



## Correlation of Novel Risk Factors with Syntax Score in Young and Elderly Males with Coronary Artery Disease

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### Abstract

Worldwide, Coronary Artery Disease (CAD) is one of the leading causes of death. Patients from the Indian subcontinent present relatively early and may have more extensive CAD. Various Conventional and Novel risk factors for CAD have been studied. In this study apart from the Conventional risk factors, we assessed the Novel risk factors like Hyperhomocysteinaemia, Lipoprotein a (Lpa), Apolipoprotein B (Apo B), Apolipoprotein A<sub>1</sub> (Apo A<sub>1</sub>) and Apolipoprotein B/A ratio in both the Elderly (>45 years) & Young (≤45 years) groups and correlated their values with the SYNTAX Score to find out if there was any correlation between the levels of the Novel risk factors and the SYNTAX score. We found that the Homocysteine levels in young patients correlated linearly with their respective Syntax scores with a highly significant 'p' value of 0.001355. This was however not so in the elderly group. It was also derived from this study that serum Homocysteine levels in young coronary artery disease patients are 83.33% sensitive, 91.67% specific and 86.67% accurate in predicting complexity of coronary lesions and thus the aggressiveness of the disease in terms of their Syntax scores.

### Introduction

The spectrum of coronary artery disease (CAD) in India reveals, that not only is CAD more diffuse & aggressive, but affects people at an earlier age<sup>1,2</sup>. We have found that one in five patients who are admitted for CABG in our unit are less than 45 years of age. Apart from the Conventional risk factors, we assessed the Novel risk factors like Hyperhomocysteinaemia, Lipoprotein a (Lpa), Apolipoprotein B (Apo B), Apolipoprotein A<sub>1</sub>(Apo A<sub>1</sub>) and Apolipoprotein B/A ratio in both the Elderly & Young group and correlated their values with the SYNTAX Score for all our patients in the study groups to find out if there

was any correlation between the levels of the Novel risk factors and the SYNTAX score.

### Objective

To find out if there is any correlation between conventional and/or novel risk factors with the severity of Coronary Artery Disease as defined by SYNTAX score in young (≤45 years) and elderly (>45 years) coronary artery disease patients.

### Methods and Materials

This prospective analytical observational study was carried out between 01.02.2014 to 31.01.2016 in the Department of CTVS Medical College Kolkata.

**Patient Population**

Patients admitted in CTVS department for CABG. They were divided into 2 groups:

- 1) Young ≤45 years
- 2) Elderly >45 years

During the study period, since there were no female patients below the age of 45 years admitted for CABG, we did not take female patients in our study.

We did not include patients who underwent:

- 1) Emergency CABG
- 2) Had previous PCI
- 3) Associated valvular heart disease and
- 4) With mechanical complications of CAD

So the number of patients in the study was 132 patients. This sample size was more than the required sample size of 98 (considering a margin of error of 5%, a confidence level of 95% and a response distribution of 50%).

Matching of the young and elderly groups was done by using a baseline criteria of BMI ≥23 (overweight, at risk of obesity, obese- I, obese-II)<sup>3</sup>.

Actual sample size after applying Matching criteria was 99.

Group A- young patients young (≤45 years)

Group B- elderly (>45 years)

Evaluation of Risk Factors:

The following CAD risk factors were evaluated in every patient:-

**Conventional risk factors for CAD**

- Smoking
- Hypertension
- Diabetes Mellitus type II
- Family H/O IHD
- Waistline
- BMI
- Total Cholesterol, HDL, LDL,TG

**Novel risk factors for CAD**

- Lipoprotein A Lp(a)
- Apo lipoprotein B (Apo B)
- Apolipoprotein A 1 (Apo A1)
- Apo B: Apo A1 ratio
- Homocysteine

SYNTAX score was calculated in each case from the preoperative Coronary Angiogram using online SYNTAX Score calculator version 2.11.

**Results**

Conventional risk factor results in two groups (Table 1)

	Group A - ≤45 Years (n=30)	Group B - >45 Years (n=69)
Smokers	22(73%)	48(70%)
Hypertensives	18(60%)	43(62%)
Diabetics	11(37%)	23(33%)
Family History of IHD	13(42%)	29(42%)
Waistline >90 cms	14(46%)	33(48%)
BMI>25	13(42%)	17(25%)
History of AMI	17(58%)	19(28%)
HDL < 40 mg/dl	22(73%)	26(38%)

To evaluate whether HDL level variance in the two groups is statistically significant, we used the “Two Sample T-test assuming unequal variance”. The p-value was <0.00254, making the result highly significant.

Novel risk factor results in two groups (Table 2)

	Group A - ≤45 Years (n=30)	Group B - >45 Years (n=69)
Homocysteine ≥30μmol/L	16(53%)	12(17%)
Lp(a)≥30mg/dl	19(63%)	49(71%)
Apo B >140mg/dl	7(23%)	7(10%)
Apo A <sub>1</sub> <110mg/dl	3(10%)	8(12%)
Apo B: A <sub>1</sub> ratio > 1	9(30%)	14(20%)

To evaluate whether this Homocysteine level variance was statistically significant in the two groups, we used the “ Two Sample T-test assuming unequal variance”. The p-value was <0.0485, making the result significant.

SYNTAX scores in the two groups (Table 3)

	Group A - ≤45 Years (n=30)	Group B - >45 Years (n=69)
Mean Syntax score	27.27 ± 8.41	24.32 ± 6.22
Low Syntax score (0-22)	12(40%)	29(42%)
Intermediate Syntax scor (23-33)	8(27%)	34(50%)
High Syntax score (>33)	10(33%)	6(8%)

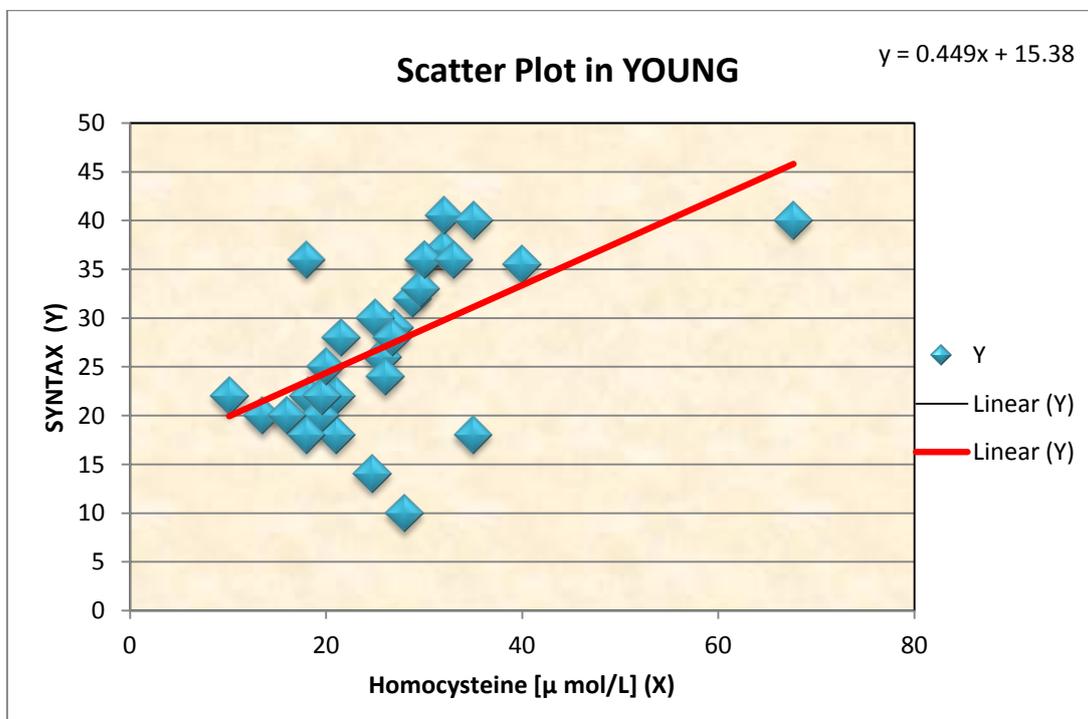
In order to find out whether there is any relationship between serum Homocysteine and SYNTAX scores in the young and elderly population, regression analysis was done. The

regression “p-value” was found to be statistically highly significant in the young group only (0.00135) as shown in table 4 and corroborated by

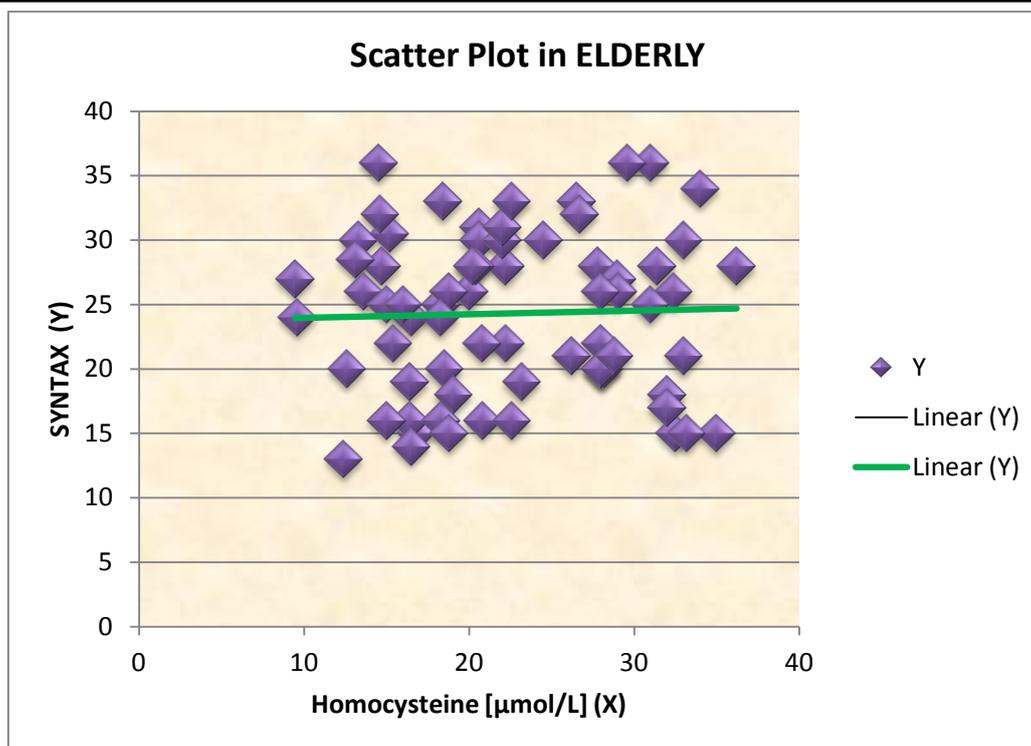
a steep slope of the scatter plot in Figure 1. However, it was not so in the elderly as in Figure 2.

**Table-4:** Regression analysis showing a significant ‘p’ value, indicating a linear relationship between Serum Homocysteine & SYNTAX score in YOUNG population ie. group A.

SUMMARY OUTPUT							
<b>Regression Statistics</b>							
Multiple R	0.557982275						
R Square	0.31134422						
Adjusted R Square	0.28674937						
Standard Error	7.104762408						
Observations	30						
<b>ANOVA</b>							
	df	SS	MS	F	Significance F		
Regression	1	638.99249	638.9925	12.65891959	0.001355517		
Residual	28	1413.3741	50.47765				
Total	29	2052.3666					
		Standard Error	t Stat	P-value	Lower 95%	Upper 95%	Lower 95.0%
	Coefficients	3.5823932					
Intercept	15.38563053	6	4.294791	0.000189762	8.047430693	22.7238304	8.047430693
X Variable 1	0.449556769	0.1263531	3.557938	<b>0.001355</b>	0.19073399	0.70837955	0.19073399
Multiple R	0.557982275						



**Figure-1:** Scatter plot relating serum Homocysteine [x-axis] with SYNTAX score [y-axis] in YOUNG [group A]. Each of the 30 young patients are represented by a **blue dot** on the chart. The statistically significant (‘p value’- **0.001355517**) **linear relationship** between the two variables is represented by the **red trend-line** which has a steep slope (equation for this trend line:  $y = 0.449x + 15.38$ ).



**Figure- 2:** Scatter plot relating serum Homocysteine [x-axis] with SYNTAX score [y-axis] in ELDERLY. Each of the 69 elderly patients are represented by a **purple dot** on the chart. The resultant **trend line in green has a flat slope** showing absence of any linear relationship between Homocysteine & SYNTAX score in ELDERLY [group B].

From this we conclude that High Homocysteine value can predict HIGH Syntax score in **young** population but **no** similar relationship could be derived in the **elderly**.

In order to find out how robust an investigation serum Homocysteine is, in predicting **complexity of coronary artery lesions in terms of SYNTAX scores in YOUNG population**, the following groups were defined:

**True Positive:** Those who have raised Homocysteine levels & Intermediate/High SYNTAX scores.

**False Positive:** Those who have raised serum Homocysteine levels & Low SYNTAX scores.

**True Negative:** Those who have normal serum Homocysteine levels & Low SYNTAX scores.

**False Negative:** Those who have normal Homocysteine levels & Intermediate/High SYNTAX scores.

These values were filled in a 2x2 contingency table & represented [Table-5] below:

**Table - 5:** True positive, False positive, True negative & False negative groups; when Serum Homocysteine is used to predict SYNTAX scores in YOUNG population [Group A]

YOUNG CAD PATIENTS	Homocysteine $\geq$ 30 $\mu\text{mol/L}$	Homocysteine $<$ 30 $\mu\text{mol/L}$
Syntax $\geq$ 23	TRUE POSITIVE [TP] n = 15	FALSE NEGATIVE [FN] n = 3
Syntax $<$ 23	FALSE POSITIVE [FP] n = 1	TRUE NEGATIVE [TN] n = 11

The following Table (Table 6) shows how good Serum Homocysteine is as a test to predict

complexity of coronary artery lesions [as SYNTAX scores], in YOUNG population.

**Table - 6:** Sensitivity, Specificity, Positive/ Negative Predictive values & Diagnostic accuracy of serum Homocysteine as a test to predict coronary artery lesion complexity in terms of SYNTAX scores in YOUNG population [group A].

SENSITIVITY	$[TP/(TP+FN)] \times 100 \%$	83.33%
SPECIFICITY	$[TN/(TN+FP)] \times 100 \%$	91.67%
POSITIVE PREDICTIVE VALUE	$[TP / (TP+FP)] \times 100 \%$	93.75%
NEGATIVE PREDICTIVE VALUE	$[TN/(FN+TN)] \times 100 \%$	78.57%
DIAGNOSTIC ACCURACY	$[(TP+TN) / (TP+FP+FN+TN)] \times 100\%$	86.67%

## Discussion

In this study, we evaluated the various risk factors in young ( $\leq 45$  Years) and elderly ( $> 45$  years) Coronary Artery Disease (CAD) patients and tried to find out if there was any direct correlation between the risk factors and the severity or extent of CAD as determined by Syntax score.

Syntax Scores have been classified into 3 groups – High ( $\geq 33$ ), Intermediate (22-32) and Low (0-22). Higher Syntax Scores indicate more complex disease and represent a bigger therapeutic challenge.

In this study we did find a strong correlation between levels of Serum Homocysteine and complexity of coronary artery disease as determined by syntax scores in Young ( $\leq 45$  Years) CAD patients. This was not however true for the Elderly ( $> 45$  years).

In fact using the scatter plot and the resultant “trend line”, we noticed a very steep slope of the trend line, indicating that, the higher the Serum Homocysteine level, the more was the Syntax score.

Boushey et al <sup>4</sup> reported a metaanalysis of 27 observational studies including about 4000 patients. A raised Homocysteine level (defined as above the 90th or 95th percentile of controls) was associated with an increased risk of fatal and nonfatal atherosclerotic vascular disease in the coronary artery (odds ratio 1.7; 95% CI 1.5-1.9). However no objective correlation was made to evaluate Homocysteine levels with the complexity and severity of atherosclerotic CAD.

In this study the Homocysteine levels in young patients correlated linearly with their respective Syntax scores with a highly significant ‘p’ value of 0.001355.

It was also derived from this study that serum Homocysteine levels in young coronary artery disease patients are 83.33% sensitive, 91.67% specific and 86.67% accurate in predicting complexity of coronary lesions and thus the aggressiveness of the disease in terms of their Syntax scores.

## Conclusion

We can conclude that in the Eastern Indian population who suffer from coronary artery disease:

- A significantly higher number of young patients with CAD have greater serum Homocysteine levels compared to elderly.
- Serum Homocysteine levels correlate linearly with the respective Syntax scores in young patients and higher Homocysteine levels are predictive of more complex disease with higher Syntax scores.
- Greater number of younger patients tend to have low HDL levels compared to elderly but no correlation could be found between low HDL levels and respective Syntax Scores.

## References

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