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Research Article

Evaluation of chest pain by holter monitoring in patients of hypertrophic cardiomyopathy

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ABSTRACT

Background: Patients with hypertrophic cardiomyopathy frequently complain of pain chest during daily activities even despite normal resting ECG and normal coronary angiogram. It seems to be related to myocardial ischemia which may lead to progressive left ventricular remodeling and fibrosis. These morphological changes may produce intractable symptoms and life threatening arrhythmia. The aim of the study is to evaluate the chest pain and clinical significance of ST-segment depression during daily normal activities in the patients with hypertrophic Cardiomyopathy as a noninvasive marker of ischemia.
Methods: Continuous 48 hours Holter monitoring was perform in 106 patients aged (40 ±12 years) with hypertrophic Cardiomyopathy. 92 patients' (86%) Holter recording were suitable for ST-segment analysis.
Results: A total of 97 episodes of ST-segment depression (≥1 mm from baseline) were recorded in 26 patients (Male 21, Female 5). In patients ≤ 30 years of age (but not ≥ 30 years) were correlated between ST-segment desperation and history of exertional chest pain (9 of 15 vs 1 of 21, P- 0011) and dyspnea NYHA II/III (9 of 14 vs 1 of 22 P-004). There was no correlation between ST-segment depression and risk factors for sudden death, such as family history of sudden death, sustained and non sustained ventricular tachycardia and history of syncope.
Conclusions: In Holter monitoring ST-segment depression is common in younger patients with history of typical pain chest of cardiac origin and dyspnea.

Keywords: Hypertrophic Cardiomyopathy, Chest pain, Dyspnea, ST-segment, Myocardial ischemia

INTRODUCTION

Chest pain is a common symptom of hypertrophic cardiomyopathy during daily normal activities even despite normal resting ECG and normal coronary angiogram.[1] It appears to be related to myocardial ischemia which may lead to progressive left ventricular remodeling, fibrosis, transmural infarction and focal fibrosis. These morphological changes may produce intractable symptoms and life threatening arrhythmia, thus may lead to syncope and even sudden death.[2] ST-segment depression has been described during resuscitated cardiac arrest and atrial pacing.[3,4,5] The prevalence of ST-segment depression and its clinical significance during normal daily activities has not been systematically analysed with Holter monitoring as a noninvasive marker of ischemia.

The aim of this study was to evaluate the chest pain during daily normal activities and its clinical significance of ST-segment depression during Holter monitoring in

patients with hypertrophic cardiomyopathy as a non invasive marker of ischaemia.

METHODS

One hundred and Six consecutive patients with hypertrophic cardiomyopathy were evaluated for chest pain with Holter monitoring at Cardiology OPD of Sri Aurobindo Medical College & P.G. Institute between January 2012 to December 2014. Cardiac medication was discontinued for 3 to 5 days prior to Holter monitoring. 22 patients were included who had been receiving amiodarone for ≥3 months. They were included to avoid bias of selection of low risk patients and were continued because of long half life of amiodarone.

Hypertrophic cardiomyopathy was defined chocardiographically by the presence of localized or generalized left ventricular hypertrophy ≥ 15 mm wall thickness in the absence of hypertension or other factors likely to result in a pressure over load of LV. All patients had left ventricular asymmetric and /or generalized hypertrophy ≥ 15mm on 2-D echocardiography in absence any other cardiac or systemic causes. Patients with Blood pressure ≥ 160/90 mmHg were excluded. Clinical history such as family history of hypertrophic cardiomyopathy, sudden death in family, history of typical angina pectoris, atypical /exertional pain chest, dyspnea on exertional and history of syncope were taken. Coronary Angiography was performed only in those patients who had clinical indication considering of age, symptoms and ECG findings.

Baseline Echocardiography (ECG)

Standard 12-leads ECG were perform in all patients using Voltage criteria for left ventricular hypertrophy : Sum of the S wave in V1 plus R wave in V6 ≥ 3.5 mm. Non sustained VT defined as ≥ 3 consecutive ventricular extrasystole at ≥ 100 beats minute^{-1} lasting for ≤ 30 seconds.

Echocardiography:

2-D and M-mode Echocardiography with conventional measurement techniques were performed.

Holter Monitoring

All patients in our study underwent Holter monitoring for 48 hours during their unrestricted daily activities. Recording were done using Philips 3 channels recording system. Computer assisted analysis was performed using Philips Holter monitoring 1810 series with Digitrak Holter software Zymed Algorithm (3 channels).

Episodes of horizontal or down sloping of ST-segment depression ≥ 1 mm from the baseline for 80 msc from the J point, were taken as positive. Each episode had to be separated from other episode ≥ 1 minute. Recording were not taken for analysis as follows a) atrial fibrillation/ flutter b) LBBB c) persistent RV pacing due to difficulty in defining the isoelectric point and secondary effect on ST-segment. Isolated episode of sudden onset offset and excessive baseline wander or artifact were not also considered for analysis. 92 recording were considered for analysis out of 106 recordings.

RESULTS

Altogether 97 episodes of ST-segment depression were detected in 26 patients (M-21, F-5) aged 18-63 years mean age 39.46±12.21 years. 43 episodes were ≥ 2 mm from base linein 14 patient during the recording period. The number of mean episodes per patient was 4 ± 6 (range 1-08). The mean number of heart rate during the recording was 139.61± 15.22 beats minutes $^{-1}$ in patients with ST-segment depression and 134 ± 24.68 patients without ST-segment depression (Table 1).

Table 1: Clinical feature of 92 patients of hypertrophic cardiomyopathy and comparison of ST-segment depression during Holter monitoring.

	ST-depression N(26)	No ST-depression N(66)
Gender M/F	20 (6)	46(20)
Age (Yrs)	39.46±12.21	38±14.62
F/H/O HCM	6(23%)	16(24%)
Dyspnea NYHA II/III	10(38%)	24(38%)
Chest pain on exertion	12	28(42%)
Syncope	2(7.6%)	5(7.5%)
NSVT	4(15%)	8(12%)
SVT	3(15%)	7(10%)
LVOT PG >40 mmHg	2(7.6)	5(7.5%)
LVEDD(mm)	46± 4	46± 5
LVESD (mm)	25±3	26± 4
LA (mm)	40±6	42± 7
IVDD (mm)	22±6	23± 7

F/H/O HCM: Family history of hypertrophic cardiomyopathy. NYHA class II/III: Dyspnea of New York Heart Association functional class II/III. NSVT: non-sustained ventricular tachycardia. SVT supraventricular tachycardia. LVOT PG: left ventricular outflow tract peak gradient. LA: Left atrial size. LVEDD: left ventricular end diastolic dimension. LVESD: left ventricular end systolic dimension. IVSDD: Intra ventricular septum diastolic diameter.

Thirty six patients were enrolled who were aged ≤ 30 years. 10 (33.33%) of them showed transient ST-segment depression with history of effort angina in 9 patients (90%). 5 (19%) patients had effort angina without ST-segment depression (P. value 0.0011). 9 Patients (90%)

had dyspnea with transient ST-segment depression and 6 patients (23%) had dyspnea without ST-segment depression (P. value 0.004).Young patient had history of chest pain and dyspnea NYHA class II/III with ST-segment depression. There were no significant differences in the mean LA size, LVIDD/ LVISDD dimension and IVSDD thickness in both the group of with and without ST-segment depression.

There were 18 enrolled patients who were on amiodarone. ST-segment were analysed of which 10 of them (M-8, F-2) had ST-segment depression during Holter monitoring. 4 out of 10 were aged ≤ 30 years amongst them 3 had ST-segment depression (Table 2).

Table 2: Comparison between ST-segment depression and clinical presentation of 36 patients aged ≤ 30 years

	ST-depression N(10)	No ST-depression N(26)
Gender M/F	9/1	23/3
Age (Yrs)	26±4	24±5
F/H/O HCM	2(20%)	4(20%)
Dyspnea NYHA II/III	9(90%)	6(23%)
Chest pain on exertion	9(90%)	5(19%)
Syncope	2(20%)	6(23%)
NSVT	1(10%)	3(11.5%)
SVT	2(20%)	6(23%)
LVOT PG >40 mmHg	1(10%)	3(11.5%)
LVEDD (mm)	46± 6	44± 5
LVESD (mm)	25±4	26± 5
LA (mm)	40±4	42± 6
IVSDD (mm)	20±6	22± 8

The patients who were taking amiodarone were included in the study so that the sample patient remained representative. Amiodarone may have reduced both the prevalence of chest pain and ST-segment depression in patients of Holter monitoring.[17,18] In young patients who were on amiodarone were excluded for evaluation of symptoms with ST-Segment depression.

Twenty two analyzed patients out of 92 (23.95%) had ECG finding of LVH according to voltage criteria (Table 3). There was no relation between LVH and ST changes during Holter monitoring in any group. Coronary Angiography was performed in 12 patients prior to Holter monitoring. 10 raveled normal coronary artery. For out of 10 had ST-segment depression during Holter monitoring. Two Patients with minor coronary artery lesion had no ST-segment depression during recording.

Table 3: Baseline ECG findings of 26 patients with episodes of ST-segment depression during Holter monitoring.

Age	Sex	Max. HB min^{-1}	No. of episodes of ST changes	≥2mm ST changes	ST change with ≥ 100 HB min^{-1}	Baseline ECG LVH	ST down1 avl V6
28	M	150	08	02	_	_	_
38	F	140	06	02	01	_	_
52	M	150	02	01	01	_	_
22	M	155	10	04	02	_	_
40	F	148	03	02	01	_	_
47	M	126	01	01	00	_	_
18	M	160	04	02	01	_	_
42	M	106	02	01	_	_	_
27	F	136	02	01	_	_	_
60	M	128	01	01	_	+	+
30	M	140	04	02	01	_	_
44	M	150	02	01	01	_	+
50	F	144	02	02	_	+	+
29	M	160	06	04	02	_	_
63	F	140	02	01	_	+	+
30	M	146	04	02	01	_	_
56	M	144	04	02	01	_	_
26	M	164	06	02	02	_	_
50	M	120	02	01	_	_	_
36	M	146	04	02	01	_	_
30	M	137	03	01	01	+	_
42	M	150	02	01	01	_	_
28	M	118	03	00	01	_	_
54	M	126	04	01	00	+	+
46	M	138	04	02	01	_	_
38	M	108	06	02	01	_	_

DISCUSSION

ST-segment depression is a validated marker of ischemia which is used to detect myocardial ischemia with chronic stable angina.[7-12] The myocardial ischaemia has been investigated by various measures of myocardial perfusion studies. There are various invasive method of detection of myocardial ischemia indirectly by metabolic marker and/or effect. One study showed prevalence of lactate extraction is 70% with hypertrophic cardiomyopathy and exercise induced ST-segment changes and 33% without ST-segment changes.[13] Metabolic evidence of ischemia is found in HCM during ST-segment depression induced by rapid atrial pacing.[14] ST-segment depression also noted preceding sudden cardiac death and /or cardiac arrest.[14,15] One report demonstrated lower coronary flow reserve in HCM during dipyridamole stress induced ST-segment depressed subject than those without ST-segment change. This may be due to abnormal myocardial metabolism in HCM.[14]

Perfusion study such as SPECT with thallium -201 failed to demonstrate an association between reversible thallium abnormalities and a history of typical exertional ischemia in HCM.[19] Coronary sinus lactate concentration as a 'gold

standard' of measure of ischemia is limited because it washout quickly and increased during adrenergic stimulation.[20] PET Scan with ^{13}N- ammonia demonstrated significantly lower coronary flow reserve in HCM patient with chest pain.[20] Mismatch between the uptake of thallium -201 and regional fatty acid metabolism assessed by radio labeled fatty acid analogue BMIPP in HCM is promising as a sensitive clinical marker of ischemia.[21]

All these studies are invasive in nature, costly and reliability has not been widely accepted as a marker of myocardial ischemia. Holter monitoring is an established technique for detection myocardial ischemia as a non invasive method and can be done in an outpatient setting.

There are number of potential mechanism of ischemia in the hypertrophic cardiomyopathy:[2]

1. Decrease coronary vasodilatory reserve due to high diastolic pressure.
2. Dysplastic small vessels which may be present in hypertrophic and non hypertrophic regions of the left ventricular and causes increase vascular resistance and altered coronary reactivity.
3. Inadequate capillary density due to extensive myocardial hypertrophy.
4. Variable degree of systolic reduction or inversion of coronary flow probably causes by compression of intramyocardial coronary vessels.
5. Systolic compression of large vessel by myocardial bridges.
6. High oxygen demand in the presence of large out flow tract gradient.
7. Concomitant epicardial atherosclerotic disease.
8. Increased oxygen demand caused by episodes of sinus tachycardia or arrhythmias.

In our study, in young patients with HCM ST-segment depression in commonly associated with exertional chest pain and dyspnea. Myocardial ischemia may be trigger for sudden death in young patients with HCM.[15] In the present study there was no significant association between recognized factors for sudden death such as family history of sudden death, syncope and non sustained VT and ST-segment depression in patients with $\leq$ 30 years of age. Myocardial ischemia is an important possible stimulus for fatal ventricular arrhythmia in sub group of patients.[17]

The association between ST-segment changes and symptoms in young patients is a pointer of clinical suspicion that this subgroup has more change to develop myocardial ischemia which may trigger VT and sudden death.

This study was conducted in a across section population who were referred for assessment of their progressive symptoms and necessary investigations and treatment. So the incidence of positive family history and number of patients taking amiodarone are high. This is a small study amongst cross section of population to evaluate ischemia in the HCM with conventional noninvasive Holter monitoring. Larger study based on more sensitive measurement of myocardial flow reserve and other novel metabolic markers of ischemia may evaluate the causes of chest pain in HCM patients.

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