SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

TRIVANDRUM - 11

LIST OF PROCEDURES DONE

PROJECT REPORT

NAME : M. ZULFIKAR AHAMED

PROGRAMME : D. M. Cardiology

MONTH AND YEAR OF SUBMISSION : November 1993

P270

CERTIFICATE

I, Dr. M. ZULFIKAR AHAMED .....hereby declare that I have actually performed all the procedures listed / carried out the projects under report.

Signature.....

Place : TRIVANDRUM

Date : 18-10-93

Name in M. ZULFIKAR AHAMED
capital letters

Forwarded. He has carried out the minimum requirement of procedures / etc.

Signature

Head of the department

LIST OF PROCEDURES DONE *
PROJECT REPORT

TITLE OF THE PROJECT: ECHOCARDIOGRAPHIC EVALUATION OF RIGHT VENTRICULAR FUNCTION IN POST OPERATIVE PATIENTS WITH SENNING'S PROCEDURE AND ROLE OF ACE INHIBITORS IN RV DYSFUNCTION.

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PROGRAMME : D.M CARDIOLOGY

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CONTENTS

INTRODUCTION

The concept of transposing the entire venous return using an intracardiac approach as treatment for ventricular arterial discordance (TGA) was suggested and experimentally performed by Albert in 1954. In 1959 Senning introduced the ingenious technique of complete intra atrial redirection of venous return[1]. It was reintroduced in 1977 by the Leiden group. In subsequent years the procedure became the operation of choice in the treatment of simple TGA[2]. Even though arterial switch operation (ASO) has reduced the role of atrial switch for patients with transposition of great vessels, atrial switching continues to be used uniformly in many centers. However inspite of low mortality, right ventricular function is often reduced following Senning repair[3]. Many long term follow up studies have highlighted this phenomenon [4,5,6,7,8].

Most studies on RV function following Senning procedure have either utilised angiography [4,7,9] or radio nuclide angiography as a tool of measuring RV ejection fraction (RVEF). However there have been studies utilising 2D echocardiography in assessment of RV function and other parameters[10,11,12]. In addition to calculation of Ejection Fraction (EF) by echocardiography

RV systolic time intervals (RVSTI) have been studied and have been found to be useful, and appear to correlate well with RVEF.[11,12] With this background the present study attempts to assess right ventricular function in survivors of Senning procedure and study the possible beneficial effect of converting enzyme inhibitors on RV function as assessed by echocardiographic RVEF and STI.

SUBJECTS AND METHODS

34 survivors of Senning repair done from 1986 to 1992 in Sri Chitra Thirunal Institute of Medical Sciences and Technology (SCTIMST), Trivandrum were called back for a complete evaluation; 29 responded. The case records were studied in detail and apart from a complete clinical evaluation including history and physical examination, chest Xray and 12 lead ECG were done. All children were evaluated echocardiographically by using ultramark 8 (ATL) machine. Both 3.5 and 5.0 MHz transducers were used wherever appropriate. M-mode measurements, 2D evaluation and Doppler interrogation were performed.

2D Ejection fraction of Right Ventricle was calculated by using Simpson's formula ($V = \pi/3\ h\ D_1\ D^2$). The views chosen were Apical 4 chamber view and subcostal view. Adequate echo window was available in all children.

This method had been validated against Radionuclide method by Vitolo et al[14]. 3 cycles were chosen and average of 3 cycles were taken as mean EF. Doppler derived Systolic Time Intervals were calculated using the soft ware in the UM8. Parameters measured were Pre Ejection (PEP) Period, Ejection Time (ET) and PEP/ET ratio of both ventricles[15].

Of the total of 29 patients 10 had significant RV dysfunction. They were put on Enalapril with 0.08-0.10 mgm/kg as initial starting dose. The dose was increased to twice daily regimen and was continued for a period of 8-12 weeks. Patients were recalled and reassessment done by X ray, ECG and Echocardiography. Both RVEF and systolic time intervals were calculated and were compared to base line (pretreatment) data. 8 patients postoperatively had a restudy and their hemodynamic data were also evaluated.

3 groups of RVEF were compared with RVSTI ratios using one way analysis of variance. Comparison was done by Student - Newman - Keuls procedure. A multiple regression model using a stepwise procedure was constructed to find out predictors of impaired RV function. Overall adjusted R^2 for the model was 0.25 (25% the variation explained by the model). For comparison of

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basal and post treatment ejection fractions and RVSTI paired t test was performed.

RESULTS

Total number of children studied was 29 Majority of children were male (82.8%). All children except one were in NYHA I status. CHF was unusual (3.4%) as was cyanosis (3.4%) Approximately 21 children had an ejection murmur at left upper sternal border, 10 of whom had grade 2/6 systolic murmur. Clinically appreciable Tricuspid Regurgitation (TR) murmur was found in 25% of patients (n-8) 2 children had abnormal (choreo-athetoid) movements and one child had spastic cerebral palsy.

Youngest child evaluated was 21 months old and oldest 10 years old (TABLE I) 24 had undergone balloon atrial septostomy previously and one of them had a blade septostomy. Mean age of Balloon atrial septostomy (BAS) was 62 days. Earliest Senning operation was at 6 months of age and oldest to have surgery was a five year old child Evaluation was done 30$\pm$ 20.5 months after Senning procedure.

All but one child who underwent Senning procedure were having TGA. One had double outlet right ventricle,

ventricular septal defect with pulmonic stenosis. Apart from presence of either a PFO (86.4%) or ASD (6.8%) associated lesions were ventricular septal defect (VSD 17.2%), persistent ductus arteriosus (PDA), (10.2%) and left ventricular out flow tract (LVOT) obstruction (27.6%). One child had a small PDA and a VSD 8 children had LVOT obstruction at the time at evaluation 4 had mild (25 - 50 mm of Hg) and one moderate (75 mm of Hg) gradient.

Cardiothoracic ratio ranged from 48 to 60% Mean CTR was 543 + 2.5 % Prominent IVC was noted in 5 and SVC in 21. Right Ventricular hypertrophy was the universal finding in ECG Normal sinus rhythm was maintained in a majority (72.4%) 2 children had intermittent junctional rhythm, 3 were in junctional rhythm and 3 had either ectopic atrial or coronary nodal rhythm. qR pattern was present in 2 (6.8%), upright T in Vl in 11 (37.8%). Right axis deviation was the rule ($+105^0$ to +180).

Basal arterial oxygen saturation was 39.8 $\pm$ 13.3% (FIG:I) Values ranged from 20% to 62%. Following BAS it improved to 70$\pm$9.2% Preoperative saturations were not available.

25 children had Doppler Tricuspid Regurgitation (TR) (86.2%). More than half (58.7%) had only trivial TR.

Only 1/3 (9) patients had significant TR 13 patients had trivial mitral regurgitation (MR). No significant MR was noted in any. In those who were in sinus rhythm, tricuspid flow velocities were computed. Most (17/21) had E/A ratio greater than one. Baffle leak was seen in two and none had significant pulmonary venous or systemic venous obstruction by Doppler study.

RV ejection fraction determined by echocardiography ranged from 35% to 64% Mean was 48.3 $\pm$ 8.0%. Children were divided into 3 groups based on their EF -Low EF (<45%), fair (45 - 55%) and good (>55%) arbitrarily. (Fig-2) Doppler derived systolic time intervals were calculated for both left ventricle and right ventricle. (Table II) RVPEP (corrected) ranged from 80 msec to 180 m sec; RVET (C) from 290 to 470 msec and PEP/ET ratio from 0.20 to 0.65 LVPEP (C) ranged from 90 to 140 Msec; ET (C) from 360 to 500 m sec; and ratio from 0.16 to 0.40 LVET/RVET ratio was 1.1 and LVPEP/RVPEP was 0.8.

Preoperative variables evaluated were by pass time aortic cross clamptime and total circulatory arrest (TCA) time. Bypass time ranged from 57 minutes to 171 minutes (mean 108 + 27 minutes. Aortic cross clamptime was 64.7$\pm$12.8 minutes and TCA time was mean of 38 + minutes.

Multivariate analysis of possible variables affecting postoperative RV function showed only age at septostomy as a predictor. Other variables tested were age at Senning, time at evaluation, post BAS saturation, aortic cross clamptime and total circulatory arrest time.

Even though the primary aim of the study was to assess RV function by echocardiography, 8 of 29 patients had a post Senning hemodynamic study. The arterial saturation was 95 $\pm$ 2 % (Range 90 to 97) and mean LV systolic pressure was 29 $\pm$ 6mm of Hg (Range 22-40mm Hg) One had a baffle leak.

In 10 patients who had unequivocal RV Dysfunction by means of EF Enalapril was started. Following are results of 8-12 weeks of follow up (Table3).

CTR decreased by 1.7 $\pm$ 2.2% Mean difference in EF which showed an increase was 4.4 $\pm$ 3.8% RVEP reduced by 23.3 $\pm$ 18.7 msec (P = 0.005) RVSTI ratio dropped from 0.45 $\pm$ 0.07 to 0.35 $\pm$ 0.05 (P = 0.05). There was no significant difference in RVET LVSTI measured did not change appreciably. (FIG IV : fig. V).

DISCUSSION

Male predominance among senning patients was expected[16]. Most survivors were in NYHA I status which is similar to the observation of Graham et al[5] and Alpert et al [10] However exercise testing may bring out the differences between these patients and control population as pointed out by Stark. Significant CHF was unusual.

Earliest BAS performed was on 3rd day and BAS was done as late as 150 days. Mean age (62 + 44 days) was high possibly reflecting delayed recognition and referral. The age at which atrial switch operation has been performed varies in different series, from mean age of 57 days reported by Chalant et al[17] to 18.5 + 7.5 months reported by Wiseheart et al[9]. The mean age of operation in the present study is 19.4 + 16.6 months. This factor depends on the experience and expertise of various surgeons and the postoperative management facilities available in the institutions.

Sinus rhythm was maintained in 21/29 patient (71.4%) More than 90% of patients were in sinus rhythm in the various series reported in the literature.

Doppler TR (mild-moderate) was found in 8 patients out of 29. In Graham's Series, 10 out of 80 children had TR Tricuspid regurgitation is expected when RV has a systemic function, facing aortic systolic pressure, flows and out put impedance. The incidence of TR by echo has generally been relatively high in other studies also.

Trowitzsch et al[7] had demonstrated usefulness of echo cardiography in assessing RV function in postoperative TGA although the study involved additional assessment of regional RV function. Ninomiya et al had highlighted the problems encountered in assessing RV function in postoperative atrial switch procedures[11]. They had used apical 4 chamber view and parasternal SAX view which were perpendicular to each other. They had demonstrated a high correlation co-efficient of 0.97 against RVEF by cineangiography. Still generally echocardiographic assessment of RV volumes is considered to be associated with problems[4,18].

In the present study RV Ejection fraction ranged from 35% to 65%. Normal values of echocardiographically determined RV Ejection fraction have not been standardised, though these values have good correlation with angiographic RVEF Normal RVEF calculation of RVEF is faced with many technical problems like intra and

interobserver variations, crescentic shape of RV which is not well suited for usual Simpson's formula used for calculation of LV volumes and prominent trabeculations of RV which make endocardial border more difficult to outline[22]. However we have used views which were superior as demonstrated by Vitolo et al. Normal RVEF by angio is 0.61 + 0.08[8]. So lower limit of normal would be 0.45. We have arbitrarily chosen EF less than 45% as cut of point for the purpose of intervention using ACEI.

10 patients had EF < 45% (34.5%) 10 had fair EF and 9 had good EF. EF was lower in postop: Senning children compared to normal as well as those who underwent ASO procedure Ninomiya et al reported EF calculated by two dimensional echocardiography ranging from 0.38 to 0.72 in 24 patients[11]. Thus it is universal to find significant proportion of patients post-operatively to have impaired RV function. There have been several postulations to explain the documented RV dysfunction in postoperative senning Scenario, the prevalence of which may increase with time and approach 20%[19]. The relative roles of increased afterload or intrinsic myocardial dysfunction has not been yet resolved[7,19]. Graham feels that it is multifactorial possible contributory factors being preoperative

myocardial damage due to hypoxia, preoperative damage due to inadequate protection of myocardium, residual dilatation of RV due to RV volume overload pre operatively and of course the high afterload RV has to face[19]. Trowitzsch suggests that abnormal wall motion patterns involving RV free wall and IVS could also be a contributory factor. Goldberg et al have stressed the role of RV shape abnormality in reduction of RV function in TGA [20].

In this study doppler derived RVPEP was longer and as also RVPEP/ET ratio. Among the RVSTI RVPEP/ET ratio is known to correlate best with RVEF[10]. Hirschfield calculated mean RVPEP/ET ratio in TGA and found it to be 0.43 (0.36 to 0.53) against LVPEP/ET ratio 0.35[13]. He found that RVEP increased with decreasing RV function and RVET decreased with impaired function thereby making PEP/ET ratio a most usual indicator of RV function independent at age and heart rate. A PEP/ET ratio of > 0.55 was considered indicating poor function. In the present study RVPEP/ET ratio was 0.38+ 0.11 (Range 0.20 - 0.64).

In the present study (FIG:III) There is a significant difference between group I (poor RV function) and group II (fair function) and between group I and

group III (good function) in terms of RVPEP and RVPEP/ET ratio. RVET did not show such correlation. By dividing EF into 3 subsets, one is reasonably sure that group I (EF <45%) had poor RV function and group III (EF >55%) had good. RV function. So significant difference in PEP and RVPEP/ET ratio between group I and group III is particularly informative.

Prolongation of RVPEP is documented in preoperative TGA also, possibly due to delay in onset of RV contraction[21]. RVET is shortened possibly due to increased afterload. Prolonged PEP could also be due to RV dysfunction. So it is not surprising that STI are altered in post operative senning patients, due to combination of altered after load and intrinsic RV dysfunction.

The only factor on multivariate analysis showing correlation with RV function was age at time of BAS. According to Graham duration or degree of cyanosis before surgery may influence long term ventricular function. But such a correlation was not found in the present study and his own data compared RV function in those with Senning done before or after 3 year of age and found no significant difference between them[5,6].

One of the reasons postulated for impaired RV function is that RV is facing systemic pressures and persistant increase in afterload affects RV function and causes full in RVEF Graham had demonstrated fall of RVEF following after load challenge in 12 out of 14 postoperative children underscoring the role of afterload in RVEF. Logically an afterload reducing agent like ACE inhibitor should alter afterload favourably and hence improve RV function. It should also improve RVSTI because of two reasons. One because RVSTI especially RVRatio is a surrogate for RVEF and secondly RVSTI are afterload dependent and hence should change favourably. We found improvement of RV function following ACEI for 8-12 weeks in 9 of our patients. The present study has also shown good correlation between 3 differing subsets of RVEF and the respective systolic time intervals. Even accepting the possibility of wider margin of error in calculating RVEF by echo it has to be stressed that doppler derived STI are quite accurate and have been found to correlate well with RV function in TGA[10,13]. The current study has shown unequivocally that after a short term therapy with ACE inhibitor, PEP/ET ratio and PEP have come down indicating that afterload reduction has occurred and

subsequently improved RV function as shown by reduction of PEP/ET ratio and improvement in Echo EF.

CONCLUSIONS

Echocardiographic evaluation of Right Ventricular Ejection Fraction in postoperative Senning patients was found to be feasible and to be correlating well with RVSTI. RVPEP increased and RVRatio decreased with decreasing RVEFraction. Approximately one third of the study group had impaired RV function. A search for identifying factors responsible for impaired RV function was made and only age at time of balloon septostomy was found to be predictive of RV function. A short term trial of ACE inhibitor (Enalapril) improved both RVEF and RVSTI.

TABLE I

AGE DISTRIBUTION OF SENNING SURVIVORS

	Age at BAS (days)	Age at Senning (MO)	Age at evaluation (MO)	time interval (MO)
	(n-24)	(n-29)	(n-29)	(n-29)
Mean	62.6	19.4	51.0	30.1
SD	44.8	16.6	22.0	20.5
Range(Min)	3.0	6.0	21.0	4.0
(max)	150	60	120.0	78.0

Table II

SYSTOLIC TIME INTERVALS (DOPPLER)

	RV		LV	
	Mean	SD	Mean	SD
C - PEP (msec)	134.9	22.4	109.4	10.8
C-ET (msec)	405.5	39.6	423.8	29.3
PEP/ET Ratio	0.38	0.12	0.26	0.06

TABLE III

EFFECT OF ACE INHIBITOR

(n - 9)

	BASAL		AFTER ACEI		P VALVE
	MEAN	SD	MEAN	SD	
1. RVEF	38.6	2.9	43.8	4.2	0.05
2. RV-PEP	151.1	15.4	127.8	13.2	0.005
3. RVET	363.4	50.4	368.4	48.3	N.S
4. PEP/ETRATIO	0.45	0.07	0.35	0.05	0.05

FIG:1
ARTERIAL SATURATIONS

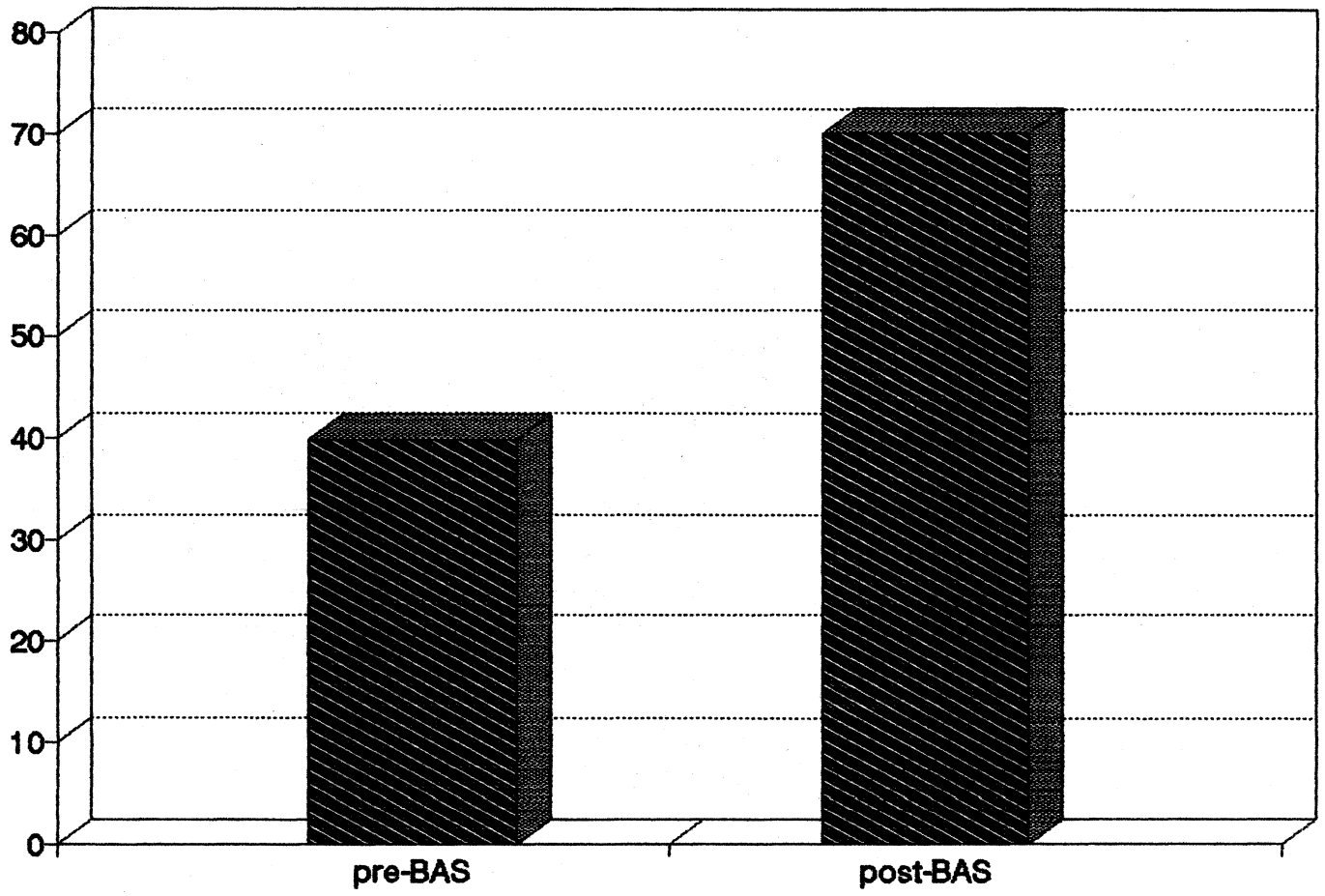


FIG:2
RIGHT VENTRICULAR EJECTION FRACTION

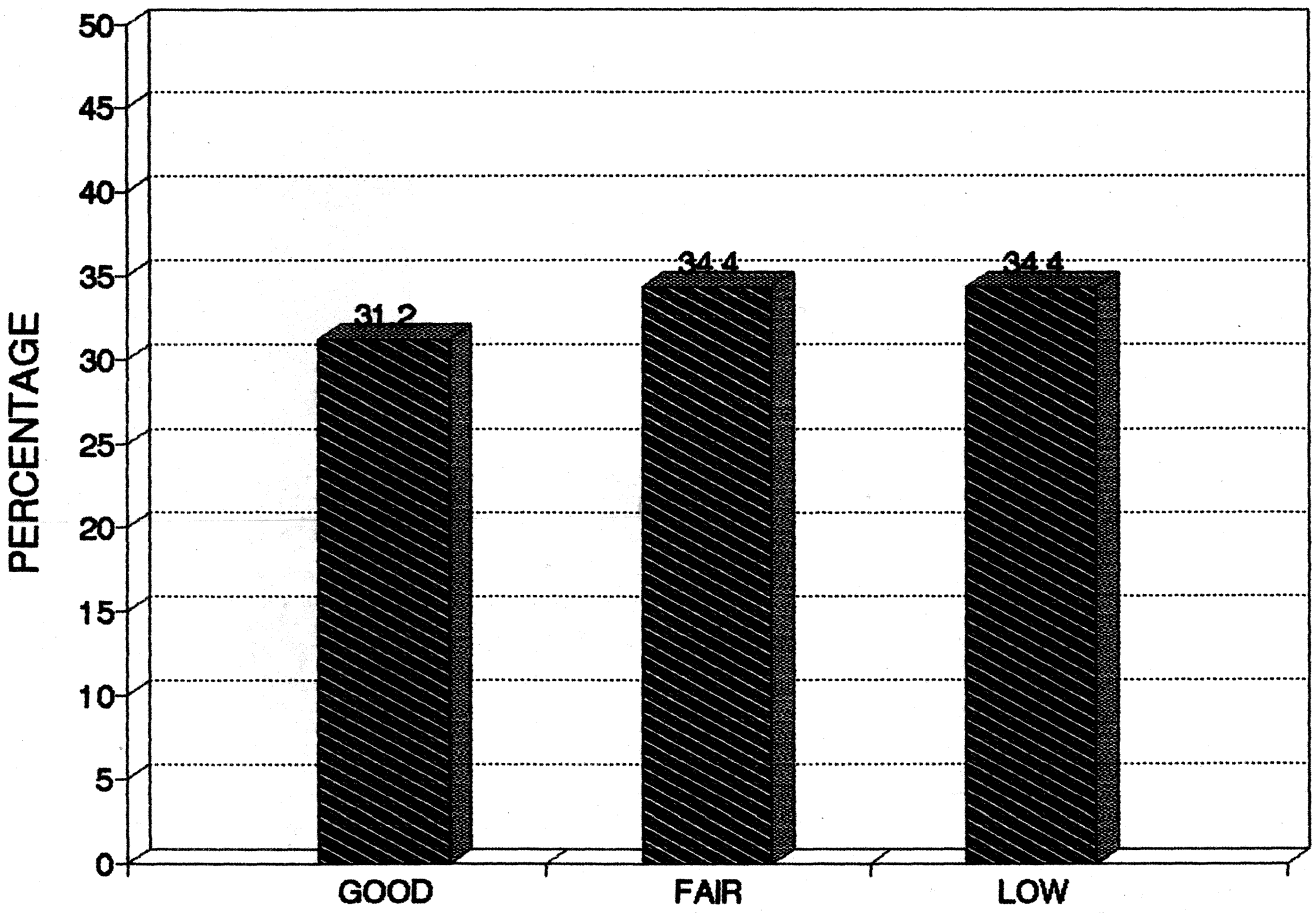


FIG: 3A
RVEF vs RV RATIO

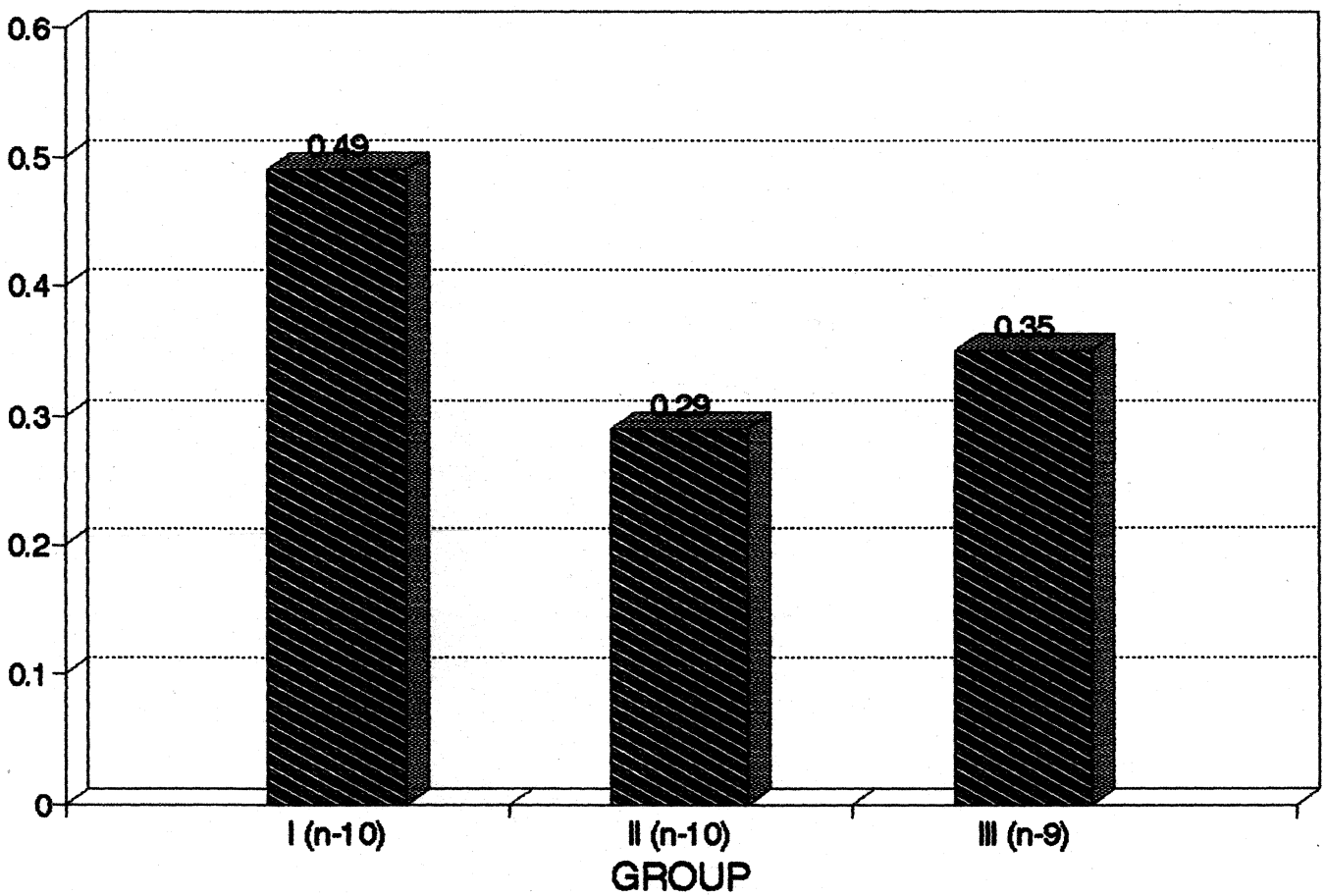


FIG: 3B
RVEF vs RVPEP

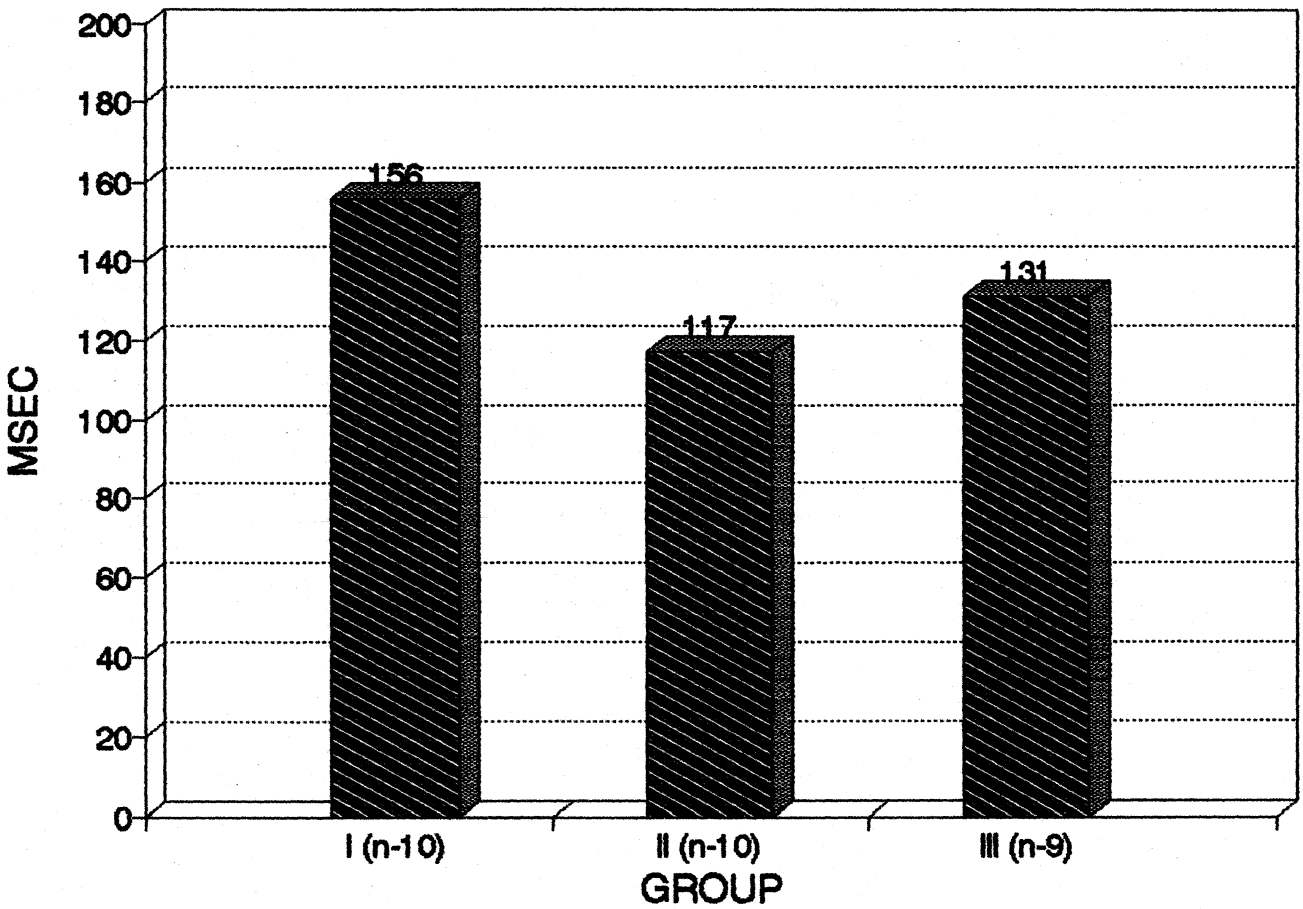


Figure 4

EFFECT OF ACE Inhibitor on RVEF

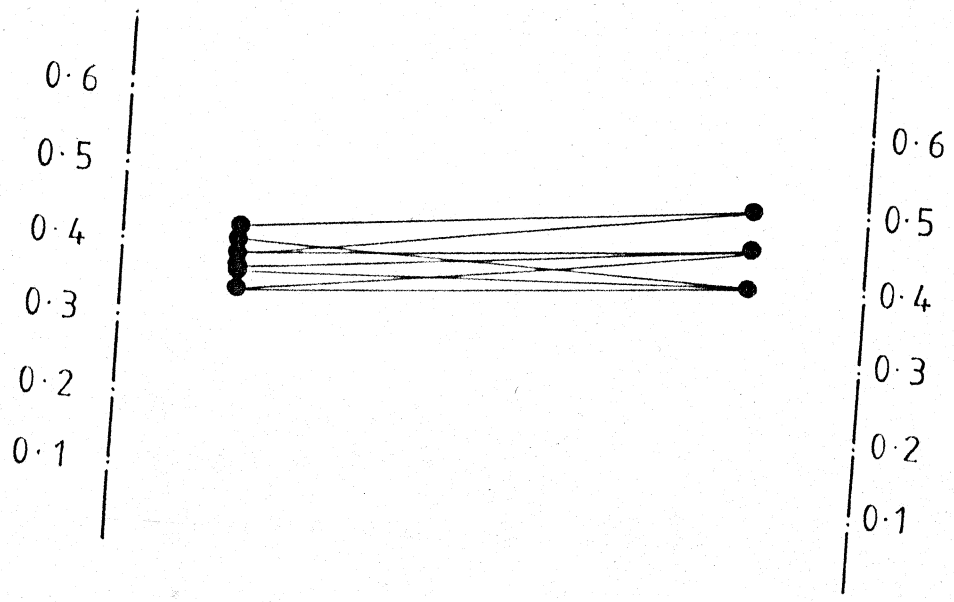
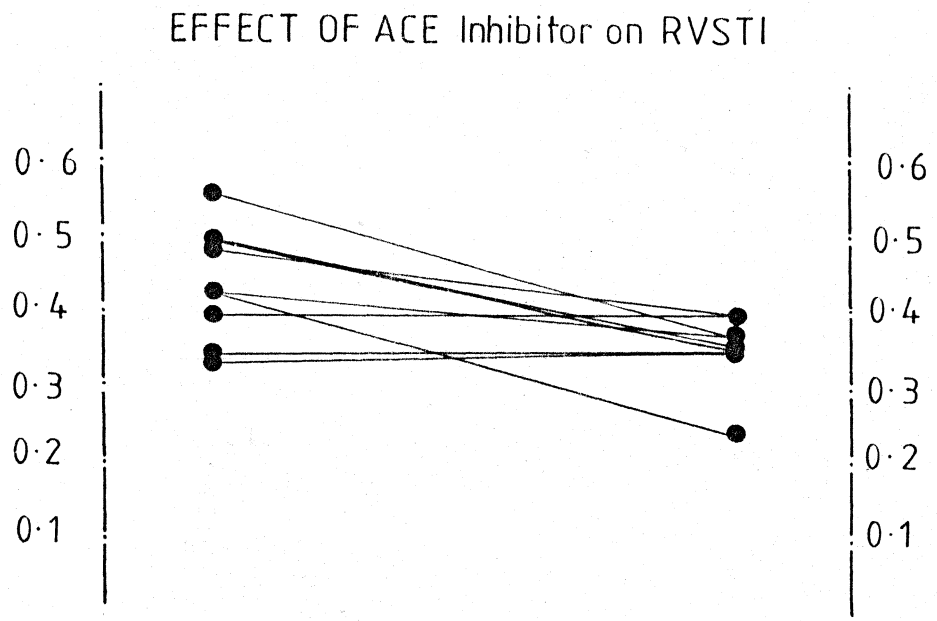


Figure 5


EFFECT OF ACE Inhibitor on RVSTI
0·6
0·5
0·4
0·3
0·2
0·1
0·6
0·5
0·4
0·3
0·2
0·1

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