues, such as the risk of lead dislodgement, anatomical challenges, elevated capture thresholds, and the risk of losing capture over both short- and long-term follow-ups, which often require more frequent lead revisions [25,26]. Therefore, the focus on LBBAP has grown in recent years. Researchers have demonstrated its feasibility and superiority in terms of LV mechanical synchrony over RVP [27]. Despite widening of the QRS complex induced by LBBAP, LV mechanical synchrony at nuclear perfusion imaging or echocardiography remains similar to native conduction [28–31].

Myocardial function remains the most important predictor of all-cause death and heart failure hospitalization. The pressure–volume analysis is the gold standard for evaluating myocardial contractility but is complex and invasive. Based on 2D speckle-tracking echocardiography, the pressure-strain loop has been developed to replace pressure–volume analysis in a simplified and non-invasive way [13,32]. This approach provides a comprehensive assessment of left ventricular (LV)

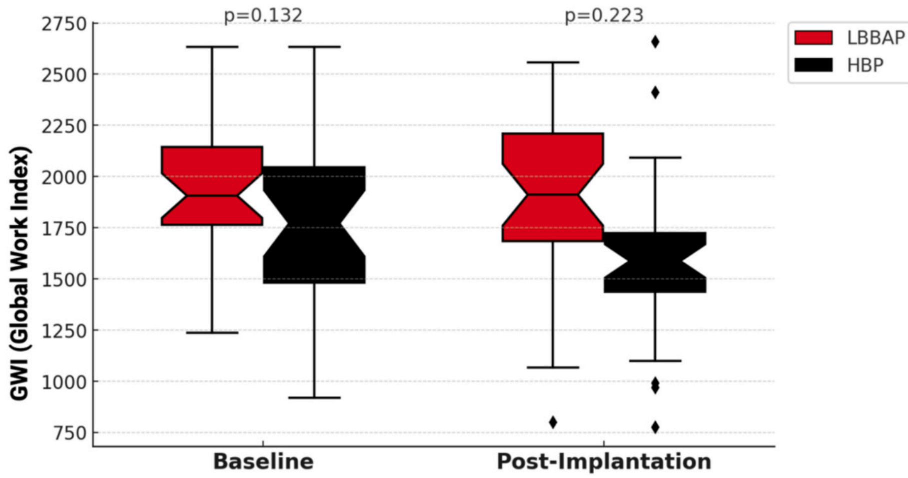

Fig. 4. Comparison of Global Work Index (GWI) between LBBAP (red) and HBP (black) at baseline and post-implantation. Box plots display data distribution, with notches indicating confidence intervals. The p-values denote statistical comparisons, and error bars represent standard deviation for each phase. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

systolic function by incorporating both pressure and strain, offering a more accurate reflection of myocardial energy consumption and efficiency compared to traditional measures like strain, especially in patients with preserved systolic function, as in our study cohort [32].

MW parameters calculated from the pressure-strain loop include the GWI, which represents the average myocardial work during the cardiac cycle and reflects overall myocardial performance. GCW measures the effective work contributing to LV contraction, including positive work during systole and negative work during isovolumic relaxation. In contrast, the GWW quantifies energy lost during inefficient myocardial activity, such as segment lengthening during systole and shortening during isovolumic relaxation. The GWE, defined as the ratio of GCW to total myocardial work, provides a comprehensive metric for myocardial energy efficiency [12].

Normal values for MW parameters were reported in a meta-analysis by Truong et al. [12]. The mean GWI and GCW across studies were 2,010 mm Hg% (95 % CI, 1,907–2,113 mm Hg%) and 2,278 mm Hg% (95 % CI, 2,186–2,369 mm Hg%), respectively. Mean global wasted work was 80 mm Hg% (95 % CI, 73–87 mm Hg%), and mean global work efficiency was 96.0 % (95 % CI, 96 %–96 %). Furthermore, gender significantly contributed to variations in normal values of GWI, GWW, and GWE, although no evidence of significant publication bias was observed. In our study, MW parameters in the LBBAP group remained within these normal ranges during follow-up, except for GWW, which was slightly elevated but consistent with baseline values. In contrast, RVP was associated with GWI and GWE below the normal range and a higher GWW, indicating functional deterioration. This highlights the potential of LBBAP in preserving LV performance with slightly higher energy consumption than native conduction. [33].

5. Limitations

The significant heterogeneity among the included studies presented a major challenge. While the aggregate comparative analysis provides valuable insights into the potential benefits of LBBAP, these findings should be interpreted with caution due to the incomplete data for certain parameters and phases, small sample sizes, and differing follow-up durations.

6. Conclusion

LBBAP demonstrated greater preservation of myocardial work and efficiency compared to RVP, with significant advantages in both GWI and GWE, particularly at last follow-up. In contrast, GCW and GWW did not differ significantly between LBBAP and RVP.

In the comparison with HBP, no significant differences were found in MW parameters, though data were available only for the post-implantation phase.

While not all differences were statistically significant, these findings suggest that LBBAP offers a physiological pacing strategy superior to RVP, maintaining myocardial work efficiency more effectively, which may have long-term clinical benefits. However, given the heterogeneity among studies, further prospective trials are needed to confirm these results and assess their clinical implications.

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CRediT authorship contribution statement

Raffaella Mistrulli: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Sara Gharehdaghi:** Data curation, Conceptualization. **Arthur Iturriagagoitia:** Writing – original draft, Conceptualization. **Elayne Kelen de Oliveira:** Writing – review & editing, Data curation. **Lucio Addeo:** Visualization, Methodology. **Stefano Valcher:** Writing – review & editing, Visualization, Methodology. **Sara Corradetti:** Writing – review & editing, Visualization, Data curation. **Michele Mattia Viscusi:** Writing – review & editing. **Peter Peytchev:** Writing – review & editing, Visualization. **Ward A. Heggermont:** Writing – review & editing, Data curation. **Marc Vanderheyden:** Writing – review & editing, Supervision. **Emanuele Barbato:** Writing – review & editing, Validation, Supervision. **Guy Van Camp:** Writing – review & editing, Visualization, Supervision. **Martin Penicka:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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