



# Serum Inflammatory Markers and Coronary Artery Calcification

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## BACKGROUND

- Elevated levels of serum inflammatory markers, such as C-reactive protein, homocysteine and lipoprotein (a) have been extensively studied as additional risk factors for coronary artery disease. The utility of these markers in relation to degree of coronary artery calcification (CAC) seen on computed tomography has yet to be conclusively established.
- Recent guidelines have suggested the threshold of CAC age- percentile ranking of  $\geq 75\%$  and absolute score of  $\geq 100$  as a marker for clinically significant atherosclerosis.

## STUDY AIMS

- This current study evaluates the association between accelerated CAC as determined by gender- and age- percentile rankings and absolute CAC score (CAC  $\geq 75\%$  and  $\geq 100$ ) and elevated levels of C-reactive protein, homocysteine and lipoprotein (a) in asymptomatic patients.

## METHODS

- Coronary artery calcification was measured non-invasively by electron beam computed tomography and CAC score calculated using the method of Agatston et al.
- Plasma high-sensitivity C-reactive protein (hsCRP), homocysteine, lipoprotein a [Lp(a)], and fasting lipid panel were measured in 400 physician-referred patients.
- The associations of hsCRP, homocysteine, Lp(a), LDL, HDL and total cholesterol with accelerated CAC ( $\geq 75\%$  and  $\geq 100$ ) were assessed by multivariate logistic regression after adjustment for conventional risk factors.

## RESULTS

- In univariate analyses, patients with accelerated CAC ( $\geq 75\%$  and  $\geq 100$ ) had significantly higher serum levels of hsCRP, homocysteine and Lp(a) ( $P < 0.001$ ) when compared to those in the lower percentile ranking (10%). Also, those patients with accelerated CAC were found to have significantly higher total cholesterol, LDL-C and TG and lower HDL-C ( $P < 0.05$ ).
- After adjustment for age, gender and other CV risk factors by multivariate logistic regression, hsCRP, homocysteine, Lp(a), total cholesterol and LDL-C remained significantly higher in those with CAC percentile ranking  $\geq 75\%$  and absolute score  $\geq 100$  than those with CAC percentile ranking = 10% [odds ratios 1.24 (1.03 - 1.50)  $P=0.02$ , 1.17 (1.02 - 1.37)  $P=0.03$ , 1.21 (1.04 - 1.41)  $P=0.01$ , 1.10 (1.07 - 1.24)  $P=0.0001$ , and 1.77 (1.13 - 3.16)  $P=0.02$ ] respectively.
- Also, HDL-C was found to be lower in those with CAC percentile ranking  $\geq 75\%$  and absolute score  $\geq 100$  than those with CAC percentile ranking = 10% [0.12 (0.05 - 0.21)  $P=0.001$ ].

Table 1. Variables Associated with CAC Score Percentiles

Variable	CAC=10%* N= 185	CAC $\geq$ 75%* N=215	P Value
Age (years)	55 $\pm$ 11	56 $\pm$ 9	0.3
Gender (male)	53% (98)	89% (191)	0.0001
Hypertension	31% (57)	45% (97)	0.003
Hypercholesterolemia	44% (81)	62% (133)	0.0001
Diabetes Mellitus	6% (11)	10% (21)	0.15
Family History of CAD	46% (85)	59% (127)	0.02
hsCRP (mg/dL)	2.7 $\pm$ 1.8	5.9 $\pm$ 2.1	0.004
Homocysteine ( $\mu$ mol/L)	10.7 $\pm$ 2.1	14.7 $\pm$ 3.5	0.001
Lp(a) (mg/dL)	2.7 $\pm$ 1.5	8.3 $\pm$ 2.3	0.001
Total Cholesterol (mg/dL)	194 $\pm$ 31	211 $\pm$ 36	0.0001
LDL-C (mg/dL)	119 $\pm$ 29	128 $\pm$ 36	0.02
HDL-C (mg/dL)	52 $\pm$ 18	45 $\pm$ 13	0.0001
Triglyceride (mg/dL)	141 $\pm$ 42	201 $\pm$ 54	0.04

## RESULTS (cont.)

Table 2. Odds Ratios of Variables Associated with CAC Score Percentiles (Multivariate Analysis Adjusted for Age, Gender, Hypertension, Diabetes Mellitus, Family History of CAD)

Variable	CAC=10%	CAC $\geq$ 75%
CRP	1.0 (Referent)	1.24 (1.03 - 1.50), $P=0.02$
Homocysteine	1.0 (Referent)	1.17 (1.02 - 1.37), $P=0.03$
LP(a)	1.0 (Referent)	1.10 (1.07 - 1.24), $P=0.0001$
Total Cholesterol	1.0 (Referent)	0.12 (0.05 - 0.21), $P=0.001$
LDL-C	1.0 (Referent)	1.77 (1.13 - 3.16), $P=0.02$
HDL-C	1.0 (Referent)	1.02 (1.00 - 1.05), $P=0.09$
Triglyceride	1.0 (Referent)	1.21 (1.04 - 1.41), $P=0.01$

## CONCLUSIONS

- In this small study, dividing patients into CAC score classifications based on gender- and age- percentile rankings as well as absolute CAC score, those in the 75<sup>th</sup> percentile or greater and absolute score  $\geq 100$  had significantly higher serum levels of hsCRP, homocysteine and Lp(a) as compared to those in the 10<sup>th</sup> percentile.
- Furthermore, accelerated CAC was significantly associated with elevated LDL-C and total cholesterol and lower HDL-C.
- CAC scores based on gender and age- percentile rankings in combination with absolute CAC score may be of more clinical utility, and further examination into its association with serum inflammatory markers may be warranted.

## REFERENCES

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