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Cardiology

A STUDY ON GLOBAL LONGITUDINAL STRAIN IN PREDICTING PACING INDUCED LEFT VENTRICULAR DYSFUNCTION OVER TIME IN POST PERMANENT PACEMAKER PATIENTS

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ABSTRACT

OBJECTIVE: The goal of this study is to predict the long term LV function in RV apical paced patients.

BACKGROUND: We have used the GLS measured by 2D STE, as a tool to predict the patients who are at high risk of developing pacing induced LV dysfunction (PIVD) or pacing induced cardiomyopathy (PCMP).

METHOD: A prospective study conducted in the cardiology department of Government Rajaji Hospital, Madurai, including 47 patients of AV block or sinus node dysfunction with preserved ejection fraction undergoing RV apical pacing. This study population was followed up with serial trans thoracic 2D echocardiography with GLS by STE for a period of 12 months for the development of PIVD (PCMP).

RESULTS: Of the study population, 42.5% (n=20) developed PIVD at 12 months and these patients had a significant fall in their GLS values at one month post pacing. (GLS -16.94% vs -17.60%; p=0.02).

CONCLUSION: GLS, a novel echocardiographic parameter can be used as a tool in predicting the decline in ejection fraction following pacemaker implantation with potential to predict the development of PIVD. GLS at one month post pacing had a high predictive accuracy for identifying those who developed PIVD later in the follow up.

KEYWORDS : Global longitudinal strain(GLS), Speckle tracking echocardiography (STE), Pacing induced cardiomyopathy (PCMP), Pacing induced LV dysfunction (PVID).

INTRODUCTION:

Left ventricular systolic function is an important prognostic predictor of cardiac mortality and morbidity. Despite the widespread clinical use of LVEF, it's assessment is limited by problems with reproducibility, dependence on image quality, subjective interpretation, and LV geometric assumptions. The recent development of two dimensional (2D) speckle-tracking echocardiography (STE) has allowed advances in the quantification of LV function beyond traditional assessment of LVEF. Global strain measurements by 2D STE have excellent correlations with LVEF validated by both three- dimensional (3D) echocardiography and cardiac magnetic resonance imaging (MRI).

Several studies have demonstrated that conventional right ventricular (RV) apical pacing causes changes of the electrical and mechanical activation pattern of the heart. These changes can result in an altered regional perfusion, mechanical dyssynchrony, and adverse left ventricular (LV) remodelling.

The development of mechanical dyssynchrony and associated LV dysfunction during long-term RV pacing rather seems to be an individual and multifactorial process. Randomised trials in RV paced individuals have shown a near 3-fold increased risk of hospitalization for heart failure when the cumulative percentage of ventricular pacing (Cum%VP) exceeds 40%.

The term pacing-induced cardiomyopathy (PICMP) has been used to describe clinically significant left ventricular systolic dysfunction (ejection fraction <45%) attributable to RV pacing, occurring in the absence of other causes of cardiomyopathy. However, lesser degrees of pacing-induced LV dysfunction (PIVD) have also been observed in up to two-thirds of patients with normal baseline LV function.

A non-invasive test able to identify such individuals is, therefore, highly desirable. Two-dimensional (2D) speckle tracking strain echocardiography (STE) has been shown to detect early signs of LV systolic dysfunction in a range of cardiomyopathies before a measurable reduction in LVEF.

AIMS AND OBJECTIVES:
To find whether the speckle tracking strain echocardiography (STE) can be used to predict the development of pacemaker induced LV dysfunction

MATERIALS AND METHODS:
Study population:
The study will be conducted in 47 pacemaker patients in GRH, Madurai during the study period from December 2019 to November 2020.

INCLUSION CRITERIA:
Patients of atrioventricular block (or) sinus node dysfunction with preserved EF who underwent permanent pacemaker implantation

EXCLUSION CRITERIA:
1. Pregnancy.
2. MI/coronary revascularisation within prior 3 months
3. Atrial fibrillation
4. Hemodynamically significant valvular heart disease[>moderate in severity]
5. Structural heart abnormality
6. LVEF <55%
7. NYHA class 3/4
8. Significant respiratory disease
9. Autoimmune disorders
10. RA/treatment with Disease modifying drugs

DATA COLLECTION:
Informed consent will be obtained from all patients to be enrolled for the study. In all patients, relevant information will be collected in a predesigned proforma.

The patients will undergo a thorough history taking, clinical examination, ECG, and two dimensional speckle tracking echocardiography.
DESIGN OF STUDY: Prospective study
PERIOD OF STUDY: From November 2019 to October 2020
ETHICAL CLEARANCE: Obtained
CONSENT: Individual informed and written consent
ANALYSIS: Statistical analysis will be performed using appropriate tests required according to data collected.
CONFLICT OF INTEREST: Nil
FINANCIAL SUPPORT: Self
PARTICIPANTS: Patients of AV block or sinus node dysfunction admitted in department of cardiology, GRH, Madurai and subsequently undergoing RV apical pacing were studied for a period of one year.

STATISTICAL ANALYSIS:

Table 1: Comparison of groups by Gender

Sex	Control	Case	Total	Chi sq	p
Male	16	10	26	0.11	0.5
Female	11	10	21		
Total	27	20	47		

Table 2: Comparison of groups by NYHA Scores

NYHA	Control	Case	Total	Chi sq	p
0	4	1	5	1.89	0.6
1	14	12	26		
2	9	7	16		
Total	27	20	47		

Table 3: Comparison of Medications between groups

MEDICATIONS	Control	Case	Total	Chi sq	p
-	3	4	7	7.4	0.3
ACEI	11	7	18		
ACEI + CCB	2	2	4		
ARB	1	3	4		
CCB	7	3	10		
D	3	1	4		
Total	27	20	47		

Table 4: Comparison of groups by base line categories

	Control	Case	Total
DM	7	5	12
SHTN	3	7	10
Smoking	9	7	16
Alcohol	8	8	16
LVH	1	6	7

Tables 5: Mean Comparison of Study variables

Variables	Group	Mean	SD	t	p
AGE years	Control	62.93	11.20	0.37	0.72
	Case	61.75	10.30		
INITIAL HEART RATE (bpm)	Control	42.11	6.92	1.33	0.19
	Case	39.55	6.00		
Hb (g/dl)	Control	12.34	1.82	2.25	**0.03**
	Case	11.23	1.43		
UREA	Control	40.63	14.70	0.14	0.89
	Case	40.05	12.67		
CREATININE	Control	1.14	0.20	-0.06	0.96
	Case	1.14	0.15		
PRE PPI QRS DURATION mS	Control	125.48	12.44	-0.22	0.83
	Case	126.20	8.97		
PRE PPI EF %	Control	62.48	4.22	-3.26	**0.001**
	Case	66.35	3.73		
PRE PPI GLS (-%)	Control	18.23	0.92	-0.35	0.73
	Case	18.32	0.65		
PACED BEATS% - POST OP	Control	43.48	26.25	-4.53	**0.001**
	Case	74.05	17.20		
QRS DURATION - ONE MONTH mS	Control	136.22	5.69	-2.21	**0.03**
	Case	141.20	9.70		
EF %- ONE MONTH	Control	62.11	3.56	-2.32	**0.03**
	Case	64.55	3.59		
GLS - ONE MONTH (-%)	Control	17.60	0.91	2.52	**0.02**
	Case	16.94	0.86		
PACED BEATS% - ONE MONTH	Control	38.00	19.25	-6.66	**0.001**
	Case	71.95	14.16		
QRS DURATION mS - 12 MONTHS	Control	140.37	4.37	-3.12	**0.001**
	Case	145.80	7.51		
EF % - 12 MONTHS	Control	60.93	3.62	2.00	0.05
	Case	58.75	3.80		
GLS - 12 MONTHS (-%)	Control	17.27	0.99	2.58	**0.01**
	Case	16.56	0.86		
PACED BEATS% - 12 MONTHS	Control	38.74	19.50	-6.37	**0.001**
	Case	71.95	14.78		

Table 6: Mean comparison of one month with 12th month among study groups

	Paired t test	Mean	SD	t	p
Control	QRS DURATION - ONE MONTH mS	136.22	5.69	-5.931	0.001
	QRS DURATION ms - 12 MONTHS	140.37	4.37		
	Ef %- one month	62.11	3.56	3.6	0.001
	Ef % - 12 months	60.93	3.62		
	Gls - one month (-%)	17.60	0.91	8.683	0.001
	Gls - 12 months (-%)	17.27	0.99		
	Paced beats% - one month	38.00	19.25	-1.914	0.067
	Paced beats% - 12 months	38.74	19.50		
Case	QRS DURATION - ONE MONTH ms	141.20	9.70	-5.596	0.001
	QRS DURATION ms - 12 MONTHS	145.80	7.51		
	Ef %- one month	64.55	3.59	16.817	0.001
	Ef % - 12 months	58.75	3.80		
	Gls - one month (-%)	16.94	0.86	3.409	0.003
	Gls - 12 months (-%)	16.56	0.86		
	Paced beats% - one month	71.95	14.16		
	Paced beats% - 12 months	71.95	14.78		

Table 7: Correlation analysis of study variables

		Correlation	p
Control	QRS DURATION - ONE MONTH & QRS DURATION ms - 12 MONTHS	0.77	0.0001
	Ef %- one month & ef % - 12 months	0.886	0.0001
	Gls - one month (-%) & gls - 12 months (-%)	0.983	0.0001

	Paced beats% - one month & paced beats% - 12 months	0.995	0.0001
Case	QRS DURATION - ONE MONTH & QRS DURATION ms - 12 MONTHS	0.94	0.0001
	Ef %- one month & ef % - 12 months	0.914	0.0001
	Gls - one month (-%) & gls - 12 months (-%)	0.836	0.0001
	Paced beats% - one month & paced beats% - 12 months	0.991	0.0001

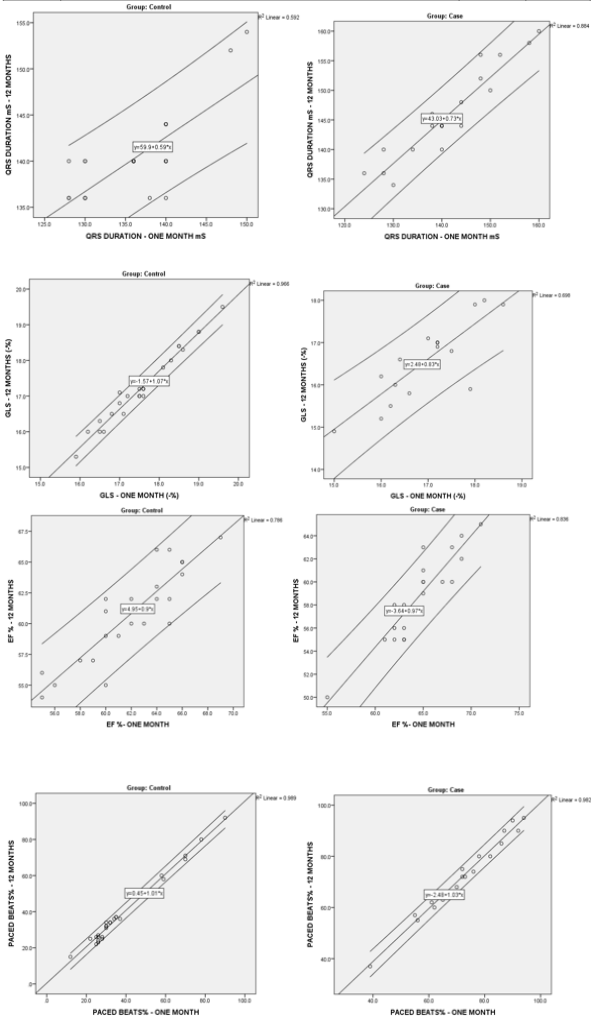

Figure 1: Scatter Plot

RESULTS:

In the study period of November 2019 to October 2020, 51 patients were screened for pacemaker induced ventricular dysfunction. Four of them were excluded from the study as per the exclusion criteria. Baseline clinical characteristics for the study participants are shown in table 1-5.

None of them developed PIVD at one month as defined by echocardiography, but 42.5% of the study population (n=20) developed PIVD at the twelfth month. In this fraction of the study population, there was no significant fall in ejection fraction at one month in comparison with their pre PPI counterparts.

Even though there was no significant variation in the baseline GLS values of the study population, there was a significant fall in one month GLS values of those who have developed PIVD later in the course when compared with those who did not (-16.94% vs -17.60%; p=0.02). The fall in GLS when compared with their own baseline was significant with a p value of <0.05 (-16.94% vs -18.32%) whereas their EF remained the same (64.55% vs 66.35%; p>0.05). Thus measurement of GLS at one month is superior and accurate in predicting the development of PIVD than EF.

GLS values measured at one month <-17.0% had a low sensitivity of 55% and a high specificity of 81.48% with accuracy of 70.21% for predicting PIVD at 12 months.

There is no significant difference between the groups due to gender (p = 0.5), NYHA (p=0.6), Medication taken (p=0.3). Table 5 explains that there were significant difference between the case and control group of Hb (p= 0.03) but age, heart rates and all other baseline blood parameters variables were not significant.

Table 6 explains the mean comparison of one month and 12th month values of QRS duration, EF(%), GLS and Paced Beats among case and control groups which were found statistically significant by paired t test (p<0.05). Table 7 shows the correlation of study variables between one month to 12th month follow up which were found statistically significant.

Figure 1 Scatter diagram explains the relationship and prediction of the study variables by regression line and coefficients, which express positive correlation. That implies as first month value increases the 12th month value also increases and vice versa.

DISCUSSION:

Though the systolic dysfunction of the left ventricle is frequently observed in those patients undergoing right ventricular pacing, the ability to predict the development of PIVD is still challenging. It has been reported in many studies that the measurement of global longitudinal strain by two dimensional speckle tracking echocardiography has proved to be a good predictor in identifying PIVD early in its course.

We hypothesised that there may be a fall in GLS before significant fall in LVEF occurs. In this study, we aimed to provide a comprehensive analysis of both LVEF and GLS by comparing pre implant data with short and midterm follow up measurements in a real world study population undergoing RV pacing. The GLS values at one month were significantly lower than the baseline values in those who developed PIVD whereas there was no significant change in EF at one month.

GLS values of less than or equal to -17.0% at one month post RV pacing had a lower sensitivity of 55%; but a higher specificity of 81.48% with an accuracy rate of 70.21%. The positive predictive value and the negative predictive value were 68.75% and 70.97% respectively for predicting the development of PIVD at twelve months. The study demonstrates the utility of one month GLS in the patients of RV pacing in predicting the development of PIVD by eventual fall in LVEF.

Serial assessment of left ventricular ejection fraction has been widely accepted as a research tool for monitoring the deleterious effects of right ventricular pacing on the left ventricular systolic function. However, the main disadvantage of PIVD follow up with LVEF is that the significant fall in LVEF occurs late in the pathophysiologic process of PIVD. In contrast, abnormal GLS may represent an earlier stage in the pathophysiology of PIVD, thus identifying those early in the course of PIVD before a significant fall in EF occurs.

LIMITATIONS:

- In this study, LVEF was calculated by 2D non contrast echocardiography; three dimensional echocardiograph was not utilised.
- The cutoff GLS for identifying PIVD was calculated as -17.0% in this study; whereas the values of GLS are software dependent and vary with different vendors.
- The effects on alternative pacing sites were not included or analysed in this study.
- Larger randomised study population is needed to validate the feasibility and clinical utility of GLS to predict PIVD
- Intervention by converting the RV pacing to biventricular or physiological pacing was not done in those with a fall in one month GLS.
- Coronary angiography was not done for all the patients in the study.

CONCLUSION:

GLS measurement at one month post pacemaker implantation shows greater potential for identifying those at high risk of developing PIVD before a significant change in the standard echocardiographic parameters occur, thus identifying the patients requiring intensive follow up with frequent echocardiographic surveillance and for considering biventricular pacing early in the course.

SUMMARY OF PRIOR PUBLICATIONS:

1. One-Month Global Longitudinal Strain Identifies Patients Who Will Develop Pacing- Induced Left Ventricular Dysfunction over Time: The Pacing and Ventricular Dysfunction (PAVD) Study

Fozia Zahir Ahmed1,2*, Manish Motwani2, Colin Cunnington2, Chun Shing Kwok3,4, Catherine Fullwood5,6, Delvac Oceandy1, Alan Fitchet7, Grahame Kevin Goode8, Matthew Luckie2, Amir Masood Zaidi2, Rajdeep Khattar9, Mamas Andreas Mamas3,4

RESULTS:

At 12 months, 15 (27%) patients developed PIVD; of these, 4 patients developed PICMP. At one month, GLS was significantly lower in the 15 patients who subsequently developed PIVD, compared to those who did not (n = 40) (GLS -12.6 vs. -16.4 respectively; p = 0.022). When patients with PICMP were excluded, one month GLS was significantly reduced com- pared to baseline whereas LVEF was not. One-month GLS had high predictive accuracy for determining subsequent development of PIVD or PICMP (AUC = 0.80, optimal GLS thresh- old: <−14.5, sensitivity 82%, specificity 75%); and particularly PICMP (AUC = 0.86, optimal GLS threshold: <−13.5, sensitivity 100%, specificity 71%).

2. Three dimensional echocardiography with left ventricular strain analyses helps earlier prediction of right ventricular pacing-induced cardiomyopathy

N.M. Sharath Babu a,⇑, Sirish C. Srinath a, Anandaroop Lahiri a, David Chase a, Bobby John a, John Roshan a

RESULTS:

The incidence of PiCMP was not only significant over a period of 6 months but also at 24 hours. Significant drops in 3D EF were noted in one (2.8%) patient at 24 hours and in another four (11.1%) patients at 6 months. A significant decrease in LV global longitudinal strain was noted in 23 (63.9%) patients by 6 months. In seven of these patients, there was significant decrease in global longitudinal strain 24 hours after implantation. In analyzing longitudinal strain, the parameter significantly influencing a decrease was a pacing percentage of 20% (p = 0.023).

3.Long-Term Impact of Right Ventricular Pacing on Left Ventricular Systolic Function in Pacemaker Recipients With Preserved Ejection Fraction: Results From a Large Single-Center Registry

Micaela Ebert, MD; Nikolaus Jander, MD; Jan Minners, MD; Thomas Blum, MD; Michael Doering, MD; Andreas Bollmann, MD, PhD; Gerhard Hindricks, MD; Thomas Arentz, MD; Dietrich Kalusche, MD;* Sergio Richter, MD*

RESULTS:

We enrolled 991 patients (7310 years, 54% male) with baseline normal (>55%) LVEF (n=791) or mildly reduced (41–55%) LVEF (n=200) who had paired echocardiographic data on LV systolic function recorded at implantation and last follow-up. According to pacing indication, patients were divided into atrioventricular block group A (n=500) and sinus node disease group B (n=491). Main outcome measures were all-cause mortality and deterioration of LV function ≥2 LVEF categories at last follow-up. Patients were followed for an average of 44 months. Death from any cause occurred in 166 (17%), and deterioration of LV function ≥2 LVEF categories in 56 (6%) patients. There was no significant difference in outcome between group A and group B either in patients with normal LVEF or in those with mildly reduced LVEF. Mean percentage of right ventricular pacing was not predictive of outcome.

CONCLUSIONS—

In a large cohort of pacemaker recipients with predominantly normal LVEF, clinically relevant LV dysfunction develops rather infrequently. No significant difference in all-cause mortality and development of severe LV dysfunction is observed between patients with atrioventricular block and sinus node disease. Accordingly, de novo biventricular pacing cannot be recommended for patients with preserved LVEF.

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