Eurasian J. Chem. Med. Pet. Res., (2026), Volume 5, Issue 2, 159-168

Eurasian Journal of Chemical, Medicinal and Petroleum Research

Journal homepage: https://www.ejcmpr.com/

DOI: https://doi.org/10.5281/zenodo.18624338

Evaluation and Comparative Analysis of Global Peak Systolic Strain in Apical versus Septal Right Ventricular Pacing

Kamran Mohammadi

Assistant Professor of Cardiology, Department of Cardiology, School of Medicine, Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article info

Received: 20.12.2025
Accepted: 11.02.2026
Available Online: 11.02.2026
Checked for Plagiarism: Yes

Keywords:
Right ventricular pacing, Septal pacing, Apical pacing, Myocardial strain

ABSTRACT

Introduction: Right ventricular pacing can profoundly influence left ventricular mechanics, particularly when non-physiological activation patterns induce mechanical dyssynchrony and impaired myocardial deformation. Global peak systolic strain is a sensitive marker for detecting pacing-related alterations in ventricular function. This study aimed to evaluate and compare global peak systolic strain in patients undergoing right ventricular apical versus septal pacing to determine the pacing site associated with more preserved myocardial mechanics.
Material and methods: This randomized historical-control study included 60 patients undergoing permanent right ventricular pacing at a tertiary cardiac center. Participants were equally assigned to apical or septal pacing. Standardized echocardiography with speckle-tracking analysis was performed to quantify global peak systolic strain, and outcomes were compared using appropriate statistical methods under blinded assessment and ethical approval.
Results: Right ventricular pacing was associated with significant impairment of left ventricular myocardial deformation. Global longitudinal strain showed a stepwise reduction from normal subjects to septal pacing and was most severely attenuated with apical pacing ($p<0.001$). Inferior and mid-inferior segmental strain was preserved with septal pacing but significantly reduced with apical pacing compared with both normal and septal groups ($p\leq0.01$).
Conclusion: This study demonstrates that the site of right ventricular pacing is a critical determinant of left ventricular mechanical performance. Although septal pacing does not fully replicate physiological ventricular activation, it is associated with relatively preserved global and regional myocardial deformation and reduced mechanical heterogeneity compared with apical pacing.

Introduction

Right ventricular pacing has remained a cornerstone therapy for the management of bradyarrhythmias and conduction system diseases for several decades. Traditionally, the right ventricular apical region has been favored for lead implantation because of its technical simplicity, procedural stability, and reliable electrical parameters. However, accumulating evidence has demonstrated that chronic right ventricular apical pacing can induce non-physiological electrical activation patterns, leading to mechanical dyssynchrony, adverse ventricular remodeling, and progressive deterioration of left ventricular systolic function.

These observations have prompted increasing concern regarding the long-term hemodynamic and structural consequences of apical pacing, particularly in patients who are pacing-dependent or require a high percentage of ventricular pacing [1].

The recognition that pacing-induced cardiomyopathy may develop even in patients without pre-existing structural heart disease has

Corresponding Author:* ***Kamran Mohammadi* *(Mohammadikamran706@gmail.com - ORCID: 0000-0002-1589-5359)*

intensified the search for alternative pacing sites that better preserve physiological ventricular activation. Right ventricular septal pacing has emerged as a promising alternative, as it is anatomically closer to the native His–Purkinje conduction system and may facilitate a more synchronous pattern of ventricular depolarization. Several electrophysiological and imaging studies suggest that septal pacing results in narrower QRS complexes and more homogeneous myocardial contraction compared with apical pacing. Despite these theoretical advantages, clinical outcomes have been heterogeneous, and the mechanistic effects of septal pacing on global and regional myocardial function remain incompletely defined [2].

Myocardial strain imaging, particularly speckle-tracking echocardiography, has revolutionized the assessment of ventricular mechanics by enabling quantitative evaluation of myocardial deformation. Among strain-derived parameters, global peak systolic strain has gained prominence as a sensitive and reproducible marker of systolic performance, capable of detecting subtle myocardial dysfunction before conventional measures such as left ventricular ejection fraction become abnormal. Global peak systolic strain reflects the integrated contractile behavior of the myocardium and provides valuable insight into the impact of altered electrical activation on ventricular mechanics. As such, it represents an ideal tool for comparing the mechanical consequences of different right ventricular pacing strategies [3].

Apical right ventricular pacing is known to generate an electrical activation sequence that mimics left bundle branch block, resulting in early septal contraction and delayed activation of the lateral and posterior walls. This abnormal sequence leads to inefficient energy utilization, regional strain disparities, and increased wall stress in late-activated segments. Over time, these alterations may contribute to myocardial fibrosis, chamber dilation, and systolic dysfunction. Global peak systolic strain, by capturing the cumulative effect of these regional abnormalities, serves as a robust surrogate marker of pacing-induced mechanical burden and may offer prognostic value beyond traditional echocardiographic indices [4].

In contrast, septal right ventricular pacing has been proposed to mitigate these adverse effects by promoting a more physiological pattern of ventricular activation. By engaging septal myocardium closer to the conduction system, septal pacing may reduce interventricular and intraventricular dyssynchrony, preserve longitudinal fiber shortening, and maintain more uniform strain distribution across myocardial segments. Several studies have reported improved regional strain profiles and reduced mechanical dispersion with septal pacing compared with apical pacing; however, the extent to which these regional benefits translate into preservation of global peak systolic strain remains a subject of ongoing investigation [5].

The assessment of global peak systolic strain in patients with right ventricular pacing is particularly relevant in contemporary clinical practice, where long-term pacing exposure is increasingly common due to aging populations and expanded indications for device therapy. Identifying pacing strategies that minimize adverse myocardial remodeling is essential for improving long-term outcomes and reducing the incidence of pacing-induced cardiomyopathy. While emerging pacing techniques such as His-bundle and left bundle branch pacing offer promising physiological alternatives, they are not universally feasible and remain technically challenging in certain patient populations. Consequently, optimizing conventional right ventricular pacing sites, including the choice between apical and septal positions, continues to hold substantial clinical importance [6].

Despite growing interest in septal pacing, existing data comparing global peak systolic strain between apical and septal right ventricular pacing remain limited and sometimes contradictory. Variability in lead positioning techniques, imaging methodologies, patient selection, and duration of pacing exposure has contributed to inconsistent findings across studies. Furthermore, many investigations have focused primarily on regional strain or electrical parameters, with less emphasis on global deformation indices that more comprehensively reflect ventricular performance. A systematic and quantitative comparison of global peak systolic strain between these two pacing strategies is therefore essential to clarify their relative mechanical impact [7].

In this context, the present study aims to evaluate global peak systolic strain in patients undergoing right ventricular apical pacing and to determine global peak systolic strain in those receiving right ventricular septal pacing, followed by a direct comparison between the two pacing sites. By leveraging advanced strain imaging, this investigation seeks to provide mechanistic insight into how pacing location influences overall ventricular mechanics. A clearer understanding of these differences may inform clinical decision-making, guide lead placement strategies, and ultimately contribute to improved preservation of myocardial function in patients requiring long-term right ventricular pacing.

Material and methods

Study Design and Setting: The present investigation was designed as a randomized clinical study with a historical control framework. The study was conducted at Shahid Madani Heart Hospital, a tertiary referral center affiliated with Tabriz University of Medical Sciences, Tabriz, Iran. Patient enrollment and data collection were carried out over a defined period spanning from the beginning of 2011 to the end of 2013. The study focused on patients undergoing permanent right ventricular pacing and aimed to assess the mechanical consequences of different ventricular lead positions on myocardial deformation parameters.

Study Population and Sampling Method: A census sampling approach was employed, whereby all eligible patients who met the predefined inclusion criteria during the study period were consecutively recruited. The final study population consisted of 60 patients, who were equally allocated into two groups: right ventricular apical pacing (n=30) and right ventricular septal pacing (n=30). This sampling strategy was chosen to minimize selection bias and to ensure adequate representation of the target population receiving long-term ventricular pacing at the study center.

Inclusion and Exclusion Criteria: Eligible participants were adult patients indicated for permanent pacemaker implantation due to symptomatic bradyarrhythmias, including high-grade atrioventricular block and sick sinus syndrome, with an anticipated high ventricular pacing burden. All included patients had preserved baseline left ventricular systolic function and no history of clinical heart failure prior to device implantation. Patients were required to have adequate transthoracic echocardiographic image quality to allow reliable strain analysis. Exclusion criteria encompassed prior myocardial infarction, known cardiomyopathies, significant valvular heart disease (greater than mild severity), congenital heart disease, atrial fibrillation or other persistent arrhythmias interfering with strain measurements, previous cardiac surgery, chronic renal failure, uncontrolled systemic hypertension, diabetes mellitus with established end-organ damage, and any condition likely to affect myocardial mechanics independently of pacing. Patients with incomplete clinical records or suboptimal echocardiographic data were also excluded from the analysis.

Randomization and Blinding: Patients were randomly assigned to receive either right ventricular apical or right ventricular septal lead placement using a computer-generated random allocation sequence. Randomization was performed prior to device implantation to ensure balanced group distribution. Due to the nature of the intervention, blinding of the implanting electrophysiologist was not feasible. However, echocardiographic image acquisition and strain analysis were conducted by experienced cardiologists who were blinded to the pacing site allocation. In addition, statistical analysis was performed by an independent investigator unaware of group assignments, thereby minimizing assessment and analytical bias.

Study Procedures: All patients underwent standard permanent pacemaker implantation according to contemporary clinical guidelines. In the apical pacing group, the ventricular lead was positioned at the right ventricular apex, confirmed fluoroscopically. In the septal pacing group, the lead was advanced and fixed to the right ventricular septum, with positioning verified using multiple fluoroscopic views to avoid inadvertent anterior or free-wall placement. Electrical parameters, including pacing threshold, sensing amplitude, and lead impedance, were assessed intraoperatively and confirmed to be within acceptable ranges.

Following implantation, patients were scheduled for standardized transthoracic echocardiographic evaluation after achieving stable pacing dependency. Echocardiographic examinations were performed using commercially available ultrasound systems equipped with speckle-tracking software. Standard two-dimensional images were acquired in accordance with current echocardiographic recommendations, ensuring optimal frame rates for strain analysis. Global peak systolic strain was derived from apical views by averaging segmental longitudinal strain values across the left ventricle.

All echocardiographic data were digitally stored and analyzed offline. Global peak systolic strain measurements were obtained by tracing the endocardial border at end-systole, with automated tracking verified and manually adjusted when necessary. Care was taken to ensure consistent region-of-interest placement and tracking quality across all segments. Measurements were averaged over three consecutive cardiac cycles to reduce beat-to-beat variability.

Statistical Analysis: Statistical analyses were performed using SPSS software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Normality of data distribution was assessed using the Kolmogorov Smirnov test. Comparisons between the apical and septal pacing groups were conducted using independent-samples t-tests or Mann Whitney U tests, as appropriate. A two-sided p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: This study was derived from the cardiology residency thesis of Dr. Kamran Mohammadi, completed in 2013, and the present analysis focuses specifically on the final three predefined specific objectives related to myocardial strain assessment. The research protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences. All procedures conformed to the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Patient confidentiality was strictly maintained, and all data were anonymized before analysis. No additional interventions beyond standard clinical care were imposed on participants as part of this study.

Results

The average duration between pacemaker implantation and echocardiographic evaluation in patients with right ventricular septal pacing was 185 ± 86 days, with follow-up periods ranging from approximately five to seven months. Left ventricular systolic performance was notably impaired in this group, with ejection fraction values substantially below normal limits. Mean ejection fraction was 42.5% using conventional two-dimensional echocardiography and 42.7% when assessed by three-dimensional imaging, both demonstrating a statistically significant reduction compared with standard reference values.

Assessment of myocardial deformation revealed a pronounced decline in global longitudinal peak systolic strain. The mean global strain value in the septal pacing cohort was -12.1%, which was markedly lower than expected for a normal left ventricle. Segment-specific analysis showed consistent attenuation of strain across all septal regions, including apical, mid, and basal segments. Comparable reductions were also observed in the anterior septal segments, indicating that septal pacing was associated with widespread impairment of septal myocardial mechanics rather than a localized effect.

In addition to septal involvement, longitudinal strain was reduced in non-septal myocardial territories. Deformation of the anterior, lateral, posterior, and inferior walls was uniformly diminished, with variability in the degree of impairment across different segmental levels. The lateral and inferior walls exhibited particularly low strain values at the apical and mid-ventricular levels, while posterior basal segments showed relatively higher but still abnormal deformation. Overall, these findings indicate a global and heterogeneous reduction in myocardial strain in patients undergoing right ventricular septal pacing (figure 1).

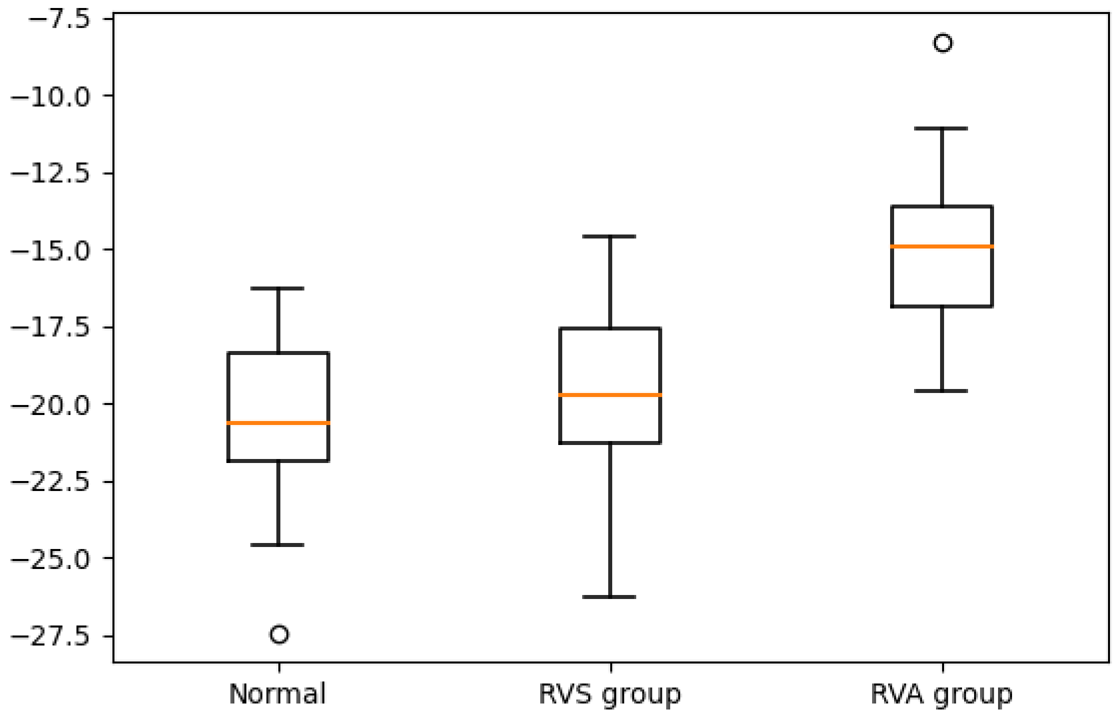

Figure 1. Left Ventricular Global Longitudinal Strain in Normal Subjects Versus Septal and Apical Right Ventricular Pacing

As shown in the boxplot, global longitudinal peak systolic strain demonstrated a statistically significant stepwise difference among the three groups. Subjects in the normal group exhibited the most negative strain values, consistent with preserved left ventricular myocardial deformation. In contrast, both pacing groups showed a significant attenuation of strain magnitude. Compared with the normal group, patients undergoing right ventricular septal pacing had significantly less negative strain values ($p<0.001$), indicating impaired longitudinal systolic function. This reduction was further accentuated in the right ventricular apical pacing group, which displayed the highest median strain values and the narrowest negative deformation range. Pairwise comparison revealed that strain impairment in the RVA group was significantly greater than in the RVS group ($p<0.01$). Additionally, the RVA group showed greater upward displacement of the interquartile range and increased dispersion, suggesting enhanced mechanical heterogeneity and ventricular dyssynchrony. Overall, these findings indicate a progressive deterioration of myocardial strain from normal subjects to septal pacing and most markedly to apical pacing, supporting the superiority of septal pacing over apical pacing in preserving left ventricular mechanical function (figure 2).

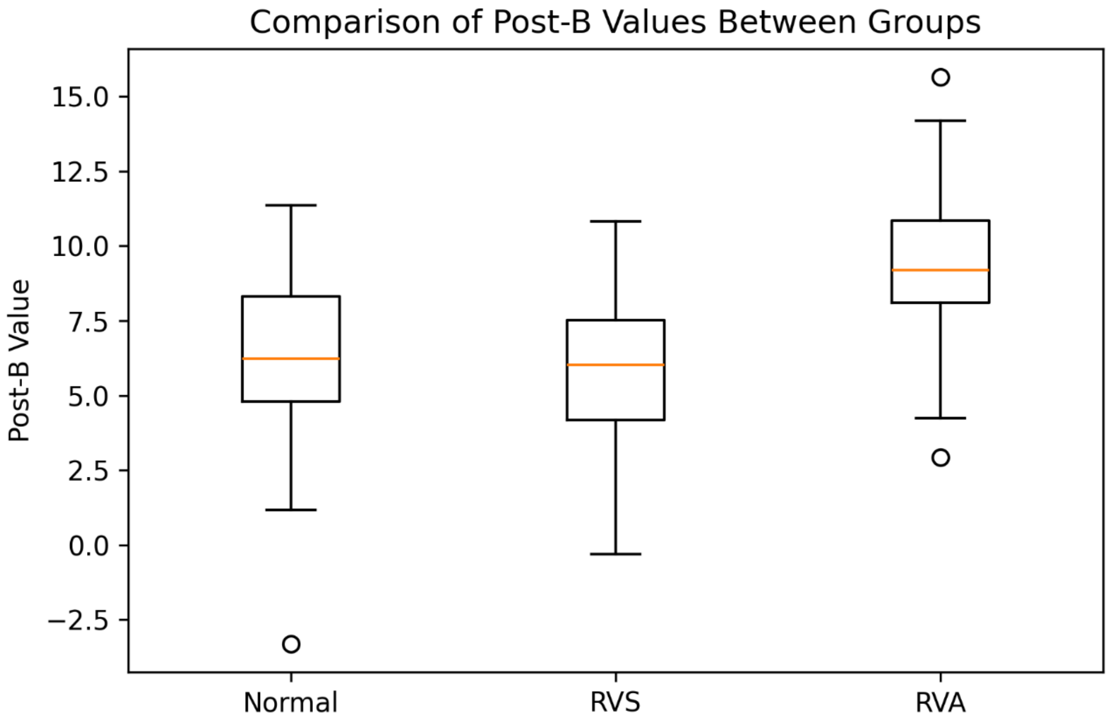

Figure 2. Comparative Analysis of Post-B Values Among Normal, RVS, and RVA Groups

The analysis of inferior segment peaks systolic strain (Inf. A) demonstrated a clear and clinically meaningful differentiation among the study groups. The normal reference group showed preserved myocardial deformation with a mean Inf. An of approximately $-20.6 \pm 2.6\%$. Patients undergoing right ventricular septal pacing (RVS) exhibited strain values that were slightly less negative but largely comparable to normal, and the difference between the RVS and normal groups did not reach statistical significance ($p=0.073$), suggesting relative preservation of inferior wall contractile mechanics with septal lead placement. In contrast, subjects with right ventricular apical pacing (RVA) showed a marked attenuation of inferior segment strain, with significantly less negative Inf. A values compared with the normal group ($p<0.001$), indicating substantial impairment of regional systolic deformation. Moreover, direct comparison between the two pacing strategies revealed significantly lower strain in the RVA group than in the RVS group ($p=0.001$), highlighting the unfavorable mechanical consequences of apical pacing on inferior myocardial function. Collectively, these findings indicate that inferior wall deformation is selectively preserved with septal pacing, whereas apical pacing is associated with pronounced regional systolic dysfunction, supporting the mechanical advantage of septal lead positioning over apical pacing (figure 3).

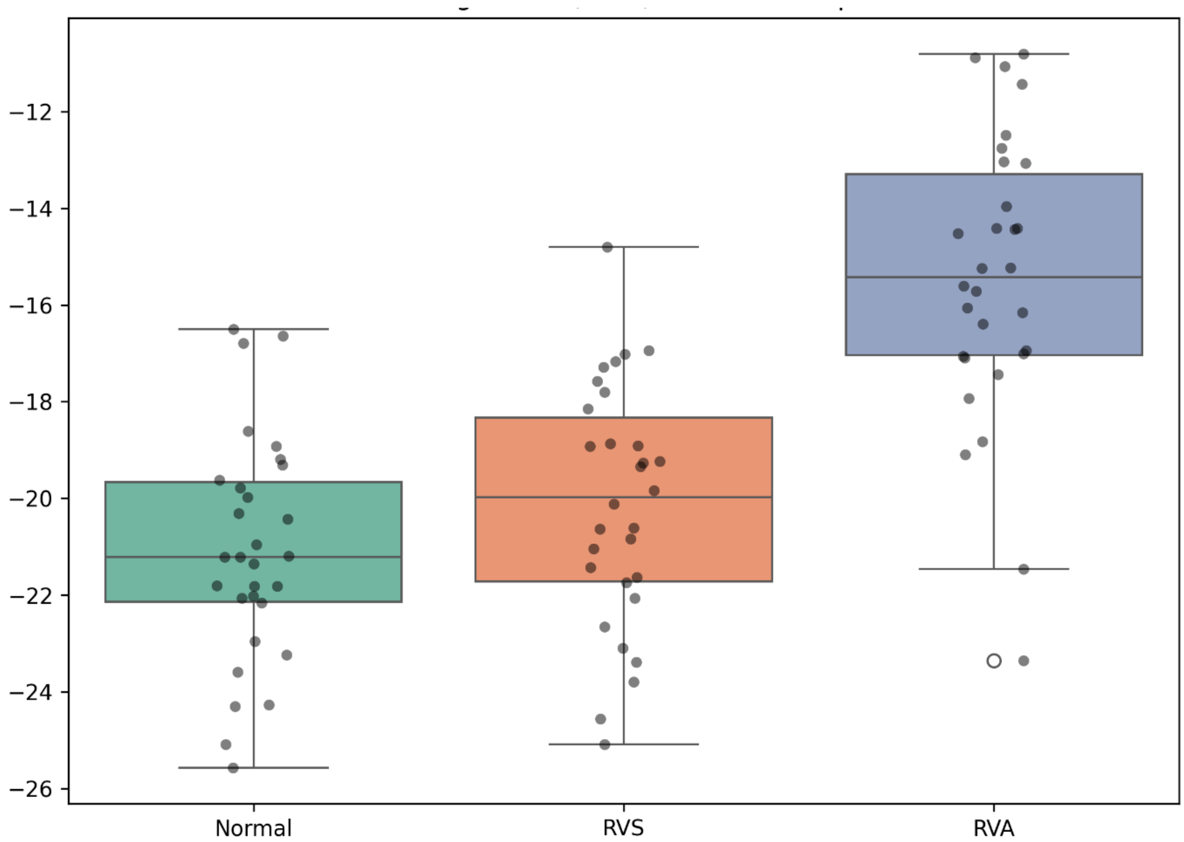

Figure 3. Inferior Segment Peak Systolic Strain (Inf. A) in Normal Subjects and Right Ventricular Pacing Sites

The comparison of inferior mid-segment peak systolic strain (SPSS-Inf. M) revealed a clear and progressive alteration in regional myocardial deformation across the three study groups. Normal subjects demonstrated preserved systolic function with a mean SPSS-Inf. M of $-20.6 \pm 2.6\%$, reflecting normal longitudinal shortening of the inferior mid-left ventricular segment. Patients with right ventricular septal pacing (RVS) showed slightly reduced but still comparable strain values ($-19.9 \pm 2.7\%$), and the difference between the RVS and normal groups did not reach statistical significance (p=0.068), suggesting that septal pacing largely maintains physiological contraction patterns in this region. In contrast, right ventricular apical pacing (RVA) was associated with a substantial reduction in strain magnitude, with mean SPSS-Inf. M values of $-16.2 \pm 2.8\%$, which were significantly less negative than those observed in normal subjects ($p<0.001$). Moreover, direct comparison between the two pacing strategies demonstrated significantly more impaired inferior mid-segment deformation in the RVA group compared with the RVS group (p=0.034). Collectively, these findings indicate that RVA pacing induces marked regional systolic dysfunction in the inferior mid-segment, whereas septal pacing better preserves myocardial mechanics and remains closer to the normal reference pattern (figure 4).

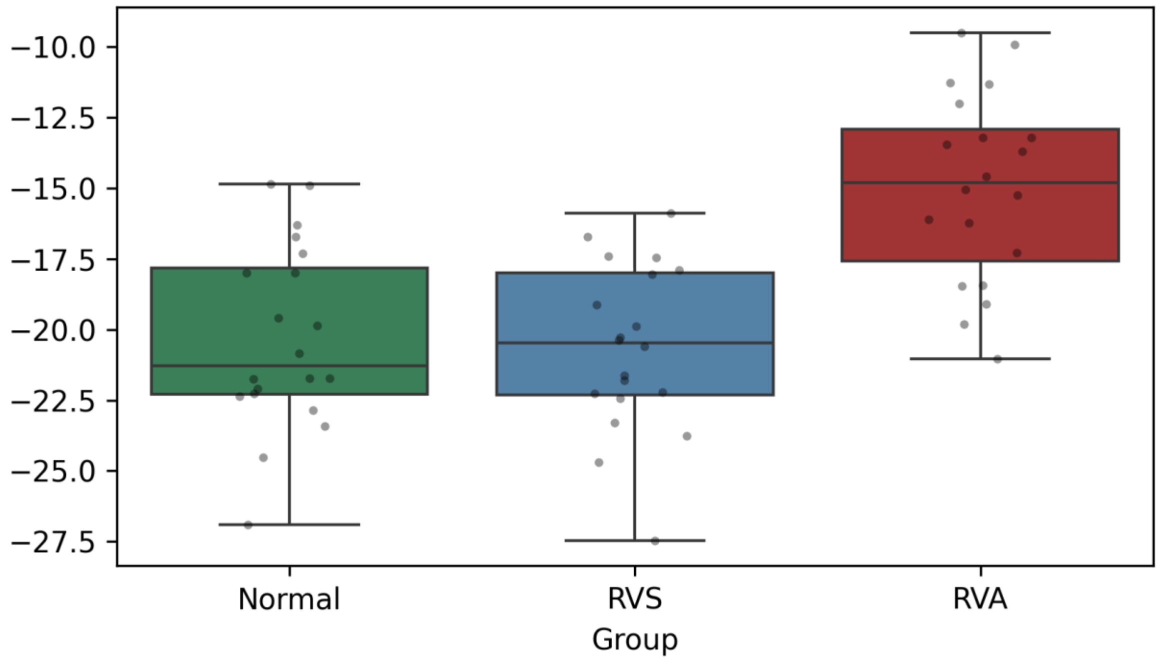

Figure 4. Comparison of Inferior Mid-Segment Peak Systolic Strain (Inf. M) Among Normal Subjects, Right Ventricular Septal Pacing, and Right Ventricular Apical Pacing

Discussion

The present study demonstrates that the site of right ventricular pacing exerts a substantial influence on left ventricular systolic performance and myocardial mechanics. In summary, patients with septal right ventricular pacing exhibited a global reduction in left ventricular contractile function and longitudinal myocardial deformation, yet these alterations were less pronounced and more homogeneous than those observed with apical pacing. In contrast, right ventricular apical pacing was associated with more severe attenuation of global strain, greater regional heterogeneity, and more marked impairment of inferior and mid-ventricular myocardial segments. Collectively, these findings suggest that septal pacing offers a mechanical advantage over apical pacing by more closely preserving physiological ventricular activation and limiting the extent of pacing-induced dyssynchrony and myocardial dysfunction (8,9).

The observed impairment of left ventricular systolic function in patients undergoing contrast, right ventricular apical pacing was associated with more severe attenuation of global strain, greater regional heterogeneity, and more marked impairment of inferior and mid-ventricular myocardial segments. Collectively, these findings suggest that septal pacing offers a mechanical advantage over apical pacing by more closely preserving physiological ventricular activation and limiting the extent of pacing-induced dyssynchrony and myocardial dysfunction (8,9).

The reduction in global longitudinal strain observed in the septal pacing group highlights the sensitivity of deformation-based indices in detecting early myocardial dysfunction. Longitudinal strain primarily reflects the function of sub endocardial fibers, which are particularly vulnerable to abnormalities in activation timing and wall stress. Even modest deviations from physiological conduction can impair the coordinated shortening of these fibers, leading to a uniform decrease in longitudinal deformation despite relatively preserved conventional systolic indices. This explains why strain analysis reveals mechanical impairment in septal pacing patients that may not be fully appreciated using traditional echocardiographic parameters alone (12,13).

Segmental analysis of septal myocardial deformation revealed that strain attenuation was not confined to a single septal region but extended across basal, mid, and apical segments. This diffuse involvement suggests that direct septal stimulation alters the longitudinal stress distribution along the entire septum rather than producing a focal mechanical disturbance. Early septal activation can generate paradoxical motion and inefficient force transfer between the septum and the left ventricular free wall, thereby compromising septal contribution to overall ventricular performance. The consistency of this effect across multiple septal levels underscores the global impact of septal pacing on interventricular mechanics (14,15).

Importantly, the reduction in myocardial deformation extended beyond the septum to involve non-septal regions, including the anterior, lateral, posterior, and inferior walls. This finding indicates that pacing-induced dyssynchrony propagates throughout the left ventricle, affecting regions remote from the pacing site. In a healthy heart, ventricular contraction relies on finely coordinated temporal interactions between different myocardial segments. Disruption of this coordination leads to abnormal load redistribution and altered myocardial fiber interactions, ultimately resulting in globally diminished strain even in regions not directly activated by the pacing stimulus (16,17).

In contrast to septal pacing, right ventricular apical pacing produced a more profound and heterogeneous impairment of left ventricular mechanics. Apical pacing initiates depolarization at a site far removed from the native conduction system, creating a markedly abnormal activation pattern characterized by delayed basal and lateral wall contraction. This reverse sequence of activation promotes substantial intraventricular dyssynchrony, inefficient myocardial work, and increased mechanical stress. Consequently, global longitudinal strain is more severely attenuated, and regional deformation becomes highly variable, reflecting the disorganized nature of ventricular contraction under apization at a site far removed from the native conduction system, creating a markedly abnormal activation pattern characterized by delayed basal and lateral wall contraction. This reverse sequence of activation promotes substantial intraventricular dyssynchrony, inefficient myocardial work, and increased mechanical stress. Consequently, global longitudinal strain is more severely attenuated, and regional deformation becomes highly variable, reflecting the disorganized nature of ventricular contraction under apical pacing conditions (18,19).

The stepwise deterioration in myocardial deformation observed from normal subjects to septal pacing and ultimately to apical pacing supports the concept of a continuum of pacing-induced mechanical dysfunction. As the pacing site deviates further from the physiological conduction pathway, the degree of electrical and mechanical dyssynchrony increases, leading to progressively worse ventricular performance. This gradient reinforces the importance of pacing site selection and suggests that even modest improvements in activation sequence, as achieved with septal pacing, can translate into meaningful preservation of myocardial mechanics (20,21).

The greater dispersion ofuced mechanical dysfunction. As the pacing site deviates further from the physiological conduction pathway, the degree of electrical and mechanical dyssynchrony increases, leading to progressively worse ventricular performance. This gradient reinforces the importance of pacing site selection and suggests that even modest improvements in activation sequence, as achieved with septal pacing, can translate into meaningful preservation of myocardial mechanics (20,21).

The greater dispersion of strain values and increased mechanical heterogeneity associated with apical pacing are particularly relevant from a pathophysiological perspective. Mechanical non-uniformity within the ventricle leads to regional differences in wall stress, energy consumption, and myocardial workload, which can promote adverse remodeling over time. Such heterogeneity is a recognized substrate for progressive ventricular dilation and functional decline. (22,23).

The relative preservation of inferior wall deformation in patients with septal pacing carries important clinical implications. The inferior wall plays a critical role in longitudinal shortening and overall left ventricular efficiency. Maintaining coordinated contraction in this region helps sustain effective ventricular emptying and limits compensatory stress on other myocardial segments. Septal pacing may better preserve inferior wall mechanics by avoiding excessive delays in activation and reducing abnormal tethering forces that commonly affect this region during apical pacing (24,25).

The pronounced impairment of inferior mid-ventricular deformation observed with apical pacing reflects the vulnerability of this region to pacing-induced dyssynchrony. Mid-ventricular segments serve as a mechanical bridge between apical and basal regions, and disruption of their contraction timing can have disproportionate effects on global ventricular mechanics. Apical pacing exaggerates temporal mismatches along this axis, whereas septal pacing maintains a more balanced activation pattern that partially preserves mid-segment function (26,27).

Overall, the findings of this study support the mechanical superiority of septal over apical right ventricular pacing in preserving left ventricular function. Although septal pacing does not fully replicate physiological activation and is associated with measurable reductions in myocardial deformation, the extent and heterogeneity of dysfunction are substantially less than those induced by apical pacing. These results emphasize the value of advanced echocardiographic techniques, particularly global and regional longitudinal strain analysis, in evaluating pacing-related myocardial effects.

Conclusion

This study demonstrates that the site of right ventricular pacing is a critical determinant of left ventricular mechanical performance. Although septal pacing does not fully replicate physiological ventricular activation, it is associated with relatively preserved global and regional myocardial deformation and reduced mechanical heterogeneity compared with apical pacing. In contrast, apical pacing induces pronounced global strain attenuation, significant regional dysfunction particularly in the inferior and mid-ventricular segments and greater dyssynchrony, reflecting unfavorable alterations in ventricular activation and contraction patterns. These findings underscore the value of strain-based echocardiographic assessment in detecting pacing-related myocardial dysfunction and support septal lead positioning as a mechanically superior strategy for preserving left ventricular function in patients requiring permanent right ventricular pacing.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Shah AM, et al., Echocardiographic Features of Patients with Heart Failure and Preserved Left Ventricular Ejection Fraction. *J Am Coll Cardiol* **2019**; 74:2858-73.

[2] Kurt M, Wang J, Torre-Amione G, Nagueh SF. Left atrial function in diastolic heart failure. *Circ Cardiovascular Imaging* **2009**; 2:10-5.

[3] Morris DA, Takeuchi M, Krisper M, Köhncke C, Bekfani T, Carstensen T, et al. Normal values and clinical relevance of left atrial myocardial function analysed by speckle-tracking echocardiography: multicenter study. *Eur Heart J Cardiovasc Imaging* **2015**; 16:364-72.

[4] Khan MS, et al., Left atrial function in heart failure with preserved ejection fraction: a systematic review and meta-analysis. *Eur J Heart Fail* **2020**; 22:472-85.

[5] Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* **2022**;145: e876-94.

[6] Bianco CM, Farjo PD, Ghaffar YA, Sengupta PP. Myocardial Mechanics in Patients with Normal LVEF and Diastolic Dysfunction. *JACC Cardiovasc Imaging* **2020**; 13:258-71.

[7] Sugimoto T, Bandera F, Generati G, Alfonzetti E, Bussadori C, Guazzi M. Left Atrial Function Dynamics During Exercise in Heart Failure: Pathophysiological Implications on the Right Heart and Exercise Ventilation Inefficiency. *JACC Cardiovasc Imaging* **2017**; 10:1253-64.

[8] Pugliese NR, De Biase N, Conte L, Gargani L, Mazzola M, Fabiani I, Natali A, Dini FL, Frumento P, Rosada J, Taddei S, Borlaug BA, Masi S. Cardiac Reserve and Exercise Capacity: Insights from Combined Cardiopulmonary and Exercise Echocardiography Stress Testing. *J Am Soc Echocardiogr* **2021**; 34:38-50.

[9] Obokata M, Negishi K, Kurosawa K, Arima H, Tateno R, Ui G, Tange S, Arai M, Kurabayashi M. Incremental diagnostic value of la strain with leg lifts in heart failure with preserved ejection fraction. *JACC Cardiovasc Imaging* **2013**; 6:749-58.

[10] Genovese D, Singh A, Volpato V, Kruse E, Weinert L, Yamat M, Mor-Avi V, Addetia K, Lang RM. Load Dependency of Left Atrial Strain in Normal Subjects. *J Am Soc Echocardiogr **2018***; 31:1221-8.

[11] Shah AM, Claggett B, Sweitzer NK, Shah SJ, Anand IS, O'Meara E, Desai AS, Heitner JF, Li G, Fang J, Rouleau J, Zile MR, Markov V, Ryabov V, Reis G, Assmann SF, McKinlay SM, Pitt B, Pfeffer MA, Solomon SD. Cardiac structure and function and prognosis in heart failure with preserved ejection fraction: findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) Trial. *Circ Heart Fail* **2014**; 7:740-51.

[12] Pritchett AM, Mahoney DW, Jacobsen SJ, Rodeheffer RJ, Karon BL, Redfield MM. Diastolic dysfunction and left atrial volume: a population-based study. *J Am Coll Cardiol* **2005**; 45:87-92.

[13] Cameli M, Mandoli GE, Loiacono F, Dini FL, Henein M, Mondillo S. Left atrial strain: a new

parameter for assessment of left ventricular filling pressure. *Heart Fail Rev* **2016**; 21:65-76.
[14] Venkateshvaran A, Tureli HO, Faxén UL, Lund LH, Tossavainen E, Lindqvist P. Left atrial reservoir strain improves diagnostic accuracy of the 2016 ASE/EACVI diastolic algorithm in patients with preserved left ventricular ejection fraction: insights from the KARUM haemodynamic database. *Eur Heart J Cardiovasc Imaging* **2022**; 23:1157-68.
[15] Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, 3rd, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P, Oh JK, Popescu BA, Waggoner AD. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* **2016**; 29:277-314.
[16] Inoue K, Khan FH, Remme EW, Ohte N, García-Izquierdo E, Chetrit M, Moñivas-Palomero V, Mingo-Santos S, Andersen ØS, Gude E, Andreassen AK, Wang TKM, Kikuchi S, Stugaard M, Ha JW, Klein AL, Nagueh SF, Smiseth OA. Determinants of left atrial reservoir and pump strain and use of atrial strain for evaluation of left ventricular filling pressure. *Eur Heart J Cardiovasc Imaging* **2021**; 23:61-70.
[17] Singh A, Addetia K, Maffessanti F, Mor-Avi V, Lang RM. LA Strain for Categorization of LV Diastolic Dysfunction. *JACC Cardiovasc Imaging* **2017**; 10:735-43.
[18] Frydas A, Morris DA, Belyavskiy E, Radhakrishnan AK, Kropf M, Tadic M, Roessig L, Lam CSP, Shah SJ, Solomon SD, Pieske B, Pieske-Kraigher E. Left atrial strain as sensitive marker of left ventricular diastolic dysfunction in heart failure. *ESC Heart Fail* **2020**; 7:1956-65.
[19] Brecht A, Oertelt-Prigione S, Seeland U, Rücke M, Hättasch R, Wagelöhner T, Regitz-Zagrosek V, Baumann G, Knebel F, Stangl V. Left Atrial Function in Preclinical Diastolic Dysfunction: Two-Dimensional Speckle-Tracking Echocardiography-Derived Results from the BEFRI Trial. *J Am Soc Echocardiogr* **2016**; 29:750-8.
[20] Morris DA, Belyavskiy E, Aravind-Kumar R, Kropf M, Frydas A, Braunauer K, Marquez E, Krisper M, Lindhorst R, Osmanoglou E, Boldt LH, Blaschke F, Haverkamp W, Tschöpe C, Edelmann F, Pieske B, Pieske-Kraigher E. Potential Usefulness and Clinical Relevance of Adding Left Atrial Strain to Left Atrial Volume Index in the Detection of Left Ventricular Diastolic Dysfunction. *JACC Cardiovasc Imaging* **2018**; 11:1405-15.
[21] Rimbas RC, Visoiu IS, Magda SL, Mihaila-Baldea S, Luchian ML, Chitroceanu AM, Hayat M, Mihalcea DJ, Dragoi-Galrinho-Antunes-Guerra R, Stefan M, Velcea A, Andronic AA, Lungeanu-Juravle L, Nicula AI, Vinereanu D. New insights into the potential utility of the left atrial function analysis in heart failure with preserved ejection fraction diagnosis. *PLoS One* **2022**;17: e0267962.
[22] Reddy YNV, Obokata M, Egbe A, Yang JH, Pislaru S, Lin G, Carter R, Borlaug BA. Left atrial strain and compliance in the diagnostic evaluation of heart failure with preserved ejection fraction. *Eur J Heart Fail* **2019**; 21:891-900.
[23] Freed BH, Daruwalla V, Cheng JY, Aguilar FG, Beussink L, Choi A, Klein DA, Dixon D, Baldridge A, Rasmussen-Torvik LJ, Maganti K, Shah SJ. Prognostic Utility and Clinical Significance of Cardiac Mechanics in Heart Failure with Preserved Ejection Fraction: Importance of Left Atrial Strain. *Circ Cardiovasc Imaging* **2016**.
[24] Nagy AI, Hage C, Merkely B, Donal E, Daubert JC, Linde C, Lund LH, Manouras A. Left atrial rather than left ventricular impaired mechanics are associated with the pro-fibrotic ST2 marker and outcomes in heart failure with preserved ejection fraction. *J Intern Med* **2018**; 283:380-91.
[25] Anker SD, Usman MS, Anker MS, Butler J, Böhm M, Abraham WT, et al. Patient phenotype profiling in heart failure with preserved ejection fraction to guide therapeutic decision making. A scientific statement of the Heart Failure Association, the European Heart Rhythm Association of the European Society of Cardiology, and the European Society of Hypertension. *Eur J Heart Fail* **2023**; 25:936-55.
[26] Fung JW, Sanderson JE, Yip GW, Zhang Q, Yu CM. Impact of atrial fibrillation in heart failure with normal ejection fraction: a clinical and echocardiographic study. *J Card Fail* **2007**; 13:649-55.
[27] Reddy YNV, Obokata M, Verbrugge FH, Lin G, Borlaug BA. Atrial Dysfunction in Patients with Heart Failure with Preserved Ejection Fraction and Atrial Fibrillation. *J Am Coll Cardiol* **2020**; 76:1051-64.