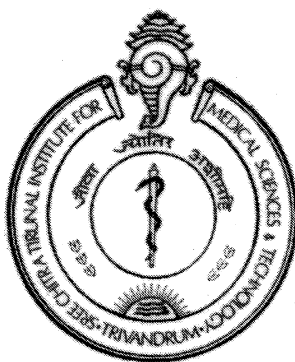


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PROJECT REPORT



Name : Dr. Krishnakumar.K

Programme : D.M. Cardiology

Month & Year of submission : November, 2002

Certificate

I, Dr. Krishnakumar.K, hereby declare that I have performed all the procedures in the work under report.

Signature



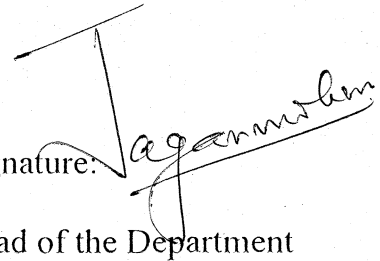
Name KRISHNA KUMAR.K

Place: Trivandrum

Date: 11-11-2002

Forwarded. He has carried out the minimum required procedures.

Signature:



Head of the Department

LIST OF PROJECTS

- ❖ **EFFICACY OF AMIODARONE IN RESTORING AND MAINTAINING SINUS RHYTHM IN RHEUMATIC HEART DISEASE AND ATRIAL FIBRILLATION.**

- ❖ **TEI INDEX AS A MARKER OF LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC DYSFUNCTION.**

Name : Dr. Krishnakumar.K

Programme : DM Cardiology

Month & Year
Of submission : November, 2002

**EFFICACY OF AMIODARONE IN RESTORING AND
MAINTAINING SINUS RHYTHM IN RHEUMATIC HEART
DISEASE AND ATRIAL FIBRILLATION**

ABSTRACT

Background

Rhythm control in AF is thought to be better than rate control and amiodarone is one of the drug option in maintaining sinus rhythm

Objective

To study the efficacy of amiodarone for reversion to sinus rhythm of chronic rheumatic atrial fibrillation and maintenance of it once reverted. Predictors of maintenance of sinus rhythm, if any, were also analyzed.

Materials and methods

Patients with AF were electrically cardioverted after a trial of amiodarone therapy. Successfully cardioverted patients were continued on amiodarone maintenance therapy. Patients were followed up every 3 months for a period of one year during which ECG, thyroid function and pulmonary function were assessed.

Results

Out of 50 patients, only 4(8%) patients reverted to sinus rhythm on amiodarone alone .In the remaining 46 patients, DC version was successful in 41(89.1%) patients. At 6 months, 72% of total patients were maintaining sinus rhythm which reduced to 60% at one year. Only significant predictor of long term maintenance of sinus rhythm was duration of AF. There was no significant adverse effects attributable to amiodarone.

Conclusion

Atrial fibrillation can be restored to sinus rhythm with a combination of electrical cardioversion and amiodarone therapy in majority of patients. Amiodarone is safe and effective in long term maintenance of sinus rhythm in such patients.

INTRODUCTION

Atrial fibrillation is common in cases of rheumatic heart disease and worsens the outcome of these patients.¹ It is associated with an increased susceptibility to embolic strokes, decreased exercise tolerance, tachycardia induced cardiomyopathy & shortened life expectancy. The overall prevalence of AF in adult population is 0.4% but frequency increases with age to approximately 2-4% in those aged > 60 yrs.

Rate control has been the mainstay in management of rheumatic atrial fibrillation but rhythm control logically seems to be ideal in these patients. Maintenance of sinus rhythm (SR) in such patients is difficult due to left atrial enlargement, long duration of atrial fibrillation and atrial scarring.

Though amiodarone is one of the most effective antiarrhythmic agents in maintaining sinus rhythm in patients with atrial fibrillation, very few studies have addressed its efficacy in atrial fibrillation associated with rheumatic heart disease.

Low dose amiodarone is effective for maintaining sinus rhythm in patients with chronic atrial fibrillation and is associated with low incidence of side effects.⁴ During loading with 600mg amiodarone for 4 weeks,

16% reverted to NSR, and with additional cardio version 84% patients achieved NSR. 53% of total patients with AF were in NSR after three years.

Short-term amiodarone with or without electrical cardio version is effective and safe in the treatment of chronic rheumatic AF after mitral valve surgery.³

Amiodarone has efficacy of reverting to SR from AF in 40% patients and in 37% patient with addition of DC version. After achieving SR 70% remained in SR at follow up of 18 months.⁷ The duration of AF ≤ 48 months alone or in combination with LA diameter < 45 mm were best predictors of long term maintenance of SR. Thus short-term amiodarone with/without DC version is effective and safe in treatment of chronic AF

NON-PHARMACOLOGICAL APPROACHES TO ATRIAL FIBRILLATION

The main stay of managing atrial fibrillation (AF) is drug therapy .Nonpharmacological approaches to management of AF includes AV junction ablation , AV nodal modification, internal atrial defibrillation, surgical procedures like maze procedure. Atrial pacing and dual site atrial pacing results in homogenous atrial depolarization. Rapid conversion of AF may decrease predisposition towards additional episodes of AF.

AIMS

- ◆ Efficacy of amiodarone for reversion of chronic rheumatic atrial fibrillation to normal sinus rhythm.
- ◆ Efficacy of amiodarone in maintenance of normal sinus rhythm after DC version in rheumatic heart disease with chronic atrial fibrillation at 6 months and 1 year.
- ◆ Evaluation of predictors of maintenance of normal sinus rhythm with amiodarone

MATERIALS AND METHODS

This is a prospective study. From Jan 2000 - December 2001, 50 patients with rheumatic heart disease and chronic atrial fibrillation were included in the study. Among the 50 patients there were 22 males and 28 females. Chronic AF was defined as duration of AF of more than 7 days.

All patients underwent detailed clinical, echocardiographic examination. ECG was done in all patients to look for current rhythm. Two dimensional and doppler echocardiographic study was done using Hewlett-Packard Sonos 1000 system and a 2.5 MHZ transducer. Mitral valve area was calculated by planimetry and pressure half time method.

Mitral regurgitation and aortic regurgitation were evaluated using color doppler. Pulmonary artery pressure was determined indirectly by calculating RV systolic pressure through doppler derived gradient of tricuspid regurgitation.

LV function was assessed by M-mode echocardiogram. Patients included in the study were both preoperative and post operative patients with RHD and atrial fibrillation of varying duration. Left atrial size was measured in parasternal long axis view as maximum distance from trailing

edge of aortic wall of LA to leading edge of posterior wall of left atrium at end of ventricular systole.

Exclusion criteria:

Pregnancy, preexisting pulmonary parenchymal disease, thyroid disorders and any contraindication for anticoagulation. Non-compliant patient and LA clot were excluded from study cohort.

Study protocol:

Informed consent from patients was obtained. All patients with rheumatic heart disease with atrial fibrillation received amiodarone 200mg thrice daily in the first week and thereafter were put on maintenance dose of 200mg once daily for one month.

Prior to giving oral amiodarone basal thyroid function tests and pulmonary function tests were done. All patients were given warfarin to maintain INR between 2 and 2.5. After the end of one month, patients were evaluated for conversion to sinus rhythm on the basis of a 12 lead ECG. Patients who persisted in AF were attempted cardioversion using DC shock. Cardioversion was performed under deep sedation with IV midazolam.

Prior to cardioversion all patients underwent trans esophageal echo to assess LA clot.

RESULTS

The basal characteristics of the patient population was as follows.

No. of patients	50
Age group	21-56 yrs
Male: Female	22: 28(44% vs 56%)
Mitral Valve disease	13/50 (26%)
Combined aortic + mitral disease:	36/50(72%)
Good LV function	48/50(96%)
LV dysfunction	2/50(4%)
Preoperative status	18/50(36%)
Post operative	32/50(64%)
Prosthetic valve patients	12/50(24%)
Post CMV	18/50(36%)
Post BMV	22/50(44%)

Out of 50 patients enrolled in the study one developed hypothyroidism at three months and hence amiodarone was stopped. Six months follow up was available in all 50 patients, 12-month follow up was available in 41 patients.

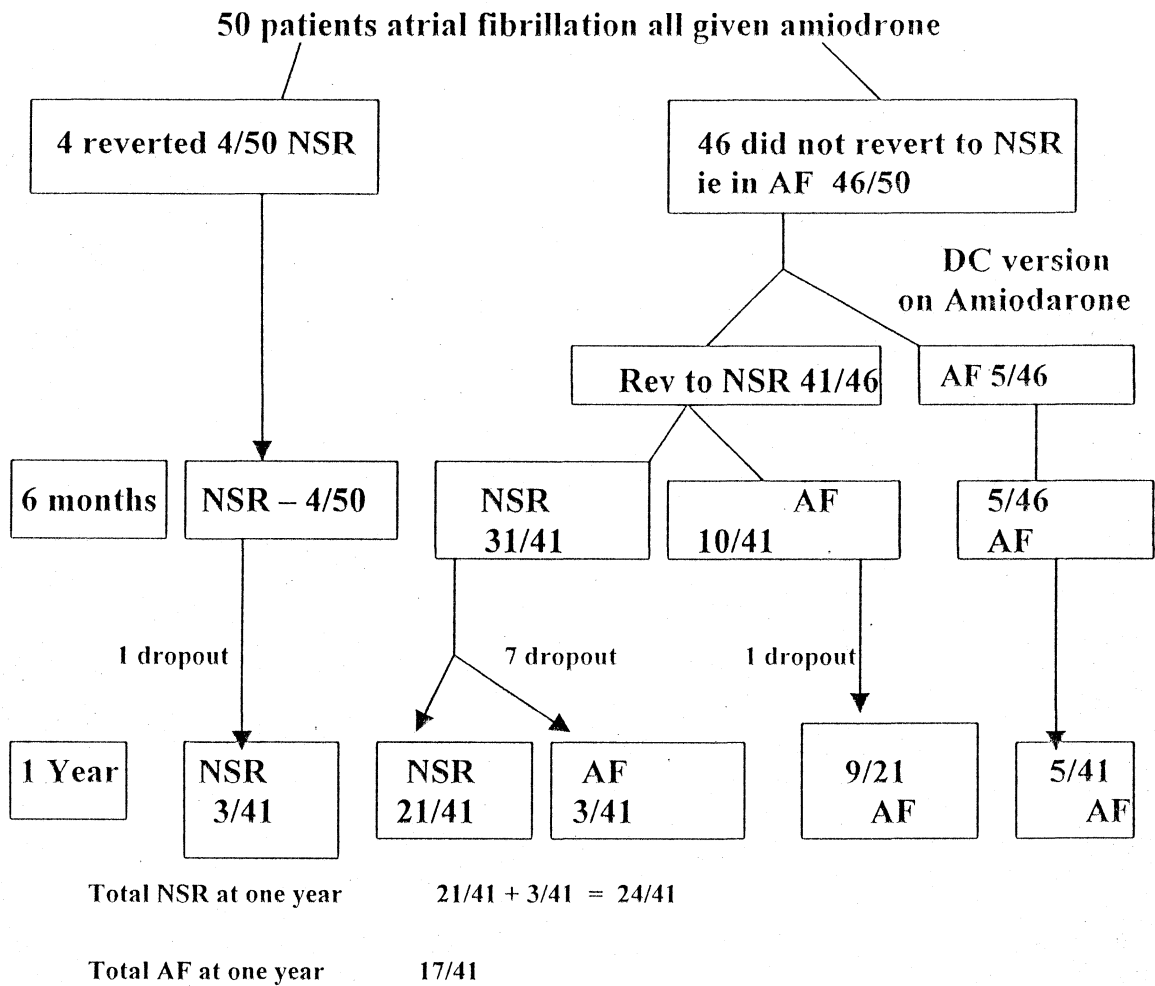
	NSR	AF	Total
1 month of amiodarone alone	4 (8%)	46 (92%)	50
After DC version	45 (90%)	5 (10%)	50
6 month after DC version	36/50 (72%)	14/50(28%)	50
1 yr after DC version	24/41 (60%)	17/41 (40%)	41

At one-month follow up 4 patients out of 50 (8%) reverted to SR with amiodarone alone. Of the remaining 46 patients DC version was successful in conversion to NSR in 41/46 (90%).

Though some patients converted at 100 Joules and some required 200J, most of patients reverted to NSR with 200 Joules. Thus at one month after DC version 45/50 (90%) reverted to NSR. 5 patients remained in AF (10%). At 6 months of the study, of the 45 patients who were in SR at one month, 9 patients (18%) had reverted to atrial fibrillation and 36 patients remained (72%) in sinus rhythm. None of 5 patients who were in atrial fibrillation at end of 1st month spontaneously reverted to NSR.

This 1st synchronized DC current shock was attempted at 150 Joules, further at 200 and 360 Joules. Patients who reverted to sinus rhythm were continued on amiodarone 200 mg daily. Patients who did not revert to sinus rhythm were put up for rate control. For these groups of patients amiodarone was discontinued.

Patients who reverted to sinus rhythm were followed up every three months. In each visit an ECG was recorded for rhythm and patients were evaluated for adverse effects of amiodarone including thyroid function and pulmonary function tests.



Statistical analysis

Continuous variables were expressed as mean \pm SD.

Comparison between discrete variables were made using chi square test.

At 6 months follow up 14 patients (28%) were in atrial fibrillation and 36 patients (72%) were in sinus rhythm.

One patient had hypothyroidism at the end of 3 months and had to be withdrawn from amiodarone therapy. 12 months follow up was available only in 41 patients.

- ◆ Of the 41 patients who came for follow up at 1 year 24/41 (60%) were in sinus rhythm and 17/41 (40%) were in AF. Of patients who were in NSR at end of 6 months (i.e. out of 36 patients) 24 remained to be in NSR (66%).Of the 4 patients who reverted to NSR with amiodarone alone ,4 came for follow up at 6 months. All 4 were in NSR (100%) 3 came for follow up at 1 year and all 3 were in NSR.
- ◆ Patients who were in atrial fibrillation following DC version continued to be in atrial fibrillation at 6 months and 1 yr.
- ◆ Of the 36 patients who were in NSR at 6 months, 24 retained NSR and 12 went back to atrial fibrillation at 1 year.
- ◆ Of the 50 patients 32 patients (64%) had undergone cardiac surgery (CMV, MVR) in the past. 18 patients had no prior surgical procedures. Of 18 preoperative patients 1 patient remained in atrial fibrillation despite DC version at one month.

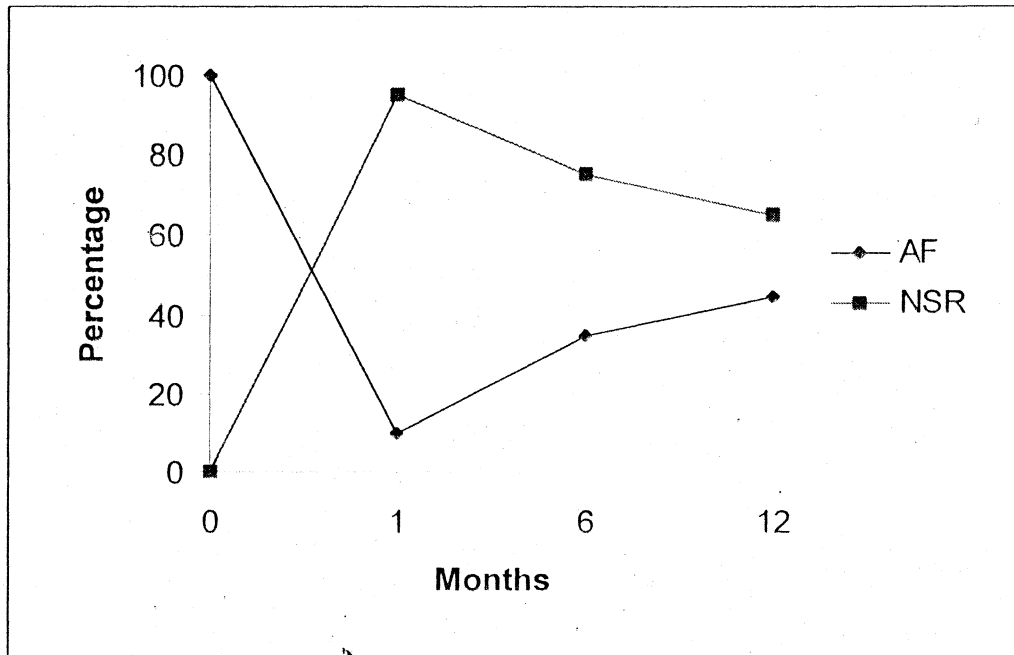
5 patients among 18 preoperative patients were in atrial fibrillation at 6 months and 1 year. 7 patients were in atrial fibrillation among 13 preoperative patients who came for follow up at 1 year.

Among 32 post operative patients 4 patients remained in AF despite DC Version at 1 month.

At 6 months follow up 9 patients were in atrial fibrillation among the 32 postoperative patients. At 1 year follow up 12 out of 27 patients who came for follow up were in atrial fibrillation. 15/27 were in sinus rhythm.

Among patients who reverted to NSR with amiodarone alone. 3 were preoperative and one was postoperative patient. 48 patients out of 50 had good LV function. Among two patients with LV dysfunction both had reverted to sinus rhythm at DC version and maintained sinus rhythm at 6 months.

◆ Out come on follow up at 6 months and one year.



PREDICTORS OF CONVERSION AND MAINTENANCE OF SINUS RHYTHM

Gender: At 1-month follow up among 5 patients who were in atrial fibrillation 4 were females and one was male. While among 45 patients in NSR 24 were in males and 21 were females.

Among 24 patients in sinus rhythm at one year 14 patients were male. 10 patients were female.

Among 17 patients with atrial fibrillation 5 were male and 12 were female,

Thus there was no gender influence as regards conversion to and maintenance of sinus rhythm.

Age: The mean age of general population was 39 ± 10.5 -year. In males the mean age was 37.7 ± 12.3 yrs. In females mean age was 40.4 ± 10.4 yrs. At follow up at 12 months the mean age of 24 patients in SR was 36.4 ± 5 yr

Mean age of 17 patients in atrial fibrillation at 12 months was 37.7 ± 5.5 year (P=NS). Age was not a significant predictor for conversion to sinus rhythm.

Duration of atrial fibrillation: The mean duration of atrial fibrillation in the 50 patients enrolled in the study was 1.5 ± 0.5 years.

At one month follow up, 45 patients were in SR and duration of atrial fibrillation in these patients was 1.25 ± 0.5 years versus 4.9 ± 2 years ($p < 0.001$) in patients remaining in atrial fibrillation.

At 12 month follow up, duration of atrial fibrillation in patients attaining SR was 1.25 ± 0.5 year versus 2.5 ± 1.0 year ($p < 0.001$) in patients who remained in atrial fibrillation.

Hence longer the preexisting atrial fibrillation the less likely was the success in restoring and maintaining SR.

LA size:

The mean LA size of patient enrolled in the study was 4.9 ± 1 cm.

The mean LA size of patients who reverted to NSR at 6 months was 45.09 ± 0.5 mm and who did not revert to NSR was $50 \text{ mm} \pm \text{SD}$.

The mean LA size of patients who did not revert to NSR at 12 months was 50.9 ± 0.5 and who reverted was 46. (p value-NS). LA size was not a significant predictor of conversion to sinus rhythm.

Pulmonary hypertension: At the time of inclusion in the study, mild PAH was present in 42 patients. Moderate PAH (50-69mmHg) was present in 5 patients. No PAH in 2 patients and severe PAH (> 70 mmHg) in none.

At 6 months follow up, of the 35 patients in NSR, 27 patients had mild PAH, 6 had moderate PAH and 2 had no PAH. In 15 patients in atrial fibrillation 1 patient had moderate PAH. 14 patients had mild PAH.

At 1 year follow up of the 24 patients in NSR, 20 patients had mild PAH, 3 patients had moderate PAH and one patient had no PAH. Of 17 patients in atrial fibrillation one patient had moderate PAH, 16 patients had mild PAH. PAH was not a significant predictor of SR restoration.

Pre/ postoperative status:

Total No. 50

Preoperative	Postoperative
18/50	32/50

Preoperative:

Amiodarone reverted AF to NSR in 4 patients. 3 were preoperative and one was postoperative.

Preoperative patients

	NSR	AF
Amiodarone	3/18 (17%)	15/18 (83%)
Dc version	17/18 (94%)	1/18 (6%)
6 month	13/18 (72%)	5/18 (28%)
1 year	7/13 (54%)	6/13 (46%)

Post operative patients

	NSR	AF
Amiodarone reversion	1/32 (3%)	
DC version	28/32 (87%)	4/32 (13%)
At 6 months	22/32 (687%)	10/32 (32%)
At one year	16/28 (57%)	12/28 (43%)

Preoperative / Post operative status did not influence reversion to NSR at 1 month, 6 month or 1 year.

- ◆ Given alone amiodarone was not effective in reversion to NSR. DC version on amiodarone was highly effective in attaining sinus rhythm. Amiodarone was highly effective in maintaining NSR at 6 months (70%), AF (30%)
- ◆ At 1 year follow up, of 41 patients who came for review 24/41 (59%) was in NSR 17/41 (41%) were in AF

The statistical analysis showed that amiodarone was highly effective in reverting to NSR combined with DC version and maintaining NSR at 6 month and at one year follow up period.

Univariate analysis showed that duration of atrial fibrillation affected maintenance of NSR at 1 year follow up.

LA size, age and sex did not affect reversion to NSR or maintenance of NSR at 6 month and at one year on amiodarone

Short duration of atrial fibrillation was associated with successful maintenance of NSR at 6 month and one year. It was not a significant predictor of restoration of SR at 1 month. LA size did not affect restoration or maintenance of sinus rhythm at 6 months or 1 year.

Adverse effects of amiodarone:

Only 1 patient had hypothyroidism. After stopping amiodarone thyroid function normalised after 3 months .

DISCUSSION

Restoration of SR in patients with rheumatic heart disease is more difficult in view of their dilated atria, longer duration of atrial fibrillation and poor tolerance to antiarrhythmic drugs⁸. On the other hand these patients would get benefit with restoration of SR.⁹

Rate of occurrence of Atrial fibrillation in various groups of Rheumatic valvular disease.

Valvular heart disease	Atrial fibrillation percentage
MS	29%
MS+MR	52%
AR	16%
AS	0%
MS+TR	64%
MS+MR+TR	70%
MS+AR	31%
MS+MR+AR	58%
MS+TR	52%

Univariate analysis of 5 echocardiographic variables including LA diameter, Trans Mitral Gradient (TMG), Mitral valve area (MVA), left ventricular end diastolic dimension (LVEDD), left ventricular end systolic dimension (LVESDD), showed that LA diameter & TMG as factors associated with increased risk of AF. Multivariate analysis showed LA diameter and age as predictors of AF.

AF is rare in aortic valvular disease. There is 1% rate of AF in aortic valvular disease. Patients with combined lesions of MS, MR & TR

constitute highest rate of AF. Atria are greatly affected hemodynamically in the presence of these lesions in combination (70%). AF occurs in 29% patients with isolated MS and 16% isolated MR.

The efficacy of amiodarone has been investigated in many trials but majority of these studies showed high incidence of adverse effects. Intolerable side effects of amiodarone was observed in 6-21 percent patients.⁸ However Grosseline et al pointed out that in these studies the mean dose of amiodarone used was high (>300mg/d).

When they used low maintenance dose (mean dose 200 ± 66 mg/dy) of amiodarone, only one (3.3%) patient had intolerable side effects.

Our results are consistent with their study. We used a maintenance dose of 200mg or less per day and only one patient showed side effects in terms of development of hypothyroidism; which required withdrawal of amiodarone.

None of the patients developed pulmonary toxicity, proarrhythmia, ophthalmological or dermatological changes.

Efficacy of Amiodarone:

Different clinical trials showed 53-79 percent success rate of amiodarone in maintenance of sinus rhythm during a mean follow up of 15-27 months.⁹

In these studies number of rheumatic atrial fibrillation patients were very few. Only Skovlarris¹⁰ studied the efficacy of amiodarone in patients with chronic atrial fibrillation who underwent successful MV replacement for rheumatic disease. The overall success rate after four weeks of amiodarone therapy with or without electrical cardioversion was 77 percent.

At a mean follow up period of 17 months 70 percent patients were in SR. In our study 8% (4 patients) reverted to SR on amiodarone only, after one month and remaining 92% (46) patients remained in atrial fibrillation.

Electrical cardioversion was successful in 41 (82%) patients in restoring sinus rhythm. So after 1 month, out of 50 patients 45/50 (90%) patients were in SR on amiodarone with or without cardioversion.

On subsequent follow up amiodarone was effective in maintenance of SR in 70% patients at 6 month and 60% patients at 1 year.

Our study showed that more than half of patients of atrial fibrillation with rheumatic heart diseases treated with amiodarone remained in sinus rhythm at 12-months follow up.

Important factors associated with maintenance of SR are; duration of atrial fibrillation, type of underlying heart disease, patient age, LV function, LA size and pharmacological agent used for maintenance of SR.¹¹

Several clinical studies have shown that out of all these predictors, LA size and duration of atrial fibrillation are significantly associated with restoration and maintenance of SR after electrical or pharmacological cardioversion.

In a retrospective study of 85 patients of atrial fibrillation Duyschaver et al. analysed predictors of long term outcome after first electrical cardioversion for atrial fibrillation.¹²

In univariate analysis the only predictor for maintenance of sinus rhythm at 100 days follow up was duration of preceding atrial fibrillation. Multivariate analysis showed that class III antiarrhythmic drugs (Sotalol, amiodarone), the duration of atrial fibrillation and old age (> 75 years) were the most important determinants of long term outcome.

Waris et al; Hall, Wood ,Gold etal. suggested that patients are unlikely to maintain sinus rhythm when AF persisted beyond one year.¹³

Waris et al and Ewy et al. showed that a patient with dilated LA more than 4.5cm is likely to have recurrent atrial fibrillation after initial successful cardioversion.¹⁴

However these studies correlating the LA size with recurrence of atrial fibrillation were done before availability of amiodarone.

Brodsky et al⁷ used amiodarone for maintenance of SR in patients of atrial fibrillation with LA dimensions above 4.5cm. Out of 10 patients who were in SR at the end of one year, nine had LA size between 4.5-6.0 cms and only one had LA size above 6 cms. They concluded that patients with LA dimension between 4.6-6cm could be maintained in SR with amiodarone therapy.

However in patients with larger LA dimension (>6cm) atrial fibrillation is likely to return in spite of antiarrhythmic therapy with amiodarone.

Further Brodsky et al in another study determined factors responsible for maintenance of SR in patients with dilated LA (>4.5cm, range 4.5-7.8cm). Factors positively associated with success were, duration of chronic atrial fibrillation < 1 year, absence of MV disease, LA dimension <6cms ($P<0.05$)¹⁵. The patient's age and LV function were not associated with

conversion to sinus rhythm. Patients with moderate LA dilatation (4.5-6cm) and a short duration of chronic atrial fibrillation (<1 year) can often be maintained in SR especially if they convert with pharmacologic intervention.

Skovlarizis et al evaluated different variables of patients like age, gender, duration of atrial fibrillation, LA diameter, LV fractional shortening, mode of therapy (amiodarone alone or in combination with DC cardioversion) with respect to success or failure to achieve and maintain SR.

In this study the only predictor of early outcome was duration of atrial fibrillation.

In patients with successful conversion to SR the mean duration of atrial fibrillation was 23.5 ± 5 month versus 55 ± 4.9 month in patients with unsuccessful cardioversion. As LA diameter over 45mm failed to predict the eventual outcome of cardioversion. None of the above variables related significantly to late success.

Several other studies have shown that success rate of electrical cardioversion is higher when atrial fibrillation is of short duration.

The success rate of chemical cardioversion for atrial fibrillation of recent onset (<24hrs) is higher¹⁶

Apart from progressive underlying heart disease, the fibrillatory process itself may cause electrophysiological and / or structural changes in atrial myocardium. These changes favour the induction and / or perpetuation of AF.

Sigffel et al showed that within few days the repetitive induction of short episodes of atrial fibrillation leads to chronic atrial fibrillation.

The increase in induction of atrial fibrillation was accompanied by a shortening of atrial refractoriness and wavelength. They introduced the concept "atrial fibrillation begets AF."

In our study age, LA size, sex, postoperative / preoperative status did not affect restoration and maintenance of SR at 1 month, 6 months & 1 year.

Duration of atrial fibrillation alone predicted maintenance of sinus rhythm at 6 months and 1 year. It did not predict restoration of SR. (1.25±0.5 Vs 4.9±2 yr).

Many trials has shown high incidence of adverse effects. However these studies used high dose of amiodarone (>300mg/day). Our study with low dose amiodarone (200mg/day) only one patient had

hypothyroidism. None had pulmonary toxicity, proarrhythmia, and ophthalmological complications

Limitations of study

Amiodarone 200mg thrice daily for 1 week & once daily for one month is probably insufficient for conversion of AF to sinus rhythm. This may be the most likely reason for the low rate of conversion to sinus rhythm by amiodarone alone.

CONCLUSIONS

Amiodarone is a safe and effective drug in maintenance of SR in patients with atrial fibrillation and rheumatic heart disease, however not for restoration of SR. Long-term maintenance of SR is lower than in other studies where majority of patient has non-rheumatic atrial fibrillation.

Age, sex and LA size were not associated with restoration or maintenance of SR.

Duration of atrial fibrillation was the only significant predictor of long-term maintenance of SR.

Long-term administration of low dose amiodarone had very low incidence of significant side effects.

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**TEI INDEX AS A MARKER OF LEFT
VENTRICULAR SYSTOLIC AND DIASTOLIC
DYSFUNCTION**

ABSTRACT

Background

Tei index is a recently described index of combined systolic and diastolic performance and is a simple and reproducible measure of cardiac function

Objective

To assess the value of Tei index as a marker of varying degrees of diastolic and systolic function.

Material and methods

100 patients with CAD were grouped into three groups. Group 1-patients with normal LV function, Group 2-patients with systolic dysfunction and Group 3-those with diastolic dysfunction. Tei index was calculated for each of these groups using IVCT,IVRT and LVET.

Results

Mean Tei index of patients with normal LV function was 0.4 ± 0.2 . It was significantly more in patients with diastolic dysfunction ($\text{Tei} = 0.54 \pm 0.1; p < 0.05$) and with systolic dysfunction ($\text{Tei} = 0.63 \pm 0.2; p < 0.05$). Among the patients with diastolic dysfunction, there was no difference among those with impaired relaxation and restrictive pattern.

Conclusion

Compared to patients with normal LV function, patients with LV dysfunction had higher Tei index which was maximally prolonged in patients with systolic dysfunction compared to diastolic dysfunction. It was not useful to discriminate among different groups of diastolic dysfunction

INTRODUCTION

Echocardiographic indices of systolic and diastolic myocardial performance are of clinical utility in both the diagnosis and management of patient with heart disease.

Presently measurements of systolic function include the ejection phase indices of volume changes like stroke volume, cardiac output and ejection fraction.

A new Doppler Index combining systolic and diastolic time intervals called Tei Index has been described. It has been initially used to assess global right ventricular function in adults especially in post Sennings patient whose right ventricle is the systemic ventricle.¹

Although the assessment of right ventricular function is important in the clinical management of children with congenital heart disease, available imaging techniques have been limited because of the complex geometry of right ventricle.

This Index has been reported to correlate well with severity of congestive heart failure and clinical outcome in adult patients with primary pulmonary hypertension.

Recently this easily measured Doppler index (Tei Index) combining systolic and diastolic time intervals has been proposed to be applicable in left ventricle also.

It is defined as the sum of isovolumetric contraction time and isovolumetric relaxation time divided by ejection time. This Index has been reported to be simple, reproducible and independent of heart rate, blood pressure, degree of valvular regurgitation.

Because this index is essentially a time ratio it is therefore independent of ventricular geometry and may be particularly useful in assessment of global LV and RV function.

Non invasive measurements of diastolic function are limited to rates of filling that may correspond to filling pressures in properly selected patients. Tei Index is a Doppler derived index that incorporates both systolic and diastolic function performance of left ventricle or right ventricle.

It has been used for sequential evaluation of left ventricular performance in children after anthracycline therapy⁵ especially in early cardiac dysfunction after anthracycline therapy.

Because the Doppler index incorporates phases of active contraction and relaxation it is hypothesized that it should correlate with invasive measures of peak positive and peak negative dp/dt .²

BRIEF REVIEW OF LITERATURE

Assessment of left ventricular function includes evaluation of both systolic and diastolic function.

Evaluation of left ventricular systolic performance

The normal values of contractility indices are as follows.

(a) Isovolumic indices

Index	Normal value
Maximum dp/dt	1650±300
Maximum dp/dt/p	44±8.4

(b) Ejection phase indices

Index	Normal value
LVSW	81±23
LVSWI	50±20
EF	72±8
Mean Vcf	1.83±0.56

LVSW-left ventricular stroke work, LVSWI-left ventricular stroke work index

EF-ejection fraction ,Mean Vcf-Mean velocity of circumferential shortening

An operational definition of systolic dysfunction is an effective ejection fraction less than 50%.

Evaluation of left ventricular diastolic performance

Normal left ventricular diastolic function can be defined as filling of the left ventricle sufficient to produce a cardiac output commensurate with the body's needs with a normal pulmonary venous pressure (less than 12 mm Hg)

A patient with systolic dysfunction requires a larger end-diastolic volume to produce an adequate stroke volume and cardiac output. If the larger left ventricular end-diastolic volume can be achieved without an abnormally high pulmonary venous pressure this can compensate for the impaired systolic performance.

However if the larger end-diastolic volume requires elevation of pulmonary venous pressure the systolic dysfunction will result in diastolic dysfunction. Thus when defined in this manner, systolic dysfunction in symptomatic patients is usually associated with diastolic dysfunction.

However diastolic dysfunction occurs in the absence of systolic dysfunction. As defined, diastolic dysfunction may be due to an obstruction to left ventricular filling or external compression.

Indices diastolic function can be organized in to 3 groups.

1. Measures of isovolumetric relaxation
2. Indices of passive left ventricular filling characteristics derived from diastolic left ventricular pressure-volume relations.
3. Measurements of pattern of left ventricular diastolic filling obtained from doppler echocardiography

Patterns of left ventricular diastolic filling

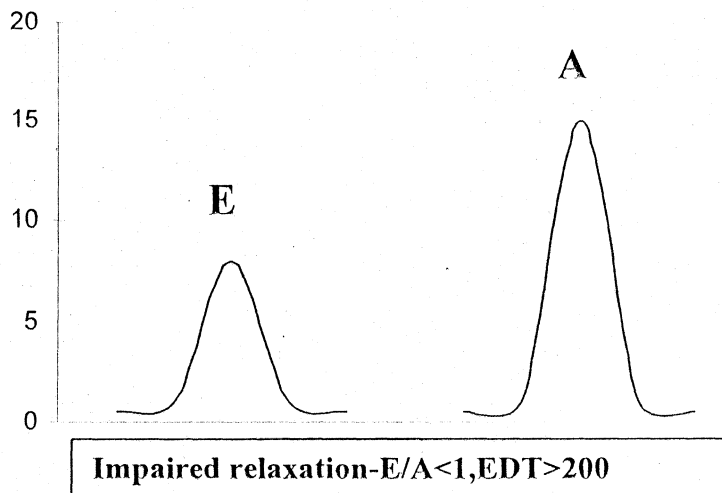
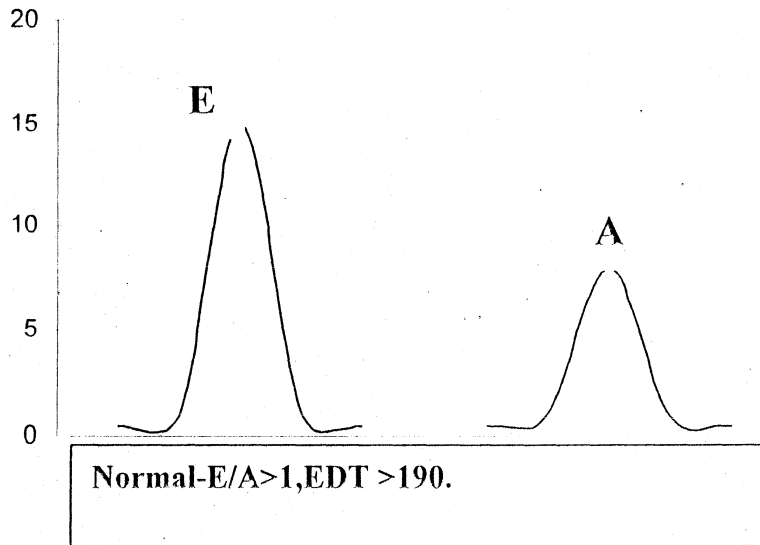
Analysis of the pattern of left ventricular filling can provide useful information about diastolic left ventricular performance.

From time of aortic valve closure until mitral valve opening the left ventricle is normally a closed chamber with a constant volume. Myocardial relaxation begins in the latter part of systole and causes a steep exponential fall in intra ventricular pressure. This is stage of isovolumetric relaxation. For first 30-40 milliseconds after mitral valve opening, relaxation of left ventricular wall tension is normally rapid enough causing rapid filling. The pressures in left atrium and left ventricle equilibrate causing little left ventricular filling- called phase of diastasis. Atrial contraction increases atrial pressure late in diastole providing a left atrial to left ventricular pressure gradient.

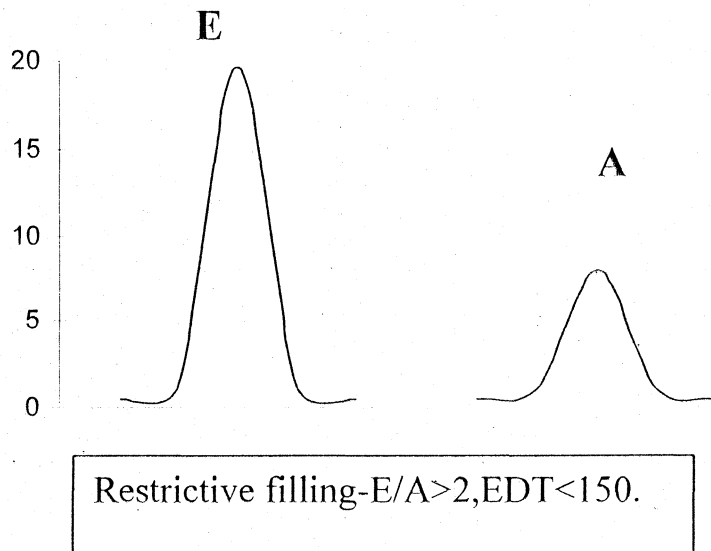
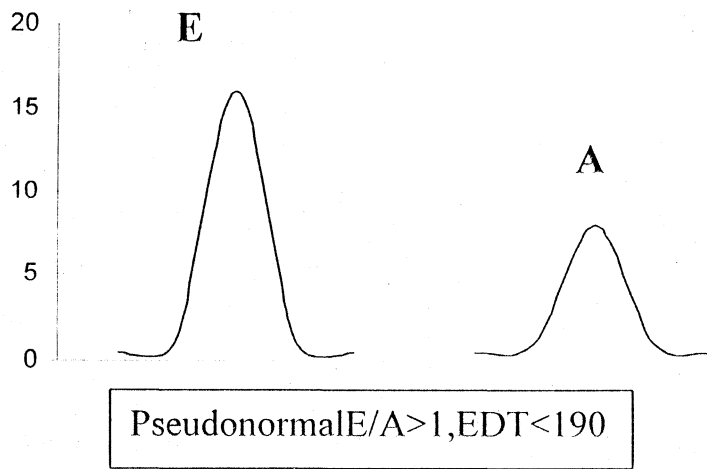
Normal pattern of left ventricular filling:

Normal pattern of left ventricular filling can be quantified by measuring the peak early diastolic filling rate or mitral flow velocity E and peak filling rate (A) or mitral flow velocity during atrial contraction. Normally E/A ratio is >1

Graph



Graph



**Normal values of parameters of left ventricular diastolic filling
measured by doppler echocardiography**

	Adults <41 (ms)	Adults >55 (ms)
Mitral peak E	76±13	63±11
Mitral peak A	8±8	52±9
Mitral E/A	2.1±0.6	1.3±0.3
Mitral E deceleration time	184±24	
IVRT	47±26	

Abnormal pattern of left ventricular filling

Three abnormal patterns have been identified indicating progressively greater impairment of diastolic function

The 1st abnormal pattern of filling has been termed delayed relaxation. A delayed relaxation pattern can be seen in patients with left ventricular hypertrophy systemic hypertension, coronary artery disease and normal elderly subjects.

The 2nd pattern of abnormal filling has been termed pseudonormalized pattern, in which E/A ratio is greater than 1.0. It is seen in patients with more severe impairment of diastolic performance than delayed relaxation. Pseudonormalized pattern of filling is distinguished from normal by a more rapid rate of diastolic flow deceleration (<190ms)

A 3rd abnormal pattern of left ventricular filling indicating a severe diastolic abnormality is the restrictive pattern. In this pattern, the early filling is increased above the control level and greatly exceed the filling that occurs during atrial contraction. E/A is usually > 2.0. Restrictive filling pattern is seen in patients with constrictive pericarditis, restrictive cardiomyopathies and is associated with poor prognosis.

AIM

Value of Tei Index as a marker of varying degrees of diastolic and systolic dysfunction.

MATERIALS AND METHODS

This was a prospective study. From January 2001 to January 2002, 100 patients with coronary artery disease were included in the study. Patients were grouped into three categories.

1. Patients with normal left ventricular systolic function ($EF > 50\%$) and normal diastolic function ($E/A > 1$, $EDT > 180\text{ms}$ with normal IRT).
2. Patients with systolic dysfunction defined as $EF < 50\%$.
3. Patients with varying degrees of diastolic dysfunction {impaired relaxation ($E/A < 1$, $EDT > 200\text{ms}$) and restrictive filling pattern ($E/A > 2$, $EDT < 150\text{ms}$)}.

Patients with valvular heart disease, including significant mitral regurgitation (2+ or more) and with rhythm other than sinus were excluded from the study.

Two dimensional, spectral Doppler and colour Doppler study was done using a Vingmed (System V) and Hewlett-Packard Sonos 1000 system and a 1.5-3.5 MHz transducer.

Tei index was calculated as follows. Two consecutive doppler mitral inflow signals were initially imaged. The time between these two left ventricular inflow signals is the sum of isovolumetric contraction time (IVCT), left ventricular ejection time (LVET) and isovolumetric relaxation time (IVRT). Left ventricular ejection time was separately measured from left ventricular out flow signal.

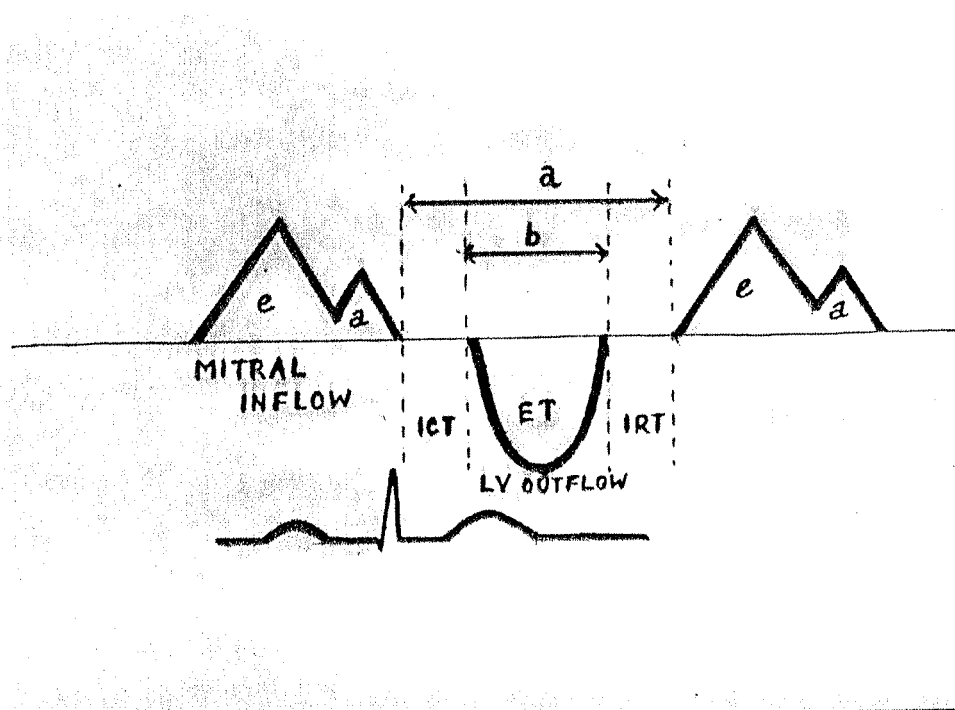
$$\text{Tei Index} = \frac{(\text{IVCT} + \text{IVRT} + \text{LVET}) - \text{LVET}}{\text{LVET}}$$

Mitral inflow signal was measured from apical 4 chamber view. It was evaluated using pulse wave Doppler sample volume positioned at tip of mitral leaflets. Measurement of LVET was done from apical 5 chamber view. Aortic out flow Doppler signal was evaluated using pulse wave Doppler sample volume positioned just below aortic valve. Left ventricular ejection time was measured from duration of left ventricular outflow velocity curve.

Schematic drawing of Doppler intervals .Tei index (a-b/b) is calculated by measuring two intervals

a= interval between cessation and onset of mitral inflow

b= ejection time of left ventricular outflow (LVET)



Mitral regurgitation, aortic regurgitation was evaluated using colour Doppler.

Left ventricular function was assessed by M-Mode and planimetric method.

Patients with left ventricular dysfunction (systolic or diastolic) were expected to have a higher Tei Index.

RESULTS

There were 100 patients with 48 females and 52 males.

Age ranged from 29-70 years (mean 55 ± 6.7 yrs).

Subgroups of study population were as follows.

Systolic Dysfunction = 25

Diastolic Dysfunction = 50

- Impaired relaxation = 40

- Restrictive pattern = 10

Normal = 25

Mean Tei Index of whole population group was 0.52 ± 0.1 .

Table I describes the *Tei Index for subgroups*.

Patients with diastolic dysfunction had much more prolonged Tei Index than normal group. Among patients with diastolic dysfunction, those with restrictive pattern of diastolic filling did not have more prolonged Tei Index than those with impaired relaxation

group. With systolic dysfunction Tei Index was prolonged much greater than with diastolic dysfunction.

Standard error of difference between 2 means was used for comparing Tei Index of various subgroups.(Table 2).There was a increase in Tei Index in patients with diastolic dysfunction as compared to normals ($p<0.05$).

On comparing patients with systolic dysfunction compared to normals, there was an increase in Tei Index in systolic dysfunction group ($p<0.05$) as also between systolic dysfunction and diastolic dysfunction($p<0.05$).

We also compared Tei Index in patients with diastolic dysfunction between the impaired relaxation and restrictive pattern subgroups.(Table 3).

There was no statistically significant difference between the Tei Index in 2 subgroups of diastolic dysfunction ($p>0.05$) that is impaired relaxation and restrictive pattern.

Table 1

Tei index for various subgroups; normal(a), diastolic dysfunction (b),
systolic dysfunction (c).

(a)

Normal	Tei Index
N=25	0.40±0.2

(b)

Diastolic Dysfunction	Tei Index
Whole group	0.54±0.1
a. Impaired relaxation n =40	0.54±0.2
b. Restrictive pattern n=10	0.52±0.1

(c)

Systolic Dysfunction	Tei Index
N= 25	.63±0.2

Table.2

Comparison between subgroups.

(a)-Between normal and diastolic dysfunction

Population study group	Tei Index
Normal	0.40±0.2
Diastolic dysfunction	0.54±0.1

SE= 0.04

OD = 0.14

P<0.05

(b) Between normal and systolic dysfunction

Study group	Tei Index
Normal	0.40±0.2
Systolic Dysfunction	0.63±0.2

SE= 0.6
OD = 0.23
P<0.05

(c) Between systolic and diastolic dysfunction.

Study group	Tei Index
Diastolic Dysfunction	0.54±0.1
Systolic Dysfunction	0.63±0.2

SE= 0.04
OD = 0.09
P<0.05

Table. 3

Comparison between different diastolic dysfunction.

Study group	Tei Index
Impaired relaxation n=40	0.54±0.1
Restrictive pattern n=40	0.52±0.1

SE-0.02
OD-0.002

P>0.05

Table-4

Echocardiographic parameters of the study subgroups.

	Normal left ventricular function	Diastolic dysfunction	Systolic dysfunction
EF	67.1±7.6 (range 55-80%)	66.8±8.5 (range 55.82%)	44±4.6 (range 35-49)
LVIDD	47±5.9 (range 39-60m)	46±5.9 (range 34±59m)	59.3±5.9 (range 54-71)
LVIDs	31.1±5.7 (range 24-45)	31.3±6.3 (range 20-40mm)	49.6±6.3 (range 37-58)
E	0.75±0.2 (range 0.5±1.0)	0.6±0.1 (range 0.4 -0.9)	0.8±0.1 (range 0.6-1)
A	0.52±0.2 (range 0.3-1)	0.73±0.2 (range 0.5-1)	0.7±0.2 (range 0.4-1.1)
E/A	1.5±0.5 (range 0.75-2.6)	0.8±0.3 (range 0.63-0.87)	1.04±0.5 (range 0.63-2.2)
Ejection time	288.8±26.5 (range 250-340)	286±37.3 (range 230-380m)	265.2±40.3 (range 210-380 m)
ICT+IRT	115.2±15.5 (100-140)	152.4±17.2 (130-170)	172.8±18.2 (150-180)

Table 5

Clinical profile and Doppler intervals of study subgroups

	Normal	Diastolic dysfunction	Systolic dysfunction
Number	25	50	25
Age	49±7.6	53±6.2	50±6.8
Tei Index	0.40±0.2	0.54±0.1	0.63±0.2
CT + IRT	115.2±15.5	152.4±17.3	172.8±18.2
ET	288.8±26.5	286.6±37.3	265.2±40.3
E	0.75±0.2	0.6±0.1	0.8±0.1
A	0.52±0.2	0.73±0.2	0.7±0.2
E/A ratio	1.5±0.5	0.8±0.3	1.4±0.5

Echocardiographic parameters(Table 4)

Mean E velocity in systolic dysfunction group was 0.8 ± 0.1 . Left ventricular and systolic diameter ranged from 20-40mm with mean LVEDS was 31.3 ± 5.3 mm.

Mean E velocity was 0.6 ± 0.1 with range from 0.4 – 0.9.

Clinical profile and doppler intervals

Tei Index did not correlate with age (P was > 0.05), so we concluded that left ventricular Index was not affected by age. No correlation was found between peak E/A ratio and age.

E/A ratio of normal versus diastolic dysfunction

Normal	Diastolic dysfunction
1.5 ± 0.5	0.8 ± 0.3

OD- 0.7
SE-0.17
P value < 0.05

Thus E/A ratio was significantly higher in normal than diastolic dysfunction

Majority (80%) patients had impaired relaxation compared to restrictive pattern in 20% in the diastolic dysfunction group.

E/A ratio of normal versus systolic dysfunction

Normal	Systolic dysfunction
1.5±0.5	1.4±0.5

OD = 0.1

SE = 0.4

p>0.05

There was no statistically significant difference in E/A ratio of normal patients versus systolic dysfunction

E/A ratio of systolic versus diastolic dysfunction

Systolic dysfunction	Diastolic dysfunction
1.4±0.5	0.8±0.3

OD =0.6

SE = 0.17, p value <0.05

There was statistically significant difference in E/A ratio of systolic dysfunction patients versus normal patients.

So E/A ratio differentiated only between normal and diastolic dysfunction, and between diastolic and systolic dysfunction.

There was no statistically significant difference in E/A ratio between normal and systolic dysfunction.

Ejection time

(a)

Normal	Diastolic dysfunction
288.8±26.5	286±37.3

P>0.05

(b)

Normal	Systolic dysfunction
288.8±26.5	265.2±45.3

P<0.05

(c)

Systolic Dysfunction	Diastolic dysfunction
265.2±45.3	286±37.3

P <0.05

Ejection time was significantly reduced in patients with systolic dysfunction compared to normal and diastolic dysfunction group. Ejection time was not significantly altered in the diastolic dysfunction group compared to normals.

IVCT + IVRT

(a)

Normal	Diastolic dysfunction
115.2±10.1	152.4±10.3

P<0.05

(b)

Normal	Systolic dysfunction
115.2±10.1	172.8±11.3

P<0.05

(c)

Systolic Dysfunction	Diastolic dysfunction
172.8±11.3	152.4±10.3

P<0.05

The sum of isovolumic relaxation time and isovolumic contraction time was significantly prolonged in diastolic dysfunction and systolic dysfunction group compared to normals.

There was progressive increase in sum of isovolumic relaxation time and isovolumic contraction time in patients with systolic dysfunction as compared to diastolic dysfunction and normals.

The increase in Tei Index in diastolic dysfunction group was due to an increase in sum of isovolumic contraction and relaxation time where as in the systolic dysfunction group in addition to increase in isovolumic contraction and relaxation time, there was a decrease in ejection time which resulted in higher Tei Index.

DISCUSSION

In this study this index of myocardial performance combining systolic and diastolic intervals was compared with conventional doppler echocardiographic variables of left ventricular function.

A measure of combined systolic and diastolic myocardial performance could be a useful predictor of outcome in patients with coronary artery disease¹⁰. Conventionally isovolumetric contraction time, relaxation time and ejection time are used to assess the myocardial performance. However these intervals demonstrate heart rate dependence. However Tei Index which combining all the three is independent of heart rate and blood pressure. In addition it is age independent^{1,7} which was evident in this study also. In Amyloidosis which has combined systolic and diastolic dysfunction Tei index is found to be a useful predictor of outcome and prognosis⁴.

Various studies have shown that Tei index prolongs with diastolic dysfunction and is maximally prolonged with systolic dysfunction.^{3,5} In our study also this index was higher in patients with diastolic dysfunction and was further prolonged in systolic dysfunction. We also noted that there was no significant difference between the

subgroups either diastolic dysfunction ;impaired relaxation vs restrictive pattern.

In our study E/A ratio was compared between various groups and it was found that it did not differentiate between normals and systolic dysfunction. In diastolic dysfunction it was significantly lower compared to normals (but majority in this group were patients with impaired relaxation in which a lower E/A ratio is expected). E/A ratio in myocardial dysfunction has limitations as it is affected by parameters like heart rate, respiration and mitral regurgitation. However Tei Index is not affected by above parameters. It is independent of loading conditions^{3,4,8,9}. In fact our study showed that even though the E/A ratio was not different between normal and systolic dysfunction ,Tei index was significantly higher in systolic dysfunction. This underscores the importance of this index.

The reasons for higher Tei index was different in various subgroups. In diastolic dysfunction, it was due to an increase in sum of isovolumic contraction and isovolumic relaxation time. LV ejection time was normal. In systolic dysfunction subgroup a decrease in ejection time also contributed in addition to prolongation of isovolumic contraction and relaxation time.

In a study⁷, 60 patients with LVEF < 30% and at least one hospitalizations for heart failure, the Tei Index was calculated. Subjects were followed up for mean duration of 24 ± 19 months from time of echocardiogram.

The median value of Tei index was 0.79. 28 died and 2 underwent heart transplant. After adjustment for potential clinical confounders, Tei Index in highest quartile was a significant predictor of composite end points. The relation was independent of age, gender, race, LVEF.

Subjects with Tei Index > 1.15 had greater than 5 fold occurrence of death or heart transplant during mean follow up for 2 years. Our study population with systolic dysfunction had a relatively lower Tei index(mean 0.63) possibly due to better LV function in them(mean LVEF was $44 \pm 4.6\%$).

Dujardine and colleagues have previously demonstrated the prognostic significance of Tei Index in a cohort of 75 patients with DCM. Tei Index was a stronger predictor of mortality than LVEF and NYHA class and had prognostic value in dilated cardiomyopathy of both ischemic and non ischemic aetiology⁸.

Cardiac time intervals are known to change with aerobic fitness. Tei Index was lower as exercise capacity increased primarily due to reduction in left ventricular isovolumetric relaxation time⁷. So this index might be useful to assess the response to various therapies also. Peak treadmill time was inversely related to Tei Index³. A reduction of left ventricular isovolumic relaxation time appeared to be the primary factor in establishing a lower index. This had shown the importance of left ventricular diastolic function in aerobic fitness.

In patients with severe Aortic stenosis (AS) the onset of heart failure is associated with mortality and increased operative risk. Heart failure may result from either diastolic, systolic or combined left ventricular dysfunction. Tei Index was significantly increased in patients with severe AS and depressed overall left ventricular function¹¹.

Tei index has been found to be important in prognosticating patients with cardiomyopathy following anthracycline therapy and has been used to sequentially evaluate LV performance⁵. It was useful in early detection of cardiac dysfunction.

STUDY LIMITATIONS

As with any echocardiographic study interpretation of these time intervals may be limited in patients with suboptimal windows. Patients with arrhythmia like atrial fibrillation, AV blocks were excluded from the study. The clinical utility of this index in such conditions is not known.

CONCLUSION

A simple measure of Doppler Index combining systolic and diastolic time intervals can be used as an expression of global myocardial performance. It is a useful marker of left ventricular diastolic or systolic dysfunction.

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