

## ***A Case Report***

# **Halting the Progression of Coronary Artery Calcification Through Diet, Exercise, and Combination Therapy**

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## ***Introduction***

The goal of cardiac CT for calcium scoring is to detect coronary artery disease (CAD) at an early stage when there are no symptoms and to determine its severity. It is a screening study that may be recommended by a physician if you have risk factors for CAD but no clinical symptoms yet. The procedure is most often suggested for men aged 45 years or older and for women who are aged 55 and above or are postmenopausal.<sup>1</sup>

The anatomic basis for the value of coronary artery calcium (CAC) imaging is the close correlation between the CAC score and the presence and extent of coronary atherosclerosis. This score, based on a system which summates the high intensity regions of calcium in the coronary vasculature, has been shown to correlate with atherosclerotic plaque calcium mass, histologic mass, the extent of coronary artery disease (CAD) measured angiographically, and the likelihood of hemodynamically significant stenoses.<sup>2</sup> Coronary calcium, as seen in the early stage of coronary artery (CAD), is closely correlated with fatty "soft" plaque, which may rupture and cause myocardial infarction.

According to Schmermund et al<sup>3</sup>, the overall mean relative progression of calcification observed in patients with positive calcium scores was 51% for total calcium scores and 42% for total calcium areas. The median values were 32% and 27%, respectively. Most of the early reports on the progression of calcification examined only asymptomatic patients. A notable study by Maher et al<sup>4</sup> reported a mean annual progression of coronary calcium scores in healthy adults (aged 46± 7 years) of 24%. Another by Budoff et al<sup>5</sup> observed almost the same progression in asymptomatic patients with several risk factors. Their mean annual progression rate was 33% and was lower in patients on lipid-lowering therapy than in the total group.<sup>3</sup>

In asymptomatic or screening populations, the most important determinants of the rate of calcium progression appear to be the initial coronary calcium score (CCS) and coronary volume score (CVS) rather than a specific risk factor, including sex and age. The results from progression studies suggest that subjects without coronary artery calcium at baseline do not rapidly develop new calcium deposits. The lower rates of CCS and CVS progression observed in women as compared with those observed in men reflect the lower initial amounts of calcium present in the distribution of the epicardial arteries. Similarly, younger subjects have significantly lower rates of calcium progression than do older subjects because younger subjects initially have smaller amounts of coronary artery calcium. Thus, demonstrating that calcium begets calcium.<sup>6</sup>

This case report study shows a patient who came in for consult and cardiac evaluation with an initial calcium score in the 96<sup>th</sup> percentile for men between the ages of 60 and 64. Current knowledge on calcium progression rate would predict this patient's score to worsen over time and thus increasing the risk for cardiovascular event for this patient.

### ***Case Report***

Patient A is a 61 year old pleasant male who first came in for consult on February 25, 2006. He had a heart scan done two weeks prior. Coronary artery calcium scanning and three-dimensional scoring was performed which showed a total calcium score of 2014.3.

He admits to having occasional chest tightness and shortness of breath on exertion. He denies palpitations, easy fatiguability, and leg edema. He is a non-smoker and non-alcoholic beverage drinker. He occasionally exercise and work as a sales representative.

Past medical history reveals hypercholesterolemia in which he is on atorvastatin 10mg once a day and obesity. He also has a strong family history of heart disease. His father died of heart failure and one brother has hypertension and had a CABG at the age of 63.

On physical examination, he was conscious, alert, not in distress, and oriented to 3 spheres. Blood pressure is around 140/80 with a heart rate of 90 bpm, respiratory rate of 15 cpm, and was afebrile. HEENT: Normal conjunctivae, normal oral mucosa. Neck: JVP is normal, no carotid bruit heard. Chest: Clear to auscultation bilaterally. Heart: S1, S2, no S3, positive S4, 2/6 systolic ejection murmur was heard in the aortic area. Abdomen: soft, non-tender, normal bowel

sounds. Extremities: No cyanosis, clubbing, nor edema. 2+ pulses in all four extremities.

An EKG was done which revealed sinus rhythm and was within normal limits. A 2-D echo with Doppler essentially revealed normal LV ejection fraction, mild aortic insufficiency, mild mitral and tricuspid regurgitation, and mild aortic sclerosis. Patient had a cardiolute stress test in which the patient walked on the treadmill for 10 minutes and 30 seconds. He reached a heart rate of 171 and had a negative maximal stress test with a normal blood pressure response. Cardiolute study showed 0% perfusion defect with LV ejection fraction by gated SPECT of around 62%.

The heart scan findings was reviewed to him in detail. His total calcium score was 2014.3 with a volume score of 1556.2. (*see Table No. 1*) This total coronary calcium score places him in the 96<sup>th</sup> percentile for men between the ages of 60 and 64. This means that 3% of men between this age group have a higher calcium score than him and 96% have a lower score. This places him on a very high risk for a cardiovascular event over the next several years.

**Table 1 Baseline Coronary Calcium score**

Vessel	Number of Lesions	Mean Density	Volume Score	Agatston Calcium Score
Left Main	0	0	0	0
LAD	6	258.8	197.3	244.4
LCX	3	196.8	42.0	33.1
RCA	23	278.7	1316.9	1736.7
<b>Total Coronary Plaque Burden</b>	<b>32</b>	<b>274.0</b>	<b>1556.2</b>	<b>2014.3</b>

Since there is a coronary plaque disease present any contributing cardiac risk factors should be reevaluated. The importance of adherence to a healthy lifestyle was discussed with him which includes low-calorie diet, regular exercise program, and weight loss since his body mass index (BMI) was >30 and is classified as obesity.

Likewise, lipids in general was also discussed as he reported having a high total cholesterol level. Based upon the CT results and current risk profile, current goals for serum lipids should be reevaluated. A target goal for total cholesterol of <200mg/dl, HDL cholesterol >60mg/dl, Triglycerides <60mg/dl, and an LDL cholesterol <60mg/dl was strongly encouraged. Modification of the current pharmacologic therapy was done. Atorvastatin 10mg was stopped and started

him on simvastatin 40mg and ezetimibe 10mg once a day. Niacin 500mg once daily was also added to the regimen. Other medications given were valsartan 80mg OD, metoprolol 50mg OD, Aspirin 81mg OD, and clopidogrel 75mg OD.

A blood test was sent to Berkeley Heartlab for advance cardiovascular lipid profile. Further workup and treatment were based on these findings.

**Follow-up #1**

Patient came back on March 20, 2006 for the evaluation of the Berkeley Heartlab findings. Total cholesterol was 156mg/dl; LDL is 87mg/dl, should be less than 60; HDL is 40mg/dl, should be more than 60; and triglycerides are 145mg/dl, should be less than 60. (see Table No. 2)

Test Date: 2-28-2006

	Normal	Inter-mediate	At Risk	Last Visit	Alert Value	ATP III Goal	Reference Range
NCEP ATP III Lipid Tests	Total Cholesterol (mg/dL)	156			>=200	<200	129 - 221
	LDL-C (mg/dL)	87			>=100	<100	59 - 145
	HDL-C (mg/dL)	40			<40	>=40	32 - 60
	Triglycerides (mg/dL)	145			>=150	<150	63 - 268

  

	Normal	Inter-mediate	At Risk	Last Visit	Alert Value	BHL Goal	Reference Range	
Advanced Cardiovascular Risk Markers	IIIa+b (%)		41.20		>=20	<=15	13.6 - 43.0*	
	LDL IVb (%)	3.2			>=10	<=5	1.7 - 9.8*	
	HDL2b (%)			5		<10	>20	7 - 30*
	Apo B (mg/dL)		85			>120	<60	60 - 140
	Lp(a), Extended Range (mg/dL)			31		>=30	<30	0 - 30
	Apoprotein A1 (mg/dL)		115			<=89	>115	110 - 180
	Homocysteine (µmol/L)		12.3			>=14	<10	4.0 - 15.4
	Apo E Genotype	3/3				3/4, 4/4		!
	Lipo PLA2 (ng/ml)	170				>223	<200	155 - 419
	CRP (hs) (mg/L)	0.7				>3.0	<1.0	0.0 - 5.0
	Fibrinogen (mg/dL)			422		>=350	<350	180 - 350
	Insulin (µU/ml)	8				>=12	<10	3 - 25
	Glucose (mg/dL)	97				>=100	<100	70 - 99

Table No. 2

Reddy Cardiac Wellness

LDL particle size revealed 41% to be pattern B, should be less than 15%; HDL 2B is 5%, should be more than 35%; ApoB is 85, should be less than 60; Lpa is 31, should be less than 10; ApoE genotype is 3/3 and is normal; LpPLA2 is 170; C-reactive protein is 0.7; fibrinogen is 422, should be less than 350; insulin is 8; glucose is 97; and TSH is 1.0.

Recommendations at this time were low-calorie diet, regular exercise, and some changes in current medications as follows: Simvastatin 20mg OD, ezetimibe 10mg OD, fenofibrate 145mg ½ tablet daily, fish oil 2000mg twice a day, niacin 500mg once a day to be increased to 1000mg once a day in 1 month, quinapril 5mg OD, metoprolol 25mg OD, Aspirin 81mg MWF, and clopidogrel 75mg MTh.

A repeat Berkeley Heartlab advanced lipid profile will be done after three months to monitor the progress and effectivity of the treatment.

**Follow-up #2**

Patient came back on July 11, 2006 for evaluation of the repeat Berkeley Heartlab findings. The total cholesterol dropped from 156mg/dl to 115mg/dl; LDL likewise dropped from 87mg/dl to 41mg/dl; HDL increased to 63mg/dl; and triglycerides went down to 54mg/dl. (see Table No. 3)

Test Date: 6-19-2006								
		Normal	Inter-mediate	At Risk	Last Visit	Alert Value	ATP III Goal	Reference Range
NCEP ATP III Lipid Tests	Total Cholesterol (mg/dL)	115			156	>=200	<200	129 - 221
	LDL-C (mg/dL)	41			87	>=100	<100	59 - 145
	HDL-C (mg/dL)	63			40	<40	>=40	32 - 60
	Triglycerides (mg/dL)	54			145	>=150	<150	63 - 268
		Normal	Inter-mediate	At Risk	Last Visit	Alert Value	BHL Goal	Reference Range
Advanced Cardiovascular Risk Markers	IIIa+b (%)			22.70	41.20	>=20	<=15	13.6 - 43.0*
	LDL Ivb (%)	1.8			3.2	>=10	<=5	1.7 - 9.8*
	HDL2b (%)		20		5	<10	>20	7 - 30*

**Table No. 3**

Interestingly, his LDL particle size changed from pattern B to pattern A and his LDL IIIa+IIIb and LDL Ivb levels or percentage dropped significantly from 44% to 24%. This significant change in the patient’s lipid profile confirms the effectivity of the current treatment.

### ***Follow-up #3***

Patient came back on October 20, 2006 for a follow-up visit. He had another heart scan done which showed a calcium score of 2007.2. Although his calcium volume had increased by about 3%, his calcium score practically remained the same. (*see Table No. 4*)

<b>Vessel</b>	<b>Number of Lesions</b>	<b>Mean Density</b>	<b>Volume Score</b>	<b>Agatston Calcium Score</b>
Left Main	0	0	0	0
LAD	8	249.2	229.0	274.8
LCX	4	192.5	34.9	24.6
RCA	25	274.0	1346.0	1707.7
<b>Total Coronary Plaque Burden</b>	<b>37</b>	<b>268.7</b>	<b>1609.8</b>	<b>2007.2</b>

*Table No. 4*

### ***Discussion***

Here is a patient who was at 96<sup>th</sup> percentile for calcium scoring for his age with a calcium score of over 2000. He was managed with aggressive lifestyle modification through diet and exercise and medical therapy. Nine months later, he had no progression of calcification in his coronary arteries. If you were to look at natural progression of calcification as per different studies, it can progress anywhere from 35% to 50% annually. In that scenario, his calcium score should have gone up 2500 to 3000 in the last nine months. This is an example of one patient who went on an aggressive low-calorie diet, lost weight and increased the HDL to 63mg/dl and dropped his LDL to 41mg/dl with a significant change in particle size, was able to halt the progression of atherosclerosis.

The major key to this attenuation of coronary calcification is lipid modification. The annual progression of coronary artery calcification (CAC) can be reduced from 25 to 30% to 0 to 6% with LDL cholesterol reduction. At treated LDL cholesterol levels somewhere below 100mg/dl, several sources of data suggest that the anatomic burden of CAD, including CAC, regresses. Additional supportive studies indicate that carotid intimal medial thickness and the volume of coronary atheroma can also be reduced by LDL cholesterol reduction in concert with elevation of HDL cholesterol.<sup>7</sup>

The ASTEROID investigation by Dr. Nissen<sup>8</sup> was the first IVUS efficacy trial to show unequivocal evidence of disease regression in atherosclerosis. The reductions in LDL levels achieved in their study were so far the lowest values ever observed in a statin/atherosclerosis progression trial and the magnitude of the elevation in HDL levels also surpassed that seen in previous statin trials. LDL was reduced from 130.4 mg/dL at baseline to 60.8 mg/dL by the end of the study, a mean reduction of 53.2% ( $p < 0.001$ ). HDL was increased from 43.1 mg/dL at baseline to 49.0 mg/dL by the end of the study, a mean increase of 14.7% ( $p < 0.001$ ). ASTEROID provides us with further scientific evidence to support the concept that lower LDL levels and higher HDL levels can cease and regress the progression of coronary disease.

If we would compare the result of ASTEROID data to the lipid profile achieved by the patient, we can see clearly that the patient had a lower LDL and a higher HDL. More than that, the patient had an HDL level more than LDL level, something that has never been achieved before. We can very well say at this point that this patient is on its way to regressing atherosclerosis.

Another thing to ponder is in relation to the process of calcification. Atherosclerotic calcification is an organized, regulated process in which calcium is deposited over arterial plaque, usually a soft plaque. The so-called 'hardening of the arteries' happens when soft plaques become hard plaques due to calcification. It is a natural process and course of progression of the disease. If a patient is burdened by soft plaques in his coronary arteries, coronary artery calcification is bound to happen and this would result in an increase in coronary calcium score. ***If we have already shown that CAD can be reversed and calcium scoring can be halted, could it be that what we have actually achieved is shrinking the soft plaques? If soft plaques are eliminated then calcification cannot proceed. If progression of coronary artery calcification can be halted, does that mean that soft plaque can stabilize and shrink in less than 4 weeks? If so, by achieving HDL more than LDL in less than 4 weeks, can the coronary events due to plaque rupture be dropped to zero? Maybe the goal for secondary prevention in the future and for primary prevention in patients with very strong family history, patients with multiple risk factors including diabetes, patients with a large soft plaque by CT-angiogram, and high calcium score of more than 400 is to have an HDL more than LDL.*** Although there has been no evidence to support this idea, it can be a challenge to the medical community to find answers to these queries through utilization of new strategies in cholesterol therapy and new technologies in imaging coronary artery disease.

**References:**

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