Coronary Artery Calcium Improves Risk Assessment in Adults with a Family History of Premature Coronary Heart Disease: Results from MESA

Supplementary Document

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Patel et al: Subclinical CAD and Family History of CHD.

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Supplemental Table 1: Crude event rates (per 1000 person-years) according to race/ethnic group stratified by a family history of premature CHD status.

	Hard ASCVD			Hard CHD		
	Negative FH	Positive FH	p-value	Negative FH	Positive FH	p-value
White	6.99	7.12	0.91	4.20	5.18	0.34
Chinese	3.44	5.62	0.49	2.38	2.81	0.79
Black	4.86	9.80	0.002	3.14	5.35	0.06
Hispanic	7.02	10.85	0.06	4.47	6.87	0.13

FH – family history of premature coronary heart disease
CHD – coronary heart disease
ASCVD – atherosclerotic cardiovascular disease

Supplemental Table 2: Hard ASCVD Events and Cox proportional hazards regression examining relation of hard ASCVD events with CAC and CIMT, stratified by FH of premature CHD.

	Cox Proportional Hazard Ratios		Number of Hard ASCVD Events	
	Negative FH (n= 4,863)	Positive FH (n= 1,262)	Negative FH (n=278)	Positive FH (n=104)
CAC 0	1 (ref)	1 (ref)	60	25
CAC 1-99	1.74 (1.21-2.50)	1.64 (0.94-2.87)	72	30
CAC 100-399	2.77 (1.90-4.05)	2.45 (1.31-4.58)	76	24
CAC ≥400	3.22 (2.15-4.84)	2.80 (1.44-5.43)	70	25
p-value for interaction	0.28			
ln (CAC+1)	1.19 (1.13-1.26)	1.17 (1.07-1.29)		
p-value for interaction	0.28			
CIMT 1st Quartile	1 (ref)	1 (ref)	30	15
CIMT 2nd Quartile	1.35 (0.86-2.10)	0.80 (0.41-1.59)	59	22
CIMT 3rd Quartile	1.12 (0.72-1.77)	1.08 (0.56-2.06)	69	29
CIMT 4th Quartile	1.45 (0.93-2.26)	0.93 (0.48-1.82)	120	38
p-value for interaction	0.29			
Continuous CIMT	1.53 (0.82-2.87)	0.89 (0.32-2.49)		
p-value for interaction	0.21			

Adjusted for age, gender, race, MESA site, cigarette smoking, hypertension, diabetes, BMI, LDL-C, HDL-C, cholesterol lowering medications. Continuous CAC units are log-transformed Agatston Units, continuous CIMT units are per millimeter change in thickness.

ASCVD – atherosclerotic cardiovascular disease
FH – family history of premature coronary heart disease
CHD – coronary heart disease
CAC – coronary artery calcium
CIMT – carotid intima-media thickness
BMI – body mass index
LDL-C – low density lipoprotein-cholesterol
HDL-C - high density lipoprotein-cholesterol

Supplemental Table 3: Hard CHD Events and Cox proportional hazards regression examining relation of hard CHD events with CAC and CIMT, stratified by FH of premature CHD.

	Cox Proportional Hazard Ratios		Number of Hard CHD Events	
	Negative FH (n= 4,863)	Positive FH (n= 1,262)	Negative FH (n=176)	Positive FH (n=67)
CAC 0	1 (ref)	1 (ref)	30	13
CAC 1-99	2.35 (1.46-3.78)	1.93 (0.91-4.10)	47	18
CAC 100-399	3.54 (2.14-5.85)	3.52 (1.58-7.84)	48	18
CAC ≥400	4.87 (2.88-8.24)	3.85 (1.65-9.02)	51	18
p-value for interaction	0.49			
ln (CAC+1)	1.25 (1.17-1.35)	1.22 (1.09-1.37)		
p-value for interaction	0.39			
CIMT 1st Quartile	1 (ref)	1 (ref)	21	8
CIMT 2nd Quartile	1.35 (0.79-2.31)	1.23 (0.51-2.93)	41	17
CIMT 3rd Quartile	0.82 (0.46-1.45)	1.11 (0.46-2.70)	34	16
CIMT 4th Quartile	1.32 (0.77-2.26)	1.28 (0.53-3.11)	80	26
p-value for interaction	0.67			
Continuous CIMT	1.31 (0.59-2.91)	1.20 (0.35-4.13)		
p-value for interaction	0.60			

Adjusted for age, gender, race, MESA site, cigarette smoking, hypertension, diabetes, BMI, LDL-C, HDL-C, cholesterol lowering medications. Continuous CAC units are log-transformed Agatston Units, continuous CIMT units are per millimeter change in thickness.

CHD – coronary heart disease
CAC – coronary artery calcium
CIMT – carotid intima-media thickness
FH – family history of premature coronary heart disease
BMI – body mass index
LDL-C – low density lipoprotein-cholesterol
HDL-C - high density lipoprotein-cholesterol

Supplemental Table 4: Cox proportional hazards regression examining relation of hard ASCVD events with CAC and CIMT, stratified by any family history of CHD (assessed at visit 1).

	No FH of CHD (n= 2,586)	Any FH of CHD (n =2,761)
CAC 0	1 (ref group)	1 (ref group)
CAC 1-99	1.65 (1.10-2.46)	1.83 (1.20-2.79)
CAC 100-399	2.33 (1.49-3.63)	2.92 (1.86-4.57)
CAC ≥400	2.85 (1.75-4.6)	3.59 (2.23-5.76)
p-value for interaction	0.93	
CIMT 1st Q	1 (ref group)	1 (ref group)
CIMT 2nd Q	1.10 (0.64- 1.90)	1.13 (0.70-1.81)
CIMT 3rd Q	1.28 (0.76-2.16)	1.05 (0.65-1.70)
CIMT 4th Q	1.42 (0.84-2.39)	1.09 (0.67-1.76)
p-value for interaction	0.10	

Adjusted for age, gender, race, MESA site, cigarette-smoking, hypertension, diabetes, BMI, LDL-C, HDL-C, cholesterol lowering medications.

ASCVD – atherosclerotic cardiovascular disease
CAC – coronary artery calcium
CIMT – carotid intima-media thickness
CHD – coronary heart disease
FH – any family history of coronary heart disease
BMI – body mass index
LDL-C – low density lipoprotein-cholesterol
HDL-C - high density lipoprotein-cholesterol

Supplemental Table 5: Cox proportional hazards regression examining relation of hard CHD events with CAC and CIMT, stratified by any family history of CHD (assessed at visit 1).

	No FH of CHD (n= 3,620)	Any FH of CHD (n = 2,686)
CAC 0	1 (ref group)	1 (ref group)
CAC 1-99	2.16 (1.24-3.78)	2.30 (1.30-4.06)
CAC 100-399	3.19 (1.74-5.86)	4.10 (2.28-7.37)
CAC ≥400	4.63 (2.43-8.81)	5.31 (2.86-9.85)
p-value for interaction	0.86	
CIMT 1st Q	1 (ref group)	1 (ref group)
CIMT 2nd Q	1.26 (0.63-2.52)	1.32 (0.73-2.38)
CIMT 3rd Q	0.98 (0.49-1.98)	1.08 (0.59-1.99
CIMT 4th Q	1.48 (0.75-2.93)	1.15 (0.62-2.11)
p-value for interaction	0.19	

Adjusted for age, gender, race, MESA site, cigarette-smoking, hypertension, diabetes, BMI, LDL-C, HDL-C, cholesterol lowering medications.

CHD – coronary heart disease
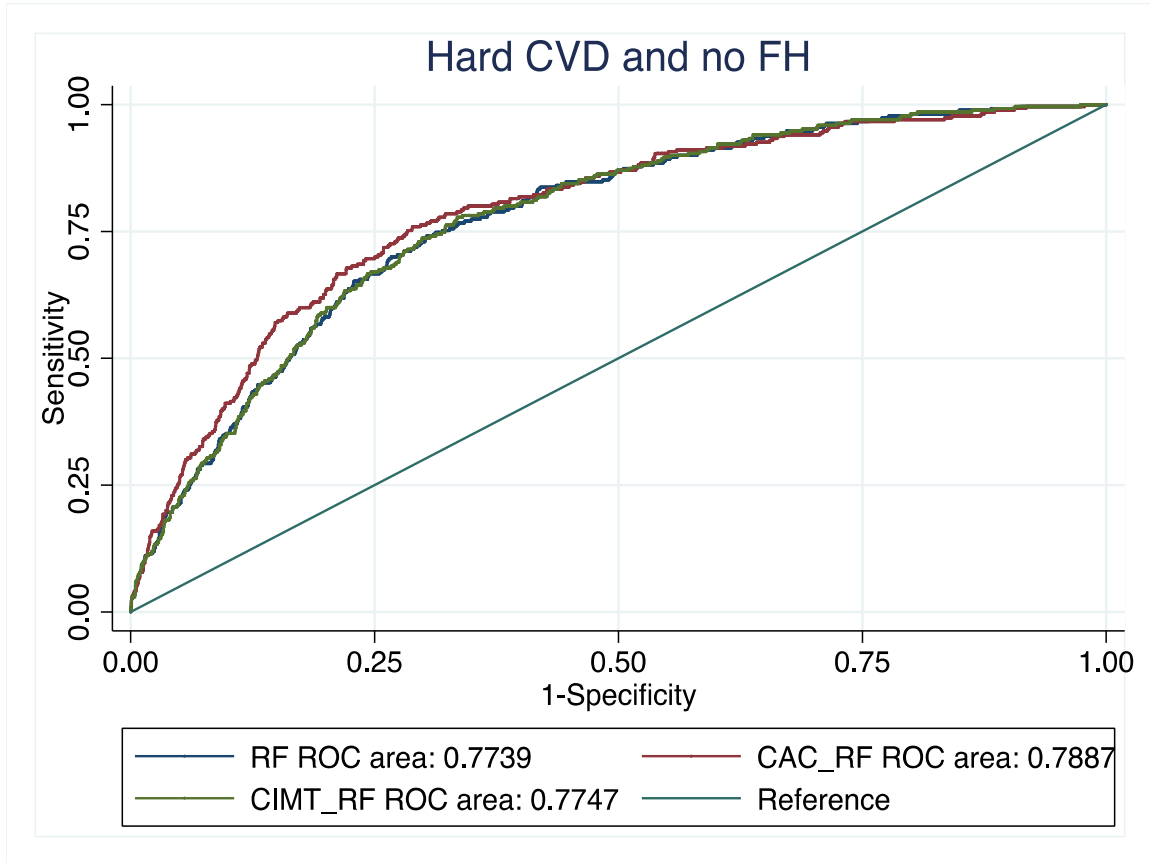CAC – coronary artery calcium
CIMT – carotid intima-media thickness
FH – any family history of coronary heart disease
BMI – body mass index
LDL-C – low density lipoprotein-cholesterol
HDL-C - high density lipoprotein-cholesterol

Supplemental Figure 1a: Receiver operating characteristic curves showing area under the curve for incident hard ASCVD among those without a family history of premature CHD*.

ASCVD – atherosclerotic cardiovascular disease
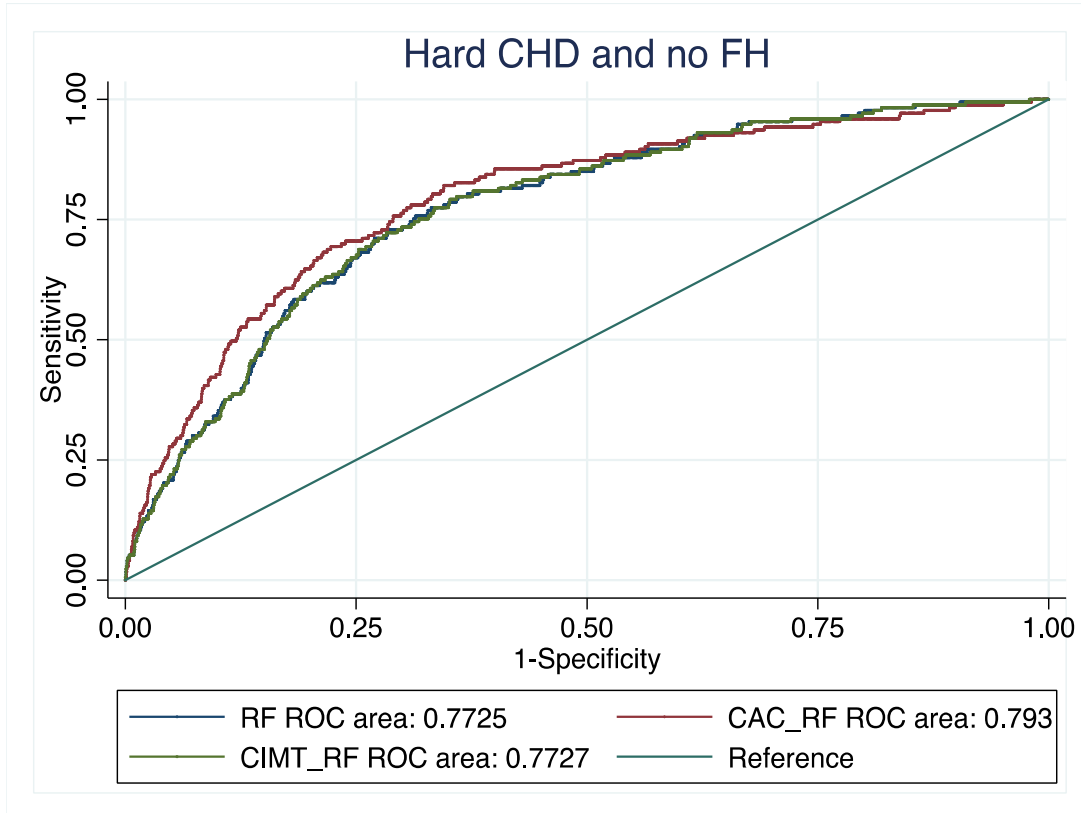FH – family history of premature coronary heart disease
CAC – coronary artery calcium
CIMT – carotid intima-media thickness
*CIMT and CAC were modelled continuously

Supplemental Figure 1b: Receiver operating characteristic curves showing area under the curve for incident hard CHD among those without a family history of premature CHD*.

CHD – coronary heart disease
FH – family history of premature coronary heart disease
CAC – coronary artery calcium
CIMT – carotid intima-media thickness
*CIMT and CAC were modelled continuously