https://doi.org/10.35336/VA-1519

MYOCARDIAL WORK AND MANIFESTATION OF CARDIAC DYSFUNCTION IN PATIENTS WITH PERMANENT LONG-TERM STIMULATION OF THE RIGHT VENTRICLE

E.V.Kukharchuk, E.M.Rimskaya, S.V.Dobrovolskaya, G.S.Tarasovsky, M.A.Saidova, S.P.Golitsyn

FSBI «National Medical Research Center for Cardiology named after academician E.I.Chazov» of the MH RF, Russia, Moscow, 15A Akademik Chazov str.

Aim. To evaluate the relationship between mechanical dyssynchrony, defined as myocardial work components and manifestations of cardiac dysfunction in patients with permanent right ventricular pacing.

Material and methods. The study included 55 patients (25 men, mean age 63±12 years) with implanted permanent pacemakers and left bundle branch block type paced QRS complex morphology and 20 healthy volunteers (15 men, mean age 32.4±7.4 years). The patients included in the study were examined twice: initially before pacemaker implantation and again at the time of study inclusion. A standard echocardiographic study was performed with an additional assessment of the degree of global longitudinal strain (GLS) and myocardial performance parameters - global constructive myocardial work (GCW), global wasted myocardial work (GWW), global work index (GWI) and global work efficiency (GWE) before and after pacemaker implantation. In all patients, segments with maximum and minimum GWI were determined. The parameters of myocardial function were analyzed depending on the localization of the pacemaker stimulating head, and a comparison was made with the parameters of myocardial function in 20 healthy volunteers.

Results. In 18.2% of patients, against the background of right ventricular pacing, a decrease in left ventricular ejection fraction (LVEF) from normal values to 55 (53.5; 55.8) % was recorded, in 5 (50%) of them, signs of chronic heart failure functional class II-III were recorded. An increase in the degree of tricuspid regurgitation (TR) was found in 29.9% of patients. In patients against the background of long-term pacing, the GLS, GWI, GCW and GWE indicators were statistically significantly lower than in the group of healthy volunteers, and the GWW indicator was higher than the reference values of the control group. Patients with an apical-septal localization of the stimulating electrode head have statistically lower GWI and GCW values than patients with a more “basal” location of the electrode head in the middle third of the interventricular septum (1042.23±308.85 versus 1430±514 mmHg%, p = 0.049 and 1457 (1256; 1766) versus 2089 (1831; 2186) mmHg%, p = 0.04).

Conclusion. The localization of the stimulating electrode head does not affect the development of negative dynamics of LVEF and TR, but has a significant effect on the myocardial performance indicators. In patients with the apical-septal localization of the electrode, the worst values of the constructive work of the myocardium were noted, and in patients with the localization of the stimulating electrode head in the right ventricular outflow tract area, the best indicators of the constructive work of the myocardium were noted.

Key words: pacing-induced cardiomyopathy; mechanical dyssynchrony; myocardial work; tricuspid regurgitation; left bundle branch block

Conflict of interest: none.
Funding: none.
Received: 30.04.2025 **Revision received:** 01.08.2025 **Accepted:** 04.08.2025
Corresponding Author: Kukharchuk Elizaveta, E-mail: ekukharchuk98@mail.ru

E.V.Kukharchuk - ORCID ID 0009-0007-5062-5374, E.M.Rimskaya - ORCID ID 0000-0002-0063-5474, S.V.Dobrovolskaya - ORCID ID 0000-0003-0580-393X, G.S.Tarasovsky - ORCID ID 0000-0002-2143-8912, M.A.Saidova - ORCID ID 0000-0002-3233-1862, S.P.Golitsyn - ORCID ID 0000-0001-9913-9974

The manuscript participated in the competition for the best scientific work of young scientists in clinical and fundamental arrhythmology within the framework of the XI All-Russian Congress of Arrhythmologists.

For citation: Kukharchuk EV, Rimskaya EM, Dobrovolskaya SV, Tarasovsky GS, Saidova MA, Golitsyn SP. Myocardial work and manifestation of cardiac dysfuction in patients with permament long-term stimulation of the right ventricle. *Journal of Arrhythmology.* 2025;32(4): 13-21. https://doi.org/10.35336/VA-1519.

Chronic heart failure (CHF) is a highly prevalent pathological condition characterised by a substantial reduction in quality of life and high patient mortality [1-3]. Results of large prospective clinical trials, such as DAVID, PACE, and BLOCK-HF, indicate that right ventricular pacing (RVP) plays a significant role among the aetiological factors associated with the development of CHF [4-6]. Observational data from patients undergoing permanent RVP for bradyarrhythmias, as well as experimental studies in laboratory animals, demonstrate that RVP may lead to pathogenetic mechanisms similar to those responsible for CHF development in the presence of left bundle branch block (LBBB) [4, 7-10].

Alterations in ventricular myocardial contraction mechanics during right ventricular stimulation, particularly with a high percentage of paced ventricular complexes, may result in the development of cardiac dysfunction even in individuals with preserved left ventricular ejection fraction (LVEF). This condition has been termed pacing-induced cardiomyopathy (PICM) in the literature. The reported incidence of PICM varies considerably among studies, ranging from 5.9% to 20.5% in patients with right ventricular pacing [11]. At the same time, the clinical manifestations of PICM may differ substantially from those of cardiomyopathy caused by electromechanical dyssynchrony secondary to LBBB [12].

It is conceivable that, in addition to electromechanical dyssynchrony, other factors contribute to the development of PICM and associated cardiac dysfunction. These include tricuspid regurgitation resulting from lead-leaflet interaction (compression, impingement, or adhesion) and the position of the pacing lead itself. Contemporary echocardiographic (echocardiography) techniques enable assessment of the contribution of each of these factors to the pathogenesis of PICM. In particular, evaluation of myocardial contraction mechanics has become possible through methods assessing myocardial work by constructing pressure-strain loops. This echocardiographic approach characterises left ventricular contraction efficiency by quantifying wasted energy and constructive work and may provide fundamentally new insights into the role of electromechanical dyssynchrony in the development of PICM in patients undergoing permanent RVP [13].

Thus, the aim of the present study was to assess the relationship between mechanical dyssynchrony-defined by myocardial work parameters-and manifestations of cardiac dysfunction in patients with permanent right ventricular pacing.

MATHERIALS AND METHODS

The study protocol was approved by the local ethics committee. Written informed consent was obtained from all participants prior to enrolment.

A total of 55 patients were enrolled in the study (25 men, 45.5%; mean age 63 ± 12 years) with implanted permanent pacemakers (PPMs): 52 (94.5%) dual-chamber and 3 (5.5%) single-chamber devices. In all cases, paced QRS complexes demonstrated a LBBB morphology. Indications for PPM implantation included high-grade atrioventricular block or the brady-systolic form of atrial fibrillation.

The primary diagnoses at the time of device implantation (Table 1) were arterial hypertension in 36 patients (65.5%), coronary artery disease (CAD) in 4 patients (7.3%), iatrogenic complete atrioventricular block following radiofrequency catheter ablation of paroxysmal atrioventricular nodal re-entrant tachycardia in 3 patients (5.5%), and congenital high-grade atrioventricular block in 2 patients (3.6%). In 10 patients (18.1%), conduction disturbances were idiopathic in nature. Patients with obstructive coronary atherosclerosis (n = 4; 7.3%) underwent timely myocardial revascularisation performed either before or after PPM implantation. At the time of implantation, 6 patients (10.9%) had type 2 diabetes mellitus.

At the time of study inclusion, 4 patients (7.3%) with severe aortic valve stenosis and 2 patients (3.6%) with manifestations of heart failure secondary to tachysystolic atrial fibrillation were receiving therapy for CHF. The remaining patients were treated with ACE inhibitors / ARBs / sacubitril-valsartan for arterial hypertension. Beta-blockers were prescribed for the presence of coronary artery disease and in 12 patients (21.8%) as antiarrhythmic therapy for atrial fibrillation.

Patients with a known history of prior myocardial infarction and/or echocardiographic evidence of hypo- or akinetic myocardial segments, as well as patients with reduced LVEF of any aetiology, haemodynamically significant valvular heart disease, or other structural myocardial disorders at the time of PPM implantation were not included in the study.

At the time of device implantation, all enrolled patients demonstrated preserved global left ventricular systolic function. LVEF was ≥60% in 100% of patients, and

Table 1.
Baseline characteristics of patients included in the study

Parameter	Value
Age (years), Me [IQR]	63[52-76]
Men, n (%)	25 (45.5)
Women, n (%)	30 (54.5)
Coronary artery disease, n (%)	4 (7.3)
Arterial hypertension, n (%)	36 (65.5)
Diabetes mellitus, n (%)	6 (10.9)
Paroxysmal AF, n (%)	12(21.8)
Persistent AF, n (%)	1(1.8)
Permanent AF, n (%)	3 (5.5)
CHF functional class I*, n (%)	1 (1.8)
CHF functional class II*, n (%)	3 (5.5)
LV end-diastolic diameter (cm), M (SD)	5.1±0.5
LV end-systolic diameter (cm), M (SD)	3.3±0.5
LVEF (%), Me [IQR]	60 [60; 60]
Paced QRS duration** (ms), M (SD)	158±28
Medical therapy at the time of pacemaker implantation	
ACEI / ARBs / valsartan + sacubitril, n (%)	37 (67.3)
Beta-blockers, n (%)	32 (58.2)
Aldosterone antagonists, n (%)	18 (32.7)
Loop diuretics, n (%)	4 (7.3)
Acetylsalicylic acid, n (%)	14 (25.5)
Anticoagulant therapy, n (%)	16 (29.1)
Statins, n (%)	20 (36.4)
No therapy, n (%)	6 (10.9)

Note: AF - atrial fibrillation; * - assessed at the time of permanent pacemaker (PPM) implantation; CHF - chronic heart failure; FC - functional class; LV - left ventricle; LVEDD - left ventricular end-diastolic diameter; LVESD - left ventricular end-systolic diameter; LVEF - left ventricular ejection fraction; ** - paced QRS complex; ARB - angiotensin II receptor blockers; ACEI - inhibitors angiotensin-converting enzyme inhibitors.

no echocardiographic signs of regional wall motion abnormalities were detected. Cardiac chamber dimensions were within normal limits: left ventricular end-diastolic diameter was 5.1 (4.6; 5.6) cm and end-systolic diameter was 3.3 (2.8; 3.8) cm. In all patients, pacing lead tip localisation for right ventricular pacing was analysed based on operative reports. The paced QRS duration was 158 ± 28 ms. Baseline patient characteristics are presented in Table 1.

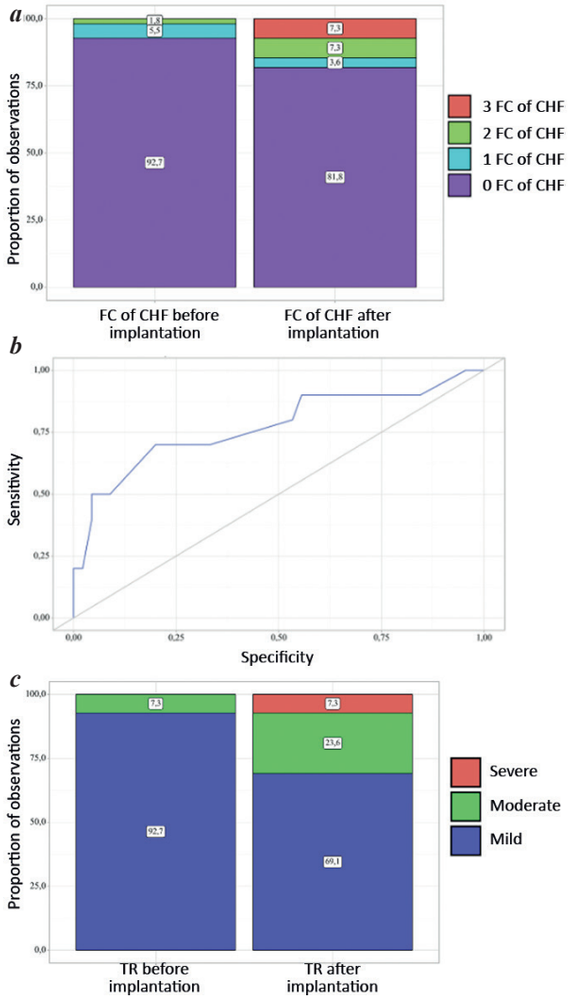

Figure 1. Changes in the functional class (FC) of chronic heart failure (CHF)during right ventricular pacing (a); ROC curve (b) illustrating the predictive value of paced QRS duration during right ventricular pacing for left ventricular ejection fraction decline (AUC = 0.772, sensitivity 70%, specificity 80%); distribution of patients according to the severity of tricuspid regurgitation (c).

Patients included in the study underwent examination twice: initially prior to PPM implantation and subsequently at the time of study inclusion. At inclusion, the duration of RVP was at least 6 months and amounted to 95.5 (33.5; 126.7) months. In addition, 20 healthy volunteers were included (15 men, 75%; mean age 32.4 ± 7.4 years), in whom clinical and instrumental evaluation revealed no evidence of organic cardiovascular disease and no pathological electrocardiographic findings.

Transthoracic echocardiography with assessment of left ventricular myocardial deformation and work

All examined patients and healthy volunteers, in addition to standard echocardiographic assessment, underwent evaluation of left ventricular (LV) global longitudinal strain (GLS, %) and myocardial work. For calculation of these parameters, echocardiographic acquisition was performed using a Vivid E9 ultrasound system (GE Healthcare, USA) equipped with an M5S phased-array transducer. Image acquisition was carried out from the apical views in accordance with current recommendations and using a previously described methodology [14].

To calculate myocardial work indices and GLS, the recorded images were analysed offline using an EchoPac PC workstation, Version 204 (GE Healthcare, USA). Based on GLS data, arterial blood pressure values, and the timing of mitral and aortic valve opening and closure manually defined on the acquired images, the software automatically constructed pressure-strain loops and calculated myocardial work indices both for each of the 17 left ventricular segments individually and for the myocardium as a whole.

The analysed myocardial work parameters included:

1. Global constructive work (GCW, mmHg%), defined as the arithmetic sum of work performed during myocardial shortening in systole and myocardial lengthening during isovolumic relaxation;
2. Global wasted work (GWW, mmHg%), calculated as the arithmetic sum of work expended during myocardial lengthening in systole and myocardial shortening during the isovolumic relaxation phase;
3. Global work index (GWI, mmHg%), corresponding to the area of the pressure-strain loop and characterising the work performed throughout systole, specifically during the time interval from mitral valve closure to mitral valve opening;
4. Global work efficiency (GWE, %), expressed as the percentage ratio of constructive work to the sum of constructive and wasted work [4].

Using the 17-segment left ventricular model (“bull’s-eye” plot), segments demonstrating maximal constructive work and maximal wasted work were identified for each patient.

Table 2.

Echocardiographic parameters of myocardial deformation and myocardial work in patients with long-term right ventricular pacing (RVP) and healthy volunteers

	Patients with long-term RVP (n = 55)	Healthy volunteers (n = 20)	p
GLS, %	-12.7 [-13.7; -11.8]	-18.0 [-18.8; -17.5]	<000.1
GWI, mmHg%	1211 [1101; 1321]	1588[1402; 1747]	<000.1
GCW, mmHg%	1719[1603; 1834]	1909 [1736; 2115]	<000.1
GWE, %	82 [78; 88]	94 [93; 95]	<000.1
GWW, mmHg%	312 [210; 432]	108 [74.3; 137.3]	<000.1

Note: RVP - right ventricular pacing; GLS - global longitudinal strain; GWI - global myocardial work index; GCW - global constructive work; GWE - global work efficiency; GWW - global wasted work.

Statistical analysis

Statistical analysis was performed using StatTech software v.4.7.0 (StatTech LLC, Russia). Quantitative variables were assessed for normality of distribution using the Kolmogorov-Smirnov test. Quantitative variables with a normal distribution were described using arithmetic means (M) and standard deviations (SD). The representativeness of mean values was expressed by 95% confidence intervals (95% CI). In the absence of normal distribution, quantitative data were described using the median (Me) and lower and upper quartiles (Q1-Q3).

Categorical variables were described using absolute values and percentages. Ninety-five per cent confidence intervals for proportions were calculated using the Clopper-Pearson method. Comparison of proportions in contingency tables was performed using Pearson's chi-square test. The strength of association between categorical variables was assessed using Cramér's V, with values interpreted according to the recommendations of Rea and Parker (2014). Differences were considered statistically significant at $p < 0.05$.

RESULTS

Localisation of the pacing lead tip in patients with RVP

Among the examined patients, the position of the RVP lead tip was basal septal in 19 patients (34.5%), mid-septal in 10 patients (18.2%), apical or near-apical (apical-septal) in 22 patients (40.0%), and located in the right ventricular outflow tract (RVOT) in 4 patients (7.3%).

Patients with different pacing lead tip localisations were comparable with respect to sex, age, baseline echocardiographic parameters (left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left ventricular ejection fraction), duration of right ventricular pacing, paced QRS duration, and comorbid conditions.

Manifestations of cardiac dysfunction during long-term RVP

Dynamics of LVEF and CHF functional class (FC) during RVP

How its indicated above, at the time of study inclusion the duration of RVP was 95.5 (33.5; 126.7) months. According to echocardiographic assessment performed during long-term RVP, a reduction in LVEF to 55.0 (53.5; 55.8)% was documented in 10 patients (18.2%); among these, 5 patients (50%) demonstrated signs of CHF of FC II-III (Fig. 1a).

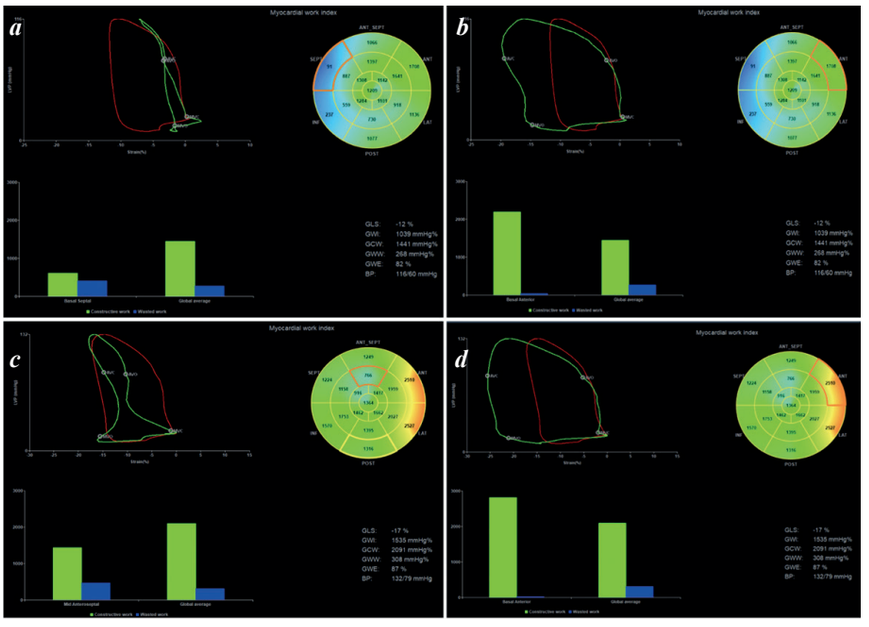

Figure 2. Examples of myocardial work in patients with apical (a, b) and mid-septal (c, d) localization of the right ventricular pacing lead. Pressure-strain loops are shown for left ventricular segments with maximal wasted myocardial work (green curve) (a, c) and maximal constructive myocardial work (b, d), compared with global myocardial work of the entire left ventricle (red curve).

Table 3.

Descriptive statistics of quantitative variables according to right ventricular pacing lead tip location.

Parameter	Pacing lead location				p
	Mid-septal (n=10)	Apical-septal (n=22)	Basal-septal (n=19)	RVOT (n = 4)	
GLS, mmHg%	-12,50 [-16,25; -10,25]	-13,00 [-14,00; -11,25]	-13,00 [-16,00; -10,50]	-15,50 [-16,50; -14,25]	0,393
GWE, mmHg%	86 [77; 88]	82 [79; 86]	82 [76; 91]	88 [82; 93]	0,495
GWI, mmHg%	1429,70±513,93	1042,23±308,85	1228,32±399,81	1515,00±244,85	0,025
GCW, mmHg%	2089,00 [1830,75; 2186,25]	1457,00 [1256,25; 1766,25]	1734,00 [1397,50; 1964,50]	2017,00 [1919,25; 2117,75]	0,017
GWW, mmHg%	355 [262; 448]	336 [235; 456]	262 [151; 354]	292 [139; 448]	0,319
Max, mmHg%	2710±791	2036±588	2254±443	2508±208	0,023
Min, mmHg%	587,00 [121,00; 786,25]	-2,50 [-234,50; 356,50]	337,00 [-30,50; 738,00]	549,00 [367,50; 781,75]	0,022

Note: Max - maximal constructive myocardial work; Min - maximal wasted myocardial work. Comparisons were performed using the Kruskal-Wallis test.

In addition to reduced LVEF, these patients were characterised by larger LV dimensions (LV end-diastolic diameter 5.5 cm vs 5.0 cm, p = 0.006; LV end-systolic diameter 3.8 cm vs 3.2 cm, p < 0.001), a significantly longer paced QRS duration (p = 0.002), and a higher prevalence of coronary artery disease in medical history (p = 0.016). At the same time, sex, age, duration of pacing, and pacing lead tip localisation did not have a significant impact on changes in LVEF.

Receiver operating characteristic (ROC) analysis demonstrated that a paced QRS duration ≥180 ms may be considered associated with a reduction in LVEF during long-term RVP (AUC = 0.772, sensitivity 70%, specificity 80%) (Fig. 1b). It should be noted that paced QRS duration did not depend on the localisation of the RVP lead (p = 0.373). It is likely that additional factors, such as baseline left ventricular myocardial condition and distal conduction disturbances, may also influence paced QRS duration during RV.

Changes in tricuspid valve function during long-term RVP

A pacing lead positioned in the right ventricle mechanically interacts with the tricuspid valve leaflets, which may potentially impair valve function. Therefore, the dynamics of tricuspid regurgitation (TR) were assessed under conditions of long-term (≥6 months) RVP. It should be noted that echocardiographic evaluation did not reveal any cases of leaflet perforation or compression by the pacing lead.

However, the proportion of patients with mild TR decreased from 92.7% to 69.1% (a reduction of 23.6%), whereas the proportion with moderate TR increased from 7.3% to 23.6% (an increase of 16.3%). In addition, severe TR was identified in 7.3% of patients during long-term RVP, whereas no cases of severe TR were present at baseline (Fig. 1c).

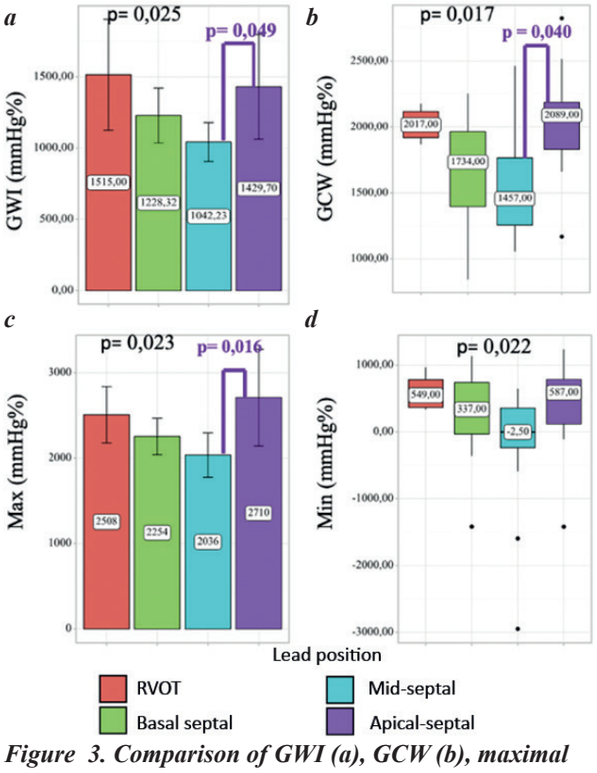

Figure 3. Comparison of GWI (a), GCW (b), maximal constructive work (c), and wasted work (d) across different right ventricular pacing lead positions. Patients with apical-septal lead localization (blue bars) demonstrate the least favorable myocardial work parameters.

Overall, progression of TR severity was observed in 16 patients (29.9%). Patients with and without worsening of TR differed significantly in CHF FC, while no statistically significant differences were found in other clinical or instrumental parameters.

Myocardial work parameters in patients with long-term RVP

When comparing myocardial work parameters and GLS calculated in the group of patients with RVP with those of healthy volunteers, substantial differences were identified. Specifically, GLS, GWI, GCW, and GWE values in the study group were significantly lower than those observed in healthy controls, while GWW was higher than the reference values of the control group (Table 2).

Thus, despite preserved LVEF in most cases, patients with RVP were characterised by less efficient myocardial work. It should be noted that segmental analysis revealed, in the same patients, LV segments with a predominance of both constructive and wasted myocardial work (Fig. 2). However, the distribution of these segments was more heterogeneous than that previously described in patients with electromechanical dyssynchrony due to LBBB [15].

The high variability of myocardial work parameters observed in the study group served as the basis for identifying factors influencing these indices. Statistical analysis revealed trends toward weak correlations between global work efficiency (GWE) and patient age (r = -0.273, p = 0.044). In addition, correlations were identified between body mass index and GLS, GWE, and GWI (r = 0.305, p = 0.025; r = -0.307, p = 0.024; r = 0.314, p = 0.021, respectively). Furthermore, correlation analysis demonstrated an association between paced QRS duration during RVP and GLS (weak positive correlation, r = 0.263, p = 0.048), as well as GWE (weak negative correlation, ρ = -0.234, p = 0.045).

Moderate correlations were also identified between RVP lead tip localisation and GWI (r = 0.407, p = 0.025), GCW (r = 0.443, p = 0.017), maximal myocardial work (Max) (r = 0.411, p = 0.023), and minimal myocardial work (Min) (r = 0.420, p = 0.022).

Comparative analysis of myocardial work parameters between patient groups stratified by RVP lead localisation (Table 3, Fig. 3) demonstrated that patients with apical-septal lead positioning had significantly lower GWI and GCW values than patients with a more “basal” lead position in the mid-portion of the interventricular septum (GWI: 1042.23 ± 308.85 vs 1430 ± 514 mmHg%, p = 0.049; GCW: 1457 [1256; 1766] vs 2089 [1831; 2186] mmHg%, p = 0.04).

At the same time, patients with apical-septal lead localisation exhibited the lowest values of both maximal constructive work (Max) and maximal wasted work (Min). In the segment with maximal wasted myocardial work in a patient with apical-septal lead positioning (Fig. 3), the value of constructive myocardial work (green bar) was nearly comparable to the value of wasted myocardial work (blue bar).

In contrast, in the segment with maximal wasted myocardial work in a patient with mid-septal lead localisation (Fig. 3), constructive myocardial work (green bar) predomi-

nated over wasted myocardial work (blue bar). Thus, the least efficient myocardial contraction was observed in patients with apical-septal pacing lead localisation. Patients with more "basal" lead positions (interventricular septum or right ventricular outflow tract) demonstrated more favourable indices of myocardial contraction mechanics (Fig. 2 and 3).

DISCUSSION

Within this study, the role of several potential pathogenetic factors contributing to the development of cardiac dysfunction under conditions of long-term RVP was assessed. The most significant determinant in the development of CHF was a reduction in LVEF. At the same time, it was found that despite the extremely long duration of RVP (95.5 [33.5; 126.7] months), both a decline in LVEF and the emergence of CHF symptoms were observed in only 18.2% of patients. These results are fully consistent with data from a larger retrospective study by S. Khurshid et al. [16]. However, the magnitude of LVEF reduction associated with RVP in that study was considerably more pronounced (from 62.1% to 36.2% over a mean follow-up of 3.3 years) than that observed in our cohort (from >60% to 55%), despite the fact that the proportion of right ventricular pacing in our patients (96.9%) exceeded that reported in the aforementioned study (≥20%).

Given that a high burden of RVP leads to LVEF decline only in a subset of patients, we analysed several factors potentially associated with this phenomenon. First, tricuspid valve dysfunction-potentially caused by mechanical fixation of valve leaflets by the pacing lead-was excluded in all cases.

The study results indicate a substantial role of paced QRS duration in the development of adverse LVEF dynamics during long-term RVP. A paced QRS duration ≥180 ms in this patient population was associated with a high likelihood of LVEF reduction (Fig. 2b), in agreement with previously published data [16-19].

In addition, the presence of CAD was identified as a predisposing factor for LVEF decline during long-term RVP. Notably, none of the patients had a history of myocardial infarction, as this diagnosis constituted an exclusion criterion for the study. This finding suggests that an initially compromised myocardial substrate is an important prerequisite for long-term RVP-particularly in the setting of a high pacing burden and marked QRS prolongation-to exert its deleterious effect in the form of reduced LVEF.

Another manifestation of cardiac dysfunction was progression of TR, observed in 18.2% of patients, in the absence of leaflet fixation or structural damage to the valve or subvalvular apparatus. The results of the present study, as well as data from a large meta-analysis, allow one to unequivocally conclude that TR progression is not related to pacing lead tip localisation [20]. It is likely that the increase in TR severity in patients with RVP is attributable to mechanisms of electromechanical dyssynchrony that differ somewhat from those observed in patients with true LBBB. Previous studies have reported TR progression during RVP within 12 months in up to 43% of patients with leadless pacemakers [21]. These observations underscore the importance of further investigation into the mechanisms of electromechanical dyssynchrony associated with RVP.

This study is the first to provide a detailed analysis of myocardial work parameters in patients with long-term RVP and the factors influencing these indices. The results demonstrate a statistically significant reduction in GCW, GWI, and GWE in this patient population, along with a significant increase in wasted work (GWW). The decline in these parameters-reflecting myocardial inefficiency-even in patients with preserved LVEF, as was the case for the majority of our cohort, may represent an early marker of progressive myocardial dysfunction. The validity of this assumption should be confirmed in a dedicated prospective study.

In addition, pronounced asynchrony of myocardial work across different LV segments was identified, resembling the dyssynchronous contraction pattern seen in LBBB, but with greater topographic variability of asynchronous segments [15]. In this context, a targeted analysis of the impact of pacing lead tip localisation on myocardial work parameters was conducted. The poorest values of constructive myocardial work were observed in patients with apical-septal lead positioning, whereas the most favourable constructive work indices were found in patients with pacing lead localisation in the right ventricular outflow tract. This finding provides an additional pathogenetic explanation for the adverse prognostic impact of apical right ventricular lead placement in patients with RVP [6, 22-24]. As in other studies, patient age and the presence of CAD were identified as factors exerting a negative influence on myocardial work parameters [25].

Study limitation

A substantial limitation of the present study is its cross-sectional and retrospective design, which may have resulted in the omission of patients who experienced more pronounced clinical deterioration in the setting of PICM. It is highly likely that time represents a critical factor in the realisation of the adverse effects of electrical dyssynchrony and the development of PICM.

It should also be noted that right ventricular function was not analysed in the present study, although it may also contribute to the progression of tricuspid regurgitation.

CONCLUSION

The results of the present study indicate that RVP is associated with a reduction in LVEF in 18.2% of patients, worsening of TR in 29% of patients, and a decrease in myocardial work parameters. Factors contributing to the development of reduced LVEF were a prolonged paced QRS duration and a history of CAD. Apical-septal positioning of the RVP lead did not contribute to adverse changes in LVEF or TR; however, it had a significant impact on myocardial work parameters. The reduction in myocardial work observed in patients with preserved LVEF suggests that this phenomenon may represent a potential early marker of subsequent cardiac dysfunction.

REFERENCES

1. Benjamin EJ, Virani SS, Callaway CW et al. American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2018 Update:

A Report From the American Heart Association. *Circulation.* 2018;137(12): e67-e492. https://doi.org/10.1161/CIR.0000000000000558.
2. Störk S, Handrock R, Jacob J, et al. Epidemiology of heart failure in Germany: a retrospective database study. *Clin Res Cardiol.* 2017;106(11): 913-922. https://doi.org/10.1007/s00392-017-1137-7.
3. Conrad N, Judge A, Tran J, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. *Lancet.* 2018;391(10120): 572-580. https://doi.org/10.1016/S0140-6736(17)32520-5.
4. Wilkoff BL, Cook JR, Epstein AE, et al. Dual Chamber and VVI Implantable Defibrillator Trial Investigators. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. *JAMA*. 2002;288(24): 3115-23. https://doi.org/10.1001/jama.288.24.3115.
5. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. MOde Selection Trial Investigators. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation.* 2003;107(23): 2932-7. https://doi.org/10.1161/01.CIR.0000072769.17295.B1.
6. Yu CM, Fang F, Luo XX, et al. Long-term follow-up results of the pacing to avoid cardiac enlargement (PACE) trial. *Eur J Heart Fail.* 2014;16(9): 1016-25. https://doi.org/10.1002/ejhf.157.
7. Lamas GA, Lee KL, Sweeney MO, et al. Mode Selection Trial in Sinus-Node Dysfunction. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. *N Engl J Med.* 2002;346(24): 1854-62. https://doi.org/10.1056/NEJMoa013040.
8. Prinzen FW, Peschar M. Relation between the pacing induced sequence of activation and left ventricular pump function in animals. *Pacing Clin Electrophysiol.* 2002;25(4 Pt 1): 484-98. https://doi.org/10.1046/j.1460-9592.2002.00484.x.
9. Delgado V, Bax JJ. Assessment of systolic dyssynchrony for cardiac resynchronization therapy is clinically useful. *Circulation.* 2011;123(6): 640-55. https://doi.org/10.1161/CIRCULATIONAHA.110.954404.
10. Barsheshet A, Wang PJ, Moss AJ, et al. Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy). *J Am Coll Cardiol.* 2011;57(24): 2416-23. https://doi.org/10.1016/j.jacc.2010.12.041.
11. Khurshid S, Frankel DS. Pacing-Induced Cardiomyopathy. *Card Electrophysiol Clin.* 2021;13(4): 741-753. https://doi.org/10.1016/j.ccep.2021.06.009.
12. Merchant FM, Mittal S. Pacing induced cardiomyopathy. *J Cardiovasc Electrophysiol.* 2020;31(1): 286-292. https://doi.org/10.1111/jce.14277.
13. Russell K, Eriksen M, Aaberge L, et al. Assessment of wasted myocardial work: a novel method to quantify energy loss due to uncoordinated left ventricular contractions. *Am J Physiol Heart Circ Physiol.* 2013;305(7): H996-1003. https://doi.org/10.1152/ajpheart.00191.2013
14. Roberto M Lang, Luigi P Badano, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal - Cardiovascular Imaging.* 2015;16(3): 233-271, https://doi.org/10.1093/ehjci/jev014.
15. Rimskaya EM, Dobrovolskaya SV, Kukharchuk EV, et al. Myocardial work in electrical dyssynchrony due to left bundle branch block. *Russian Journal of Cardiology.* 2025;30(2): 5955. (In Russ.). https://doi.org/10.15829/1560-4071-2025-5955.
16. Khurshid S, Epstein AE, Verdino RJ, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy. *Heart Rhythm.* 2014;11(9): 1619-25. https://doi.org/10.1016/j.hrthm.2014.05.040.
17. Kim JH, Kang KW, Chin JY, et al. Major determinant of the occurrence of pacing-induced cardiomyopathy in complete atrioventricular block: a multicentre, retrospective analysis over a 15-year period in South Korea. *BMJ Open.* 2018; 8(2): e019 - 048. https://doi.org/10.1136/bmjopen-2017-019048.
18. Cho SW, Gwag HB, Hwang JK, et al. Clinical features, predictors, and long-term prognosis of pacing-induced cardiomyopathy. *Eur J Heart Fail.* 2019; 21(5): 643-651. https://doi.org/10.1002/ejhf.1427.
19. Lee SA, Cha MJ, Cho Y, et al. Paced QRS duration and myocardial scar amount: predictors of long-term outcome of right ventricular apical pacing. *Heart Vessels.* 2016;31(7): 1131-9. https://doi.org/10.1007/s00380-015-0707-8.
20. Schleifer JW, Pislaru SV, Lin G, et al. Effect of ventricular pacing lead position on tricuspid regurgitation: A randomized prospective trial. *Heart Rhythm.* 2018;15(7): 1009-1016. https://doi.org/10.1016/j.hrthm.2018.02.026.
21. Beurskens NEG, Tjong FVY, de Bruin-Bon RHA, et al. Impact of Leadless Pacemaker Therapy on Cardiac and Atrioventricular Valve Function Through 12 Months of Follow-Up. *Circ Arrhythm Electrophysiol.* 2019;12(5): e007124. https://doi.org/10.1161/CIRCEP.118.007124.
22. Choi BJ, Cho KI, Kim SM, et al. Impact of right ventricular apical pacing and its frequency on left atrial function. *J Cardiovasc Ultrasound.* 2012;20(1): 42-8. https://doi.org/10.4250/jcu.2012.20.1.42.
23. Karpawich PP, Mital S. Comparative left ventricular function following atrial, septal, and apical single chamber heart pacing in the young. *Pacing Clin Electrophysiol.* 1997;20(8 Pt 1): 1983-8. https://doi.org/10.1111/j.1540-8159.1997.tb03605.x.
24. Buckingham TA, Candinas R, Attenhofer C, et al. Systolic and diastolic function with alternate and combined site pacing in the right ventricle. *Pacing Clin Electrophysiol.* 1998;21(5): 1077-84. https://doi.org/10.1111/j.1540-8159.1998.tb00153.x.
25. Morbach C, Sahiti F, Tiffe T, et al. STAAB consortium. Myocardial work - correlation patterns and reference values from the population-based STAAB cohort study. *PLoS One.* 2020;15(10): e0239684. https://doi.org/10.1371/journal.pone.0239684.