

## Association of Serum Parathyroid Hormone with Severity of Coronary Artery Disease

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### Original Research Article

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**Abstract:** Elevated serum parathyroid hormone (PTH) levels are associated with increased risk of systemic hypertension, left ventricular hypertrophy, diastolic dysfunction, reduced cardiac contractility, atherosclerosis, vascular calcification, ischemic heart disease and peripheral vascular diseases especially in chronic kidney disease and haemodialysis patients. This prospective study aims to evaluate the association between serum parathyroid hormone concentration and coronary angiogram in patients of stable coronary artery disease. Serum PTH level was measured in angiographically confirmed chronic stable angina patients. Patients were divided into groups according to serum parathyroid level as follows: group 1, Serum level  $\leq 29$  pg/ml; group 2, 30 to 70 pg/ml & group 3,  $\geq 71$  pg/ml. Coronary angiographic profile including number(s) of coronary artery, pattern of segmental coronary artery involvement and syntax score for complexity of lesions were correlated with the serum parathyroid hormone concentration. One hundred and forty (140) patients were evaluated. Mean serum PTH level were 24.10 pg/ml, 50.44 pg/ml and 85.5 pg/ml in groups 1, 2 and 3 respectively. Higher serum PTH levels were directly correlated with number of coronary artery involvement, syntax score and not with the pattern of segmental coronary artery (LAD / LCx / RCA).

**Keywords:** serum parathyroid hormone, stable coronary artery disease, syntax score.

### INTRODUCTION

Cardiovascular diseases are the leading cause of mortality and disability worldwide. Early risk stratification of patient with coronary artery disease is the subject of research.

In the human body, parathyroid hormone (PTH), is a polypeptide hormone which is crucial for the maintenance of calcium homeostasis, has been associated with increased cardiovascular risk like atherosclerosis, vascular calcification, systemic hypertension, left ventricular hypertrophy, diastolic heart failure, reduced cardiac contractility, ischemic heart disease, peripheral vascular disease etc [1]. It is secreted by the parathyroid glands in response to hypocalcaemia which is detected by the calcium sensing receptor [2]. Classic PTH effects on bone and kidney are important for the control of calcium homeostasis, but PTH receptors are also expressed in the vessel walls and the myocardium suggesting direct effects on the cardiovascular system. Primary hyperparathyroidism, characterized by inadequately high PTH levels with subsequent hypercalcaemia, has been associated with increased cardiovascular risk and mortality, which could be significantly reduced by parathyroidectomy [1]. Secondary hyperparathyroidism due to vitamin D deficiency or chronic renal failure may affect cardiac muscle contractility, promote

atherosclerosis and vascular calcification, have permissive role for cardiac fibrosis and is associated with elevated blood pressure resulting in increased prevalence of cardiovascular disease and subsequent mortality [3, 4].

Recent studies have shown link between disturbances in PTH metabolism reflected by too high PTH concentrations and the presence of CVD events [5, 6].

### MATERIALS AND METHODS

#### Study population

Overall 140 subjects were included for the study at the department of cardiology, Rajendra Institute of Medical Sciences, Ranchi, in between January 2017 to December 2017. Patients with confirmed cases of coronary artery disease on coronary angiogram were eligible for the study. The study was approved by institutional ethics committee. Patients who presented with acute coronary syndrome and those

who were known case of primary hyperparathyroidism were excluded from the study.

**Collection of samples and measurement:**

Blood samples were collected after an overnight fast. Venous blood was drawn in plain tubes. Plasma was separated after centrifugation at 3500 rpm for five minutes, and stored at - 70° C until analysis. Analysis of blood sugar, lipid profile, renal function test and serum parathyroid hormone were done with AU2700 plus, Backman Coulter machine. Normal range of serum parathyroid hormone is 12 – 88 pg / ml.

**Outcomes**

End point of the study was to evaluate the association of the serum parathyroid hormone level with the atherosclerotic coronary artery anatomy

(number) and complexity of coronary artery disease (SYNTAX score).

**Statistical Analysis**

Mean of the variables and significance (p-value) of the study among the groups were analyzed by the two sample t-test and Pearson chi square test respectively using SPSS software (version 20).

**RESULTS**

A total of 140 patients were recruited for the present study. Group 1, 2 and 3 consisted of n = 55 (39.28 %), 70 (50 %) and 15 (10.71 %) patients, respectively. Base line characteristics are shown in table 1 and 2. The mean age of participants at the time of enrolment was 59.9 years and majority (74.3 %) were males with no significant difference between groups (p = NS).

**Table-1: Age and sex distribution**

	Total population	Group 1 (N=55)	Group2 (N=70)	Group3 (N=15)	p-value
Mean age (years)	59.9 years	58.9 years	59.64 years	61.7 years	0.472
Male N (%)	104 (74.3 %)	44 (80 %)	49 (70 %)	11 (73.3 %)	0.929
Females N (%)	36 (25.7 %)	11 (20 %)	21 (30 %)	4 (26.6 %)	0.866

**Table-2: Distribution of Risk Factors**

	Total population	Group 1	Group 2	Group 3	p-value
Systemic Hypertension	79 (56.4 %)	28 (50.90 %)	40 (57.14 %)	11 (73.33 %)	0.162
Diabetes Mellitus	74 (52.9 %)	18 (32.72 %)	46 (65.71 %)	10 (66.66 %)	0.257
Dyslipidemia	82 (58.6 %)	24 (43.63 %)	44 (62.85 %)	14 (93.33 %)	0.004
Current Smoking	32 (22.9 %)	18 (32.72 %)	11 (15.71 %)	3 (20 %)	0.679
Chronic Kidney Disease	4 (2.9 %)	1 (1.81 %)	2 (2.85 %)	1 (6.6 %)	0.349

**Left Ventricular Function**

100 patients (71.4 %) had normal LV function while 16 (11.4 %) had mild LV dysfunction. 13 (9.3 %) and 11 (7.9 %) had moderate and severe ventricular dysfunction, respectively.

**Angiographic Profile**

Significant coronary artery disease was defined as more than fifty percent (50 %) luminal diameter stenosis for individual arteries. Patients were then classified into single, double or triple vessel disease or left main disease on the basis of the number of coronary artery involvement.

**Table-3: Shows involvement of coronary artery in different groups.**

	SVD(N=60)	DVD (N=38)	TVVD (N=42) mo	p-value
Group 1	39 (70.9 %)	11 (20 %)	5 (9.09 %)	<0.05
Group 2	20 (28.5 %)	27 (38.5 %)	23 (32.8 %)	<0.05
Group 3	1 (6.6 %)	0	14 (93.3 %)	<0.05

Single vessel coronary artery disease was the most common finding (70.9 %) in group 1 where as triple vessel coronary artery disease was more prevalent in group 3 group with significant difference between the groups (p < 0.05).

The group wise prevalence of number of significant coronary artery involvement is given in figure 1.

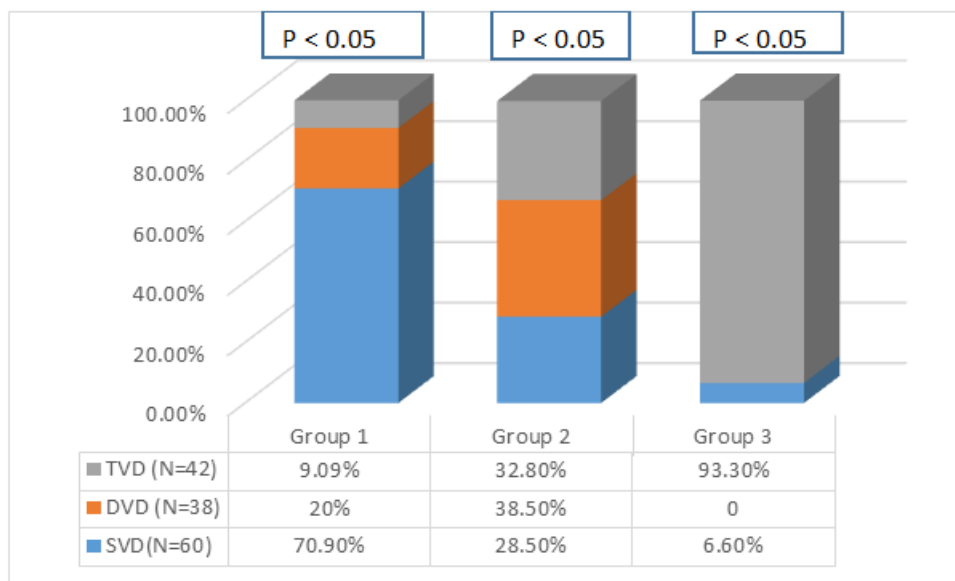


Fig-1: Bar diagram showing pattern of coronary artery involvement in different groups

Table-4: Shows odds ratio in groups for the coronary artery disease

		Odd Ratio	P value for difference
Group 1	SVD VS DVD	0.77	NS
	SVD VS TVD	20.14	< 0.05
	DVD VS TVD	25.96	< 0.05
Group 2	DVD VS SVD	1.55	NS
	DVD VS TVD	1.29	NS
Group 3	TVD VS SVD	197	< 0.05

In Group 1, SVD was more prevalent compared to TVD (OR – 20.14,  $p < 0.05$ ) whereas TVD was more prevalent in Group 3 (OR – 197,  $p < 0.05$ ) (Table-4).

Mean serum PTH concentration was 24.1, 50.44 and 85.55 pg/ml in groups 1, 2 and 3, respectively with significant difference ( $p < 0.05$ ). There was no significant difference in coronary artery disease according to the number of coronary artery involvement for mean serum PTH concentration ( $p = NS$ ) (Table-5).

Table-5: Shows mean serum parathyroid hormone concentration in different groups and coronary artery involvement

Level	GROUP				CAD			
	Group 1	Group 2	Group 3	P value	SVD	DVD	TVD	P value
Mean PTH (pg/ml)	24.10	50.44	85.55	<0.05	26.72	43.57	61.92	NS

Table-6: Distribution of individual coronary artery involvement in groups

	SVD (N=60, 42.85 %)				DVD (N=38, 27.14 %)			TVD (N=42, 30 %)
	LAD (N=25, 41.6%)	LCx (N=20, 33.3%)	RCA (N=15, 25 %)	P value	LAD+ LCx (N=4, 10.56 %)	LAD+ RCA (N=12, 31.57 %)	RCA+ LCx (N=22, 57.89 %)	
Group 1	16	14	9	NS	2	4	5	5(13.5 %)
Group 2	9	5	6	NS	2	8	17	23(62.1 %)
Group 3	0	1	0	NS	0	0	0	14(37.8 %)

There was no difference in the artery involvement among single vessel disease in different groups. In group 2, combination of RCA plus LCx

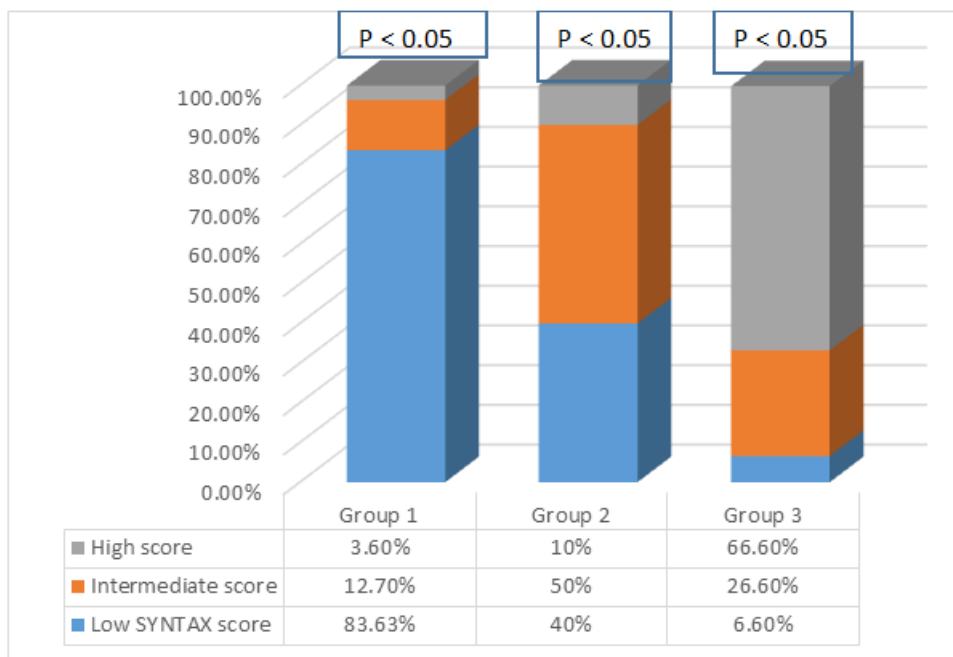
involvement was more common compared to LAD plus LCx and LAD plus RCA combination.

**Table-7: Distribution of SYNTAX scores**

	Low SYNTAX score	Intermediate score	High score	p-value
Group 1	46 (83.63 %)	7 (12.7 %)	2 (3.6 %)	<0.05
Group 2	28 (40 %)	35 (50 %)	7 (10 %)	<0.05
Group 3	1 (6.6 %)	4 (26.6 %)	10 (66.6 %)	<0.05

Low syntax score was more prevalent in group 1 whereas high syntax score was more prevalent in group 3 with significant difference in groups ( $p < 0.05$ ).

The group wise SYNTAX score is given in figure 2.



**Fig- 2: Bar diagram showing SYNTAX scoring system in different groups.**

**Table-8: Shows odd ratio for SYNTAX score**

Group	SYNTAX score	Odd Ratio	P value for difference
Group 1	Low VS Intermediate	35.24	<0.05
	Low VS High	138.10	<0.05
Group 2	Intermediate VS Low	1.50	<0.05
	Intermediate VS High	9.00	<0.05
Group 3	High VS Low	28.16	< 0.05
	High VS Intermediate	5.50	< 0.05

**DISCUSSION**

In this study 140 patients of chronic stable angina of moderate to high risk were enrolled by non invasive stratification.

**Conventional risk factors (Table-1 & 2)**

The mean age in this study was 59.9 years in contrast to 71 years of previous study, [6] as they included more frail elderly. In accordance to previous studies, [7] the prevalence of dyslipidemia was significantly different between groups in this study. Prevalence of the systemic hypertension (56.4 %), and smoker (22.9 %) was in accordance to previous study [6] while prevalence of diabetes mellitus was higher (52.9 %) in contrast to previous study [6] (11.2 %).

**Left Ventricular Function**

There was no significant difference in normal LV function, mild, moderate and severe LV dysfunction between groups ( $P = NS$ ).

**Serum Parathyroid Hormone Concentration (Table-5)**

Mean serum parathyroid hormone concentration were 24.10 pg/ml, 50.44 pg/ml and 85.5 pg/ml in groups 1, 2 and 3 respectively. There was no significant difference in the mean serum parathyroid concentration in segmental atherosclerotic coronary artery disease involvement ( $P = NS$ ).

### Angiographic profile (Table-3, 4, 5 and 6)

Angiographically, in group 1, SVD – 39 (70.9 %) was most common followed by DVD – 11 (20 %) while in the group 2, DVD – 27 (38.5 %) and group 3 TVD – 14 (93.3 %) was the most common coronary artery involvement. In group 1, SVD was more prevalent found compared to TVD (OR – 20.14,  $p < 0.05$ ) whereas TVD was more prevalent in group 3 (OR – 197,  $p < 0.05$ ).

There was no significant difference in individual segmental artery distribution (LAD / LCx / RCA) among groups ( $p=NS$ ). Low syntax score (46, 83.63 %) followed by intermediate syntax score (7, 12.7 %) was more prevalent in group 1, intermediate – 35 (50 %) followed by low – 28 (40 %) score in group 2 and high – 10 (66.6 %) followed by intermediate – 4 (26.6 %) score in group 3 groups. In groups 1, 2 and 3, the low ( $p < 0.05$ ), intermediate ( $p < 0.05$ ) and high ( $p < 0.05$ ) syntax score were significantly different, respectively.

### Principal Finding

Observations of the present study are

- In accordance to previous study [7], dyslipidemia is significantly different in all groups.
- Higher serum levels of PTH are associated with more complex coronary anatomy in terms of numbers of coronary artery involvement.
- Above results remained essentially unaltered even in participants with serum PTH within normal range which is in accordance with previous studies [6-9].
- Pattern of individual segmental coronary artery (LAD / LCx / RCA) involvement was similar in three groups.

### Comparison with the literature

There is paucity of literature correlating increased PTH level as predictor of cardiovascular risk outcome [8]. Even previous literatures are not accounting the coronary anatomy as the risk assessment of cardiovascular outcome. One literature reported the association of circulating PTH and the risk for cardiovascular disease [10] but it was limited by a cross-sectional study design. Thus, the prospective association between plasma PTH level and cardiovascular outcome has not been previously reported. Moreover, no previous studies have reported the higher PTH is associated with higher incidence of complex coronary anatomy.

### Limitation

In this study, the major limitation is lack of healthy control group. Patients were enrolled from the same ethnic background. Renal function status was assessed by blood urea and creatine level only not by eGFR so cases of subclinical secondary

hyperparathyroidism and other mineral metabolism disorder cannot be ruled out.

### CONCLUSION

Early risk stratification of the coronary artery disease patients is essential and the foremost step in the prognostication and management. Higher serum levels of parathyroid hormone are associated with more number(s) of the coronary artery involvement and higher syntax score as the complexity of the lesion even in patients with normal renal function. These results are unaltered even in patients with upper normal limit of serum parathyroid hormone concentration.

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