# "EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS"

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*In partial fulfillment of the requirements for the award of the degree of*

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# CERTIFICATE

This is to certify that the dissertation entitled "**EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS**" is the bonafide original work of Dr.S.SRIKUMAR, in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2013.The period of postgraduate study and training was from August 2010 to July 2013.

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# DECLARATION

I, **Dr.S.SRIKUMAR**, solemnly declare that this dissertation entitled, "**EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS**" is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2010 – 2013 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor V.E.Dhandapani M.D.D.M. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology**.

Place: Chennai

Date:

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## CONTENTS

# INTRODUCTION

The right (RV) and left (LV) ventricles differ markedly in shape and myocardial contractile element density. Despite these differences, the synchronous electrical excitation and mechanical contraction of both the ventricles and the ventricular interdependence maintains the biventricular function in balance [13]. This is known as ventricular synchrony. Certain disease states like ischemic heart disease (IHD), acute pulmonary embolism, conduction disorders like left bundle branch block (LBBB), preexcitation, and ventricular pacing alters this balance resulting in ventricular dyssynchrony.

RV apical permanent pacemaker implantation (PPI) with ventricular inhibited pacing (VVI) mode is known to produce ventricular dyssynchrony by abnormal electrical and mechanical activation of the ventricles. Long-term RV apical pacing is also associated with detrimental effects on cardiac structure and left ventricular (LV) function[15]. Echocardiographic evaluation of LV and RV systolic function by measuring mitral annular plane systolic excursion (MAPSE) [8] and tricuspid annular plane systolic excursion (TAPSE)[9] and their ratio (MAPSE/TAPSE ratio)[12] has been shown to correlate with ventricular synchrony in normal healthy individuals. M-mode echocardiographic evaluation of MAPSE, TAPSE, and their ratio can provide information regarding the degree of ventricular dyssynchrony in patients with VVI pacing.

## AIMS AND OBJECTIVES

1. To assess the systolic function of left and right ventricle by mitral and tricuspid annular plane systolic excursions in patients with VVI pacing.

2. To analyse the interventricular systolic relationship using MAPSE/TAPSE ratio in patients with VVI pacemaker implantation.

# REVIEW OF LITERATURE

## Conduction System of the Heart

### Automaticity

The inherent ability of the electrically active cells of the heart to spontaneously depolarize resulting in electrical activation of the heart is known as automaticity. The sinoatrial (SA) node is the dominant pacemaker of the heart, consisting of a collection of pacemaker cells, located in the upper portion of the right atrium (RA), close to the insertion of the superior vena cava (SVC). The SA nodal discharge typically produces a heart rate of around 70 beats per minute (bpm) in a healthy person. The SA nodal discharge rate responds to various physiological events and increases heart rate during exercise, fever and emotional stress, and decreases heart rate during rest or increased vagal tone. These changes are mediated by the changes in the neural balance maintained between the sympathetic and the vagal system.

The intrinsic discharge rate of the atrial myocardial cells is usually around 40-50 bpm and hence are suppressed by the higher rate of discharge by the SA node. But occasionally, atria may show increased automaticity leading to an atrial premature contraction (APC) or an atrial tachycardia. In addition, slowing of the sinus heart rate can allow the atrioventricular (AV) node to discharge and pace the heart with a junctional rhythm with a stable rate of about

40 or 50 bpm[31]. Myocardial ischemia, myocarditis, digitalis toxicity and cardiac surgery can lead to a more rapid junctional rhythm called non-paroxysmal junctional tachycardia.

The ventricle is at the bottom of the hierarchy. In patients with complete heart block (CHB), the sinus nodal discharge does not reach the ventricle in a one-to-one ratio due to the block. So, the ventricle starts discharging producing a ventricular escape rhythm. This rhythm, in the presence of complete heart block, is ominous and usually occurs at a very slow rate of around 20-30 bpm. This extremely slow rhythm is potentially lethal as it results in prolongation of the QT interval which may precipitate polymorphic ventricular tachycardia (VT).

**Sinus Node and Atrium:**

The sinus node is located subepithelially in the high RA near the junction of SVC. SA nodal cells undergo spontaneous depolarization at a rate of approximately 60-100 bpm. The electrical discharge from the SA node is not routinely recorded with electrophysiologic studies and standard intracardiac catheters. The sinus node is highly responsive to a variety of physiologic stimuli, adjusting the discharge rate by going slow or fast, as appropriate. This physiological response by the SA node can be reproduced to some extent by rate-adaptive pacemakers.

The atrium is the chamber that conducts electrical discharge from the sinus node down to the AV node. Cardiac myocytes are electrically coupled with one another through the gap junctions. These gap junctions allow the transmission of electrical impulses to travel through the atrial myocardium towards the AV node. The gap junctions are mainly composed of intercellular adhesion molecules called connexions. This atrial depolarization forms a P wave on the electrocardiogram. The total time taken for the transmission of impulses through the atria to the AV node is approximately 100 msec. The atria also function as conduits for the returning venous blood that is pushed into their respective left (LV) and right (RV) ventricles. The atrial contribution to ventricular filling accounts for as much as 30% of the total stroke volume. This in turn results in an improvement in cardiac output through the Frank-Starling mechanism. Maintaining atrioventricular synchrony is an important goal with dual-chamber pacemakers.

**AV Node:**

The atria are separated from the ventricles by the two atrioventricular valves and their supporting fibrous tissue. This fibrous skeleton essentially acts as an insulator preventing the simultaneous electrical activation of the upper and lower chambers. The only normal electrical pathway between the atria and the ventricles is the through the AV node which is situated subepithelially in the RA close to the coronary sinus.

The electrical impulses from the SA node travelling down towards the ventricles are slowed down by the AV node. This atrioventricular delay is approximately 80 msec. This brief delay in the conduction of the depolarization wave from atria to the ventricles, also known as “electrical modulation”, has great functional significance because this delay allows the blood to be emptied near completely from the atria into the ventricles. This atrial contraction augmented emptying of blood accounts for an additional contribution to the end-diastolic ventricular volume by approximately 30%, thus allowing for more efficient cardiac output.

The AV node is responsive to both vagal and sympathetic input. Heightened vagal activity in trained athletes can result is marked slowing of the heart rate, producing asymptomatic episodes of intermittent block in the AV node. The delayed AV nodal conduction may further get impaired in certain disease states like degenerative nodal calcification and myocardial ischemia, resulting in atrioventricular conduction blocks, including complete heart block, necessitating ventricular pacemaker. The AV node also has the property of retrograde conduction, allowing ventriculo-atrial (VA) conduction during ventricular tachycardias and ventricular pacing.

**His-Purkinje System:**

The electrical activity from the SA node that has been briefly slowed in the AV node enters the His-Purkine system, which constitutes the first portion

of the specialized conduction system of the heart having rapid conducting properties. The Purkinje fibers are very long fibers with abundant concentrations of gap junction. This contributes to the very high conduction speeds of 3-4 m/sec in the His-Purkinje as opposed to the relatively slow conduction (0.3-1 m/sec) speed of the working myocardium.

The initial portion of this part of the conduction system is the bundle of His and is a fairly thick bundle of cells. The His-Purkinje system is essentially a trifascicular network. The bundle of His almost immediately splits into the two components of the Purkinje system: the right and left bundle branches. The left bundle is further divided into the left anterosuperior and left posteroinferior fascicles. This can be explained teleologically as a rapidly conducting electrical system that spreads through the LV and RV myocardium to allow almost simultaneous, synchronized, contraction of the ventricles. The recent advance in cardiac resynchronization therapy (CRT) for congestive heart failure (CHF) represents an effort to reproduce this effect. Disruption of these bundles is quite common and results in left bundle branch block (LBBB) and right bundle branch block (RBBB) which are routinely diagnosed on surface electrocardiogram (ECG). The clinical significance of these blocks is dependent on the clinical scenario and can range from completely benign to pathological.

**Ventricular myocardium:**

The ventricular myocardium is electrically isolated from the His-Purkinje system in all the regions except at the Purkinje-myocardial junction. The regions of the ventricular myocardium that are activated earliest are the RV anterolateral wall and the LV inferolateral wall. This is followed by early apical activation, and further spread of the electrical impulses occur in a apex-to-base sequence. Simultaneously, there also occurs endocardial-to-epicardial spread of excitation front. The last parts of the RV to be activated are the AV sulcus and the pulmonary conus. Similarly, the last part of the LV to be activated is the posterobasal area. The time interval between the impulses arriving at the His bundle and the first ventricular activation is around 20 msec. The complete ventricular activation is completed in around 60-80 msec.

**Mechanical activation under physiological states:**

The electrical activation of the heart results in mechanical contraction of the myocardial fibers, mediated by the process of "electro-mechanical coupling". The spontaneous depolarization of the SA nodal cells is followed by spread of the depolarization wave along the entire cardiac conduction system. This results in the opening up of the calcium (Ca2+) channels in the surface of the myocardial cells, resulting in increased calcium entry into the cells. This calcium further mediates the release of more calcium from the sarcoplasmic reticulum (SR) through calcium-induced calcium release (CICR) channels, thereby increasing the intracytoplasmic calcium concentrations upto ten times.

Calcium then binds with the troponon-C protein causing activation of the troponin complex. This is followed by an increase in the actin-myosin interaction which produces myocardial fiber contraction.

Ventricular contraction is followed by relaxation of the myocardial fibers. At the end of myocardial contraction, with the depletion of adenosine triphosphate (ATP), the calcium ions dissociate themselves from the troponin complex and are released into the cytoplasm. This released calcium is removed from the cytoplasm by two major systems: the reuptake of calcium into the SR by the sarcoplasmic reticulum Ca2+-ATPase (SERCA) and the efflux of calcium outside of the cells through the sarcolemmal sodium-calcium exchanger (NCX) pump. The SERCA mechanism is the dominant mechanism accounting for the removal of upto 80% of the cytoplasmic calcium under physiological states and the NCX accounts for upto 10-15% of total calcium efflux. This finally results in myocardial relaxation.

## Interventricular relationship and Ventricular dyssynchrony

### Synchronous Ventricular Contraction:

The left ventricle (LV) and the right ventricle (RV) differ markedly in shape, thickness and density of the myocardial contractile elements. In spite of these differences, both the ventricles function in a smooth and coordinated manner maintaining normal biventricular function. This is mediated by the

synchronous excitation of the cardiac conduction system as well as the contraction of the myocardial fibers. The electrical activation of the heart begins in the sinoatrial (SA) node and spreads through the atrioventricular (AV) node to the His bundle, bundle braches and Purkinje fibers finally resulting in the activation of the myocardial fibers through the Purkinje-myocardial coupling. The His-Purkinje system is extremely important in maintaining the synchronous activity of the myocardium, because of its widespread distribution in the ventricles and unique propagation properties. The result of this is a high degree of coordinated mechanical contraction between remote regions of the myocardium.

**Ventricular dyssynchrony:**

Ventricular dyssynchrony can be defined as an abnormality of the normal, organized electromechanical coupling of the ventricles and this disturbance is the consequence of an intra or interventricular conduction delay[1]. Ventricular dyssynchrony results in the early electrical activation of the RV before LV activation. Also, RV depolarization and mechanical contraction occurs earlier followed by LV depolarization and mechanical contraction. This altered ventricular activation sequence has the following hemodynamic effects :

(i) Reduction in the LV contractility

(ii) Decreased LV diastolic filling times with reduced preload

(iii) Mitral regurgitation due to delayed activation of the posteromedial papillary muscle

(iv) Paradoxical septal motion resulting in reduced contribution of the interventricular septum (IVS) to LV stroke volume

These hemodynamic effects are particularly troublesome in patients with heart failure resulting in progressively downhill course with increased morbidity and mortality.

***Electrical dyssynchrony*** is defined by an abnormally widened surface QRS duration exceeding 120 msec in any electrocardiographic limb lead. ***Mechanical dyssynchrony*** refers to presence of abnormal activation timing within or between the ventricles as evidenced by echocardiography[2].

**Types of Ventricular Dyssynchrony:**

Left ventricular dyssynchrony occurs in the settings of impaired ventricular interaction and is of 3 types:

1. Atrioventricular dyssynchrony resulting from atrial and ventricular activation occurring out of phase.
2. Interventricular dyssynchrony resulting from altered activation timings between the ventricles.

3. Intraventricular dyssynchrony resulting from differential activation among the various segments of the LV itself.

**Echocardiographic assessment of Ventricular dyssynchrony:**

*Atrioventricular dyssynchrony* is assessed echocardiographically by measuring the LV diastolic filling time (DFT) using pulsed wave doppler (PWD) in the apical 4-chamber view. DFT is measured from the beginning of the E- wave to the end of the A wave in the mitral inflow velocity recordings. Atrioventricular dyssynchrony is present if the DFT is < 40% of the cardiac cycle.

*Interventricular dyssynchrony* is currently best assessed by measuring the interventricular mechanical delay (IVMD). IVMD is defined as the time difference between left and right ventricular pre-ejection intervals measured by PWD. The pre-ejection intervals are measured from the beginning of the QRS complex to the beginning of the pulmonary (Q-PV) or aortic ejection (Q-AV). Normal IVMD is < 40 milliseconds (ms). Interventricular dyssynchrony is present if IVMD is > 40 ms[3]. Tissue doppler imaging (TDI) is also used in the assessment where any delay between the onset of systolic motion between the basal RV free wall and the most delayed LV segment is measured. A delay > 56 ms is considered abnormal.

*Intraventricular dyssynchrony* is assessed by various methods, but the two most widely accepted methods are:

(i) M-mode echocardiographic measurement of septal-to-posterior wall motion delay (SPWMD). SPWMD is obtained in the parasternal short axis view at the papillary muscle level by measuring the delay between the peak systolic excursion of the anterior (septal) and the posterior walls. SPWMD value of 130 ms or more is considered abnormal [4].

(ii) Color-coded TDI showing a delay $\geq$ 65ms between any two walls ( usually between septal and lateral walls) from QRS onset to peak contraction, assessed in either the apical 3-, 4-, or 5-chamber view. The color-coded TDI method is the most preferred method for assessing intraventricular dyssynchrony and patient outcomes[5].

## Mitral Annular Plane Systolic Excursion (MAPSE)

**Mitral annular ring:**

The harmony of the mitral valve opening and closure, and LV filling and emptying is maintained by the anatomical integrity of the "left atrial- mitral valve-left ventricular complex". An essential component of this complex is the mitral annular ring providing support to the mitral valve. During LV contraction and relaxation, this mitral annular ring also undergoes a complex motion composed of three components: motion in long-axis (base-to-apex), constricting

motion in a sphincter-like fashion, and rotation. The base-to-apex motion of the mitral annular ring was first described in details by Zaky et al[6].

**LV systolic function by echocardiography:**

Left ventricular systolic function is traditionally assessed by echocardiography using a variety of parameters including LV ejection fraction (LVEF), using either Teichholz method or modified Simpson method, LV fractional shortening (LVFS), LV fractional area change (LV FAC), LV outflow tract acceleration time, and mitral dP/dt. Among these, the most widely accepted and used parameter is the LVEF. Left ventricular ejection fraction is a measure of the LV systolic function along both its circular and longitudinal axis and reduced ejection fraction has been correlated with prognosis, both short term and long term, in various heart diseases.

**Longitudinal motion of left ventricle:**

The systolic contraction and diastolic relaxation of the LV myocardium is mediated mainly by two groups of muscle fibers: longitudinal fibers present in the subendocardial layer, subepicardial layers as well as in papillary muscles, and circular muscle fibers present predominantly in the subepicardial layer. During myocardial contraction, the longitudinal fibers begin to contract earlier than the circular fibers.

In disease states with altered contractility, both the longitudinal and rotational motion of the myocardium is affected. But, it has been shown by Bolognesi et al that in diseased states like myocardial ischemia or infarction, the longitudinal motion is affected first[7]. Thus, echocardiographic evaluation of longitudinal motion of myocardium may help in diagnosing cardiac dysfunction at an early stage of disease process itself.

**Mitral annular plane systolic excursion:**

MAPSE is an echocardiographic parameter useful in assessing the longitudinal function of the left ventricle. It is measured by M-mode echocardiography by placing the patient in the left lateral position and obtaining an apical-4-chamber view. The M-mode beam is placed along the lateral annulus of the mitral valve and the maximal excursion of the mitral annular plane in systole is measured. The annular plane is identified in M-mode recording as the first continuous line seen immediately below the LV cavity.

The normal range for MAPSE is 12 +/- 2 mm (men: >13 mm and women >11 mm). Values less than 10 mm is considered abnormal and correlates with LVEF and cardiac dysfunction. Reduction in the MAPSE has been demonstrated in many disease states like ischemic heart disease, acute myocardial infarction, severe aortic stenosis, cardiomyopathies. The systolic LV function as assessed by MAPSE has also been shown to have high correlation with brain natriuretic peptide (BNP) levels in patients with heart failure[8].

# Tricuspid Annular Plane Systolic Excursion (TAPSE)

## Tricuspid annular ring and its motion:

Similar to the left side of the heart, the coordinated functioning of the right sided chambers is effectively maintained by the "right atrial-tricuspid valve-right ventricle complex" and tricuspid annular ring is an essential component of this complex. The contractile elements of the right ventricle (RV) are predominantly aligned in the longitudinal axis of RV. So, during RV systole, the myocardial shortening takes place mainly in the longitudinal plane. This systolic longitudinal motion of the RV is best assessed by TAPSE.

## RV systolic function by echocardiography:

RV systolic function can be assessed echocardiographically by various parameters. But, the parameters that have been widely accepted and used are right ventricular index of myocardial performance (RIMP), TAPSE, two-dimensional RV fractional area change (2D RV FAC) and tissue Doppler-derived tricuspid lateral annular systolic velocity (S'). Various cut-off points for distinguishing normal and abnormal states for each of the above parameters have been defined. In the recent years, the significance of TAPSE in evaluating RV function has been validated in many trials beyond doubt.

**Tricuspid annular plane systolic excursion:**

TAPSE is measured using M-mode echocardiography by placing the M-mode beam along the lateral annulus of the tricuspid valve in the apical-4-chamber view. The difference in the distance between the tricuspid annulus and the RV apex during systole and diastole as obtained in M-mode echocardiography gives the measure of TAPSE.

Normal value for TAPSE is 18mm or above. Values below 17mm is considered abnormal RV function. Various studies have shown significant correlation between low levels of TAPSE and RV function in many disease states including acute myocardial infarction, pulmonary embolism, cor pulmonale. Samad et al showed that in patients with first myocardial infarction, lower TAPSE levels were associated with worse outcomes and higher mortality [9]. Their study showed that patients with a TAPSE value < 15mm had a significantly high mortality of 45% at 2 years as compared to patients with TAPSE levels >20mm who had a low mortality of around 4%. Lower levels of TAPSE has been shown to be a predictor of poor outcomes in patients having dilated cardiomyopathy and pulmonary hypertension[10].

Gupta.S et al in their study to evaluate the interventricular relationships and ventricular dyssynchrony in patients with heart failure observed that patients with LV systolic dysfunction had significantly reduced levels of TAPSE. Patients with bi-ventricular dyssynchrony had the lowest levels of

TAPSE, and levels were highest for those without any ventricular dyssynchrony. The association between TAPSE and LV dyssynchrony was found to be independent of the RV and LV ejection fraction. In conclusion, they remarked that TAPSE may serve as a useful indicator of LV dyssynchrony, especially because it is both easily measurable and reproducible [11].

The main advantages of TAPSE are: it is a simple, readily available, easily reproducible parameter that can be repeated as needed and does not need any specialized echocardiographic machine. But there are certain disadvantages of using TAPSE because it measures the longitudinal motion of the RV at one plane and assumes that this is reflective of global RV function. Also, TAPSE may be angle-dependent and so needs precise alignment of the M-mode beam parallel to the RV free wall- tricuspid annulus plane for obtaining correct values. Based on the above evidences from various studies, as well the advantages, American Society of Echocardiography (ASE) recommends that TAPSE should be used routinely as a simple method of estimating RV function, with a lower reference value for impaired RV systolic function of 16 mm [25].

## MAPSE/TAPSE Ratio

The left and right ventricular interrelationship is the most important physiological mechanism that maintains the cardiovascular homeostasis in

normal healthy individuals. This relationship may get altered in various disease states like ischemic heart disease, acute myocardial infarction, arrhythmias, constrictive pericarditis, cardiac tamponade, RV dysfunction due to pulmonary hypertension, pulmonary embolism, and cor pulmonale. The assessment of this relationship using echocardiography has been an area of interest for many decades and various parameters have been described. A novel approach using MAPSE/TAPSE ratio has recently been described for the quantitative assessment of interventricular systolic relationship [12].

Bruhl et al, in their pilot study, evaluated 51 healthy personnel using resting echocardiography for the quantitative assessment of interventricular relationship by measuring MAPSE, TAPSE, MAPSE/TAPSE ratio, peak annular systolic velocity of left (LVs) and right (RVs) ventricles by M-mode and tissue Doppler method[12]. They also further analyzed these parameters for variance across age, gender and body surface area (BSA). They found that TAPSE was greater than MAPSE by over 54.5% (22.1 ± 2.9 mm vs 14.3 ±2.6 mm) and MAPSE/TAPSE ratio was 0.66 ± 0.14. These relationships were remarkably consistent regardless of age, sex or BSA. Similarly consistent results were also noted with the TDI derived parameters. Based on these observations, the investigators concluded that MAPSE/TAPSE and LVs/RVs ratios are good surrogate measures of left and right ventricular systolic relationship and interdependence.

Bruhl et al, also suggested that, despite the markedly reduced muscle mass, the consistently higher RV systolic excursions along the longitudinal plane and systolic velocities compared to the LV parameters, was due to the relatively low pulmonary vascular resistance against which the RV contracts compared to the systemic vascular resistance [12]. Also, upto 80% of RV stroke volume is due to systolic contraction along its longitudinal axis, while contraction along this plane accounts only for 60% of LV stroke volume and the rest of the contraction involves circular and torsional movements[13].

The normal MAPSE/TAPSE ratio may be altered by disease states involving either side of the ventricles. The clinical application of this novel parameter involves conditions producing RV dysfunction like pulmonary hypertension, acute pulmonary emboli and RV infarctions as well as conditions producing LV dysfunction like aortic stenosis, acute myocardial infarction. The ratio may also be altered in dyssynchronous ventricular contraction states like right (RBBB) and left bundle branch block (LBBB), RV or LV pacing and accessory pathway conduction.

## Permanent Pacemaker Implantation (PPI)

Ever since the development of implantable cardiac pacemakers in the mid 20th century, cardiac pacing has remained the mainstay of therapy in managing patients with both bradyarrhythmias and tachyarrhythmias. In recent years, the indications for pacing has been expanded to diseases like drug-refractory heart

failure and hypertrophic cardiomyopathy. However, the most important indications for cardiac pacing are atrioventricular blocks and sick sinus syndrome.

There are various types of pacemakers and they are described by the Pacemaker code system developed by the NASPE/BPEG[14] (Table.A).

**Table.A NASPE/BPEG Generic Code for Antibradycardia Pacing**

| **POSITION** | **I** | **II** | **III** | **IV** | **V** |
|---|---|---|---|---|---|
| Category | Chamber(s) paced | Chamber(s) sensed | Response to sensing | Rate modulation | Multisite pacing |
| | O = None | O = None | O = None | O = None | O = None |
| | A = Atrium | A = Atrium | T = Triggered | R = Rate modulation | A = Atrium |
| | V = Ventricle | V = Ventricle | I = Inhibited | | V = Ventricle |
| | D = Dual (A + V) | D = Dual (A + V) | D = Dual (T + I) | | D = Dual (A + V) |
| Manufacturers' designation only | S = Single (A or V) | S = Single (A or V) | | | |

Application of magnet over a pacemaker converts the pacemaker programming into asynchronous mode of operation like DOO, AOO, or VOO. In the case of ICDs, magnet application does not alter the programmed pacing function, but does inhibit the detection of ventricular tachycardia (VT) / ventricular fibrillation (VF) by the ICDs.

The various types of pacemakers have their advantages and disadvantages that are dependent on the timing cycle of individual pacemaker mode.

**Ventricular Inhibited Pacing (VVI):**

The most commonly used mode in PPI is the VVI mode. VVI pacing mode is capable of sensing a ventricular event and responds by inhibiting the pacemaker output. VVI pacemakers have a period of refractoriness after a paced or sensed ventricular event, during which any ventricular event is not sensed. This interval is called the ventricular refractory period. During this period, ventricular events do not reset the cycle timing. VVI pacing is especially protective in life threatening bradycardias. The main disadvantage of VVI pacing mode is the lack of AV synchrony.

**Atrial Inhibited Pacing (AAI):**

AAI pacing mode has timing cycles similar to VVI pacing, but the major difference is that both pacing and sensing takes place from the atrium and responds to a sensed atrial event by inhibiting the pacemaker output. An atrial event, either paced or sensed, is followed by a refractory period similar to VVI pacing during which no intrinsic atrial event changes delivery of the next pacing stimulus. The next atrial pacing stimulus is delivered when the first atrial timing cycle ends, irrespective of ventricular events. This occurs because, by

pacemaker programming, an AAI pacemaker should not sense ventricular events. The only exception to this rule is “far-field sensing” where a large ventricular signal may inappropriately be sensed by the atrial lead, resulting in resetting of the atrial timing. This abnormality can be partially corrected by decreasing the sensitivity of the atrial channel or by prolonging the atrial refractory period.

**AV Sequential, Non–P-Synchronous Pacing (DDI):**

DDI pacing mode is characterised by dual-chamber sensing, which prevents competitive atrial pacing. The response of the DDI ventricular mode is inhibition only. There is no tracking of P waves and hence, pacing occurs only at the programmed rate. DDI is rarely a preferred mode, but it is still a programmable option in most of the current dual-chamber pacemakers. The DDI pacing mode can be particularly helpful during intermittent atrial tachyarrhythmia as it results in atrial undersensing and thereby prevents mode switching.

**Dual-Chamber Pacing and Sensing with Inhibition and Tracking (DDD):**

In the DDD mode, the basic timing circuit associated with lower rate pacing is divided into two intervals: the ventriculoatrial (VA) interval and the atrioventricular interval (AVI). The AVI results in AV sequential pacing, which is initiated by pacing producing subsequent intrinsic ventricular conduction.

Alternately, it may be initiated by a native P wave producing subsequent ventricular pacing.

**Rate-Adaptive Sensors**:

Incorporation of rate-adaptive sensor in the pacemaker provides rate responsiveness when the sensor is on, based on changes in the level of physical activity. Rate-adaptiveness of a pacing mode is represented by adding an R in the fourth position of the code (e.g., VVIR, AAIR, DDIR, and DDDR). The sensors most commonly used are the accelerometer which is based on activity, and minute ventilation, based on measuring transthoracic impedance.

## Right ventricular apical pacing with VVI mode

Due to the ease of site accessibility and stability of the pacemaker lead, the pacing lead in the endocardium is traditionally positioned at the right ventricular apex. In general, patients tolerate pacing from the RV apical position very well and is effective in relief of symptoms. However, it is now known that adverse effects, may arise from RV apical pacing, on cardiac structure and LV function[15]. This may be related to the altered electrical and mechanical activation pattern of the ventricles (i.e, ventricular dyssynchrony) caused by RV apical pacing.

**Altered ventricular activation sequence in RV apical pacing:**

During RV apical pacing, the electrical activation sequence of the ventricles is altered. The RV apex where the lead is positioned is activated first, followed by the spread of the electrical impulses to other regions of the right and left ventricle. This spread of electrical activation takes place through the ventricular myocardium and not through the His-purkinje conduction system. The result of this abnormal spread of the electrical wave front is slow propagation and also heterogenous mechanical activation of the ventricles, similar to that of LBBB. The consequence of this abnormal activation, is that, the total time required for activation of the entire ventricular myocardium, expressed as QRS duration, is at least twice that during normal sinus rhythm. In most cases, the site of earliest mechanical activation is the interventricular septum. This single breakthrough at the interventricular septum is followed by abnormal activation of other regions of the ventricles and the last part of activation at the inferoposterior base of the LV[16].

RV apical pacing thus results in changes, not only of the initiation of mechanical contraction, but also in the sequence of mechanical contraction. The regions of the RV that are near the pacing site and hence are activated early show early meachanical coupling with rapid systolic contraction. This causes the regions that are activated later to be stretched due to this early contraction. These regions that are late-activated, thereby undergo a delayed systolic shortening which, in turn imposes systolic stretch, to the early activated regions

that are at present undergoing premature relaxation. The end result of these abnormal contraction patterns involving different regions of the LV is a redistribution of myocardial strain and work which produces a contraction that is comparatively less effective.

**RV apical pacing and its detrimental effects:**

The altered sequences of electrical activation and mechanical contraction of the ventricles in RV apical pacing may result in a variety of detrimental effects on the metabolism, perfusion dynamics, remodelling, hemodynamics and mechanical function. Long-term RV apical pacing can cause changes in both regional perfusion and oxygen demands of the myocardium, resulting in myocardial perfusion defects, mainly in regions near the pacing site, in upto 65% of patients even in the absence of underlying obstructive coronary artery disease (CAD).

Chronic RV apical pacing may also cause abnormal LV remodelling, like asymmetrical hypertrophy of the RV and LV myocardium. The regions of myocardium that are activated early undergo thinning while the late-activated regions undergo thickening. The abnormal contraction sequence may result in ventricular dilation during long-term RV pacing. Progressive LV dilation may also cause functional mitral regurgitation that also gradually worsens. Left atrial (LA) remodelling is another consequence of chronic RV pacing that may result in heterogeneity in atrial electrical excitation with resultant atrial fibrillation.

Histopathological changes in the ventricular myocardium include intercellular and intracellular alterations showing myofiber disarray and degenerative fibrosis, variations in the mitochondrial organisation, abnormal expression of myocardial contractile proteins. There also occurs a gradual reduction in protein kinases and proteins associated with calcium homeostasis[17].

Abnormality in the sequence of electrical and mechanical activation of the LV may result in global mechanical dysfunction and associated adverse hemodynamic properties. Pacing at the RV apex and associated dyysynchrony results in longer durations of the isovolumic contraction (IVC) and isovolumic relaxation (IVR) phases of the cardiac cycle. This may result in altered filling and contractile properties of the LV with a resultant decrease in cardiac output. Alterations in myocardial strain and timing of regional strain also may occur during RV apical pacing resulting in varying degrees of mechanical dyssynchrony.

**Evidence from Pacing Mode Trials**:

The association between a high percentage of RV apical pacing and adverse clinical outcomes has been shown by a number of large randomized clinical trials on pacing mode selection.

The investigators of the MOST (Mode Selection Trial), through a substudy, concluded “ strong association between RV pacing and the risk of

hospitalization due to heart failure and atrial fibrillation in patients who had both the physiological dual-chamber pacing (DDDR) and single-chamber ventricular pacing [VVIR]"[18]. It was noted that ventricular pacing for more than 40% of the time in the DDDR group was associated with an increased risk of hospitalization for heart failure (hazard ratio [HR]: 2.60; 95% confidence interval [CI]: 1.05 to 6.47; $p< 0.05$). Similarly, ventricular pacing for more than 80% of the time in the VVIR group was also associated with a higher risk of heart failure hospitalization (HR: 2.50; 95% CI: 1.44 to 4.36; $p< 0.05$). The results of the MOST study demonstrated that the cumulative percentage of ventricular pacing is a strong predictor of hospitalization for heart failure in patients with a normal baseline QRS duration. There was also a linear association between the cumulative percentage of ventricular pacing and an increased risk of atrial fibriilation.

In the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial[19], patients with underlying indication for defibrillator implantation, but without any indication for antibradycardia pacing, were randomized to receive either physiologic pacing using DDDR mode with lower rate of 70 beats/ min or ventricular backup pacing using VVIR mode with lower rate of 40 beats/min. The median follow-up period was 8.4 months. The primary outcome measures studied were: (i) freedom from death and (ii) absence of hospitalization for new or worsened heart failure. These outcomes were lower in the VVIR group than

in the DDDR group (relative hazard: 1.61; 95% CI: 1.06 to 2.44; p< 0.03). Importantly, the investigators noted that patients with a high pacing percentage at the 3-month follow-up had a pattern toward a worse survival at 12 months [19]. The above trials concluded that there is absence of any clinical benefit of physiologic DDDR pacing over VVIR. The reason for the absence of significant benefit in these studies was explained by the short programmed AV interval that caused a higher percentage of ventricular pacing in the DDDR groups. Thus, the beneficial effect of maintaining AV synchrony by physiologic DDDR pacing may be neutralized by the deleterious effects due to RV apical pacing itself.

Unfortunately, these trials did not provide conclusions about the exact amount of RV apical pacing that is associated with negative effects on the cardiac function. Ventricular pacing, by means of maintaining physiologic AV synchrony, may in reality be beneficial to a certain extent. But, certain patient populations are more likely to be prone to the negative effects of RV apical pacing , especially, patients with underlying conduction disorder, ischemic heart disease, patients requiring pacing for a longer period of time and patients with reduced LV function at baseline[20].

**Mechanisms of mechanical dyssynchrony during RV apical pacing:**

Mechanical dyssynchrony secondary to right ventricular apical pacing can result in both interventricular dyssynchrony as well as intraventricular dyssynchrony.

The extent of ventricular dyssynchrony and the activation sequence during abnormal conduction are determined, at least by four myocardial properties which as follows:

a) Myocardial fibers conduct electrical impulses slower by up to four times compared to conduction through the Purkinje system.

b) Velocity of conduction along the length of the muscle fibers is approximately two times than perpendicular to them. Therefore, the pacing site is surrounded by an elliptical-shaped wave front, particularly in the epicardial and midmyocardial layers[21].

c) Reentry of impulses that originate from the working myocardium into parts of the rapidly conducting His-Purkinje system is rare. Even though Purkinje-myocardial junctions are present to facilitate the transmission of electrical impulses from the conduction system into the myocardium, the reverse is not true. So, in majority of cases, the myocardial activation sequence during ventricular pacing is determined predominantly by slow conduction through the normal myocardium, away from the pacing site.

d) Conduction of impulses through most of the endocardial fibers is faster than the rest of the LV wall fibers. Also, the circumference

of the endocardium is smaller than its epicardial counterpart. So, total electrical activation time is shorter with LV endocardial pacing compared with LV epicardial pacing[22].

In heart failure patients, an increased risk of cardiac morbidity and mortality has been proven in the presence of ventricular dyssynchrony. In addition, the LV systolic function and functional capacity of the patients is also reduced in patients with mechanical dyssynchrony following long term RV apical pacing. Cardiac resynchronization therapy (CRT) results in normalization of LV systolic function by restoring the synchronized cardiac contraction thereby improving the functional capacity[23]. This suggests that there is a direct relationship between abnormal activation pattern (LBBB-like pattern) during RV apical pacing or ventricular dyssynchrony and a deterioration of LV function. Therefore, valuable information can be obtained from assessing ventricular dyssynchrony by echocardiography in patients with VVI pacing.

## MATERIALS AND METHODS

This was a prospective case control study done between March 2012 and February 2013 at the department of cardiology, Government General Hospital Chennai. The study cohort comprises of 40 patients, who had permanent pacemaker implantation done (RV apical pacing with VVI mode) more than one year back, who attended the Pacemaker clinic of our department for follow-up. The patients with the presence of any comorbid conditions like diabetes mellitus, hypertension, ischemic heart disease were excluded from the study. The control group consists of 30 age matched healthy individuals. Patients and controls both belonged to the age group of 30- 75 years. Informed, written consent was obtained from all the patients and controls. The study protocol was evaluated and approval was obtained from the Institutional Ethics Committee.

**Inclusion criteria:**

All patients with VVI pacemaker implantation (with RV apical pacing) done between one to two years before the start of the study period.

**Exclusion criteria:**

1. Known case of IHD, MI or regional wall motion abnormalities
2. Known case of cardiomyopathy, heart failure or LV dysfunction
3. Known case of valvular heart disease

4. Diabetes mellitus

5. Hypertension

6. Chronic kidney disease

7. Chronic lung disease

**Patient evaluation:**

All of the 40 patients and controls were subjected to the following assessment:

1. Detailed history taking

2. Thorough clinical examination

3. Standard 12-lead electrocardiogram, especially the paced QRS (pQRS) duration

4. Echocardiographic evaluation

**Echocardiographic examination:**

Echocardiographic examination was done with a 2.5 MHz transducer using the Esaote myLab equipment available in our Echo lab. The examination was done with the patients in the left lateral decubitus position. Echocardiographic examination and measurements were recorded according to the American Society of Echocardiography recommendations [24- 25].

The LV end diastolic and end systolic volumes were measured from the apical 4- and 2- chamber views using the modified Simpson method and LV ejection fraction was calculated from the volumes obtained. The patients were analyzed under two groups: normal (LV EF>55%) and reduced (LV EF <55%) LV systolic function. Presence of LV diastolic dysfunction was assessed in the apical 4-chamber view with the pulsed wave Doppler sample placed at the mitral inflow region. The presence of any associated mitral regurgitation was noted by the standard protocols. Mitral (MAPSE) and tricuspid (TAPSE) annular plane systolic excursions were measured in the apical 4-chamber view by placing the M-mode cursor along the lateral annulus of the mitral and the tricuspid valves. The difference in the distance between the mitral annulus and the LV apex during systole and diastole was obtained in M-mode echocardiography to get MAPSE. Similar measurements of the tricuspid annular excursions during systole and diastole were obtained to get TAPSE. The MAPSE/TAPSE ratio was calculated from the above values. MAPSE value of 10mm or less and TAPSE value of 16mm or less were considered abnormal. Based on the suggestions by Bruhl et al and the observed values of controls in our study, a MAPSE/TAPSE ratio of <0.64 was taken as the cut-off for the presence of interventricular dyssynchrony.

Baseline demographic and clinical characteristics for continuous variables were expressed as mean ± SD and tested for differences using the

Student’s t-test. The study population was also divided into 3 groups based on age including those < 40 years, 40-60 years, and > 60 years old as well as by sex. Comparison of multiple echo measurements across age groups was done by Analysis of variance (ANOVA). For all measurements, a two-sided P-value of less than0.05 was considered statistically significant. All statistical analysis was performed using SPSS for Windows, version 17.0, SPSS Inc, Chicago, Illinois, USA.

## RESULTS

The study population included 40 patients with VVI pacemaker implantation and 20 healthy controls. The average age of the patients was 50.35 ± 11.28 years and of the control group was 49.21± 8.82 years. The average percentage of males and female in both the groups was 55% and 45% respectively (Fig.1). There was no difference in the age or sex distribution between the two groups. Baseline profile and echocardiographic parameters of the study population is given in Table.1.

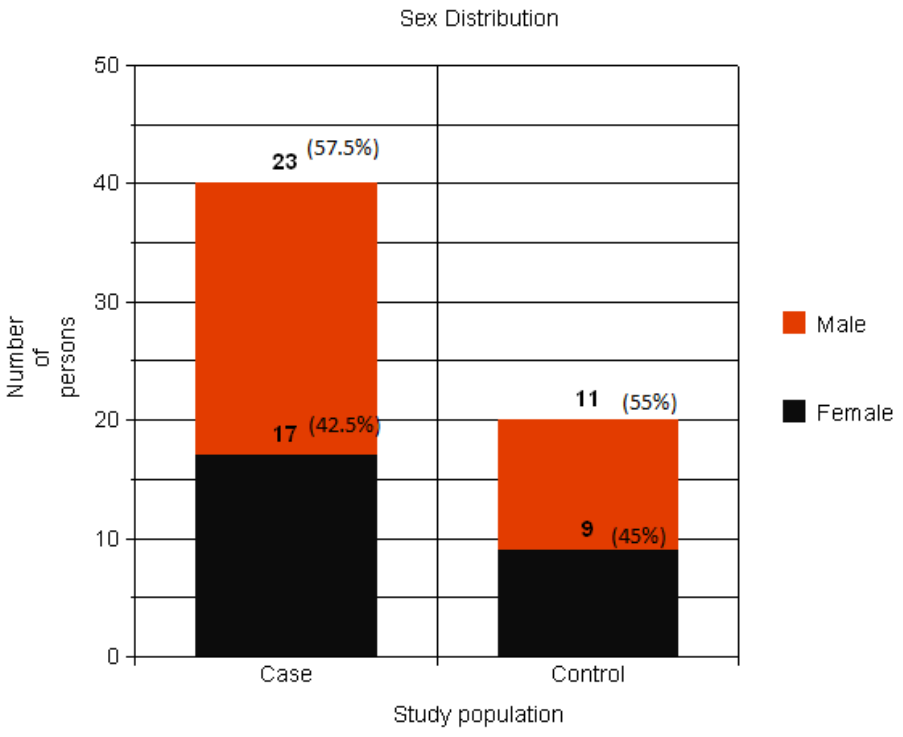


Fig.1:

Stacked bar diagram showing the percentage of sex distribution among the study population.

Among the 40 patients, 28 (70%) patients had CHB and 12 (30%) patients had SSS as the underlying conduction disorder for pacemaker implantation (Fig.2). All the patients had undergone pacemaker implantation before 1 to 2 years from the start of the study period. The average pQRS duration in the patient group was 162.5 ± 8.39 msec and in the control group was 107.05 ± 11.18 msec (P<0.0001).

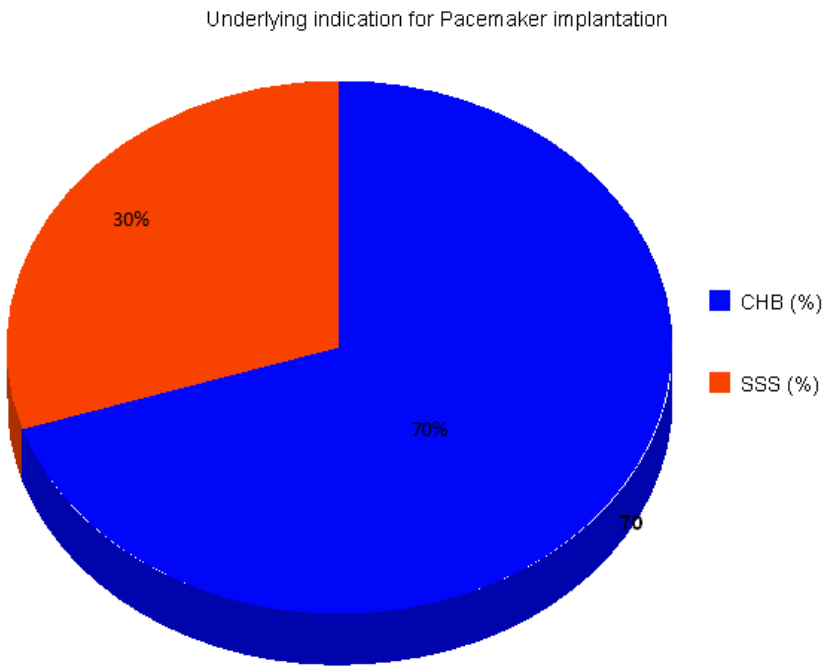


Fig.2 showing the percentage distribution of patients having underlying CHB and SSS

Table.1 Baseline characteristics

| Characteristics | Patients (n=40) | Controls (n=20) | P value |
|---|---|---|---|
| Age (years) | 50.35 ± 11.28 | 49.21 ± 8.82 | 0.069 |
| Sex | | | |
| Males | 23 (57.5%) | 11 (55%) | |
| Females | 17 (42.5%) | 9 (45%) | |
| Indication for Pacemaker | | | |
| CHB | 28 (70%) | - | |
| SSS | 12 (30%) | - | |
| pQRS duration (msec) | 162.5 ± 8.39 | 107.05 ± 11.18 | <**0.0001** |
| Echocardiographic parameters: | | | |
| LV EDV (ml) | 125.9 ± 24.87 | 117.68 ± 26.54 | 0.242 |
| LV ESV (ml) | 58.94 ± 20.94 | 47.03 ± 12.12 | **0.022** |
| LV EF (%) | 53.64 ± 9.93 | 60.05 ± 4.41 | **0.008** |
| LV DD: | | | |
| Grade 1 | 5 (12.5%) | 2 (10%) | |
| Grade 2 | - | - | |
| Grade 3 | 2 (5%) | - | |
| Grade 4 | - | - | |
| MR severity: | | | |
| Mild | 2 | - | |
| Moderate | 2 | - | |
| Severe | 1 | - | |
| MAPSE (mm) | 13.11 ± 1.72 | 13.92 ± 0.54 | **0.045** |
| TAPSE (mm) | 20.57 ± 2.62 | 21.13 ± 1.36 | 0.371 |
| MAPSE/TAPSE ratio | 0.639 ± 0.039 | 0.659 ± 0.01 | **0.028** |

(CHB- Complete heart block, SSS- Sick sinus syndrome, EDV- End diastolic volume, ESV-End systolic volume, EF- Ejection fraction, DD- Diastolic dysfunction, MR- Mitral regurgitation, MAPSE- Mitral annular plane systolic excursion, TAPSE- Tricuspid annular plane systolic excursion, pQRS – paced QRS)

The LV systolic function assessed by EF in the patient group was reduced significantly compared to the controls (53.64 ± 9.93% vs 60.05 ± 4.41%; P = 0.008). Among the 40 patients, 15 (37.5%) had reduced EF <55% suggesting underlying LV systolic dysfunction. The mean MAPSE was 13.11 ± 1.72 mm in the patients compared with average MAPSE of 13.92 ± 0.54mm (P = 0.045) in control groups. LV diastolic dysfunction of grade 3 was noted in 2 patients (5%) with pacemaker who had severe LV dysfunction . There was no severe LV diastolic dysfunction in the control group.

The mean TAPSE values, suggestive of RV systolic function, were also lesser in the patient group compared to the controls, though not statistically significant (20.57 ± 2.62 vs 21.13 ± 1.36; P=0.374).

The average MAPSE/TAPSE ratio in the normal healthy controls was 0.659 ± 0.01and 0.63 ± 0.033 in the patiens (P=0.028). As mentioned previously, a cut-off value of 0.64 for MAPSE/TAPSE ratio was taken as suggestive of ventricular dyssynchrony. The patients were further subdivided into two groups: MAPSE/TAPSE ratio below 0.64, and equal to or above 0.64, and correlation of these values with other echocardiographic parameters of ventricular functions were analyzed.

Table.2 Measured pQRS duration and echocardiographic variables by age.

| **Parameters** | **Age <40 years (n=8)** | **Age 40-60 years (n=24)** | **Age >60 years (n=8)** | **P value (ANOVA)** |
|---|---|---|---|---|
| pQRS duration (ms) | 155.62 ± 4.95 | 162.08 ± 6.90 | 170.62 ± 9.03 | **0.001** |
| LV EF (%) | 58.7 ± 6.17 | 55.51 ± 7.96 | 42.96 ± 11.47 | **0.001** |
| MAPSE (mm) | 14.06 ± 0.87 | 13.45 ± 1.42 | 11.12 ± 1.77 | 0 |
| TAPSE (mm) | 22.57 ± 1.24 | 20.81 ± 2.34 | 17.83 ± 2.31 | 0 |
| MAPSE/TAPSE ratio | 0.63 ± 0.033 | 0.64 ± 0.038 | 0.62 ± 0.04 | 0.431 |

(ANOVA- Analysis Of Variance)

Patients with VVI pacing were divided into three age groups of less than 40 years, 40-60 years and more than 60 years (Table.2) and the multiple Echocardiographic parameters were analyzed by ANOVA. There was a statistically significant correlation for increasing age with QRS duration on the ECG and LV EF (Fig.3). Patients with age above 60 years had markedly prolonged pQRS duration (mean: 170.62 ± 9.03 msec) thereby increasing the risk of electrical dyssynchrony and also reduced LV EF (mean: 42.96 ± 11.47 %) compared to the other age groups. No significant association between age and MAPSE, TAPSE or MAPSE/TAPSE ratio was noted.

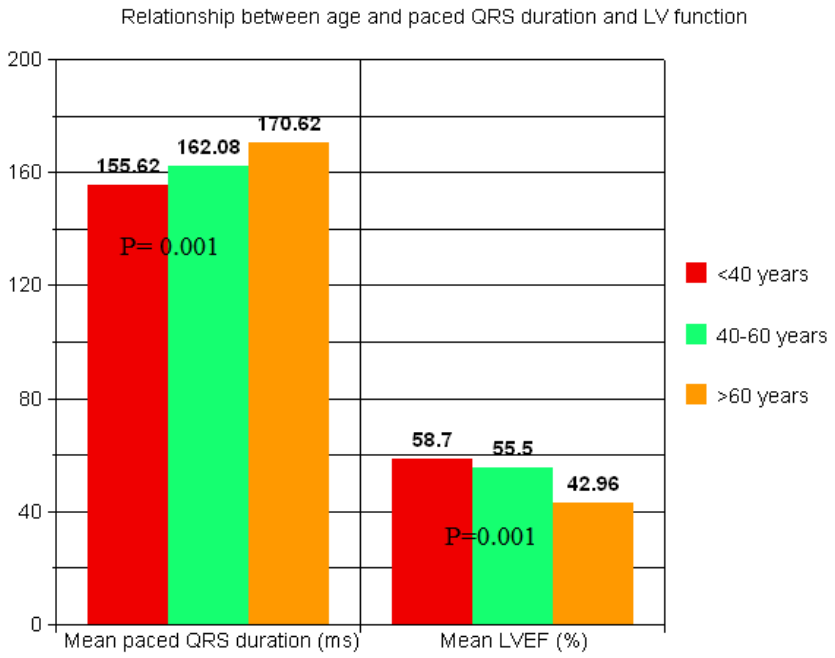


Fig.3 showing the relationship between increasing age, paced QRS duration and LV function

Table.3 Measured pQRS duration and echocardiographic variables by gender

| | **Male (n=23)** | **Female (n=17)** | **P value** |
|---|---|---|---|
| pQRS duration (ms) | 163.26 ± 7.77 | 162.77 ± 10.60 | 0.86 |
| LV EF (%) | 53.98 ± 8.61 | 51.54 ± 13.33 | 0.48 |
| MAPSE (mm) | 13.44 ± 1.69 | 12.49 ± 1.80 | 0.097 |
| TAPSE (mm) | 21.06 ± 2.43 | 19.61 ± 2.98 | 0.098 |
| MAPSE/TAPSE ratio | 0.64 ± 0.038 | 0.63 ± 0.041 | 0.431 |

There was no difference either in the pQRS duration or echo derived variables of ventricular function/ dyssynchrony and gender (Table.3).

Table.4 Measured pQRS duration and echocardiographic variables by indication for pacemaker

| | **CHB (n=28)** | **SSS (n=12)** | **P value** |
|---|---|---|---|
| pQRS duration (ms) | 162.5 ± 9.37 | 162.5 ± 5.83 | 1.00 |
| LV EF (%) | 52.33 ± 11.25 | 56.69 ± 4.97 | 0.207 |
| MAPSE (mm) | 12.74 ± 1.86 | 13.97 ± 0.89 | **0.036** |
| TAPSE (mm) | 20.38 ± 2.93 | 21.00 ± 1.71 | 0.499 |
| MAPSE/TAPSE ratio | 0.62 ± 0.03 | 0.66 ± 0.02 | **0.0001** |

(CHB- Complete heart block, SSS- Sick sinus syndrome)

The underlying indication for pacemaker implantation did show an influence on ventricular synchrony (Table.4). Patients who had underlying CHB had a lower MAPSE levels compared with patients who had SSS (12.74 ± 1.86 vs 13.97 ± 0.89; P = 0.036). They also had a more marked reduction in the MAPSE/TAPSE ratio than the SSS group (0.62 ± 0.03 vs 0.66 ± 0.02; P = 0.001).

Table.5 Measured echocardiographic variables by pQRS duration

| | **QRS duration ≤ 165 ms (n=33)** | **QRS duration > 165 ms (n=7)** | **P value** |
|---|---|---|---|
| LV EF (%) | 57.25 ± 5.93 | 39.17 ± 9.75 | **<0.0001** |
| MAPSE (mm) | 13.72 ± 1.18 | 10.66 ± 1.33 | **<0.0001** |
| TAPSE (mm) | 21.52 ± 1.83 | 16.75 ± 1.57 | **<0.0001** |
| MAPSE/TAPSE ratio | 0.639 ± 0.039 | 0.635± 0.041 | 0.80 |

Patients with marked prolongation of the pQRS duration (>165 ms) had lower LV EF (39.17 ± 9.75 vs 57.25 ± 5.93; P <0.001) than patients with lesser degrees (< 165 ms) of pQRS prolongation (Table.5 and Fig.4).

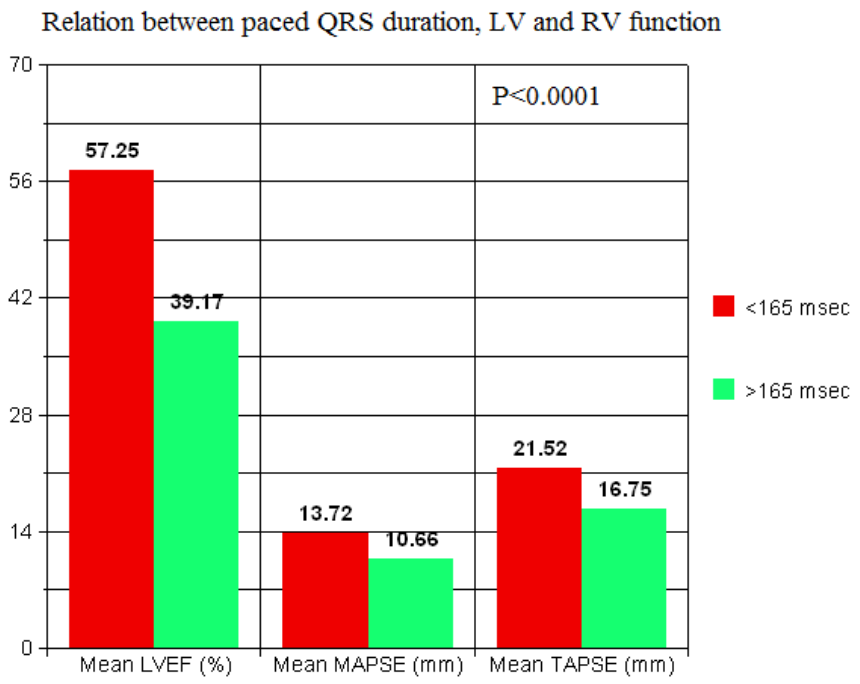


Fig.4 showing the relationship between paced QRS duration, LV and RV function

Both MAPSE and TAPSE were also significantly reduced in patients with pQRS duration >165ms as compared to patients with pQRS duration < 165 ms. However, there was no difference in the MAPSE/TAPSE ratio between the two groups.

Table.6 Measured pQRS duration and echocardiographic variables by LVEF

| | LV EF ≥55% (n=25) | LV EF <55% (n=15) | P value |
|---|---|---|---|
| pQRS duration (ms) | 158.8 ± 5.25 | 168.66 ± 9.15 | **<0.0001** |
| MAPSE (mm) | 14.1 ± 0.66 | 11.46 ± 1.69 | **<0.0001** |
| TAPSE (mm) | 22.12 ± 0.87 | 17.98 ± 2.52 | **<0.0001** |
| MAPSE/TAPSE ratio | 0.637 ± 0.037 | 0.64 ± 0.043 | 0.81 |

(LV EF- LV ejection fraction)

When patients were analyzed based on the presence of normal LVEF (>55%) and reduced LVEF (<55%), the paced pQRS duration, MAPSE and TAPSE were significantly reduced in the group with LV dysfunction compared with the group with normal LV function (Table.6 and Fig.5 & 6). However, there was no difference in the MAPSE/TAPSE ratio between the two groups.

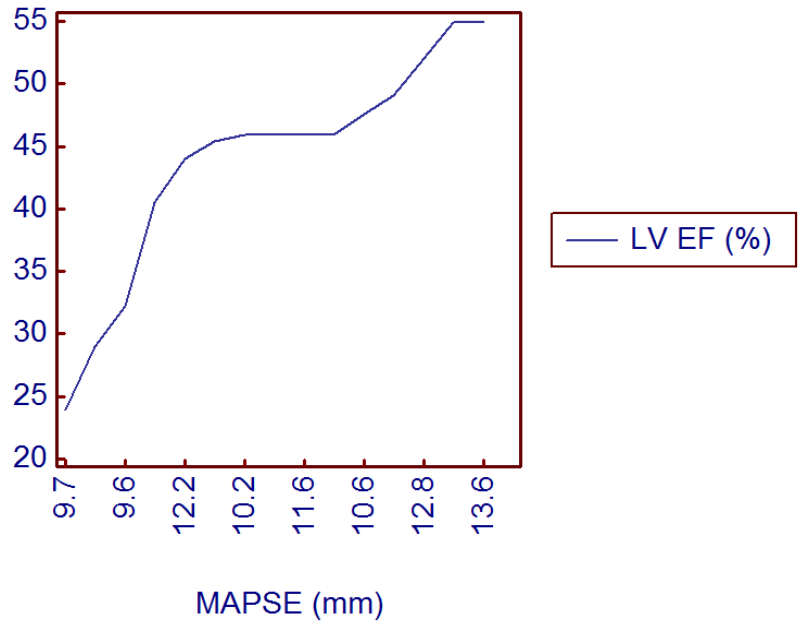


Fig.5 showing the linear relationship between LVEF and MAPSE.

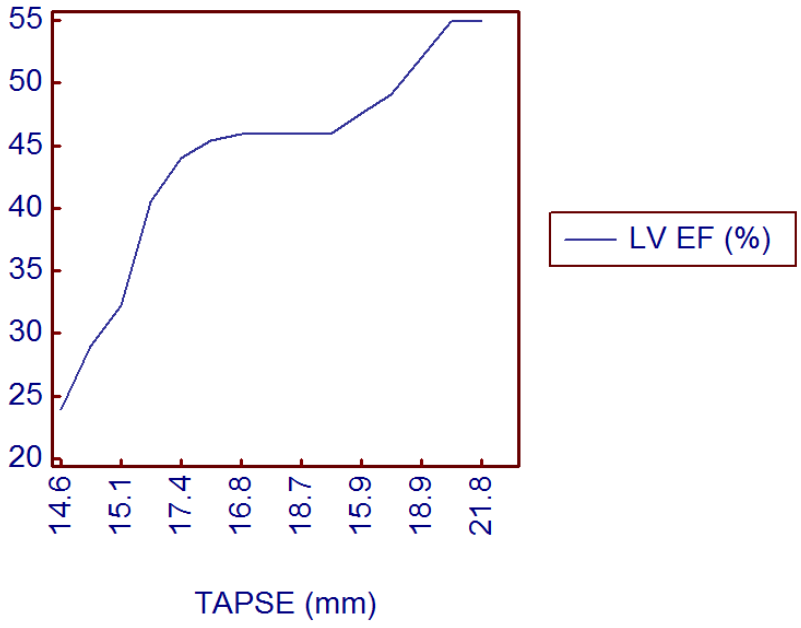


Fig.6 showing the linear relationship between LVEF and TAPSE

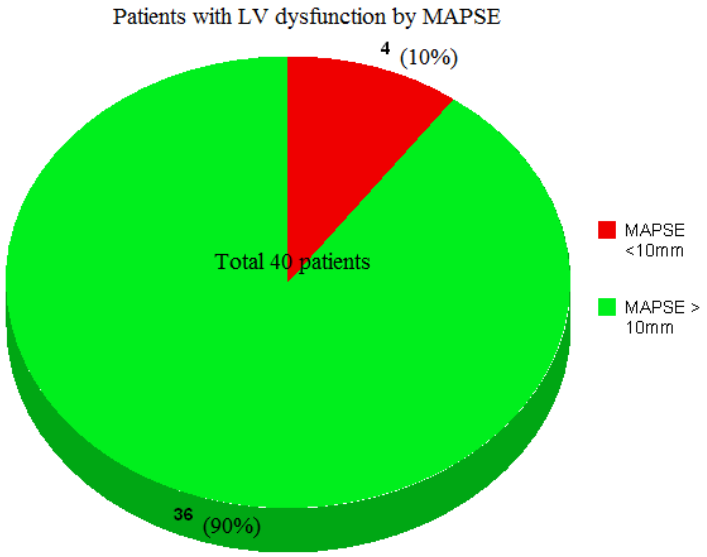


Fig.7 showing percentage of patients with LV dysfunction by MAPSE

Out of the 40 patients studied, 4 patients (10%) had MAPSE <10 mm suggestive of LV dysfunction (Fig.7)

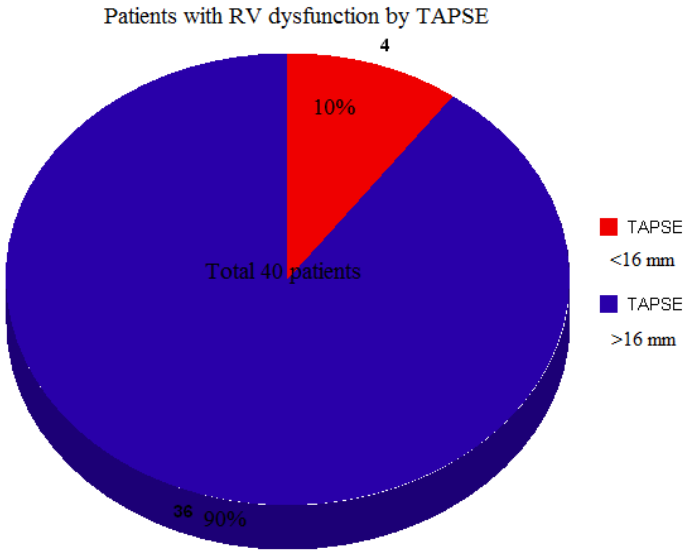


Fig.8 showing percentage of patients with RV dysfunction by TAPSE

The same 4 patients had TAPSE <16mm suggestive of associated RV dysfunction (Fig.8).

Table.7 Measured pQRS duration and echocardiographic variables by MAPSE/TAPSE ratio

| | MAPSE/TAPSE ratio <0.64 (n=19) | MAPSE/TAPSE ratio >0.64 (n=21) | P value |
|---|---|---|---|
| LV EDV (ml) | 130.43 ± 24.88 | 121.82 ± 24.73 | 0.279 |
| LV ESV (ml) | 63.37 ± 23.61 | 54.92 ± 17.83 | 0.206 |
| LV EF (%) | 52.75 ± 10.30 | 54.44 ± 9.77 | 0.059 |
| pQRS duration (ms) | 162.89 ± 9.32 | 162.14 ± 7.67 | 1.00 |

The patients were then subdivided into two groups based on the MAPSE/TAPSE ratio: patients with LV dyssynchrony (ratio <0.64) and no LV dyssynchrony(ratio > 0.64) and, relationship if any, with pQRS duration, LV functional parameters was assessed. Nearly 50% (19) of the patients had MAPSE/TAPSE ratio <0.64 suggesting the presence of some degree of LV dyssynchrony. But, there was no statistically significant difference noted between the two groups in these variables (Table.7). However, there was a trend towards an association between lower MAPSE/TAPSE ratio and reduced LV EF (Fig.9).

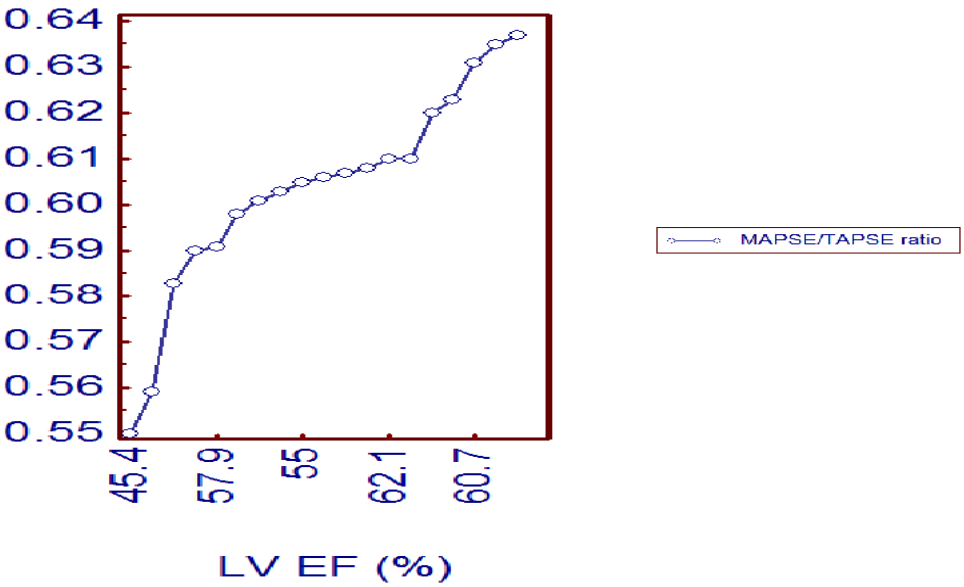


Fig.9 showing the linear relationship between MAPSE/TAPSE ratio and LVEF

# DISCUSSION

Single chamber RV pacing using VVI pacemaker is the most common type of pacemaker implantation done worldwide for various conduction disorders. The advantages of VVI pacing, in terms of survival benefit is well known. But, long term RV apical pacing is also associated with detrimental effects on the cardiac structure and function. Prior studies have showed the adverse effects of RV apical pacing on both LV and RV function. Chronic RV apical pacing is also known to result in some degree of ventricular dyssynchrony due to the altered electrical activation pattern.

## Chronic VVI pacing and LV function

Paxinos G et al, in their study, evaluated LV function in patients with sick sinus syndrome who had undergone VVI pacing and showed that VVI pacing in the long term resulted in reduction in LV EF[26]. In our study, all the patients studied had undergone pacemaker implantation between 1 to 2 years before the start of the study. The patient group had a lower LV EF compared to the control group (53.64 ± 9.93% vs 60.05 ± 4.41%; P = 0.008). This shows that the reduction in LV function can be noted as early as 1 year after implantation.

**Determinants of LV dysfunction in VVI pacing**

Among the patients with VVI pacing, in our study, LV dysfunction as assessed by reduced LV EF (<55%) was present in 15 (37.5%) patients. The major factors affecting the reduction in LV function were the paced QRS duration, age of the patient and underlying prior CHB.

The paced QRS complex duration is a major determinant in the adverse effects of chronic VVI pacing. Su Y et al, proved in their study that paced QRS duration ≥ 180 ms is associated with progressive LV dilation and worsening LV EF[27]. In our study also, the patients with paced QRS duration >165 ms had significant reduction in the LV EF, MAPSE and TAPSE compared to patients with lesser duration of paced QRS complex.

Advancing age was a major determinant affecting LV function. Those patients above the age of 60 years had more marked prolongation of the paced QRS complex and higher reduction in the LV EF. The biventricular function assessment did not show significant difference between males and females.

In our study, patients with underlying CHB as the indication for pacemaker implantation had significantly lower MAPSE and MAPSE/TAPSE ratios compared to patients with SSS. This difference may possibly be due to the fact that in patients with CHB, there is uninterrupted pacing discharge from

the VVI pacemaker to maintain the heart rate. As a result of this, the ventricles are continuously contracting out of phase, resulting in early onset of LV dysfunction. In contrast, the presence of intermittent intrinsic rhythm in patients with sick sinus syndrome, reduces the repetitive pacing discharges; thereby lowering the detrimental effects of chronic VVI pacing on the ventricular function.

**Mitral regurgitation in VVI pacing**

The development of mitral regurgitation of varying degrees in VVI pacing had been demonstrated in previous studies[29]. In our study also, moderate to severe MR was present in 3 (8%) patients. It was demonstrated by Sassone B et al that the functional MR developing in pacemaker implantation was due to the presence of both AV dyssynchrony and alteration in the ventricular activation sequence, with the latter playing the major role[30].

**Role of MAPSE and TAPSE**

Those patients with reduced LV EF <55% had significantly increased QRS duration compared to patients with normal LV function. There was a linear correlation between levels of LV EF below 55% and reduction in MAPSE and TAPSE; lower the LV EF, lower were the MAPSE and TAPSE levels.

The usefulness of MAPSE as a surrogate marker of LV systolic function was demonstrated previously by Pai R G et al[28]. In our study, 10% of pacemaker group had reduced MAPSE (<10mm) and there was a linear correlation between MAPSE levels and reduced LV EF. These 10% patients also had lower TAPSE (<16mm) possibly due to biventricular dysfunction as a result of ventricular dyssynchrony.

In our study, the absolute value of TAPSE was more than MAPSE in both the patient and control by around 50%. This further favours the previous conclusion by various studies[(12-13)] that the tricuspid annular plane systolic movement is more than mitral annular movement during systole. This is explained by the predominant systolic movement of the RV along its longitudinal axis compared to the LV systolic movement along longitudinal, circular and radial axis[13].

**MAPSE/TAPSE ratio and interventricular dyssynchrony in VVI pacing**

Bruhl et al concluded in their study that concluded that MAPSE/TAPSE and LVs/RVs ratios are good surrogate measures of left and right ventricular systolic relationship and interdependence[12]. In their study, MAPSE/TAPSE ratio was 0.66 ± 0.14 in normal healthy individual and concluded that reduced levels of this ratio can be used to study interventricular relationship and ventricular dyssynchrony. In our study, the average MAPSE/TAPSE ratio in the normal healthy controls was 0.659 ± 0.01and 0.63 ± 0.033 in the patients

(P=0.028). Based on the above studies, a cut-off value of 0.64 for MAPSE/TAPSE ratio was taken as the cut-off suggestive of LV dyssynchrony. The patients were further subdivided into two groups: MAPSE/TAPSE ratio below 0.64 and above 0.64, and correlation of these values with other echocardiographic parameters of ventricular functions were analyzed. There was no statistically significant difference noted between the two groups in these variables. However, there was a trend towards a linear association between lower MAPSE/TAPSE ratio <0.64 and reduced LV EF, thus strongly favouring the direct relationship between LV dyssynchrony and worsening LV function.

## LIMITATIONS OF THE STUDY:

1. All of the pacemaker patients had undergone VVI implantation only between 1 to 2 years before the start of the study. The effect of VVI pacing in patients with longer duration (>2 years) of implantation was not done.

2. Even though the linear correlation between lower LV EF and ventricular dyssynchrony by MAPSE/TAPSE ratio was shown, no statistically significant association between the two variables could be demonstrated. This might have been overcome by a larger study population.

3. Even though M-mode and 2D echocardiography was done for measuring the variables in our study, the current Echo method of choice for assessing ventricular function and wall motion is TDI with strain rate imaging.

## CONCLUSIONS

1. Chronic VVI pacing from RV apex is associated with varying degrees of LV and RV dysfunction.

2. The degree of prolongation of the paced QRS duration is a powerful determinant of worsening ventricular function.

3. Advanced age is associated with both a marked prolongation of the paced QRS duration and progressive ventricular dysfunction in patients with VVI pacing.

4. MAPSE and TAPSE are useful parameters for quickly assessing LV and RV functions in VVI pacing.

5. LVEF and MAPSE/TAPSE ratio have linear correlation for LV dysfunction in VVI pacing.

6. MAPSE/TAPSE ratio is a novel indicator of ventricular dysfunction and lower levels are suggestive of associated interventricular dyssynchrony. However, this ratio needs further validation by larger randomized studies.

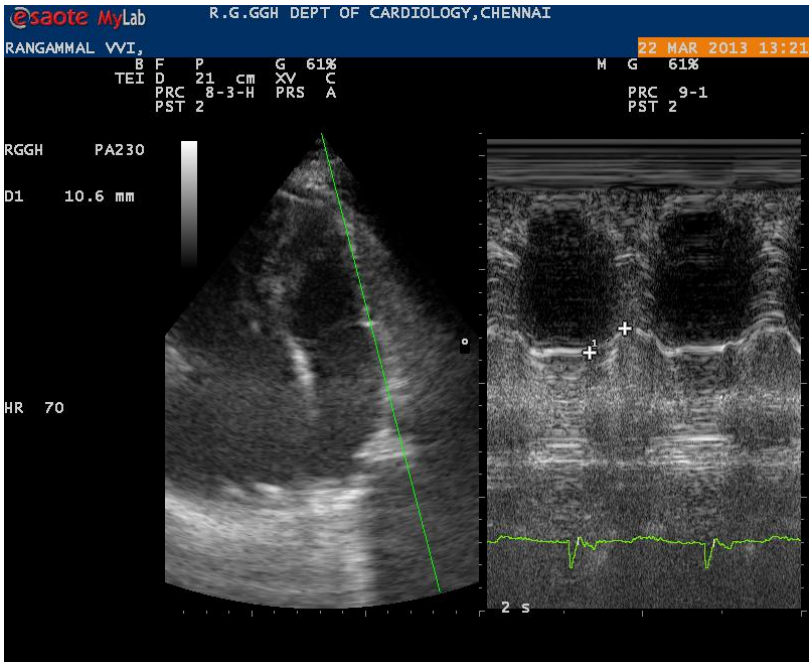


Fig.A showing Apical 4-chamber view for measuring MAPSE. The M-mode cursor placed along the lateral annulus of the mitral valve

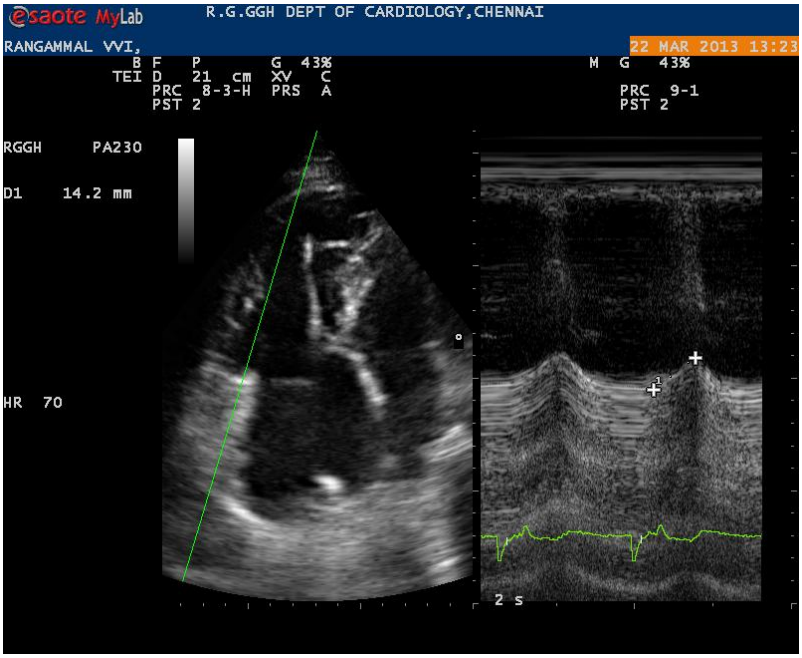


Fig.B showing Apical 4-chamber view for measuring TAPSE. The M-mode cursor placed along the lateral annulus of the tricuspid valve

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## ABBREVIATIONS AND ACRONYMS

| | | |
|---|---|---|
| AAI | : | Atrial inhibited pacing |
| APC | : | Atrial premature contraction |
| ATP | : | Adenosine triphosphate |
| AV | : | Atrioventricular |
| BNP | : | Brain natriuretic peptide |
| CHB | : | Complete heart block |
| CRT | : | Cardiac resynchronization therapy |
| CICR | : | Calcium induced calcium release |
| DD | : | Diastolic dysfunction |
| DDI | : | AV sequential, Non-P synchronized pacing |
| DDD | : | Dual chamber pacing and sensing with inhibition and tracking |
| DFT | : | Diastolic filling time |
| EDV | : | End diastolic volume |
| EF | : | Ejection fraction |
| ESV | : | End systolic volume |
| FAC | : | Fractional area change |
| IMP | : | Index of myocardial performance |
| IVMD | : | Interventricular mechanical delay |
| IVR | : | Isovolumic relaxation |
| LBBB | : | Left bundle branch block |
| LV | : | Left ventricle |
| MAPSE | : | Mitral annular plane systolic excursion |

| | | |
|---|---|---|
| NCX | : | Sodium-calcium exchanger pump |
| PPI | : | Permanent pacemaker implantation |
| RBBB | : | Right bundle branch block |
| RV | : | Right ventricle |
| SA | : | Sinoatrial |
| SERCA | : | Sarcoplasmic reticulum calcium ATPase |
| SPWMD | : | Septal-to-posterior wall motion delay |
| SSS | : | Sick sinus syndrome |
| SVC | : | Superior vena cava |
| TAPSE | : | Tricuspid annular plane systolic excursion |
| TDI | : | Tissue Doppler imaging |
| VT | : | Ventricular tachycardia |
| VVI | : | Ventricular inhibited pacing |

**PROFORMA**

CD No:

Name: Age: Sex:

Year of pacemaker implantation:

PR:

BP:

ECG:

**Echo parameters:**

LVEDV (ml): LVESV (ml): LV EF (%):

LV DD:

MR severity:

TR:

RVSP:

MAPSE (mm):

TAPSE (mm):

MAPSE/ TAPSE ratio:

# INFORMATION TO PARTICIPANTS

**Title** : EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS

**Principal Investigator: Dr. S .Srikumar**

**Co-Investigator(if any):**

**Name of Participant:**

**Site : RGGGH& MMC, Chennai**

You are invited to take part in this research/ study/procedures/tests. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

**What is the purpose of research?**

Despite the differences in the right and left ventricles in shape and myocardial contractile element density, the synchronous electrical excitation and mechanical contraction of both the ventricles and the ventricular interdependence maintains the biventricular function in balance.

VVI pacemaker implantation with RV apical pacing disturbs this balance by abnormal electrical and mechanical activation of the ventricles (or ventricular dyssynchrony) with detrimental effects on cardiac structure and left ventricular (LV) function

Echocardiographic evaluation of LV and RV systolic function by measuring MAPSE and TAPSE and their ratio (MAPSE/TAPSE ratio) has been shown to correlate with ventricular synchrony in normal healthy individuals. So,in our study we are using the M-mode echo measurement of MAPSE, TAPSE, and their ratio to obtain information regarding the degree of ventricular dyssynchrony in patients with VVI pacing.

We have obtained permission from the Institutional Ethics Committee.

**The study design**

It is a prospective case control study.

**Study Procedures**

- The study involves evaluation of detailed history along with clinical presentation and assessment of echocardiographic parameters, including LV and RV function assessment

by MAPSE, TAPSE and MAPSE/TAPSE ratio for evaluating ventricular dyssynchrony in patients with VVI pacemaker implantation.

The results of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.

**Confidentiality of the information obtained from you**

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, Institutional Ethics Committee and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

**How will your decision to not participate in the study affect you?**

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not loose any benefits to which you are entitled.

**Can you decide to stop participating in the study once you start?**

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment/discontinuing of procedures etc.

Signature of Investigator
Date

Signature of Participant
Date

## PATIENT CONSENT FORM

**STUDY TITLE :**

**EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS**

*Patient may check (✓) these boxes.*

PARTICIPANT NAME : DATE:

AGE: SEX: C.D.NO. :

1. The details of the study have been provided to me in writing and explained to me in my own language. ☐
2. I confirm that I have understood the purpose of the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction. ☐
3. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected. ☐
4. I understand that investigator, the institution, regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐
5. I hereby consent to, undergo complete physical examination ,and diagnostic tests including hematological, biochemical, radiological and urine examinations ☐
6. I have been given an information sheet giving details of the study .
7. I hereby consent to participate in the above study ☐

Signature of the Participant

| Name | Age (yrs) | Sex | QRS durn ms) | EDV (ml) | ESV (ml) | LV EF (%) | LV DD | MR | MAPSE (mm) | TAPSE (mm) | MAPSE/TAPSE Ratio |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Rajendran | 52 | M | 114 | 142 | 54 | 61 | NIL | NIL | 14.2 | 22.5 | 0.631 |
| Gurusamy | 44 | M | 120 | 138 | 48 | 65 | NIL | NIL | 13.8 | 23.1 | 0.597 |
| Kavitha | 47 | F | 120 | 70 | 27 | 61.4 | NIL | Trivial | 13.7 | 21.5 | 0.637 |
| Ramasamy | 65 | M | 110 | 147 | 65.9 | 55.2 | Grade 1 | NIL | 14.7 | 23.4 | 0.628 |
| Gajendran | 40 | M | 90 | 129 | 58.1 | 55.1 | NIL | NIL | 13.3 | 22 | 0.604 |
| Angalammal | 56 | F | 110 | 97.3 | 27 | 72 | NIL | NIL | 14.4 | 20.6 | 0.699 |
| Manimegalai | 38 | F | 90 | 88 | 35 | 60 | NIL | NIL | 13.5 | 19.7 | 0.685 |
| Rajamanickam | 37 | M | 110 | 147 | 61.9 | 57.9 | NIL | NIL | 14.6 | 21.2 | 0.688 |
| Pavithra | 57 | F | 120 | 129 | 50.8 | 60.7 | NIL | Trivial | 12.8 | 22.4 | 0.571 |
| Pachaiyappan | 45 | M | 110 | 107 | 35 | 67.4 | NIL | NIL | 14.8 | 19.8 | 0.747 |
| Mahendran | 42 | M | 120 | 153 | 58.1 | 62.1 | NIL | NIL | 13.9 | 23.4 | 0.594 |
| Kaliammal | 55 | F | 120 | 97.3 | 40.9 | 57.9 | NIL | NIL | 13.7 | 19.4 | 0.706 |
| Divya | 37 | F | 90 | 112 | 50.8 | 55 | **NIL** | NIL | 13.6 | 20.7 | 0.657 |
| Sangaraiyan | 65 | M | 110 | 141 | 61.9 | 56 | Grade 1 | NIL | 14.2 | 19.4 | 0.731 |
| Moorthy | 60 | M | 100 | 107 | 44.1 | 58.9 | NIL | NIL | 14.6 | 20.7 | 0.705 |
| Thulasi | 48 | F | 100 | 97.3 | 40.9 | 57.9 | NIL | Trivial | 13.4 | 20.6 | 0.623 |
| Dinakar | 53 | M | 110 | 153 | 58 | 62 | NIL | NIL | 14.1 | 21.5 | 0.655 |
| Poosam | 46 | F | 90 | 107 | 44.1 | 58.9 | NIL | NIL | 13.5 | 20.3 | 0.665 |
| Pothumponnu | 48 | F | 100 | 74.2 | 32.2 | 56.6 | NIL | NIL | 13.7 | 19.3 | 0.709 |

| Name | Age (yrs) | Sex | PPI Indicn | Years since PPI | QRS durn (ms) | LV EDV (ml) | LV ESV (ml) | LV EF (%) | LV DD | MR severity | MAPSE (mm) | TAPSE (mm) | MAPSE/TAPSE ratio |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kala | 31 | F | CHB | 1 | 150 | 87.6 | 35 | 60 | NIL | NIL | 13.3 | 20.6 | 0.645 |
| Krishnamoorthy | 33 | M | CHB | 1 | 150 | 141 | 61.9 | 56.1 | NIL | NIL | 13.4 | 22.2 | 0.603 |
| Murugan | 33 | M | CHB | 1 | 155 | 107 | 35 | 67.4 | NIL | NIL | 14.4 | 23.6 | 0.61 |
| Pandian | 33 | M | SSS | 1 | 160 | 107 | 44.1 | 58.9 | NIL | NIL | 15.2 | 23.5 | 0.648 |
| Vijaya | 34 | F | CHB | 2 | 155 | 70 | 27 | 61.4 | NIL | NIL | 14.2 | 23.6 | 0.601 |
| Kulanthai Therasa | 34 | F | CHB | 1 | 155 | 97.3 | 40.9 | 57.9 | NIL | NIL | 12.6 | 21.3 | 0.591 |
| Murugesan | 37 | M | CHB | 1 | 155 | 129 | 50.8 | 45.9 | NIL | Trivial | 14.7 | 23.9 | 0.674 |
| Ganesh | 38 | M | SSS | 1 | 165 | 153 | 58 | 62 | NIL | NIL | 14.7 | 21.9 | 0.671 |
| Sheikh Kasim Ali | 42 | M | CHB | 2 | 160 | 153 | 58.1 | 62.1 | NIL | NIL | 13.8 | 22.5 | 0.61 |
| Lakshmi | 44 | F | CHB | 1 | 160 | 118 | 61.9 | 47.6 | NIL | Trivial | 10.6 | 15.9 | 0.666 |
| Kaniammal | 44 | F | SSS | 1 | 160 | 97.3 | 40.9 | 57.9 | NIL | NIL | 13.7 | 20.9 | 0.655 |
| Shanmugam | 45 | M | SSS | 1 | 160 | 153 | 58.1 | 62.1 | NIL | NIL | 14.8 | 21.8 | 0.678 |
| Adhiyammal | 45 | F | CHB | 1 | 180 | 166 | 112 | 32.2 | Grade 1 | Mild | 9.6 | 15.1 | 0.635 |
| Indira Gandhi | 46 | F | CHB | 1 | 150 | 107 | 44.1 | 58.9 | NIL | NIL | 12.7 | 22.7 | 0.559 |
| Jayaraman | 48 | M | SSS | 2 | 150 | 141 | 54.4 | 57.9 | NIL | NIL | 14.1 | 21.6 | 0.652 |
| Balu | 48 | M | SSS | 2 | 155 | 153 | 65.9 | 57.1 | NIL | Trivial | 14.8 | 20.7 | 0.714 |
| Pandi | 48 | M | CHB | 1 | 165 | 129 | 58.1 | 55.1 | NIL | NIL | 14.8 | 21.6 | 0.685 |
| Veerappan | 48 | M | SSS | 1 | 165 | 147 | 61.9 | 57.9 | NIL | NIL | 14.1 | 21.4 | 0.658 |
| Chinnappa | 48 | M | CHB | 1 | 175 | 129 | 70 | 45.9 | Grade 1 | Mild | 11.6 | 18.7 | 0.62 |
| Pushpa | 49 | F | SSS | 1 | 165 | 112 | 50.8 | 54.9 | NIL | NIL | 13.3 | 19.3 | 0.689 |
| Kulasekaran | 49 | M | SSS | 2 | 165 | 129 | 50.8 | 60.7 | NIL | NIL | 14.4 | 22.8 | 0.631 |
| Govindaraj | 50 | M | SSS | 1 | 170 | 141 | 78 | 44 | NIL | Mild | 12.2 | 17.4 | 0.701 |
| Rajendran | 51 | M | CHB | 1 | 160 | 147 | 65.9 | 55.2 | Grade 1 | NIL | 13.4 | 22.7 | 0.59 |
| Vimala | 52 | F | CHB | 2 | 160 | 97.3 | 27 | 72.2 | NIL | NIL | 14.6 | 22.1 | 0.66 |
| Perumal | 52 | M | CHB | 1 | 160 | 147 | 65.9 | 55.2 | NIL | NIL | 14.2 | 23.4 | 0.606 |
| Kalirathinam | 53 | M | CHB | 1 | 165 | 129 | 58 | 55 | NIL | NIL | 13.8 | 22.8 | 0.605 |
| Krishnaveni | 55 | F | SSS | 1 | 165 | 102 | 50.8 | 54.9 | NIL | NIL | 13.6 | 21.8 | 0.623 |
| Muniammal | 58 | F | CHB | 1 | 155 | 129 | 50.8 | 60.7 | NIL | NIL | 13.7 | 22.5 | 0.608 |
| Nithya | 58 | F | CHB | 1 | 160 | 74.2 | 32.2 | 56.6 | NIL | NIL | 14.6 | 21.2 | 0.688 |
| Shakunthala | 58 | F | CHB | 1 | 165 | 83 | 29.5 | 64.4 | NIL | NIL | 14.5 | 22 | 0.659 |
| Masilamani | 58 | M | CHB | 2 | 165 | 147 | 61.9 | 57.9 | NIL | NIL | 14.8 | 21.9 | 0.675 |
| Babyammal | 60 | F | CHB | 1 | 155 | 107 | 58.1 | 45.9 | NIL | NIL | 11.3 | 16.8 | 0.672 |
| Kanniappan | 62 | M | SSS | 1 | 170 | 112 | 54 | 52 | NIL | NIL | 12.8 | 18.9 | 0.677 |
| Kesavan | 62 | M | CHB | 1 | 175 | 147 | 87.6 | 40.5 | Grade 1 | Moderate | 9.4 | 15.7 | 0.598 |
| Rajeswari | 66 | F | CHB | 1 | 160 | 130 | 70 | 45.4 | NIL | NIL | 10.3 | 18.7 | 0.55 |
| Lakshmi | 66 | F | CHB | 1 | 165 | 129 | 65.9 | 49.1 | NIL | Trivial | 12.9 | 19.4 | 0.664 |
| Amirthavalli | 66 | F | CHB | 1 | 185 | 141 | 107 | 23.9 | Grade 3 | Moderate | 9.7 | 14.6 | 0.664 |
| Sivalingam | 67 | M | CHB | 2 | 160 | 129 | 54.4 | 57.9 | NIL | NIL | 13.9 | 21.8 | 0.637 |
| Thirupathi | 68 | M | CHB | 1 | 180 | 166 | 118 | 29 | Grade 3 | Severe | 9.8 | 16.8 | 0.583 |
| Pachaiyappan | 75 | M | CHB | 1 | 170 | 153 | 83 | 45.9 | Grade 1 | NIL | 10.2 | 16.8 | 0.607 |

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“EVALUATION OF THE INTERVENTRICULAR SYSTOLIC RELATIONSHIP IN PATIENTS WITH RIGHT VENTRICULAR APICAL PACING WITH VENTRICULAR INHIBITED PACING MODE BY ECHOCARDIOGRAPHY USING MITRAL AND TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSIONS” Dissertation submitted to THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY In partial fulfillment of the requirements for the award of the degree of D.M. BRANCH - II CARDIOLOGY MADRAS MEDICAL COLLEGE RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI 600 003 THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI, INDIA AUGUST 2013 INTRODUCTION The right (RV) and left (LV) ventricles differ markedly in shape and myocardial contractile element density. Despite these...

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*Dissertation submitted to*

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

*In partial fulfillment of the requirements for the award of the degree of*

D.M. BRANCH - II CARDIOLOGY

MADRAS MEDICAL COLLEGE
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL,
CHENNAI 600 003

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI -3**

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## CERTIFICATE OF APPROVAL

To
Dr.S.Srikumar
PG in DM Cardiology,
MMC, Chennai -3.

Dear Dr.S.SRIKUMAR

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Evalution of the interventricular systolic Relationship in patients with VVI pacing by Ecocardiography using Tricuspid and mitral Annular peak systolic Excursions" No.03032013.

The following members of Ethics Committee were present in the meeting held on 05.03.2013 conducted at Madras Medical College, Chennai -3.

1. Dr.SivaKumar, MS FICS FAIS --- Chairperson
2. Prof. R. Nandhini MD -- Member Secretary
   Director, Instt. of Pharmacology ,MMC, Ch-3
3. Prof. Shyamraj MD -- Member
   Director i/c , Instt. of Biochemistry , MMC, Ch-3
4. Prof. P. Karkuzhali. MD -- Member
   Prof., Instt. of Pathology, MMC, Ch-3
5. Prof. A. Radhakrishnan MD -- Member
   Prof of Internal Medicine, MMC, Ch-3
6. Prof. S. Deivanayagam MS -- Member
   Prof of Surgery, MMC, Ch-3
7. Thiru. S. Govindsamy. BABL -- Lawyer
8. Tmt. Arnold Saulina MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nadini

Member Secretary, Ethics Committee