Published in final edited form as:

Am Heart J. 2009 June ; 157(6): 1001–1009. doi:10.1016/j.ahj.2009.03.018.

Evaluation of coronary artery calcium screening strategies focused on risk categories: The Dallas Heart Study

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Abstract

Background—A strategy using coronary artery calcium (CAC) screening to refine coronary heart disease risk assessment in moderately high risk (MHR) subjects (10-year risk 10%–20%) has been suggested. The potential impact of this strategy is unknown.

Methods—Coronary artery calcium screening strategies focused on MHR subjects were modeled in 2,610 subjects aged 30 to 65 years undergoing Framingham risk scoring and CAC assessment in the Dallas Heart Study. The proportions of subjects eligible for imaging and reclassified from MHR to high risk (HR) (10-year risk >20%) based upon CAC scores were determined.

Results—Only 1.0% of women and 15.4% of men were at MHR by Framingham risk scoring and thus eligible for imaging, and <0.1% and 1.1% respectively, changed from MHR to HR using a CAC threshold ≥ 400 . Coronary artery calcium imaging targeting MHR subjects was also relatively inefficient (>100 women, 14.3 men scanned per subject reclassified). Restricting to an older age range (45–65 years) or expanding the MHR group to 6% to 20% risk had virtually no impact on risk assessment in women. In a secondary analysis, a proposed imaging strategy targeting promotion of subjects from lower risk to MHR was more efficient and had greater yield than current recommendations targeting promotion from MHR to HR.

Conclusions—Coronary artery calcium screening strategies focused on MHR subjects will have a negligible impact on risk assessment in women and a modest impact in men. Further studies are needed to optimize the use of CAC screening as an adjunct to coronary heart disease risk assessment, especially for women and those at seemingly lower risk.

Measurement of coronary artery calcification (CAC) provides a noninvasive assessment of coronary atherosclerotic burden.¹ Higher CAC scores are independently associated with coronary heart disease (CHD) events and incrementally improve estimations of CHD risk when used in conjunction with traditional risk assessment protocols.^{2–5} As a result, screening for CAC with computed tomography is now recognized by several professional organizations as a potential adjunct to traditional CHD risk assessment strategies in select individuals.^{1,6–8}

Current recommendations^{7,8} target the use of CAC screening to individuals deemed to be at moderately high (also referred to as “intermediate”) CHD risk, with a 10-year CHD risk estimate of 10% to 20% by the Framingham risk score (FRS).^{6,9} Subjects identified with high-risk CAC scores can be reclassified and promoted to high-risk status, with accompanying changes in low-density lipoprotein treatment goals.^{6–8} The rationale for restricting screening to the moderately high risk (MHR) group is based upon Bayesian probability theory: posttest risks are more significantly influenced by test results among subjects whose pretest risks are intermediate, rather than low or high. However, although theoretically sound, the utility and efficiency of this strategy when applied on a population basis remain unclear.

Given the uncertain implications of this strategy, we evaluated the impact of applying CAC screening in MHR subjects in the Dallas Heart Study (DHS), a large probability-based population sample.

Methods

Study population

The Dallas Heart Study is a single-site, multiethnic, probability-based population study. Complete details of the DHS design have been described elsewhere.¹⁰ Briefly, 6,101 subjects aged 18 to 65 years were recruited from 2000 to 2002 in Dallas County and completed 3 sequential visits: visit 1—in-home survey and anthropometric measurements (n = 6,101); visit 2—blood and urine samples (n = 3,399, aged 30–65 years); visit 3—imaging tests (n = 3,072). Demographic variables, body mass index, and blood pressure were similar between subjects completing the initial visit, and visits 2 and 3.¹⁰ The present study is limited to 2,610 subjects aged 30–65 years who had clinical data and fasting blood samples to estimate 10-year CHD risks using a modified FRS⁶ and electron-beam computed tomography scans for CAC assessment. All subjects provided prospective written informed consent to participate in the research protocol, which was approved by the University of Texas Southwestern Medical Center institutional review board.

Study definitions

The details of blood pressure and plasma lipid measurements and the definition of diabetes have previously been reported.¹¹ Assays for high-sensitivity C-reactive protein levels have been previously described.¹²

The cohort was stratified according to estimated 10-year CHD risks based on the National Cholesterol Education Program (NCEP) modified version of the FRS devised by Wilson et al.^{6,9} For statin users (n = 156 or 5.7%), measured total cholesterol was adjusted to reflect a 30% lowering from baseline levels based on average treatment effects observed in the Heart Protection Study.^{13,14} Sensitivity analyses were performed without this adjustment and by excluding statin users. As per the modified NCEP-Adult Treatment Panel III guideline, subjects with diabetes mellitus, self-reported history of myocardial infarction/stroke, or FRS estimated 10-year CHD risk >20% were defined as the high-risk subset.⁶ The MHR group was defined by FRS 10-year CHD risk estimate of 10% to 20% and the lower risk (LR) group by <10%.

Coronary artery calcium

Two consecutive electron-beam computed tomography scans were performed for measurement of CAC using a Imatron C-150XP scanner (GE Healthcare, Chalfont St. Giles, UK), as has been previously described.¹¹ CAC severity was quantified using Agatston units, and the mean of 2 consecutive scans was used as the final Agatston score.

Statistical analysis

The proportions of subjects aged 30 to 65 years in the LR, MHR, and high-risk groups were determined. Next, the proportion of subjects at MHR who would be reclassified and promoted to high-risk status based on high-risk CAC scores (≥ 400 Agatston units)^{2,4,6,7} was evaluated. This analysis was repeated with a more expansive pool of imaging candidates (FRS 10-year risk 6%–20%).⁷ The effects of using CAC thresholds ≥ 100 ,¹ ≥ 75 th percentile for age and sex (calculated in 5-year increments),⁷ and screening an older cohort (aged 45–65 years) were also evaluated. These analyses were also repeated among subjects with FRS 10-year risk of 10% to 20% plus ≥ 2 traditional CHD risk factors, to determine whether requiring ≥ 2 risk factors, per the NCEP definition of MHR, altered the findings.⁶

The impact of 2 alternative CAC screening strategies was then assessed: (1) bidirectional reclassification strategy and (2) select LR strategy. For the bidirectional strategy, reclassification was defined as follows: (a) upward—LR with CAC ≥ 100 and MHR with CAC ≥ 400 ; (b) downward—high risk with CAC < 400 and MHR with CAC < 100 . For the LR strategy, subjects categorized as LR by FRS with CAC ≥ 100 were defined as misclassifications. Various eligibility criteria for CAC scanning were evaluated for efficiency assessed by minimizing the number needed to scan (NNS) to identify one misclassified subject and maximizing the percentage of misclassified subjects identified. The most efficient eligibility criteria were used to develop a potential CAC screening strategy for LR subjects.

The efficiency of these CAC screening strategies was evaluated also using the NNS approach,¹⁴ as well as by determining the proportion of all subjects in the cohort with underestimated risk detected by each strategy. The NNS for the LR strategy was confirmed using resampling techniques involving 500 cross-validations.

All analyses were stratified by sex, sample-weight adjusted, and performed using SAS software version 9.1 (SAS Institute, Cary, NC). Sampling weights, formulated based upon a subject's initial selection probability and then rescaled to adjust for attrition between visits, were used to estimate population frequencies in Dallas County.¹⁰ All proportions presented are sample weight adjusted, whereas all numerical values are unadjusted. The Dallas Heart Study was funded by the Donald W. Reynolds Foundation (Las Vegas, NE) and was partially supported by USPHS GCRC grant #M01-RR00633 from NIH/NCRR-CR. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Results

Baseline characteristics stratified by sex are presented in Table I. The distribution of FRS-determined risk categories for subjects aged 30 to 65 years is presented in Figure 1. One percent ($n = 19$) of women and 15.4% ($n = 179$) of men were at MHR and would thus be eligible for CAC screening according to present recommendations. Defining the MHR group by FRS-estimated 10-year risk of 10% to 20%, $< 0.1\%$ of women ($n = 1$) and only 1.1% of all men ($n = 13$) would be reclassified to the high-risk group based on the presence of CAC ≥ 400 (Table II). Expanding the pool of imaging candidates to include subjects with FRS 10-year risk of 6% to 20%⁷ had minimal effect on the proportion of women eligible for imaging (3.4%) and had no effect on the proportion promoted to the high-risk category ($< 0.1\%$). In men, using this expanded group greatly increased the proportion eligible for imaging (27.0%), but had negligible effect on those reclassified to high risk (1.8%). The above results were not significantly altered by including the ≥ 2 traditional CHD risk factor criteria as part of the NCEP definition for MHR. Furthermore, sensitivity analyses adjusting the

effect of statin treatment on total cholesterol and excluding statin users did not significantly alter the results (data not shown).

Table II displays the impact of varying the CAC imaging strategy by (a) restricting the cohort eligible for imaging to subjects aged 45 to 65 years and (b) using different CAC thresholds for risk category promotion.^{1,7} Restricting to an older age range only increased the proportion of women eligible for imaging to 2.1%, but had no impact on the proportion promoted to the high-risk group. Using an alternate CAC threshold of ≥ 100 or ≥ 75 th percentile for age/sex did not appreciably change the small proportion of women that would change risk categories ($<1\%$). On the other hand, in men, there was a small increase in the proportion of men promoted to the high-risk group when screening was restricted to the older age range (from 1.1% to 2.5%); however, this was accompanied by a large increase in the proportion of men eligible for imaging, from 15.4% to 29.8%. A greater proportion of men changed risk categories using a CAC threshold of ≥ 100 or ≥ 75 th percentile for age/sex compared to ≥ 400 , particularly among the older age group.

Table III demonstrates the efficiency of a CAC screening strategy targeting the MHR group. With a CAC threshold of ≥ 400 for reclassification of risk, >100 women (aged 30–65 years) would need to be scanned to detect one subject whose risk category would change and $>99\%$ of women with underestimated risk would remain undetected. In men, 14.3 subjects would need to be scanned to identify one informative subject and almost three quarters of all LR and MHR men with underestimated risk would fail to be detected. Whereas altering the age range of the cohort had little effect on the efficiency of CAC screening, using a CAC threshold of ≥ 100 greatly improved the efficiency of CAC scanning for both sexes. However, only a small proportion of those in the LR or MHR groups with CAC above this score would be detected in women and still just over half of such men. The efficiency of scanning was maximized using the threshold of ≥ 75 th percentile for age/sex, but resulted in further reductions in the proportion of LR and MHR subjects with underestimated risk that were detected.

The impact of using a bidirectional reclassification strategy for CAC scanning is demonstrated in Figure 2. When applied to the entire population aged 30 to 65 years, 27.5% of men and 12.5% of women would be reclassified, with the majority of these being downward reclassifications (23.2% and 9.6% of each sex, respectively). The NNS to identify one subject for reclassification was 3.6 in men and 8.0 in women overall, and 1.2 and 1.6 when restricting to just the MHR and high-risk subgroups.

In women aged 30 to 65 years, 72.3% of those with CAC scores of 100 to 399 and 23.6% of those with CAC ≥ 400 were in the LR group, representing 2.6% and 0.3% of the overall female population, respectively. In men, 29.9% and 26.9% of those with CAC scores 100 to 399 and ≥ 400 , respectively, were found in the LR group, representing 2.4% and 0.8% of the male population. Thus, to develop an alternate strategy of CAC scanning in select LR subjects, the prevalence of CAC within 5-year age bins of LR subjects was evaluated (Figure 3). Less than 0.1% of men aged <40 years and women aged <45 had CAC ≥ 100 , meaning scanning such individuals would have little yield. On the other hand, more than one half of all CAC values ≥ 100 were found in men aged ≥ 50 years or women ≥ 60 years, resulting in an NNS of 5.7 and 4.1 in these older age groups, respectively.

The efficiency of various other eligibility criteria to target CAC screening to select LR subjects is presented in Table IV. The only eligibility criteria that reduced the NNS to <10 were FRS 10-year risk 6% to 9% among men and 3% to 9% among women, and only age and FRS adequately discriminated subjects with CAC ≥ 100 (c statistics 0.8), whereas all other risk factors did not (c statistics ≤ 0.6).

With the use of the most efficient eligibility criteria of age and FRS, a simple CAC screening strategy for LR subjects was developed (Figure 4). Based upon this strategy, 15.0% of all men and 12.7% of all women aged 30 to 65 years would be eligible for CAC screening. The cross-validated estimates of the NNS to identify one subject with CAC ≥ 100 were 6.8 for men (95% CI 4.6–13.3) and 5.2 for women (95% CI 3.4–11.4), and 51.1% of men and 84.2% of women with underestimated risk from the whole cohort would have been detected using this strategy (Table V). Applying this same LR screening strategy to detect subjects with CAC ≥ 75 th percentile for age/sex improved the efficiency but slightly reduced the overall yield of CAC screening.

Discussion

Our study has 4 principal findings. First, the MHR group, defined by an FRS estimated 10-year CHD risk of 10% to 20%, represents a very small proportion of women. Second, a CAC screening strategy focused on the MHR group had virtually no impact on risk assessment in women and only a minor impact in men. Third, altering the pool of imaging candidates by increasing age cut-offs or using a lower CAC threshold (≥ 100) for risk category promotion had essentially no impact on risk assessment in women. In men, these changes individually had a modest impact on the proportion of men promoted to the high-risk group; however, increasing the age cut-off significantly increased the pool of imaging candidates. Fourth, a meaningful percentage of women and men at LR by FRS have at least MHR CAC and are thus potentially misclassified in the LR group. In an exploratory analysis, an imaging strategy solely targeted toward promoting subjects from the LR to MHR was more efficient and had greater yield in detecting clinically relevant coronary calcium than current imaging recommendations targeting promotion from MHR to high-risk status. Thus, we conclude that applying CAC screening to the subgroup classified as MHR would have only a minimal effect on risk stratification in the population and would fail to detect a relevant number of seemingly LR women and men with significant atherosclerosis and underestimated risk.

Moderately high risk women

One of the most meaningful observations in our study is the much smaller percentage of women (1.0%) than men (15.4%) aged 30 to 65 years in Dallas County presently characterized as moderately high or intermediate risk. Even after excluding women aged <45 , still only 2.1% of women were characterized as MHR. Despite differences in the absolute proportion of women categorized as MHR because of differing age ranges, both the National Health and Nutrition Examination Survey and MESA studies reported similar findings that only a small proportion of women are characterized as MHR in the population.¹⁵ As a result, novel risk stratification tools aimed at the MHR group in women are unlikely to significantly improve the current inadequacies of traditional risk assessment strategies in this group.¹⁶ Given these problems in risk assessment as well as unfavorable trends in cardiovascular disease mortality in women,¹⁷ new strategies are needed to more effectively apply emerging risk stratification tools in women.

Coronary artery calcium screening in MHR subjects

Several major organizations consider the use of CAC scanning to refine risk assessment in MHR subjects with FRS 10-year risk of 10% to 20% as a reasonable strategy.^{1,6–8} However, no prior studies have examined the ramifications of this imaging strategy by correlating the proportion of women and men belonging to this group with CAC scanning data. Given the small number of MHR women as well as their low prevalence of clinically relevant elevated CAC scores, implementation of this strategy would have effectively no impact in women aged 30 to 65 years. Moreover, despite the substantially larger size of the

MHR group in men, this strategy would have only a modest effect on risk reclassification in men and would also be relatively inefficient.

An alternate CAC screening strategy that has been proposed is to expand the pool of imaging candidates to include subjects with FRS 10-year risk of 6% to 20%.⁷ In our study, increasing the imaging pool to include these subjects minimally increased the proportion eligible for imaging from 1.0% to 3.4% in women and had virtually no impact in the proportion of women reclassified to high-risk status (<0.1%). Using this strategy in men significantly increased the eligible cohort of men from 15.4% to 27.0%; however, relative to this large increase in men eligible for imaging, only a small increase was observed in the proportion of men reclassified to high-risk status (from 1.1% to 1.8%), which raises important questions regarding the efficiency of this strategy.

It is plausible that the inclusion of younger subjects in our study may have skewed our results by (1) expanding the size of the LR group and diminishing the proportion of subjects at MHR and thus eligible for imaging, and (2) lowering the prevalence of elevated CAC scores. However, even after restricting our cohort to an older age range (aged 45–65 years), the proportion of women eligible for imaging remained so low that an imaging strategy focused on the MHR group still had a negligible effect on risk classification. Among men, the older age range restriction resulted in a substantial increase in the proportion eligible for imaging (almost 30% of the population), but only a small increase in the proportion promoted to the high-risk group, once again raising concerns about the efficiency of this strategy. Although the DHS did not include subjects >65 years of age who would have higher calcium scores, cardiovascular risk assessment strategies that are only applicable in older segments of the population will not maximize the yield of preventive interventions.

Calcium threshold for high cardiovascular risk

The appropriate CAC threshold that corresponds to high CHD risk and warrants upward risk reclassification of FRS risk categories remains controversial. A scientific statement published in 2006 by the American Heart Association recommended that a CAC score >100 should be equated with high risk for CHD events (>20% 10-year risk).¹ However, a subsequent expert consensus document from the American College of Cardiology/American Heart Association in 2007 reviewed recent data on CAC imaging as an adjunct to FRS assessment and stated that “intermediate-risk FRS patients with CAC scores ≥ 400 would be expected to have event rates that place them in CHD risk equivalent status ($\geq 20\%$ risk over 10 years).”⁷ This secondary analysis from 4 published studies as well as findings from other studies^{2,4} confirms that CAC thresholds of >400 (or >300) were accompanied by an extrapolated 10-year CHD event rate of >20%, whereas lower thresholds were not.

Although a CAC threshold of ≥ 400 appears more appropriate for risk reclassification of MHR subjects, we also evaluated a CAC threshold of ≥ 100 and CAC ≥ 75 th percentile for age/sex.⁷ Using these lower thresholds greatly improved the efficiency of CAC scanning, but still had a negligible impact on risk reclassification in women. In contrast, they did have a more meaningful impact in men, particularly in the older age group. The improved efficiency resulted from a larger proportion of MHR subjects with CAC scores ≥ 100 and ≥ 75 th percentile for age/sex, but a significant proportion of LR subjects also had CAC scores higher than these levels. Thus, a sizeable percentage of LR or MHR women (88%) and men (49%) with CAC ≥ 100 would still fail to be detected by current imaging strategies, and an even greater proportion using CAC ≥ 75 th percentile age/sex (92% and 71%, respectively).

Bidirectional reclassification

While present CAC imaging recommendations focus on upwards reclassification of risk based upon high CAC scores, bidirectional reclassification may improve the utility of CAC scanning. Indeed, using such a strategy in the current study greatly improved the efficiency of CAC scanning and resulted in a large proportion of the population that would undergo risk reclassification (10%–30%). However, the majority of reclassifications using this strategy were in the downwards direction, as has been reported in one previous study.¹⁸ Although a bidirectional reclassification strategy of CAC scanning warrants further evaluation, there is currently no consensus as to what CAC values merit downgrading risk in MHR and high-risk subjects and there are no prospective studies with outcomes data reporting the impact of such a strategy.

Potentially underestimated risk in the LR group

An imaging strategy focused on the MHR group is appropriately based upon Bayesian probability theory, which supports the use of screening in intermediate-risk populations. In this case, however, based upon the small size of the MHR group in women and the significant number of seemingly LR subjects with at least MHR CAC scans observed in our study, pretest risk assessments using FRS alone may inadequately characterize the MHR group as the intermediate-risk population.

There are an important number of seemingly LR subjects (FRS 10-year risk <10%) whose risks are likely underestimated based upon disproportionately high CAC scores.¹⁹ Coronary artery calcium scores of 100 to 399 may not be informative in subjects already classified in the MHR group by FRS, but they can reasonably serve as the basis for promoting subjects from the LR group to MHR based upon several studies demonstrating a 10-year risk of CHD events of 10% to 20% with this level of CAC.^{2–4} Indeed, a recent report from the MESA study confirmed the predictive value of CAC scanning in women considered LR by FRS.²⁰

Reclassification of risk among LR subjects is likely to have greater clinical ramifications than reclassification among MHR individuals, because LR subjects are presently ineligible for more intensive primary prevention strategies, such as the use of statins with aggressive low-density lipoprotein cholesterol goals (<100 mg/dL) and the use of aspirin, which are already options for moderately high and high-risk subjects.^{6,21} As such, CAC scanning among seemingly LR individuals by FRS estimation may be a particularly valuable option. However, given the large size of the LR population, screening for CAC in this entire group is clearly not feasible and not advocated. In an exploratory analysis, we demonstrated that simple eligibility criteria based upon age and FRS may identify a subgroup in which CAC scanning can be efficiently applied. In fact, a CAC screening strategy for LR subjects based upon these criteria was much more efficient than presently recommended strategies focusing on MHR subjects and identified the vast majority of subjects in the entire population with underestimated risks. Although these findings were robust to cross-validation, they require confirmation in additional cohorts.

Limitations

Although the multiethnic, population-based design of our study enhances the generalizability of these findings, the study also has many important limitations. First of all, the cross-sectional nature of the study did not permit us to correlate CAC thresholds and risk reclassification with clinical outcomes. In addition, the younger age of our cohort results in a lower prevalence of CAC, and the restricted analyses of those aged 45 to 65 years do not address the impact of CAC imaging in even older populations (>65 years).

Conclusions

Our study demonstrates that CAC screening strategies focused on a MHR population are unlikely to fully realize the potential of imaging in CHD risk assessment. Very few women aged 30 to 65 years (or 45–65 years) are presently stratified into the MHR group, making a screening strategy directed to this group virtually ineffective. Despite a substantially larger MHR group in men, screening for CAC in this group is inefficient and would only have a modest impact on risk assessment. In addition, a meaningful number of both women and men with significant atherosclerosis remain undetected and likely misclassified in the LR group, providing an opportunity for further studies in optimizing the use of CAC scanning for CHD risk assessment.

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Figure 1.
Distribution of Framingham risk categories.

Figure 2.

Distribution of Framingham risk categories after screening for CAC using a bidirectional reclassification strategy. Part **A**, Women; Part **B**, men. Upwards reclassification occurred for low-risk subjects with $CAC \geq 100$ or MHR subjects with $CAC \geq 400$. Downwards reclassification occurred for high-risk subjects with $CAC < 400$ or MHR subjects with $CAC < 100$.

Figure 3. Coronary artery calcium prevalence by age categories in LR subjects. Part **A**, Women; Part **B**, Men. *Number needed to scan to identify one subject with CAC ≥ 100 in each respective age category.

Figure 4.
Coronary artery calcium screening strategy for select LR subjects.

Table I

Baseline characteristics stratified by sex

	Women (n = 1,449)	Men (n = 1,161)
Age, y *	44.7 (0.4)	43.6 (0.4)
Black race, %	19.3	15.8
Systolic blood pressure, mm Hg *	117.8 (0.6)	124.1 (0.6)
Total Cholesterol, mg/dL *	186.9 (1.7)	188.8 (1.8)
Low-density lipoprotein cholesterol, mg/dL *	109.4 (1.5)	116.1 (1.6)
High-density lipoprotein cholesterol, mg/dL *	53.4 (0.6)	43.3 (0.4)
Tobacco use, %	19.8	28.7
Diabetes, %	7.3	8.2
History of myocardial infarction, %	1.3	1.4
History of stroke, %	1.6	1.2
Hypertensive therapy, %	13.5	11.5
Statin therapy, %	6.7	4.7

* Represents mean (SEM).

Table II

Impact of varying calcium thresholds and age range

	CAC threshold	Proportion eligible for imaging	Proportion promoted to high-risk category
<i>Part A: Women</i>			
Aged 30–65 y (n = 1,449)	≥400	1.0%	< 0.1%
	≥100	1.0%	0.4%
	≥75th percentile age/sex	1.0%	0.6%
Aged 45–65 y (n = 732)	≥400	2.1%	< 0.1%
	≥100	2.1%	0.8%
	≥75th percentile age/sex	2.1%	1.2%
<i>Part B: Men</i>			
Aged 30–65 y (n = 1,161)	≥400	15.4%	1.1%
	≥100	15.4%	3.3%
	≥75th percentile age/sex	15.4%	3.7%
Aged 45–65 y (n = 559)	≥400	29.8%	2.5%
	≥100	29.8%	7.6%
	≥75th percentile age/sex	29.8%	8.0%

Table III

Efficiency of imaging strategies targeted to MHR subjects

	CAC threshold	NNS to detect 1 subject with CAC above threshold	% of all subjects with underestimated risk detected*
<i>Part A: Women</i>			
Aged 30–65 y (n = 1,449)	≥400	> 100	0.3% ^a
	≥100	2.6	11.8% ^b
	≥75th percentile age/sex	1.8	7.9% ^c
Aged 45–65 y (n = 732)	≥400	>100	0.3% ^a
	≥100	2.6	12.4% ^b
	≥75th percentile age/sex	1.8	9.9% ^c
<i>Part B: Men</i>			
Aged 30–65 y (n = 1,161)	≥400	14.3	25.1% ^a
	≥100	4.6	50.9% ^b
	≥75th percentile age/sex	4.1	29.5% ^c
Aged 45–65 y (n = 559)	≥400	12.1	29.1% ^a
	≥100	3.9	55.9% ^b
	≥75th percentile age/sex	3.7	40.1% ^c

* Underestimated risk refers to subjects

^a categorized as LR with CAC score ≥100 or MHR with CAC ≥400;

^b LR or MHR with CAC ≥100;

^c LR or MHR with CAC ≥75th percentile for age/sex.

Table IV

Efficiency of various eligibility criteria for CAC screening in LR subjects

Potential eligibility criteria	Lower risk women		Lower risk men	
	NNS to identify 1 subject with CAC ≥ 100	Proportion of LR* subjects with CAC ≥ 100 identified	NNS to identify 1 subject with CAC ≥ 100	Proportion of LR* subjects with CAC ≥ 100 identified
Hypertension	14.3	33.7%	17.8	13.0%
Hypercholesterolemia	14.2	53.3%	20.0	28.2%
Smoking	15.5	37.5%	26.9	19.2%
Family history of MI	57.4	4.8%	13.8	12.5%
Low HDL-C	59.7	8.7%	23.9	34.5%
Hypertriglyceridemia	15.4	19.7%	36.8	10.3%
Glucose intolerance	22.3	25.4%	48.5	8.9%
Obesity by WC	26.3	68.2%	17.9	50.5%
≥ 1 Traditional RF**	25.6	69.1%	20.2	79.2%
≥ 2 Traditional RF	12.2	55.9%	22.3	27.9%
Hs-CRP >3 mg/L	24.2	62.4%	17.6	31.5%
Metabolic syndrome	18.3	46.7%	18.8	27.1%
FRS 10-year risk 0%–2%	58.4	47.7%	94.4	15.3%
FRS 10-year risk 3%–5%	7.8	28.7%	14.5	30.4%
FRS 10-year risk 6%–9%	3.5	23.6%	6.6	54.3%

MI, Myocardial infarction; HDL-C, high-density lipoprotein cholesterol; WC, waist circumference; RF, risk factors; LDL-C, low density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein.

* Lower risk indicates FRS 10-year risk $<10\%$.

** Traditional RF indicates hypertension, hypercholesterolemia, smoking, family history of MI, low HDL-C.

Table V

Efficiency of an imaging strategy targeted to select LR subjects

	CAC threshold	NNS to detect 1 subject with CAC above threshold	% of all subjects with underestimated risk detected [*]
Women			
Aged 30–65 y (n = 1,449)	≥100	5.2	84.2% ^a
	≥75th percentile age/sex	4.2	92.1% ^b
Men			
Aged 30–65 y (n = 1,161)	≥100	6.8	51.1% ^a
	≥75th percentile age/sex	3.7	42.9% ^b

Data evaluate the efficiency of the LR strategy outlined in Figure 4.

^{*} Underestimated risk refers to subjects^a categorized as LR with CAC score ≥100 or MHR with CAC ≥400;^b LR or MHR with CAC ≥75th percentile for age/sex.