SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY. THIRUVANANTHAPURAM.

PROJECT REPORT

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PROGRAMME : DM CARDIOLOGY

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CERTIFICATE

I, Dr. Sanjay G, hereby declare that the projects in this book were undertaken by me under the supervision of the faculty, Department of Cardiology, SCTIMST.

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Date: 25.10.2007

Forwarded,

The Candidate, Dr. Sanjay G has completed the projects satisfactorily.

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ANALYSIS OF P WAVE SLOPE IN ATRIAL ENLARGEMENT

INTRODUCTION

The sino-atrial node initiates the activation of the atria which is completed in 0.099$\pm$ 0.012 second. (1). The right atrial activation begins first, reflected by the ascending limb of the P wave in the frontal plane leads, and ends at the apex of the P wave. The left atrial activation begins when the impulse waves reach the interatrial septum about 0.03 second after the onset of right atrial activation and constitutes the distal half or descending limb of P wave in standard lead II. The electrical stimulus next reaches the atrioventricular node and then completes the depolarization of the right atrium while left atrial depolarization continues until the end of the P wave (13).

The normal P wave is usually best seen and studied in the standard lead II because the frontal plane P wave axis (+45 to +60 degrees) is usually directed to the positive pole of this lead. The P wave is pyramidal in shape with a somewhat rounded apex. Rarely, the apex of P wave can be notched in lead II normally. The duration of the P wave is usually not greater than 0.11 sec. The maximum amplitude normally does not exceed 2.5mm or 0.25mV. (2)

In lead V1, the initial and terminal components of the P wave may be clearly identified and the morphology may be biphasic with an initial positivity and terminal negativity. The initial positivity is due to the initial right atrial activation vector which is directed anteriorly and slightly to the left. Left atrial activation begins slightly later than right atrial activation and overlaps with the terminal activation of the right atrium. The activation vector of left atrium is directed posteriorly and inscribes a terminal negative component in V1.

LEFT ATRIAL ENLARGEMENT

Left atrial enlargement will result in three basic electrocardiographic effects

i. prolongation and delay of the terminal or left atrial component of atrial activation

ii. increased posterior deviation of the left atrial vector

iii. left axis deviation of the mean frontal P wave axis

<u>ELECTROCARDIOGRAPHIC CRITERIA OF LEFT ATRIAL ENLARGEMENT</u>

(3, 4)

- Duration of terminal negative P wave deflection in lead V1 > 0.04 sec
- Amplitude of terminal negative P wave deflection in lead V1 > 0.10 mV
- Duration between peaks of P wave notches > 0.04 sec
- Maximal P wave duration ≥ 0.12 sec
- Ratio of P wave duration to PR segment duration > 1.6
- left axis deviation of P wave from -30 to +45 degrees

RIGHT ATRIAL ENLARGEMENT

With right atrial enlargement, the initial or right atrial component of the P wave is increased both in amplitude and in duration. The P wave amplitude exceeds 2.5mm (0.25mV) and is usually best seen in lead II. But in patients with acquired heart disease, there may be an associated right axis deviation of P wave in frontal plane and in patients with congential heart disease; the P wave axis may be normal or even leftward. (1)

ELECTROCARDIOGRAPHIC CRITERIA FOR RIGHT ATRIAL ENLARGEMENT

- Peaked P waves with amplitudes greater than 0.25 mV in lead II
- Rightward shift of the mean P wave axis to greater than +75 degrees
- Increased area under the initial positive portion of the P wave in lead V_1 to >0.06 mm-sec

Additional features involving QRS morphology include QR morphology in V1 in the absence of infarction, diminution in the size of QRS deflection in V1 with marked increase in QRS amplitude in V2, etc.

SLOPE OF P WAVE IN LIMB LEADS AND V1

Right atrial enlargement is characterized by an increase in P wave amplitude in lead II and an increase in P initial force in lead V1. But, the total duration of P wave is not altered significantly, because the right atrium in the normal course gets activated first and is fully activated before the completion of left atrial activation. Whereas, in left atrial enlargement, the duration of left atrial activation is prolonged. It is known that left atrial enlargement results in deepening and lengthening of the terminal P wave in V1. There are few studies which have assessed the effect of either atrial enlargement or combined atrial enlargement in the slope of atrial activation vector. By assessing the upslope of P wave in limb leads and the slope between the initial and terminal components in V1, we can analyze the effect of atrial enlargement on the activation vectors of both atria.

ECHOCARDIOGRAPHIC ASSESSMENT OF ATRIAL ENLARGEMENT:

M-mode echocardiography has been established as a reliable technique for measuring the anteroposterior dimension of the left atrium (10). Atrial volume estimation using bi-plane Simpson's method and single-plane area length method have been found to correlate well with autopsy studies (7,11,12, 14) both in left and right atria. The mean indexed left and right atrial volumes in normal subjects were found to be 22ml/sq m in these studies which has been used in the current study as well. (9, 15) The technique of measurement of atrial volume by echocardiography is elaborated along with the methods.

OBJECTIVES OF THE STUDY

- To analyze the effect of enlargement of atria independently and combined on the slope of P wave in limb leads and lead V1
- To compare the P wave slope with various electrocardiographic indicators of atrial enlargement.

MATERIALS AND METHODS

Patients who attended the out-patient department cardiac assessment or who were hospitalized in the cardiology department of this institute for management of their underlying condition above the age of 12 years were included for the study. The patients underwent evaluation of their cardiac condition which included clinical examination, chest Roentgenogram, electrocardiogram and echocardiography. The patients, prior to inclusion were first evaluated for the presence of atrial enlargement by echocardiography.

Method of estimating the right atrial volume:

Apical 4- chamber images were obtained in the left lateral decubitus position using the available imaging system. Planimetric measurement of the right atrial volume was done in the end-systolic frame using the single plane method of discs (6). The right atrium was outlined by tracing a line around the inner atrial border. The computer then inserted the discs at equal intervals within the outline, perpendicular to the longest atrial dimension and automatically calculated the volume as the sum of the areas of the disc. Subsequently, the obtained volume was indexed to the body surface area.

Assessment of left atrial volume:

Both apical four chamber and apical two chamber images were obtained. Planimetric assessment of left atrial volume using the single plane method of discs was done both in apical four chamber and apical two chamber views. The outline of atrial endocardium was traced in both the views. At the mitral annulus, a straight line was extrapolated connecting the attachment point of the leaflets to the valve ring.

Then, a perpendicular was drawn from this line to the roof of the left atrium. The computer then inserted the discs at equal intervals and calculated the left atrial volume in both the views. The average of the result obtained was taken and was indexed to the body surface area (ml/ sq.m)

Eighty patients were selected consecutively, with twenty in each of the following four groups – with left atrial enlargement (indexed left atrial volume $\geq$ 23ml/sqm) (9), with right atrial enlargement (indexed right atrial volume $\geq$ 23ml/sqm) (9), those with bi-atrial enlargement, and those with normal atrial volume.

The following parameters of the patients were noted – age, gender, height (cm), weight (kg), body surface area, and then electrocardiographic analysis was performed.

Electrocardiographic analysis

A routine 12 lead surface electrocardiogram was taken for all the patients. For better assessment, amplified surface electrocardiogram was obtained using the Bard-EP system and the following aspects analysed:

Lead II – P wave amplitude (mV), time to peak P wave amplitude (sec), P wave duration, presence of double peaking of P wave with inter-peak distance $\geq$ 0.04 second (and if present, the amplitude of both the peaks in mV), PR interval in seconds and the PR segment (from the end of P wave to the onset of QRS complex) in seconds. The following parameters were derived: (i) P wave upslope in lead II – obtained by dividing the P wave amplitude by the duration to peak (mV/sec)

(ii) P/PR segment ratio: P wave duration in lead II divided by the PR segment duration. In case the axis of P wave was shifted, the limb lead with maximum P wave amplitude was selected for the analysis, i.e, lead III for patients with right axis deviation of P wave and lead I for those with left axis deviation.

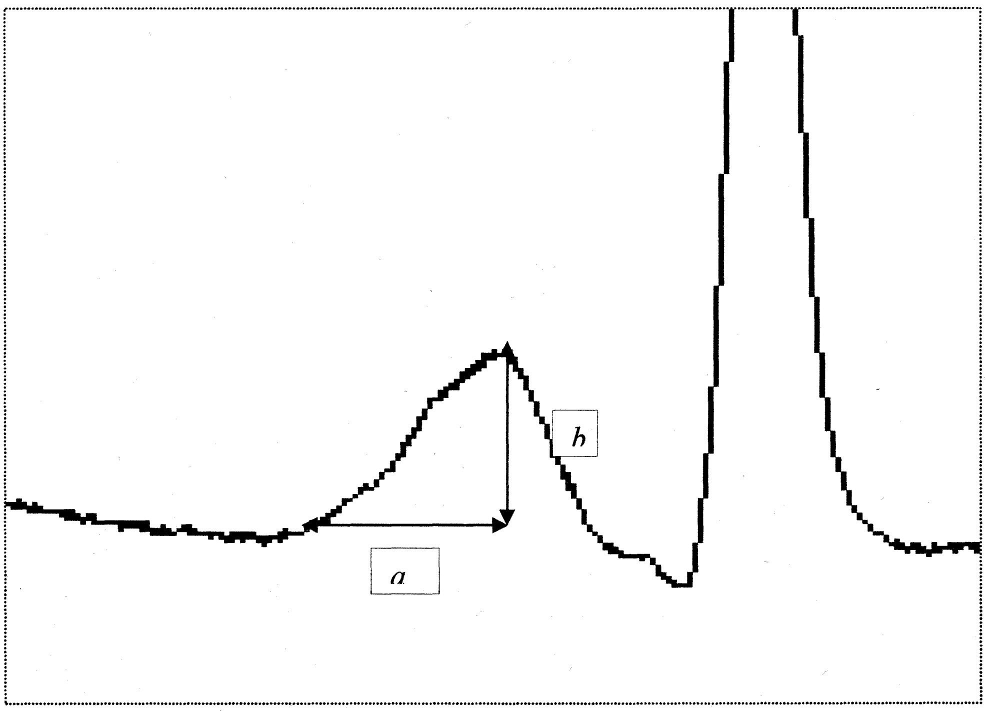


Figure 1 : Calculation of upslope of P wave in standard limb lead

'*a*' = duration of upslope in second

'*b*' = amplitude of P wave in millivolts

UPSLOPE = b/a

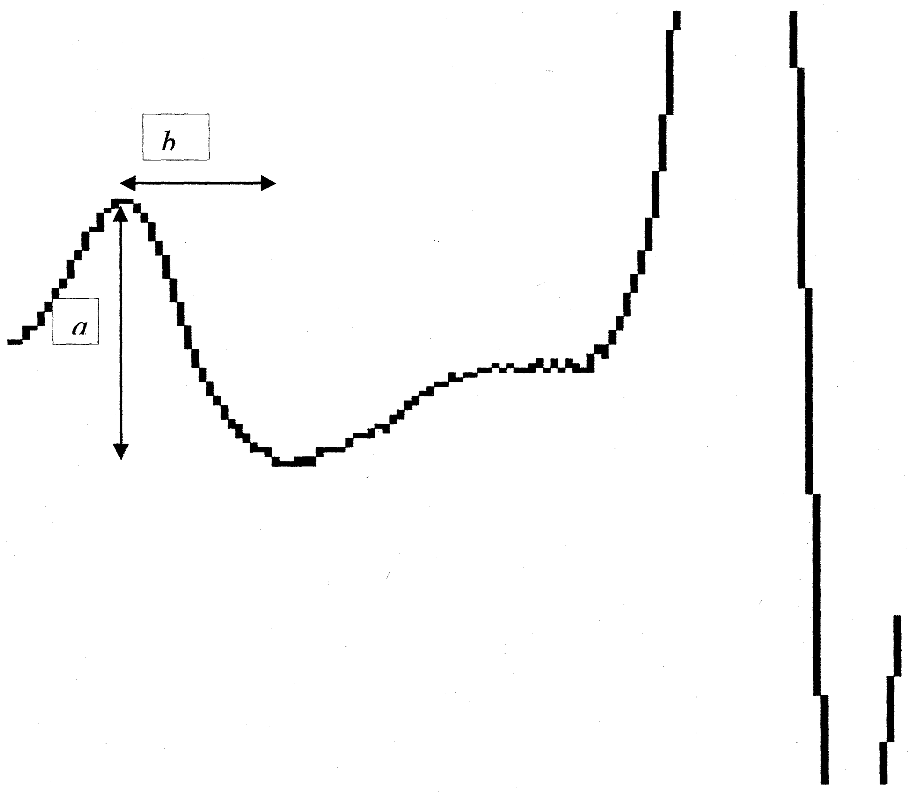


Figure 2: Calculation of downslope in lead V1

'**a**' = amplitude of P wave in lead V1 in millivolts

'**b**' = duration between the peak and nadir of P wave in lead V1 in second

<u>DOWNSLOPE = a/b</u>

Lead V1 – the amplitude and duration of the positive components of the P wave, the amplitude and duration of the negative component of the P wave, the total amplitude of the P wave, the duration from the peak of the positive component to the nadir of the negative component. The following parameters were derived:

(i) initial P force = amplitude of positive component X duration of the positive component (mV.sec)

(ii) terminal P force = amplitude of the negative component X duration of the negative component (mV.sec)

(iii) downslope of P wave in lead V1 = Amplitude of P wave divided by the duration from peak to nadir (mV/sec)

(The direction of the vectors were discarded and the results were expressed as absolute integers)

In addition to these, the routine surface electrocardiogram was also analyzed for the axis of P wave, the axis of QRS wave and the presence of left ventricular hypertrophy or right ventricular hypertrophy by voltage criteria (4)

EXCLUSION CRITERIA:

The following categories of patients were excluded from the study

- Patients with any rhythm other than sinus
- Patients with any manifest supraventricular tachyarrhythmias, ventricular arrhythmias, ventricular pre-excitation, any forms of A-V block.
- Patients without an intact atrial septum
- Ebstein anomaly of tricuspid valve, complex congential heart diseases with atrio-ventricular discordance, situs abnormality etc.
- Post mitral- valve replacement patients

STATISTICS

The results of parametric data are expressed as mean ± standard deviation. P values <0.05 were taken as significant. Significance between the means of the continuous variables between the groups was assessed using independent T test or Pearson correlation. Linear regression model with P wave upslope and P wave downslope in lead V1 as dependent factors and continuous variables against various variables were assessed separataely.

RESULTS

DEMOGRAPHIC VARIABLES

The demographic data of all patients are given in table 1. The mean age of the patients was 36.2 years. Altogether, there were 39 males and 41 females. (table 2)

Table 1 demographic and electrocardiographic data of all patients

PARAMETER	N	Minimum	Maximum	Mean	Standard deviation
Age (years)	80	13	66	36.20	12.71
Height in cm	80	136	180	159.79	9.24
Weight in kg	80	32	74	53.48	8.89
Body surface area (sq m)	80	1.15	1.81	1.534	0.162
P wave axis degrees	80	-15	90	45.94	26.72
P duration lead II (sec)	80	0.078	0.160	0.112	.023
P amplitude II (mV)	80	0.085	0.525	0.228	0.11
P' ampl II (mV)	23	0	.4000	0.247	0.089
P P' duration (sec)	23	0	.0500	0.042	0.009
upslope duration (sec)	80	0.032	.0820	0.047	0.011
P upslope (mV/sec)	80	2.1	10.2	4.78	1.97
P duration in V1 (sec)	80	0.065	0.156	0.102	0.021
Initial P height V1 (mV)	80	0	0.32	0.114	0.095
Terminal P ht V1 (mV)	80	0	0.07	0.027	0.009
P initial force (mV.sec)	80	0	0.027	0.006	0.007
P terminal force (mV.sec)	80	0	0.080	0.009	0.01
P amplitude in V1 (mV)	80	0.065	0.525	0.241	0.12
Downslope duration V1 (sec)	80	0.028	0.072	0.54	4.46
P slope V1 (mV/sec)	80	1.8	17.5	5.77	3.05
PR interval (sec)	80	0.14	0.23	0.164	0.025
PR segment (sec)	80	0.04	0.64	0.074	0.065
P/PR segment (sec)	80	1	4.	1.74	0.68
QRS axis (degrees)	80	-30	135	54.19	34.37
Indexed LA vol (ml/sq m)	80	16	152	47.93	29.47
Indexed RA vol (ml/sq m)	80	15	125	43.19	26.61

Table 2. Gender distribution between groups

Group	Males	females
Normal	9	11
Left atrial enlargement	8	9
Bi-atrial enlargement	12	8
Right atrial enlargement	10	10
Total	39	41

Underlying cardiac illness in various groups :

Left atrial enlargement : 19 had rheumatic heart disease with severe mitral stenosis in 16 and severe mitral regurgitation in 3. One patient had hypertrophic cardiomyopathy with LV diastolic dysfunction.

Bi-atrial enlargement :

- Rheumatic heart disease with significant pulmonary arterial hypertension and tricuspid regurgitation – 14 patients
- Dilated cardiomyopathy with biventricular dysfunction – 3 patients
- Hypertrophic obstructive cardiomyopathy with severe pulmonary arterial hypertension - 1 patient
- Ruptured sinus of valsalva aneurysm to right ventricle with tricuspid valve regurgitation – 1 patient
- Anterior wall myocardial infarction with severe left ventricular dysfunction and significant pulmonary arterial hypertension – 1 patient

Right atrial enlargement:

- Primary pulmonary hypertension – 10 patients
- Eisenmenger syndrome (secondary to ventricular septal defect or persistant arterial duct) – 4 patients
- Tetralogy of fallot with ventricular dysfunction or tricuspid regurgitation – 3 patients
- Post intracardiac repair of Tetralogy of Fallot with significant tricuspid regurgitation or Right ventricular hypertension – 2 patients
- Inferior wall myocardial infarction with right ventricular infarction , severe tricuspid regurgitation, good left ventricular function and right ventricular dysfunction – 1 patient

Normal atrial volume:

- Atrioventricular nodal re-entrant tachycardia (in sinus rhythm) without structural heart disease – 19 patients
- Mild mitral valve regurgitation – 1 patient

Tables 3,4,5,6 provide the demographic and electrocardiographic data of patients with left atrial enlargement, those with bi-atrial enlargement, right atrial enlargement and normal atrial volumes respectively.

DEMOGRAPHIC & ECG DATA OF PATIENTS WITH LEFT ATRIAL ENLARGEMENT

Table 3

PARAMETER	N	Minimum	Maximum	Mean	Standard Deviation
Age (years)	20	17	56	34.20	11.32
Height (cm)	20	136	174	158.25	10.22
Weight (kg)	20	36	65	51.9	9.14
Body surface area (sq m)	20	1.21	1.73	1.51	0.17
Paxis (degrees)	20	-15	30	14.25	12.38
P duration lead II (seconds)	20	0.12	0.15	0.13	0.01
P amplitude lead II (mV)	20	0.10	0.34	0.19	0.07
P' amplitude lead II (mV)	12	0.12	0.34	0.22	0.07
P P' duration lead II (sec)	12	0.038	0.050	0.044	0.004
upslope duration (sec)	20	0.03	0.08	0.053	0.015
P upslope (mV/sec)	20	2.50	5.00	3.45	0.76
P duration lead V1 (sec)	20	0.096	0.130	0.112	0.010
Initial P height V1 (mV)	20	0	0.12	0.04	0.040
Terminal P ht V1 (mV)	20	0.075	0.280	0.170	0.055
P initial force (mV.sec)	20	0	0.003	0.0011	0.0008
P terminal force (mV.sec)	20	0.008	0.030	0.0149	0.005
P amplitude in V1 (mV)	20	0.110	0.38	0.231	0.074
Downslope duration V1 (sec)	20	0.030	0.06	0.048	0.008
P slope V1 (mV/sec)	20	2.50	9.50	5.15	1.67
PR interval (sec)	20	0.166	0.210	0.178	0.009
PR segment (sec)	20	0.04	0.064	0.048	0.003
P/PR segment	20	1.45	3.75	2.11	0.46
QRS axis (degrees)	20	0	60	41.25	17.5
Indexed LA vol (ml/sq m)	20	51	108	70.3	15.5
Indexed RA vol (ml/sq m)	20	16	22	21.3	2.7

DEMOGRAPHIC & ELECTROCARDIOGRAPHIC DATA OF PATIENTS WITH BI-ATRIAL ENLARGEMENT

Table 4

PARAMETERS	N	Minimum	Maximum	Mean	Standard Deviation
Age (years)	20	13	62	32.8	13.9
Height (cm)	20	146	177	159.7	9.4
Weight (kg)	20	32	65	49	9.6
Body surface area (sq m)	20	1.15	1.77	1.47	0.18
Paxis (degrees)	20	15	75	49.5	21.3
P duration lead II (seconds)	20	0.100	0.160	0.133	0.016
P amplitude lead II (mV)	20	0.18	0.46	0.28	0.068
P' amplitude lead II (mV)	11	0.22	0.40	0.29	0.06
P P' duration lead II (sec)	11	0.034	0.050	0.044	0.004
upslope duration (sec)	20	0.03	0.08	0.05	0.01
P upslope lead (mV/sec)	20	3.90	7.80	5.65	0.96
P duration lead V1 (sec)	20	0.105	0.156	0.125	0.013
Initial P height V1 (mV)	20	0.1	0.26	0.165	0.059
Terminal P ht V1 (mV)	20	0.124	0.3	0.185	0.047
P initial force (mV.sec)	20	0	0.017	0.011	.004
P terminal force (mV.sec)	20	0.007	0.030	0.013	0.005
P amplitude in V1 (mV)	20	0.230	0.500	0.341	0.082
Downslope duration V1 (sec)	20	0.040	0.072	0.054	0.010
P slope V1 (mV/sec)	20	4.5	8.3	6.36	0.93
PR interval (sec)	20	0.150	0.230	0.191	0.019
PR segment (sec)	20	0.04	0.09	0.058	0.013
P/PR segment	20	1.56	4.00	2.41	0.72
QRS axis (degrees)	20	-30	120	46.5	41
Indexed LA vol (ml/sq m)	20	53	152	77.1	23.4
Indexed RA vol (ml/sq m)	20	47	124	64.2	18.9

DEMOGRAPHIC & ECG DATA OF PATIENTS WITH RIGHT ATRIAL ENLARGEMENT

Table 5

PARAMETERS	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	20	17	57	32	11.9
Height (cm)	20	145	180	161	8.1
Weight (kg)	20	34	62	52.8	6.9
Body surface area (sq m)	20	1.19	1.72	1.52	0.13
Paxis (degrees)	20	45	90	65.2	12.2
P duration lead II (seconds)	20	0.08	0.13	0.09	0.012
P amplitude lead II (mV)	20	0.18	0.53	0.33	0.09
upslope duration (sec)	20	0.03	0.06	0.04	0.006
P upslope (mV/sec)	20	4.10	10.20	7.15	1.38
P duration lead V1 (sec)	20	0.075	0.125	0.090	0.013
Initial P height V1 (mV)	20	0.00	0.32	0.22	0.083
Terminal P ht V1 (mV)	20	0.00	0.07	0.02	0.008
P initial force (mV.sec)	20	0.000	0.027	0.020	0.007
P terminal force (mV.sec)	20	0.000	0.005	0.002	0.001
P amplitude in V1 (mV)	20	0.180	0.525	0.305	0.096
Downslope duration V1 (sec)	20	0.028	0.042	0.033	0.004
P slope V1 (mV/sec)	20	4.70	17.50	9.25	2.96
PR interval (sec)	20	0.150	0.220	0.180	0.021
PR segment (sec)	20	0.07	0.10	0.08	0.012
P/PR segment	20	1.00	1.57	1.23	0.154
QRS axis (degrees)	20	0	135	89.2	28
Indexed LA vol (ml/sq m)	20	16	22	20.30	1.34
Indexed RA vol (ml/sq m)	20	45	125	67.90	19.1

DEMOGRAPHIC & ECG DATA OF PATIENTS WITH NORMAL ATRIA

Table 6

PARAMETERS	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	20	35	66	45.8	8.6
Height (cm)	20	142	172	160.2	9.6
Weight (kg)	20	52	74	60.1	5.8
Body surface area (sq m)	20	1.41	1.81	1.63	0.12
Paxis (degrees)	20	30	60	42.7	10.1
P duration lead II (seconds)	20	0.078	0.100	0.086	0.005
P amplitude lead II (mV)	20	0.09	0.16	0.122	0.024
upslope duration (sec)	20	0.03	0.05	0.04	0.004
P upslope (mV/sec)	20	2.10	3.80	2.85	0.51
P duration lead V1 (sec)	20	0.065	0.090	0.078	0.006
Initial P height V1 (mV)	20	0.00	0.05	0.04	0.011
Terminal P ht V1 (mV)	20	0.03	0.06	0.04	0.011
P initial force (mV.sec)	20	0.000	0.002	0.001	0.0004
P terminal force (mV.sec)	20	0.001	0.005	0.002	0.0007
P amplitude in V1 (mV)	20	0.065	0.120	0.086	0.013
Downslope duration V1 (sec)	20	0.028	0.046	0.037	0.004
P slope V1 (mV/sec)	20	1.80	3.12	2.32	0.37
PR interval (sec)	20	0.140	0.172	0.156	0.009
PR segment (sec)	20	0.06	0.08	0.06	0.006
P/PR segment	20	1.10	2.00	1.23	0.11
QRS axis (degrees)	20	0	75	39.7	18.3
Indexed LA vol (ml/sq m)	20	14	22	19.4	1.5
Indexed RA vol (ml/sq m)	20	15	22	19.3	2.1

Comparison between LAE and Normal (N=20 each) - independent T test (two-tailed, 95% confidence intervals)

Table 7

PARAMETER	LEFT ATRIAL ENLARGEMENT		NORMAL		T value	P value
	mean	Standard deviation	Mean	Standard deviation		
Paxis (degrees)	14.25	12.38	42.7	10.1	-7.98	0.0001
P duration lead II (seconds)	0.13	0.01	0.086	0.005	18.21	0.0001
P amplitude lead II (mV)	0.19	0.07	0.122	0.024	3.69	0.001
upslope duration (sec)	0.053	0.015	0.04	0.004	3.23	0.003
P upslope (mV/sec)	3.45	0.76	2.85	0.51	2.9	0.006
P duration lead V1 (sec)	0.112	0.010	0.078	0.006	12.12	0.0001
Initial P height V1 (mV)	0.04	0.040	0.04	0.011	0.086	0.932
Terminal P ht V1 (mV)	0.170	0.055	0.04	0.011	9.85	0.0001
P terminal force (mV.sec)	0.0149	0.005	0.002	0.0007	11.2	0.0001
P amplitude in V1 (mV)	0.231	0.074	0.086	0.013	8.7	0.0001
Downslope duration V1 (sec)	0.048	0.008	0.037	0.004	1.004	0.01
P slope V1 (mV/sec)	5.15	1.67	2.32	0.37	7.38	0.0001
PR interval (sec)	0.178	0.009	0.156	0.009	6.45	0.001
PR segment (sec)	0.048	0.003	0.06	0.006	4.38	0.001
P/PR segment	2.11	0.46	1.23	0.11	8.17	0.0001
QRS axis (degrees)	41.25	17.5	39.7	18.3	0.27	0.793
Indexed LA vol (ml/sq m)	70.3	15.5	19.4	1.5	13.24	0.0001
Indexed RA vol (ml/sq m)	21.3	2.7	19.3	2.1	0.71	0.32

On comparison between patients with isolated left atrial enlargement and those with normal atria (table 8) the patients with enlarged left atria had significantly higher P wave duration in leads II and V1, upslope in limb leads, left axis deviation of P wave, higher terminal P wave forces in lead V1, downslope in V1, PR interval and P/PR segment ratios. But there was no difference in initial P height in V1.

Comparison between BAE and Normal (N=20 each)- independent T test (two-tailed, 95% confidence intervals)

Table 8

parameters	Bi-atrial enlargement		normal		T value	P value
	Mean	Standard deviation	Mean	Standard deviation		
Paxis (degrees)	49.5	21.3	42.7	10.1	1.283	.207
P duration lead II (seconds)	0.133	0.016	0.086	0.005	12.529	.0001
P amplitude lead II (mV)	0.28	0.068	0.122	0.024	10.125	.0001
upslope duration (sec)	0.05	0.01	0.04	0.004	2.993	.005
P upslope (mV/sec)	5.65	0.96	2.85	0.51	11.471	.0001
P duration lead V1 (sec)	0.125	0.013	0.078	0.006	14.087	.0001
Initial P height V1 (mV)	0.165	0.059	0.04	0.011	8.684	.0001
Terminal P ht V1 (mV)	0.185	0.047	0.04	0.011	12.746	.0001
P initial force (mV.sec)	0.011	.004	0.001	0.0004	8.980	.0001
P terminal force (mV.sec)	0.013	0.005	0.002	0.0007	8.738	.0001
P amplitude in V1 (mV)	0.341	0.082	0.086	0.013	13.767	.0001
Downslope duration V1 (sec)	0.054	0.010	0.037	0.004	6.395	.0001
P slope V1 (mV/sec)	6.36	0.93	2.32	0.37	17.944	.0001
PR interval (sec)	0.191	0.019	0.156	0.009	7.313	.0001
PR segment (sec)	0.058	0.013	0.06	0.006	-3.651	.001
P/PR segment	2.41	0.72	1.23	0.11	7.183	.0001
QRS axis (degrees)	46.5	41	39.7	18.3	.672	.506
Indexed LA vol (ml/sq m)	77.1	23.4	19.4	1.5	10.109	.0001
Indexed RA vol (ml/sq m)	64.2	18.9	19.3	2.1	10.531	.0001

All the electrocardiographic parameters except for the P wave axis in frontal plane and QRS axis were significantly different and higher in patients with bi-atrial enlargement compared with normal atria.

Comparison between RAE and Normal (N=20 each)- independent T test (two-tailed, 95% confidence intervals)

Table 9

parameters	RIGHT atrial enlargement		normal		T value	P value
	Mean	Standard deviation	Mean	Standard deviation		
Paxis (degrees)	65.2	12.2	42.7	10.1	9.761	0.0001
P duration lead II (seconds)	0.09	0.012	0.086	0.005	3.961	0.0001
P amplitude lead II (mV)	0.33	0.09	0.122	0.024	9.982	0.0001
upslope duration (sec)	0.04	0.006	0.04	0.004	2.316	0.026
P upslope (mV/sec)	7.15	1.38	2.85	0.51	12.994	0.0001
P duration lead V1 (sec)	0.090	0.013	0.078	0.006	4.830	0.0001
Initial P height V1 (mV)	0.22	0.083	0.04	0.011	9.675	0.0001
Terminal P ht V1 (mV)	0.07	0.02	0.04	0.011	1.525	0.136
P initial force (mV.sec)	0.020	0.007	0.001	0.0004	8.719	0.0001
P terminal force (mV.sec)	0.002	0.001	0.002	0.0007	1.127	0.351
P amplitude in V1 (mV)	0.305	0.096	0.086	0.013	10.105	0.0001
Downslope duration V1 (sec)	0.033	0.004	0.037	0.004	-2.702	0.001
P slope V1 (mV/sec)	9.25	2.96	2.32	0.37	10.356	0.0001
PR interval (sec)	0.180	0.021	0.156	0.009	4.493	0.06
PR segment (sec)	0.08	0.012	0.06	0.006	3.603	0.07
P/PR segment	1.23	0.154	1.23	0.11	-.152	0.88
QRS axis (degrees)	89.2	28	39.7	18.3	6.449	0.0001
Indexed LA vol (ml/sq m)	20.30	1.34	19.4	1.5	-6.089	0.07
Indexed RA vol (ml/sq m)	67.90	19.1	19.3	2.1	11.303	0.0001

On comparison, all the parameters except terminal P wave amplitude, P- terminal force in lead V1, PR interval, PR segment, and P/PR segment ratios were significantly different between the two groups.

Comparison between RAE and LAE (N=20 each)- independent T test (two-tailed, 95% confidence intervals)

Table 10

parameters	Left atrial enlargement		Right atrial enlargement		T value	P value
	mean	Standard deviation	Mean	Standard deviation		
Paxis (degrees)	14.25	12.38	65.2	12.2	-16.213	0.0001
P duration lead II (seconds)	0.13	0.01	0.09	0.012	8.744	0.0001
P amplitude lead II (mV)	0.19	0.07	0.33	0.09	-5.986	0.0001
upslope duration (sec)	0.053	0.015	0.04	0.006	1.931	0.061
P upslope (mV/sec)	3.45	0.76	7.15	1.38	-10.460	0.0001
P duration lead V1 (sec)	0.112	0.010	0.090	0.013	4.635	0.0001
Initial P height V1 (mV)	0.04	0.040	0.22	0.083	-8.758	0.0001
Terminal P ht V1 (mV)	0.170	0.055	0.07	0.02	1.522	0.001
P initial force (mV.sec)	0.0011	0.0008	0.020	0.007	-8.646	0.0001
P terminal force (mV.sec)	0.0149	0.005	0.002	0.001	2.028	0.005
P amplitude in V1 (mV)	0.231	0.074	0.305	0.096	-2.718	0.0001
Downslope duration V1 (sec)	0.048	0.008	0.033	0.004	1.006	0.001
P slope V1 (mV/sec)	5.15	1.67	9.25	2.96	-5.367	0.0001
PR interval (sec)	0.178	0.009	0.180	0.021	1.001	0.02
PR segment (sec)	0.048	0.003	0.08	0.012	.321	0.01
P/PR segment	2.11	0.46	1.23	0.154	8.033	0.0001
QRS axis (degrees)	41.25	17.5	89.2	28	-6.343	0.0001
Indexed LA vol (ml/sq m)	70.3	15.5	20.30	1.34	14.236	0.0001
Indexed RA vol (ml/sq m)	21.3	2.7	67.90	19.1	-10.805	0.0001

All the electrocardiographic parameters were significantly different as expected when compared between patients with isolated left and isolated right atrial enlargements.

One way ANOVA for the comparison between the quartile groups (N=20 each)

Table 11

VARIABLES	F VALUE	P VALUE
Paxis deg	62.566	.0001
P duration lead II	80.556	.0001
P amplitude II mv	40.892	.0001
upslope duration	4.470	.006
P upslope	85.621	.0001
P duration in V1	68.222	.0001
Initial P amplitude in V1	53.374	.0001
Terminal P amplitude in V1	8.767	.0001
P initial force	54.169	.0001
P terminal force	7.449	.0001
Total P amplitude in V1	47.341	.0001
Downslope duration in V1	1.004	.396
P slope V1	52.184	.0001
PR interval	1.003	.396
PR seg	.920	.435
P/PR seg	37.879	.01
QRS axis	14.034	.0001
Lavolml/m2	89.823	.0001
Ravol ml/m2	76.202	.0001

One way ANOVA was performed to compare various parameters between the groups which demonstrated that all variables except for downslope duration in lead V1, PR interval, and PR segment were significantly different among the groups.

P wave slope in various patient groups

Tables 12 &13

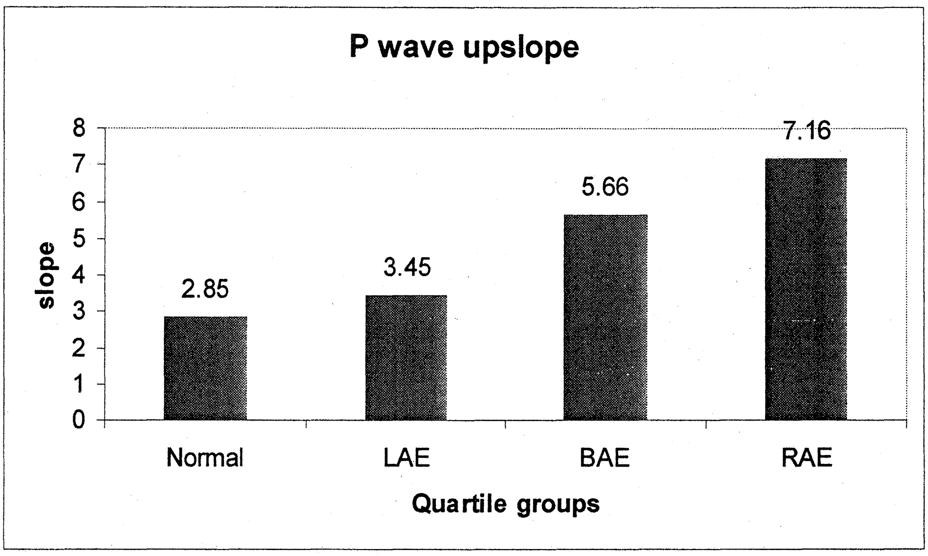
PARAMETER	Group	N	Mean	Minimum	Maximum	Std. Deviation	Std. Error
P wave upslope	LAE	20	3.45	2.50	5.00	.76	.17
	BAE	20	5.65	3.90	7.80	.96	.21
	RAE	20	7.15	4.10	10.20	1.38	.31
	normal	20	2.85	2.10	3.80	.51	.11
	Total	80	4.77	2.10	10.20	1.97	.22

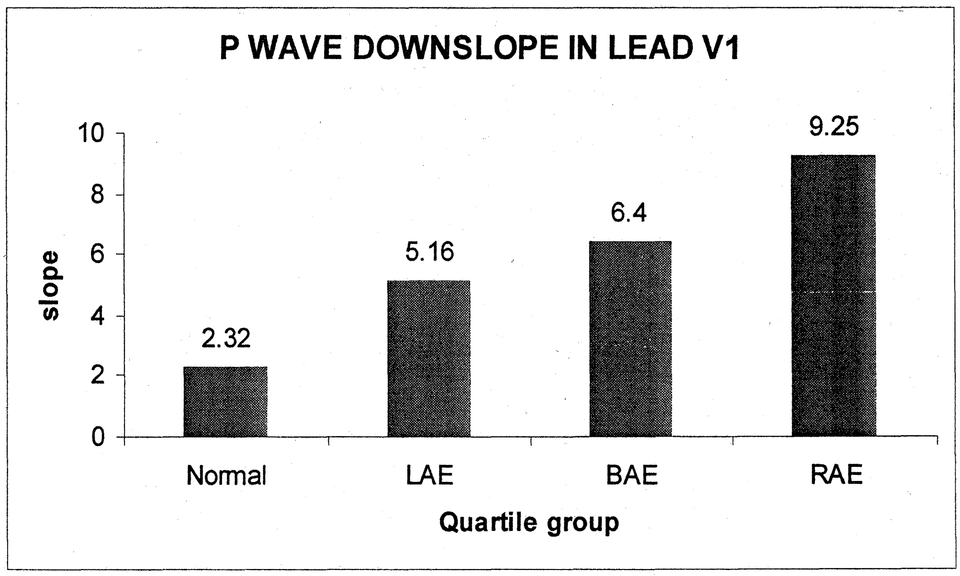
PARAMETER	Group	N	Mean	Minimum	Maximum	Std. Deviation	Std. Error
P wave downslope in lead V1	LAE	20	5.15	2.50	9.50	1.67	.37
	BAE	20	6.36	4.50	8.30	.93	.21
	RAE	20	9.25	4.70	17.50	2.96	.66
	normal	20	2.32	1.80	3.12	.37	.08
	Total	80	5.77	1.80	17.50	3.04	.34

Note: the slope is expressed as an absolute integer, ignoring the direction of the vector

LAE – left atrial enlargement, RAE – right atrial enlargement, BAE – biatrial enlargement

Among the four groups, patients with isolated right atrial enlargement had the highest values for both the P wave upslope in limb leads and the downslope in lead V1, followed by patients with bi-atrial enlargement, with isolated left atrial enlargement and the lowest in patients with normal atria


P wave upslope
slope
8
7
6
5
4
3
2
1
0
2.85
3.45
5.66
7.16
Normal
LAE
BAE
RAE
Quartile groups


P WAVE DOWNSLOPE IN LEAD V1
slope
10
8
6
4
2
0
2.32
5.16
6.4
9.25
Normal
LAE
BAE
RAE
Quartile group

Sensitivity and specificity of ECG parameters in Left Atrial Enlargement

TABLE 14

PARAMETER	Sensitivity	Specificity	Positive Predictive value	Negative Predictive Value
P terminal amplitude inV1 >0.01 mV	70	90	63.6	92.3
P termimal force in V1≥ 0.004 millivolt.second	100	90	90.9	100
P mitrale with interpeak duration≥ 0.04 sec	52.5	100	100	67.8
P duration in II ≥ 0.12sec	97.5	85	86.7	97
P/ PR segment ≥ 1.6	92.5	92.5	92.5	92.5
P wave upslope (>3.1mV/sec)	77.5	35	54.4	60.9
P wave downslope V1 (>2.73mV/sec)	97.5	47.5	65	95

A lower cutoff value of upslope & downslope was used for assessing the sensitivity and specificity for left atrial enlargement, which inturn was the median value of upslope and downslope after excluding patients with co-existing or isolated right atrial enlargement.

Sensitivity and specificity of Slopes in left atrial enlargement after excluding the patients with right atrial enlargement

Table 15

PARAMETER	Sensitivity	Specificity	Positive Predictive value	Negative Predictive Value
P wave upslope (>3.1mV/sec)	55	70	64.7	60.9
P wave slope V1 (>2.73mV/sec)	95	95	95	95

The downslope of P wave in V1 had better sensitivity and specificity for left atrial enlargement in patients without co-existing right atrial enlargement whereas P wave upslope in limb leads had low sensitivity, specificity, positive and negative predictive values for left atrial enlargement.

Sensitivity and specificity of ECG parameters in Right Atrial Enlargement

Table 16

PARAMETER	Sensitivity	Specificity	Positive Predictive value	Negative Predictive Value
P wave amplitude lead II ≥ 0.25mV	80	95	94	82.6
QRSaxis≥90 degrees	40	100	100	62.5
P initial force in V1 ≥ 0.006mV.sec	87.5	100	87.5	100
Right ventricular hypertrophy in ECG	55	100	100	69
P wave upslope (>4.3 mV/sec)	90	90	90	90
P wave downslope in V1 (>5.6mV/sec)	85	90	89.5	85.7
QRS axis ≥ 75degrees	65	97.5	96.3	73.6

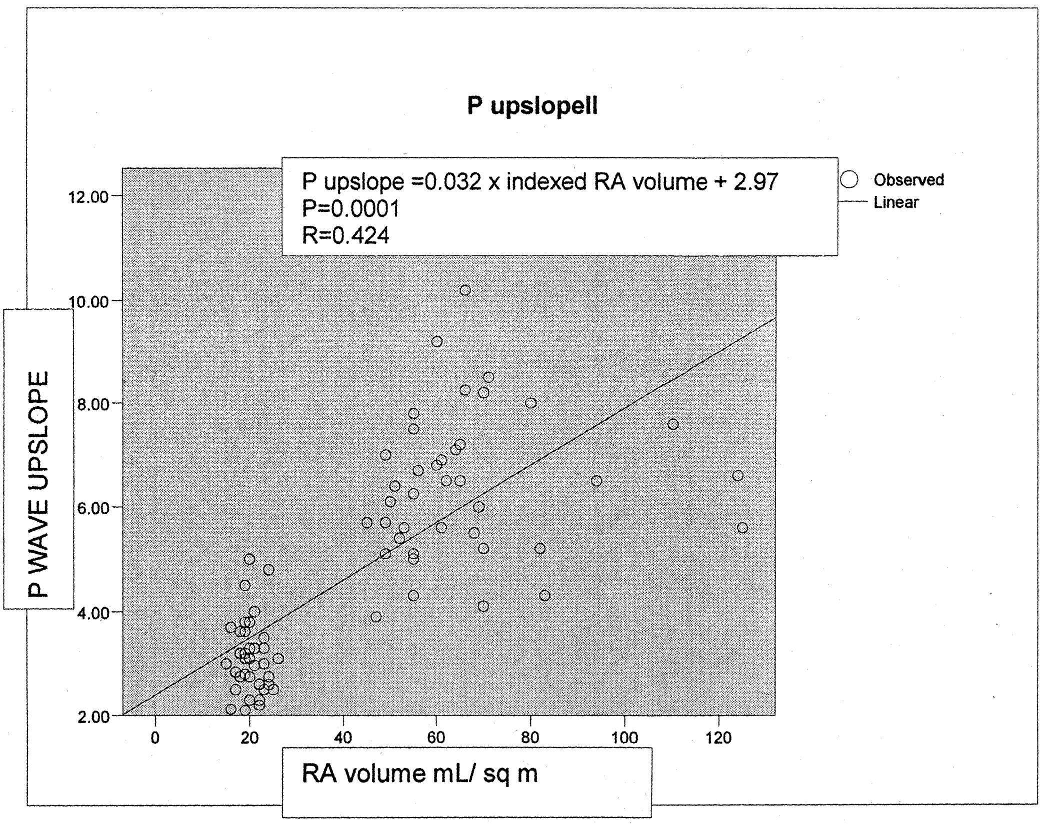
The sensitivity, specificity, positive predictive value and negative predictive value of the upslope of P wave (median value of 4.3 was tested) in lead II and the downslope of P wave in lead V1 (median value of 5.6 was tested) were high for the diagnosis of right atrial abnormality.

Regression model for P wave upslope and predictors

Linear regression model with P wave upslope as a dependent factor and continuous variable, against the following characteristics given in the following table as the independent variable was assessed. Right atrial volume was found to be the most important predictor of P wave upslope (β coefficient 0.424, P value < 0.0001). Presence of right ventricular hypertrophy was also a significant predictor of P wave upslope. (β coefficient 0.381). The left atrial volume was not found to be a significant predictor of P wave upslope

Table 17 **Regression model for P wave upslope against variables**

Model	Parameters	Standardized Coefficients	T value	P value
	LA volume ml/m2	-.027	-.259	0.797
	RA volume ml/m2	.424	4.266	0.0001
	Body surface area	-.023	-.303	0.763
	P wave axis	.114	.915	0.363
	Right ventricular hypertrophy	.381	3.556	0.001
	Left ventricular hypertrophy	.154	1.901	0.061



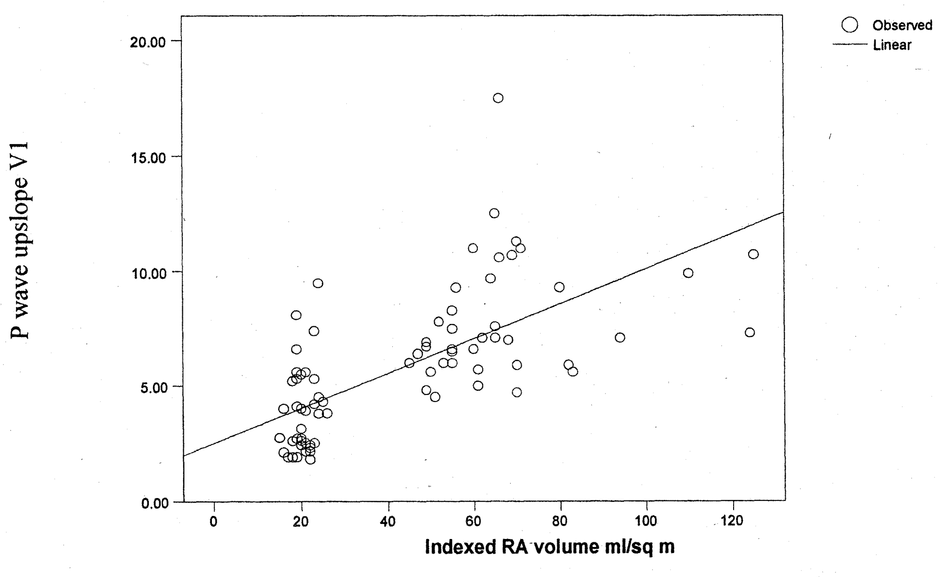
Relation of P wave upslope with indexed right atrial volume.

Regression Model of P wave Downslope in Lead V1 and predictors.

Table 18

Model	Parameters	Standardized Coefficients	T value	P value
	LA volume ml/m2	.016	1.381	.172
	RA volume ml/m2	.408	3.482	.0001
	Body surface area	-.044	-.485	.629
	P wave axis	-.078	-.528	.599
	Right ventricular hypertrophy	.460	3.145	.001
	Left ventricular hypertrophy	.134	1.404	.165

Right atrial volume (β coefficient 0.408, P value < 0.0001) and the presence of right ventricular hypertrophy were the significant predictors of P wave downslope(β coefficient 0460.). The left atrial volume was found to be a weak predictor of P wave downslope in V1.



P slope V1 =0.047 x indexed RA volume + 4.332
P=0.001 R=0.408

DISCUSSION

Einthoven is credited with being the first to recognize that P wave abnormalities on the surface electrocardiogram reflected altered atrial depolarization. Subsequently, numerous criteria for the ECG recognition of right and left atrial enlargements have been proposed.

Regarding right atrial enlargement, the most emphasized of the criteria is tall peaked P wave in lead II, III and aVF with a rightward deviation of the P wave axis in the frontal plane. But this finding was weakly validated in early autopsy studies. (18). In the study by Kaplan et al in 52 patients with sinus rhythm, P wave height > 2.5 mm in lead V1 had only 6% sensitivity, but had 100% specificity in the diagnosis of right atrial abnormality (6). The current study had a sensitivity and specificity of 80% and 95% for the same, perhaps due to the lesser numbers and more severe underlying disease. Previous studies have shown that the electrocardiographic markers for right atrial enlargement have a low sensitivity but higher specificity. In the study by Kaplan et al, the P initial force in lead V1 had the maximum sensitivity (50%) but the least specificity (76%). Right ventricular hypertrophy or mean frontal QRS axis had lower sensitivity than other parameters for detecting right atrial enlargement, reflecting the influence of coexisting left sided cardiac lesions or non pulmonary arterial hypertensive diseases resulting in right atrial enlargement. A lesser extent of shift of QRS axis to the right also did not increase the sensitivity appreciably. Greater right atrial mass results in greater electrical force early during the atrial activation with augmentation of the initial P wave deflection in V1.

There is strong evidence that left atrial enlargement, as determined by echocardiography, is a strong predictor of cardiovascular outcomes (16). Initial studies in smaller number of patients without echocardiographic data have mentioned modest to high sensitivity and specificity of electrocardiographic criteria for left atrial enlargement. In a study of 87 patients with left sided valvular heart disease, Morris et al reported 92% true positivity for increased terminal P force in V1, whereas P/PR segment ratio had only 52% true positivity in the diagnosis of left atrial enlargement (17). Subsequent ECG – echocardiographic correlation studies showed that the various parameters had lower sensitivity, but higher specificity. In the study by Alpert et al, the P- terminal force in V1 had the maximum sensitivity of 83% whereas the other criteria tended to have sensitivity between 30 – 60% (4, 5). In the current analysis, except for the presence of P mitrale, other parameters had good sensitivity and specificity for left atrial enlargement, which could be due to the severe degree of atrial enlargement.

P WAVE SLOPE:

In the current study, the patients with normal atrial volume had the lowest values for P wave upslope as well as downslope in V1, followed by those with isolated left atrial enlargement, those with bi-atrial enlargement and then patients with isolated right atrial enlargement who had the maximum values for both the slopes. The downslope of P wave in lead V1 was found to be significantly different in patients with left atrial enlargement and in patients with right atrial enlargement, with the latter group having a steeper downslope than the former. The sensitivity and specificity of P wave upslope (the part of P wave which represents depolarization of right atrium) was 90% each for right atrial enlargement. As expected, P wave upslope in limb leads had poor sensitivity and specificity for right atrial enlargement, which was confirmed after excluding patients with co-existing right atrial enlargement. The downslope of P wave in lead V1 had better sensitivity and specificity for right atrial enlargement (85& 90% respectively). For left atrial enlargement, the sensitivity of the same parameter was good (97.5%), but had low specificity. After excluding patients with co-existing right atrial enlargement, the specificity and positive predictive value improved to 95% each. Regression analysis showed that only right atrial volume was a good predictor for both P wave upslope in standard limb leads and also P wave downslope in lead V1, whereas left atrial volume correlated poorly with both variables. It is logical that right atrial enlargement has a steep upslope in lead II and a steep downslope in V1, because there is an increase in amplitude without much increase in the total duration of atrial activation. In lead II, a steep upslope indicates that the completion of the increased right atrial mass occurs fairly rapidly and subsequently, the rest of left atrium which is normal, gets activated normally. The steep downslope in lead V1 is contributed by the same phenomenon in patients with right atrial enlargement. The less steep slopes in patients with left atrial enlargement was further made more steep with co-existence of right atrial enlargement. This study did not attempt to analyse the differential effect of pressure versus volume overload of the right atrium, but the patient with non hypertensive tricuspid valve regurgitation (secondary to right ventricular myocardial infarction) had the lowest value for P wave upslope of 4.7.

Patients with isolated left atrial enlargement had significantly more upslope in lead II than patients with normal atria (5.15 vs 2.32, $p < 0.0001$). This could be explained by the onset of left atrial activation before completion of right atrial activation. It had only modest sensitivity and specificity for isolated left atrial enlargement. The patients with isolated left atrial enlargement had steeper downslopes in V1 when compared to normal atria, which could be due to the higher increment in the amplitude of P wave than the increment in the duration of left atrial activation.

Moreover, the mean indexed left atrial volume in these patients was very high. The patients with lesser degrees of left atrial enlargement are likely to have less steep downslope in V1.

CONCLUSION

- P wave upslope in standard limb lead along the axis of the P wave and the downslope of P wave in lead V1 correlate with right atrial enlargement.

- P wave downslope in lead V1 correlate with left atrial enlargement only if co-existing right atrial enlargement is ruled out.

- P wave downslope differs significantly in patients with left atrial enlargement from patients with right atrial enlargement, with the latter patients having a significantly steeper downslope in V1

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ANGIOGRAPHIC ANALYSIS

OF

CORONARY COLLATERALS

IN PATIENTS WITH

CHRONIC TOTAL OCCLUSION

INTRODUCTION

Blood flow to the myocardium, the viability and function of the myocardial cell and thus the clinical presentation and symptoms of a patient with coronary artery disease are influenced by the rate of progression of the coronary obstructive lesions and also by the rate at which anastomotic vessels develop into functioning collateral channels. These anastomotic channels cannot be visualized in patients with normal or mild coronary artery disease generally as carry only minimal flow and have a small caliber (<0.2mm) which is beyond the spatial resolution of coronary imaging systems. Once significant stenosis (generally to the severity of 90%) develops, the perfusion pressure distal to the obstruction falls and a pressure gradient is created across the proximal part of the anastomotic channels in the feeder vessel and the distal part which connects beyond the site of occlusion. This dilates the pre-existing anastomotic channels which become visible angiographically as the collaterals.

The presence of collaterals at the time of acute occlusion of a coronary artery may slow down cell death of the myocardial tissue and may limit necrosis to the least perfused layers (3). Collateralization hardly improves during the initial minutes of acute coronary occlusion, but repeated occlusions may stimulate recruitment of collaterals and condition myocardium for better tolerance of ischemia.

DETERMINANTS AND DEVELOPMENT OF CORONARY COLLATERAL CIRCULATION

Recurrent and severe myocardial ischemia may stimulate the development of coronary collateral circulation. In a study, patients with chronic angina pectoris before an acute MI had smaller infarcts compared with patients with angina pectoris of short duration before an acute MI. They had, however, a higher 1-year mortality rate and a higher risk of reinfarction, probably reflecting more extensive coronary artery disease in these patients, with a higher risk of death (4). The mechanisms of collateral development include vasculogenesis, angiogenesis, and arteriogenesis. (5) Vasculogenesis refers to the initial events in vascular growth, in which endothelial cell precursors (angioblasts) migrate to discrete locations, differentiate in situ, and assemble into solid endothelial cords, later forming a plexus with endocardial tubes. Angiogenesis is the subsequent growth, expansion, and remodeling of these primitive vessels into a complex, mature vascular network. Myocardial ischemia, through induction of angiogenic growth factors (TGF–α, VEGF and basic FGF) can enhance this process. But collaterals can develop in non ischemic tissue as well by a process of pressure gradient between the vessels and subsequent shear stress due to the increased flow across the channels, which inturn enhance arteriogenesis. (Transformation of preexisting arterioles into functional collateral arteries, by addition of a thick muscular coat, with acquisition of viscoelastic and vasomotor properties) (5). Shear stress induces release of factors like TGF-β, GM-CSF and basic FGF which promote arteriogenesis. Impaired formation of collaterals have been described in patients with diabetes, hyperlipidemia and in elderly which may be secondary to impaired expression of various growth factors.

Angiographic studies revealed conflicting reports regarding the influence of diabetes mellitus in the development of collaterals. There were studies which reported impaired development as well as ones which had the opposite conclusion (9, 10). But analysis of collaterals using invasive Doppler derived indices showed that there were no overall differences in the coronary collateral flow between diabetic and non-diabetic patients (11, 12). Hypercholesterolemia was found to predict better angiographic collateral grade (13)

In chronic total occlusions, the collaterals are capable of complete preservation of myocardial function or of providing a minimum perfusion for the hibernating myocardium (14, 16). Regional left ventricular contraction is better in segments supplied by adequate collateral circulation than in segments supplied by inadequate collaterals (15). Preservation of ventricular function is dependent upon the presence of a collateral circulation which is already developed simply being 'recruited' at the time of infarct. Studies have highlighted the role of pre-infarct angina on better early outcomes after and acute coronary event (17, 18). Although collaterals have a role in reducing the infarct size and preserving LV function during an acute event, or in reducing the immediate or 6 month MACE after elective angioplasty, this has not been translated to improvement in long term mortality (19).

CORONARY COLLATERAL ANATOMY (2, 6)

Coronary collaterals are broadly divided in to INTERCORONARY anastomoses which connect branches of the three different major coronary arteries and HOMOCORONARY anastomoses which arise proximal to the occluded segment of the artery and connect distal to the occlusion. These, in turn could be either BRIDGING collaterals (which grow out of vaso vasora) or could arise from the proximal part of the vessel or its named branches and link with the distal part of the vessel or its branches.

INTERCORONARY ANASTOMOSES BETWEEN LEFT ANTERIOR DESCENDING ARTERY (LAD) AND RIGHT CORONARY ARTERY (RCA):

- via conus branch (described by Vieussens)
- via right ventricular branch – these run across the anterior wall of the right ventricle and meet similar LAD branches at various levels along the course of the vessel
- via Acute marginal branch to branches of LAD
- Posterior descending branch of RCA to anterior descending or vice versa through septal collaterals
- Termino-terminal connections between posterior descending and posterior ascending (part of LAD after it curves around and ascends into the posterior interventricular groove)

INTERCORONARY ANASTOMOSES BETWEEN LEFT ANTERIOR DESCENDING ARTERY (LAD) AND LEFT CIRCUMFLEX ARTERY (LCX):

- between the obtuse marginal branch of LCX (or Ramus intermedius, if present) and the diagonal branch of LAD
- between the OM branch and apical segment of LAD
- between the terminal portion of the LAD and the posterior descending branch (PDA) from the dominant LCX

INTERCORONARY ANASTOMOSES BETWEEN RCA AND LCX:

- Between the terminal portion of the RCA and the terminal portion of the LCX at the postero-inferior part of the Atrio-ventricular groove

- Between the proximal atrial branches of the RCA and proximal atrial branches of the LCX (sinus node artery included) – rarely seen
- Between proximal atrial branches of the RCA and other atrial branches of the LCX (Kugel's artery included) – seen in upto 6% of patients (7)
- Between the atrial circumflex and the terminal portion of the RCA, seen especially when the distal circumflex is diminutive
- Between the posterolateral branches of the LCX and the left ventricular branches of the RCA.

HOMOCORONARY COLLATERALS

Apart from the bridging collaterals and other unnamed ones, the usual forms of collaterals which are seen between named segments or branches include:

RCA: between conus and RV branches, conus and acute marginal branch, between RV branches, between RV and acute marginal, between PDA and posterior LV branches, and as part of Kugel's anastomoses – between proximal and distal RCA. (Kugel's artery or *arteria anastomotica auricularis magna* is a small vessel which originates either from the proximal RCA or LCX, then passes down the anterior margin of the atrial septum to anastomose with the AV node artery)

LAD: between the diagonal branches, between the septal branches, between diagonal and apical branches.

LCX: between OM and posterolateral branches to LV, between left PDA and left posterolateral branches, between proximal and distal atrial branches.

OBJECTIVES OF THE STUDY

- to analyze the patterns of collaterals in various sites of chronic total occlusion
- to assess the prevalence of various coronary risk factors in patients with adequate and inadequate coronary collaterals
- to study the association of symptomatic status and left ventricular function in patients with good and inadequate collaterals.

MATERIALS AND METHODS

The patients who had chronic total coronary occlusion (CTO) among the coronary angiograms performed in this Institute from 1st January 2006 to 31st December 2006 were studied retrospectively. Chronic total occlusion is defined as a total coronary occlusion greater than three months from the coronary event (1). The clinical parameters of the patients studied included age, gender, family history of premature coronary artery disease, presence of diabetes mellitus, systemic arterial hypertension, smoking status, whether the female patients had attained menopause and serum fasting lipid levels. Total cholesterol, HDL cholesterol, triglycerides were assayed and serum LDL cholesterol levels and serum total cholesterol: HDL cholesterol ratios were derived

LDL cholesterol = Total cholesterol – [triglycerides/5 + HDL cholesterol]

Smoking status was categorized into never smoker, ex-smoker (if the patient discontinued smoking more than a year ago) and current smoker.

Data regarding coronary artery disease included presence of angina, presence of dyspnea, the duration of such symptoms and their stratification according to the NYHA functional capacity at the time of presentation. History of left ventricular failure or congestive heart failure was noted. Regarding the acute coronary event, the particulars considered were the type of event (ST segment elevation myocardial infarction –STEMI or non-ST segment elevation acute coronary syndromes – NSTEMI and unstable angina), the number of events, time of the last event, whether fibrinolytic therapy was administered during STEMI and the site of myocardial infarction. The site of myocardial infarction was broadly divided into 1- Anterior wall myocardial infarction (AWMI, which included anteroseptal infarcts, anterolateral infarcts), 2- Inferior wall myocardial infarction (IWMI, which included inferior wall infarcts, inferior wall with posterior wall, lateral wall and right ventricular infarcts), 3 -Lateral wall myocardial infarction alone and 4 –combined AWMI + IWMI. The time to coronary angiography from the last coronary event was noted in months.

The angiographic parameters analyzed included the dominance of coronary circulation, site of the total occlusion, presence of other significant coronary lesion (lesions > 70% diameter stenosis in the major coronary arteries or their major branches, or >50% diameter stenosis in the left main coronary artery), both of which were categorized by the segment of the vessel involved as given below: (2)

Segments of left anterior descending artery (LAD)

Proximal – from point of origin from left main coronary artery till the major septal

Mid – from major septal origin till the bend (about 90 degree angle the artery makes as it turns around the pulmonary artery, best appreciated in the shallow right anterior oblique view. Usually the second major diagonal arises at this point)

Distal – from this point till the termination

Major diagonal – if the lesion or total occlusion is in a large diagonal branch.

Segments of the left circumflex artery (LCX)

Proximal – from the take off of the LCX from the left main coronary artery till the origin of the major Obtuse Marginal artery (OM)

Distal – from this point till termination of the circumflex, or till crux if it is the dominant vessel

Major OM – the largest among the obtuse marginal branches

Ramus intermedius if present

Left posterior descending artery, if LCX is the dominant vessel

Postero-lateral branch from LCX

Segments of the right coronary artery

Proximal – from the ostium to the main right ventricular branch take off

Mid – from the right ventricular branch to acute margin

Distal – from the acute margin to the origin of the posterior descending artery

Posterior descending artery

STUDY OF COLLATERALS:

The coronary collaterals were broadly divided into Homocoronary (bridging & others) and Intercoronary collaterals. The prevalence of the named intercoronary collaterals was noted against the site of occlusion. The homocoronary and intercoronary collaterals were graded by Rentrop grading (8).

0 – no collaterals present

1- Barely detectable collateral flow. Contrast medium passes through collateral channels, but fails to opacify the epicardial vessel at any time

2- Partial collateral flow. Contrast medium enters, but fails to opacify the target epicardial vessel completely

3 – Complete perfusion. Contrast material enters and completely opacifies the target epicardial vessel.

STATISTICS

The results were expressed as mean ± standard deviation for quantitative data and frequency and percentage for qualitative data. Significance between the means of the continuous variables between the groups was assessed using independent T test and those of the qualitative data, using Chi-square test.

RESULTS

DEMOGRAPHIC AND CLINICAL DATA OF PATIENTS

Parameter	N	Frequency	percent
Male	158	141	89.2
Hypertension	158	76	48.1
Diabetes mellitus	158	87	55.1
Family history of CAD	158	35	22.2
Post menopause	17	15	88.2
Angina	158	155	98.1
Dyspnea	158	64	40.5
History of LVF	158	14	8.9
STEMI	158	101	63.9
Fibrinolytic therapy	101	37	23.4
AWMI	158	45	28.5
IWMI	158	67	42.4
LWMI	158	3	1.9
AW+IWMI	158	18	11.4
Antiplatelets	158	158	100.0
Beta receptor antagonists	158	149	94.3
Calcium channel blockers	158	32	20.3
Nitrates	158	147	93.0
Statins	158	158	100
Insulin	71	17	23.9
Oral hypoglycemic agents	71	62	86.1
ACE inhibitors / Angiotensin receptor blockers	158	81	51.3
Regional wall motion abnormality	158	127	80.4
Akinesia	158	45	28.4
LV aneurysmal segment	158	9	5.7
History of angina pre-acute coronary event	158	18	11.4
Single vessel disease	158	51	32.3
Double vessel disease	158	48	30.4
Triple vessel disease	158	59	37.3

TOBACCO SMOKING: Ex smoker 72 (45.6%), current smoker 38 (24.1%), never smoker 48 (30.4%)

(Ex smoker – a person who quit smoking one year prior)

Descriptive Statistics

PARAMETER	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	158	37	77	53.9	8.5
Total cholesterol (mg/dl)	158	89	340	179.7	40.3
HDL cholesterol (mg/dl)	158	18	64	35.4	7.4
Triglycerides (mg/dl)	158	54	317	149.6	49.2
HDL (mg/dl)	158	34	289	114.4	37.9
Total cholesterol : HDL cholesterol ratio	158	2.2	14.2	5.3	1.7
LV ejection fraction (%)	158	24	71	54.9	10.3
Time to CAG from last acute event (months)	158	3	240	17.3	30.9

37.9 % of patients were $\leq$ 50 years of age (table 1, appendix)

Majority of the patients had poorly controlled serum lipid levels (see figures 1-5, appendix)

Majority of the patients had a single acute coronary event (67.7%) (Table 2, appendix)

PATTERN OF CORONARY ARTERY DISEASE IN PATIENTS (N=158)

Coronary lesion	Frequency	percentage
LAD disease only	23	14.6
LCX disease only	7	4.4
RCAdisease only	21	13.3
LAD + LCX disease	14	8.9
LCX + RCA disease	14	8.9
LAD + RCA disease	20	12.7
Three vessel disease	59	37.2

(For calculation, LMCA disease was taken to be equivalent to LAD + LCX disease. Significant LMCA disease was present in 9 patients)

DISTRIBUTION OF THE TOTALLY OCCLUDED ARTERY

LAD: 67 (42.4%)

LCX: 29 (18.4%)

RCA: 72 (45.6%)

10 patients had total occlusion in more than one coronary artery.

DISTRIBUTION OF THE VARIOUS TYPES OF INTERCORONARY COLLATERALS BASED ON THE SITE OF CTO: (in next page)

1. CTO IN LEFT ANTERIOR DESCENDING ARTERY:

CTO site	N	Collateral name	Frequency	%
PROXIMAL LAD	31	Conus-LAD	22	70.1
		RV branches - LAD	17	54.8
		RCA –PDA-septal - LAD	20	64.5
		RPDA-LAD (end-end)	6	19.4
		LCX-OM-Diagonal- LAD	6	19.4
		LCX -OM- apical LAD	3	9.7
		RI - LAD	0	0
		LPDA to distal LAD	0	0
MID LAD	31	Conus-LAD	16	51.6
		RV branches - LAD	14	45.2
		RCA –PDA-septal - LAD	24	77.4
		RPDA-LAD (end-end)	8	25.4
		LCX-OM-Diagonal- LAD	11	35.5
		LCX -OM- apical LAD	3	9.7
		RI - LAD	0	0
		LPDA to distal LAD	0	0
DISTAL LAD	2	RV branches - LAD	1	50
		RCA –PDA-septal - LAD	2	100
		RPDA-LAD (end-end)	1	50
		Conus - LAD	0	0
		LCX-OM-Diagonal- LAD	1	50
		LCX -OM- apical LAD	1	50
		RI - LAD	0	0
		LPDA to distal LAD	0	0
Major Diagonal	3	LCX-OM-Diagonal	2	66
		RI - diagonal	0	0

2. CTO IN LEFT CIRCUMFLEX ARTERY

CTO site	N	Collateral name	Frequency	%
Proximal LCX	10	Terminal RCA- LCX	3	30
		RCA- SA Node branch - LCX	0	0
		RCA – proximal atrial – LCX (Kugels)	1	10
		Distal RCA – Atrial Cx - LCX	5	50
		RCA- PLB - LCX	1	10
		LAD- Diagonal – OM - LCX	5	50
		Distal LAD-OM - LCX	0	0
		LAD – LPDA - LCX	0	0
Distal LCX	11	Terminal RCA- LCX	4	36.4
		Distal RCA – Atrial Cx - LCX	6	54.5
		RCA- PLB - LCX	1	9.1
		LAD- Diagonal – OM - LCX	3	27.3
		Distal LAD-OM - LCX	0	0
		LAD – LPDA - LCX	0	0
Major OM	8	LAD – diagonal – Major OM	8	100

3. CTO SITE IN RIGHT CORONARY ARTERY

CTO site	N	Collateral name	Frequency	%
Proximal RCA	35	LAD- Septal – PDA- RCA	20	57.1
		LAD – RV branches – RCA	7	20
		LAD – PDA (end-end) – RCA	5	14.3
		LAD – Acute marginal – RCA	5	14.3
		LCX – SA Nodal branch – RCA	0	0
		LCX – proximal atrial – RCA (Kugels)	2	5.7
		LCX- atrial CX – distal RCA	25	71.4
		LCX- terminal RCA in AV groove	21	60
		LCX-OM/ PLB – RCA	8	22.9
Mid RCA	30	LAD- Septal – PDA- RCA	21	70
		LAD – PDA (end-end) – RCA	4	13.3
		LAD – Acute marginal – RCA	4	13.3
		LCX- atrial CX – distal RCA	23	76.7
		LCX- terminal RCA in AV groove	15	50
		LCX-OM/ PLB – RCA	8	26.7
Distal RCA	7	LAD- Septal – PDA- RCA	5	71.4
		LAD – PDA (end-end) – RCA	2	28.6
		LCX- atrial CX – distal RCA	4	57.2
		LCX- terminal RCA in AV groove	3	42.9
		LCX-OM/ PLB - RCA	1	14.3

DISTRIBUTION OF GRADING OF INTERCORONARY COLLATERALS:

Grade 0: 7 (4.4 %)

Grade 1: 35 (33.3 %)

Grade 2: 48 (30.4 %)

Grade 3: 68 (43%)

DISTRIBUTION OF HOMOCORONARY COLLATERALS:

None: 60 (38%)

Only bridging collaterals: 27 (17.1%)

Homocoronary collaterals other than bridging: 43 (27.2%)

Both types of homocoronary collaterals: 28 (17.7%)

DISTRIBUTION OF HOMOCORONARY COLLATERAL GRADE

Grade 0: 60(38 %)

Grade 1: 49 (31 %)

Grade 2: 35 (22.1 %)

Grade 3: 14 (8.9%)

All the patients had atleast some type and degree of collaterals. There was no patient without any collateral.

One way ANOVA to compare the differences of various parameters among patients with all grades of intercoronary collaterals.

VARIABLES	F VALUE	P VALUE
AGE	1.48	0.222
Gender	2.68	0.049
Smoking status (non smoker vs anytime smoker)	1.82	0.144
Hypertension	3.18	0.026
Diabetes	1.33	0.265
Total cholesterol	.98	0.404
HDL cholesterol	3.88	0.010
triglycerides	.82	0.480
LDL cholesterol	.63	0.593
Angina NYHA class	2.17	0.093
History of LVF	4.38	0.005
STEMI	3.84	0.011
No. of acute coronary events	4.26	0.006
Site of MI	4.32	0.006
ACEI / ARB	7.30	0.0001
LV ejection fraction	12.54	0.0001
Time to CAG from last ACS	1.89	0.133

The parameters which significantly differed among the groups (intercoronary collateral grade 0, 1, 2, 3) include gender, hypertension, serum levels of HDL cholesterol, history of LVF, history of ST elevation MI, site of myocardial infarction, and LV ejection fraction.

The collaterals were in turn graded into Good (Rentrop grade III) and Inadequate (grade 0, 1, 2) for the sake of comparison of various parameters. Of 158 patients, 68 patients had good and 90 patients had inadequate intercoronary collaterals. (This was on the basis that only Grade III collaterals result in a TIMI III flow distal to the occluded segment in the coronary angiogram).

Comparison of various characteristics in patients with 'Good' intercoronary collaterals and inadequate intercoronary collaterals

PARAMETERS	Good collaterals		Inadequate collaterals		T value	P value
	Mean	Standard deviation	Mean	Standard deviation		
AGE (years)	53.9	8.55	53.8	8.4	.098	.922
Serum Total cholesterol	174.4	39.4	183.7	40.7	-1.435	.153
Serum HDL cholesterol	34.7	5.9	35.9	8.4	-1.054	.294
Serum triglycerides	143.9	40.9	153.9	54.5	-1.277	.203
Serum LDL cholesterol	110.9	36.6	116.9	38.9	-.982	.328
Total cholesterol : HDL cholesterol	5.17	1.44	5.38	1.87	-.785	.434
LV ejection fraction	59.6	6.09	51.2	11.3	5.473	.0001
Time to coronary angiography (months)	23.6	42.92	12.5	15.93	2.257	.0001

PARAMETER	Good collaterals n=68	%	Inadequate collaterals n = 90	%	P value
Female gender	6	8.8	11	12.2	.495
Any time smoker	47	69	63	70	.905
Hypertension	36	52.9	46	51.1	.82
Diabetes	28	41.2	43	47.8	.409
Family history of CAD	16	23.5	19	21.1	0.717
History of LVF	2	3.2	12	13.3	.023
ACEI or ARB	28	41.2	53	58.9	.027
STEMI	35	51.5	66	73.3	0.005
Fibrinolytic therapy †	13/35	37.1	24/66	36.4	0.938
Significant angina on presentation (NYHA III or IV)	5	7.3	21	23.3	0.005
RWMA	52	76.4	75	83.3	0.282
AKINESIA OR ANEURYSM	5	7.3	38	42.2	0.0001
More than 1 Acute coronary event	12	17.7	39	43.3	0.001
Coexisting 'good' homocoronary collaterals *	8	11.8	6	6.7	0.264
Significant disease in the feeder vessel proximal to the site of collateral origin	16	23.5	35	38.9	0.041
HDL cholesterol > 40mg/dl	8	11.8	21	22.3	0.063
Total cholesterol : HDL cholesterol < 3.5	7	10.3	12	13.3	0.366
Angina prior to acute coronary event	8	11.8	10	11.1	0.546

† 35 patients in good collateral group and 66 in inadequate collateral group were eligible for fibrinolytic therapy at the time of acute coronary event

* The same grading system for good and inadequate intercoronary collaterals is used

LINEAR REGRESSION ANALYSIS with good collateral grade as the dependent variable showed that only LV ejection fraction was an independent predictor of good collaterals (Rentrop grade 3) with beta coefficient of (-0.383), p value <0.0001. Presence of hypertension, diabetes and high HDL cholesterol levels in serum were not independent predictors of the degree of collaterals.

DISCUSSION

DISTRIBUTION OF COLLATERALS

In total occlusion of LAD, the common types of collaterals seen were conus to LAD in 71% of patients, predominantly if the site of occlusion was either in proximal or mid segments of LAD. The other channels from RCA were via RV branches to LAD in 47.8% of patients and from PDA via septals in 69% of patients. The septal collaterals were prevalent irrespective of the site of CTO in LAD. The chief supply of collaterals from LCX was via OM which was found in 29.8% patients. Apart from these, some degree of non-bridging homocoronary collaterals occurred in 28.3% patients (table 3, Appendix)

In LCX total occlusions, the commonest source was from LAD via diagonal and OM which was seen in 55% of patients. Collaterals were also given off from RCA in a good number of patients. (Distal RCA to atrial circumflex in 38% and terminal RCA – LCX along atrio-ventricular groove in 24%). Non bridging types of homocoronary collaterals were found in 58% of patients which involved collaterals between proximal and distal OM branches mainly and to a lesser extent, between proximal and distal atrial branches.

In total occlusions involving RCA, LCX was found to give the maximum collateral supply with atrial circumflex or distal atrial branches of LCX supplying distal RCA in 72%, and terminal LCX- RCA along atrioventricular groove in 54.2% of patients. Septal collaterals from LAD to PDA occurred in 64% of patients. Homocoronary collaterals (excluding bridging collaterals) were found in 55% of patients. Anastomosis involving Kugel's artery was found in 1.9% of patients with either LCX or RCA occlusion.

COLLATERAL GRADING

No differences in age, gender, smoking status, hypertension, diabetes, and presence of wall motion abnormality were noted between patients with good collaterals and those with inadequate intercoronary collaterals. The mean fasting lipid profile was also similar. Patients with good collaterals had higher ejection fraction. History of LVF was more in patients with inadequate collaterals and they tended to be more symptomatic. Such patients suffered from multiple acute coronary events, had higher chance for transmural infarction with consequent akinesia or LV aneurysm reflecting on non-viability and tended to be sicker and were on treatment with ACE inhibitor or angiotensin receptor blocker. This is also reflected in the tendency for earlier coronary angiography in patients with inadequate collaterals after an acute coronary event when compared to the patients with adequate collaterals. The risk of a significant disease in the feeder vessel proximal to the take-off of collaterals was higher in patients with inadequate collateral grades. But the degree of adequacy of homocoronary collaterals was similar between the groups. The lesser development of collaterals in such patients could be secondary to the extensive atherosclerotic process as evidenced by significant disease in feeder vessel proximally.

CONCLUSIONS

- Patients with preserved LV function and less severe symptoms tended to have better degrees of collaterals in a chronic total occlusion
- There was no association between the degree of collaterals and the various coronary risk factors like smoking, diabetes, hypertension and low HDL.
- There was no relation between the degree of development of intercoronary collaterals and that of homocoronary collaterals
- Inadequate degrees of development of intercoronary collaterals were seen in patients with disease in the feeder vessel
- The usual patterns of intercoronary collateral circulation included septal collaterals between LAD and PDA, conus to LAD, between the terminal of RCA and LCX, between the distal atrial branches of RCA and atrial circumflex and between diagonals and obtuse marginals.

APPENDIX

Table 1: Age distribution of patients

Age groups (years)	Frequency	Percent
≤ 40	7	4.4
41-50	53	33.5
51-60	66	41.8
61-70	26	16.5
≥ 71	6	3.8
Total	158	100.0

Figure 1 Distribution of serum total cholesterol levels among patients

(expressed in mg/dl)

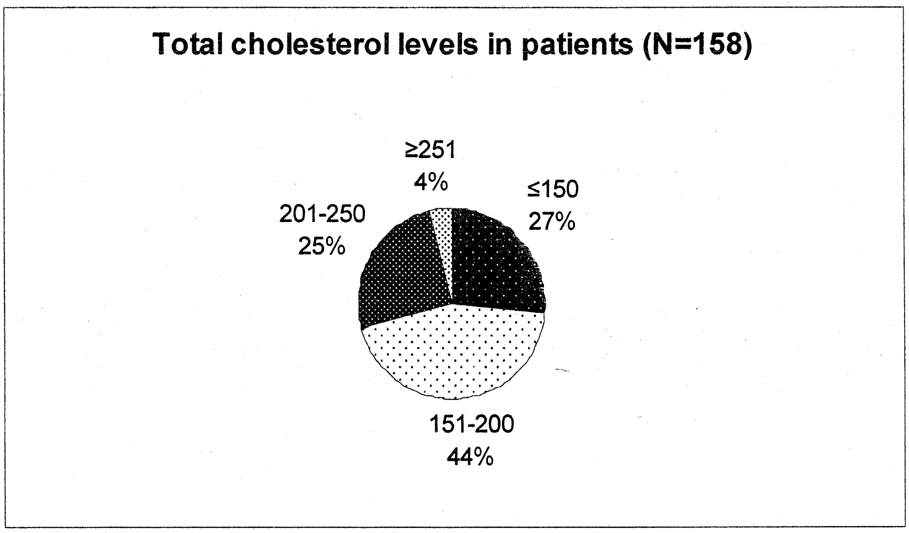


Figure 2: distribution of HDL cholesterol levels among patients (mg/dl)

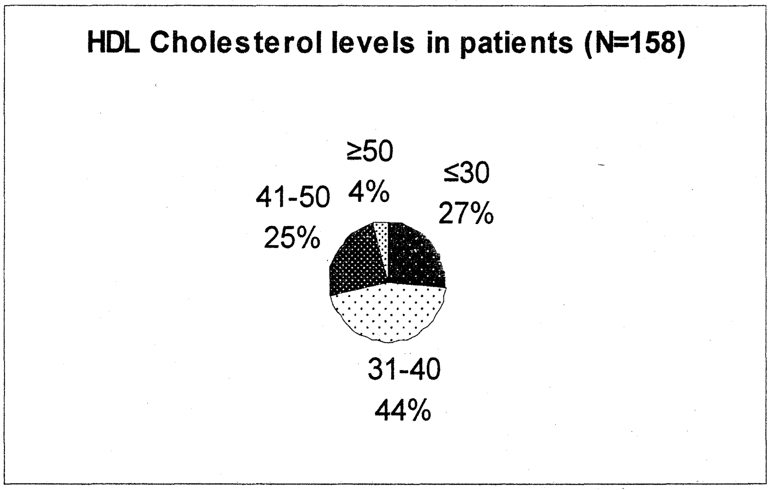


Figure 3: distribution of serum LDL cholesterol levels in patients (mg/dl)

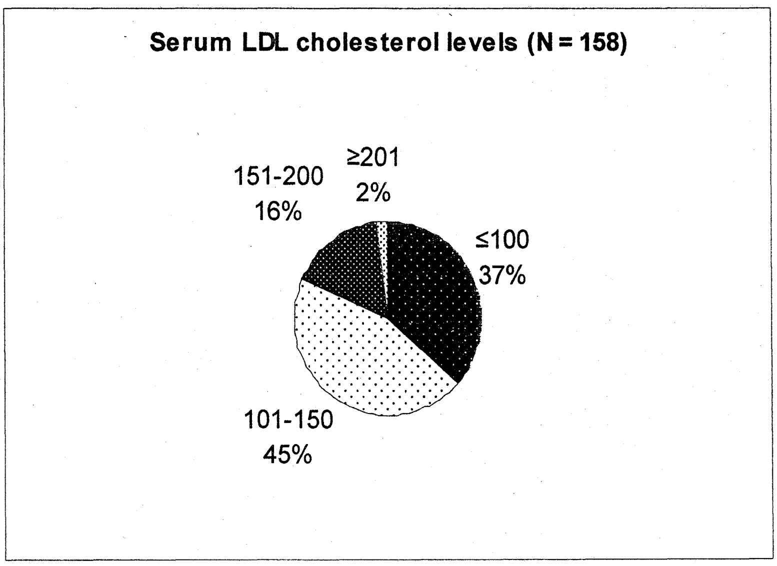


Figure 4: distribution of Serum triglyceride concentrations in patients (mg/dl)

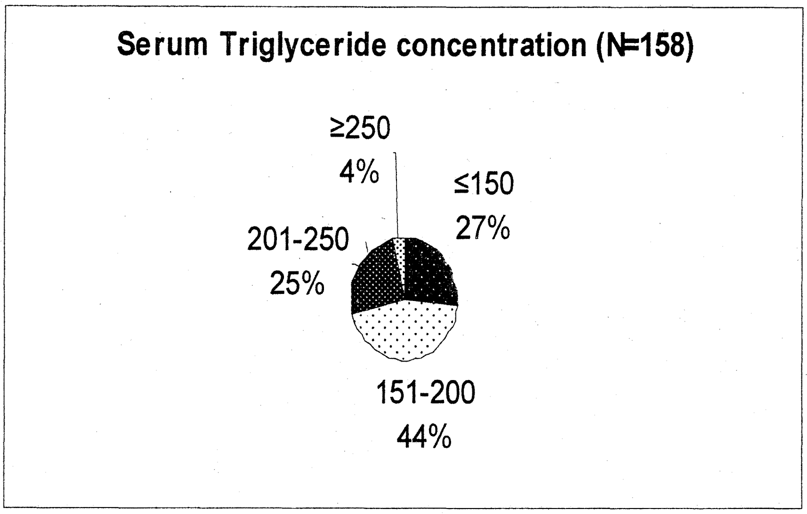


Figure 5: distribution of total cholesterol: HDL cholesterol ratio in patients

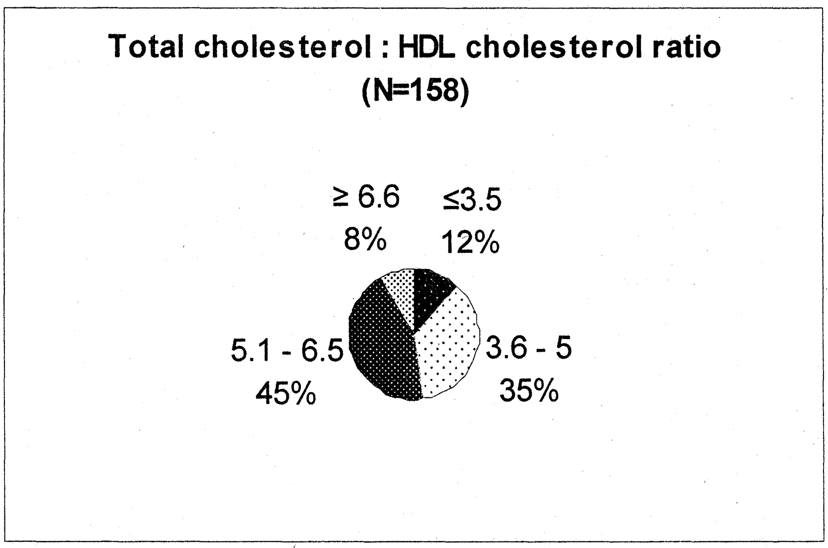


Table 2: Acute coronary events in patients

No. of events	Frequency	percent
1	107	67.7
2	40	25.3
≥3	11	7

Table 3
HOMOCORONARY COLLATERALS IN VARIOUS TOTAL OCCLUSIONS

VESSEL INVOLVED (CTO)	BRIDGING COLLATERALS ONLY		OTHERS (BRIDGING COLLATERALS ABSENT)		BOTH PRESENT	
	N	%	N	%	N	%
LAD N=67	15	22.4	10	14.9	9	13.4
LCX N=29	2	6.9	9	31.9	8	27.6
RCA N=72	11	15.3	24	33.3	16	22.2

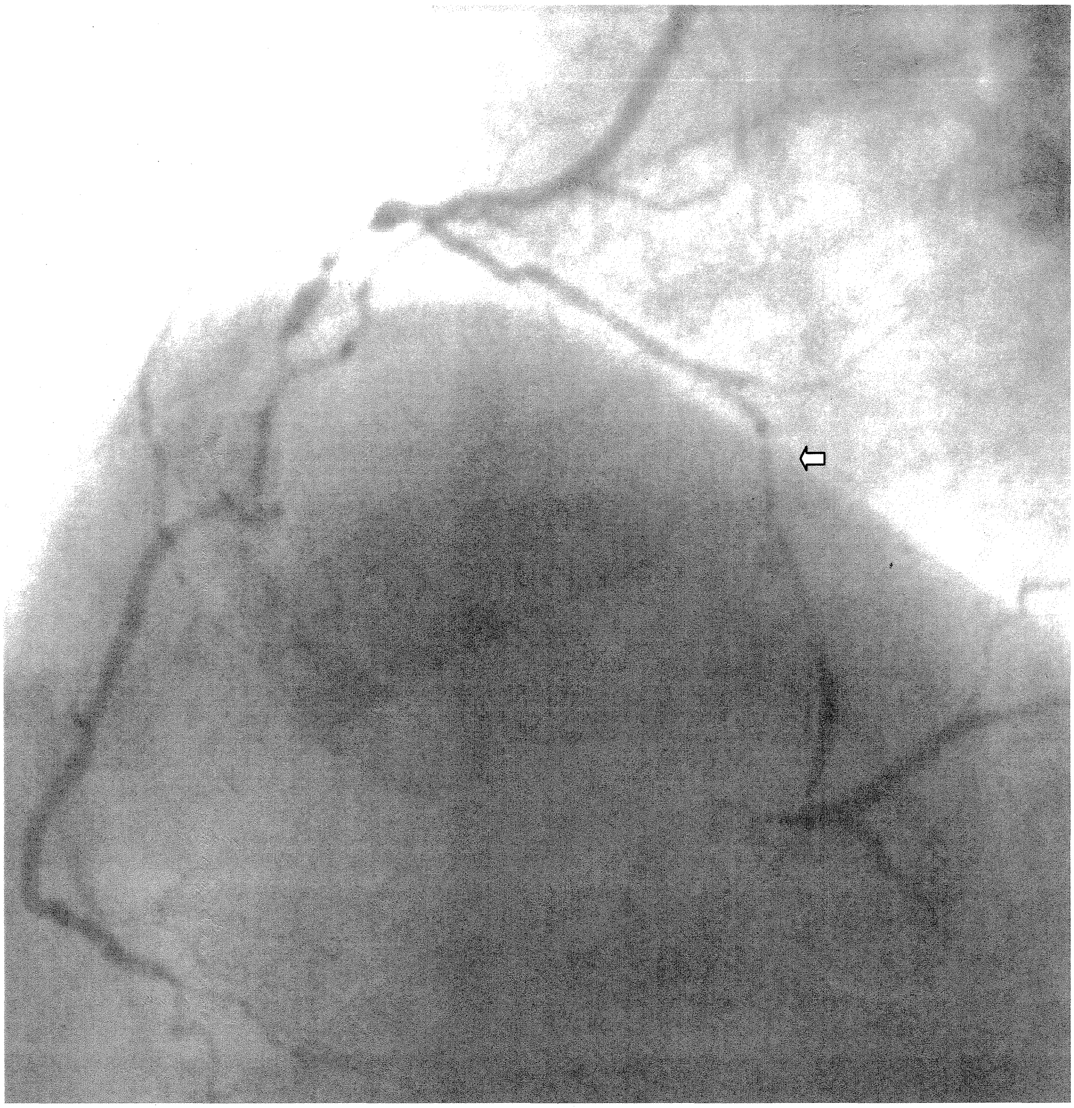
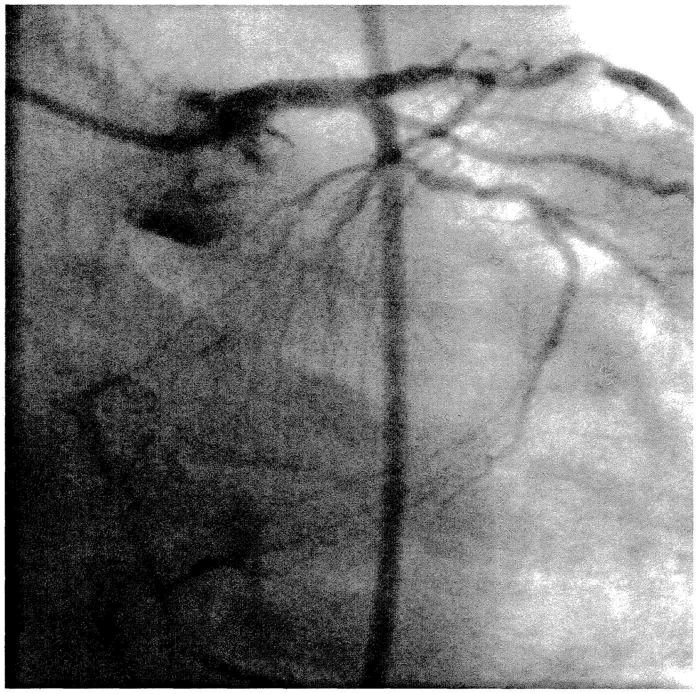
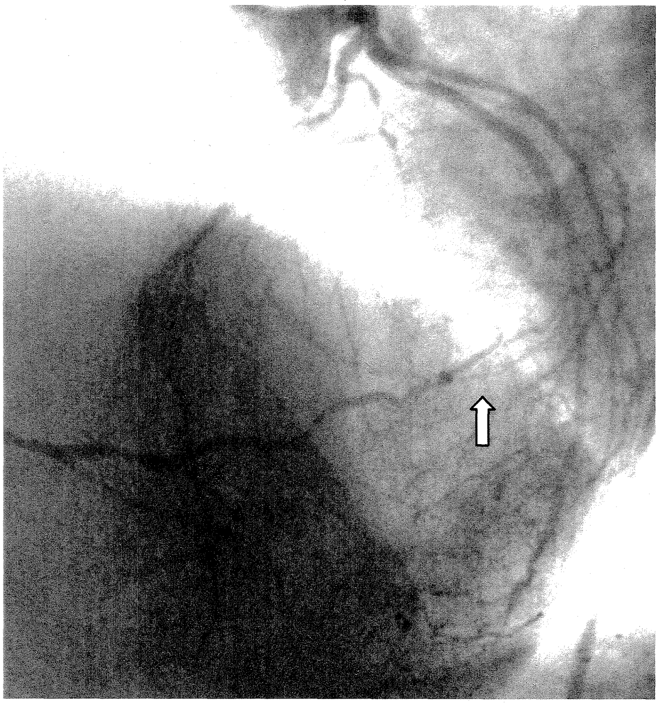


Figure 1 Proximal RCA- distal RCA via Kugel's artery



Figures 2 - a, b: LCX - RCA collaterals



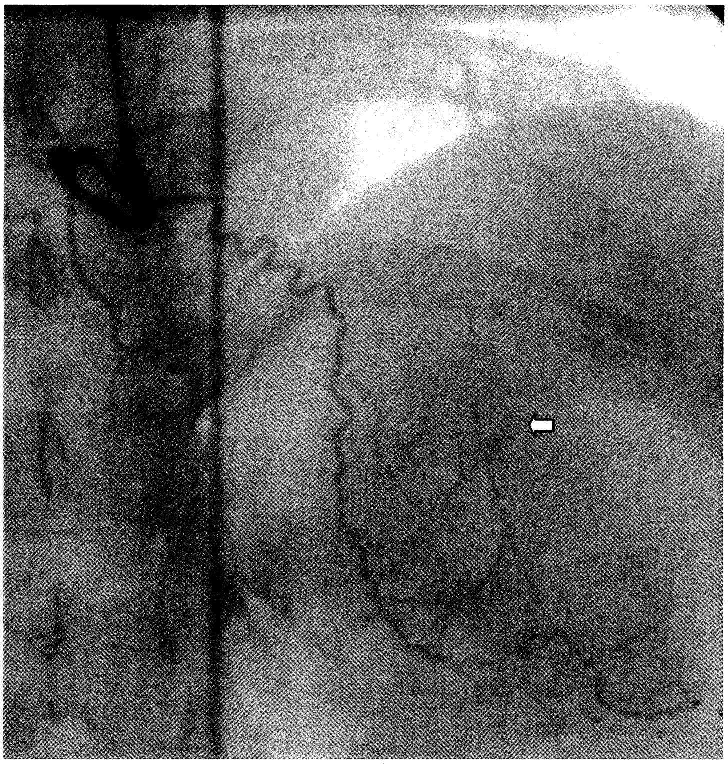


Figure 3 Conus- LAD in the same patient as 2b

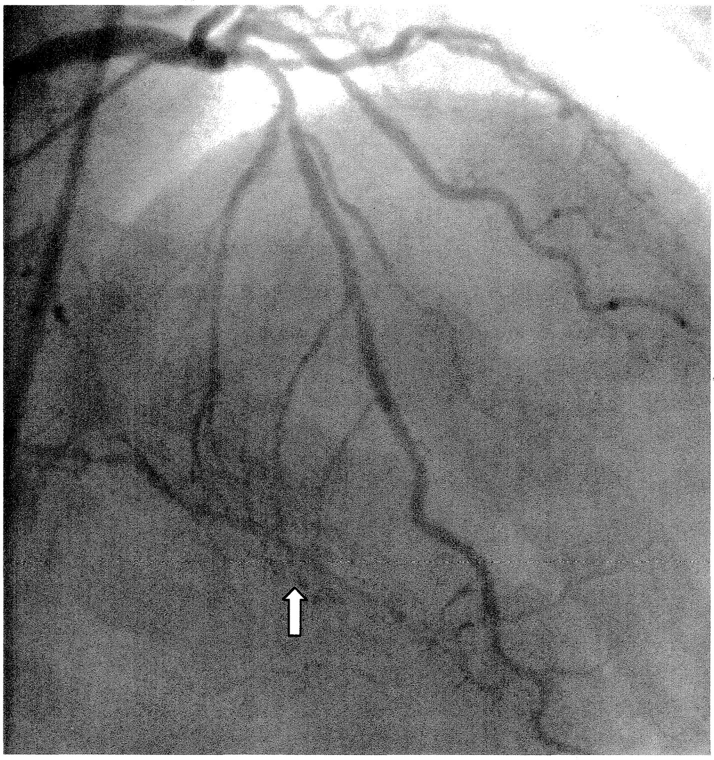


Figure 4 LAD - septals - PDA

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