Population screening with coronary computed tomography angiography and the prevention of coronary events

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EDITORIAL

Population Screening With Coronary Computed Tomography Angiography and the Prevention of Coronary Events

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Coronary heart disease is the most common cause of death worldwide and is responsible for the death of approximately 9 million persons each year.[1] This condition often presents with an unheralded acute coronary event, such as a myocardial infarction or a sudden cardiac death, but coronary atherosclerosis has invariably been present for years before the onset of symptoms. Despite having effective, low-cost treatments that prevent acute coronary events, our current approach to prevention is based on population estimates of risk rather than on diagnostic testing with coronary imaging. Probabilistic risk scores are imprecise and may result in both unnecessary life-long therapies in those without disease and failure to initiate treatment in those at greatest risk. Furthermore, although the use of probabilistic risk scores is widespread, their effectiveness has not been validated by clinical trial evidence.[2]

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In recent years, the use of invasive and noninvasive coronary imaging has become the standard of care for persons with symptomatic coronary artery disease.[3] In particular, the use of coronary computed tomography angiography (CCTA) has been shown to improve diagnosis and change treatment, potentially leading to reduced risk of future myocardial infarction.[4,5] Modern scanners and imaging protocols enable rapid and accurate quantification of coronary atherosclerosis at a low radiation dose and raise the possibility that CCTA could play a wider role in the targeting of preventative therapies through population screening.

To inform the design of future strategies to prevent coronary heart disease, an essential first step is to define the true prevalence of coronary atherosclerosis in the general population. Previous estimates have been based on postmortem evidence; small, selected populations; or coronary artery calcification (CAC), an incomplete measure of disease. In this context, the findings of the SCAPIS trial (Swedish Cardiopulmonary Bioimage Study) are particularly important.[6]

The SCAPIS investigators recruited 30 154 men and women 50 to 64 years of age who were randomly selected from the population to undergo a comprehensive assessment including the measurement of risk factors and CCTA imaging.[7] Their aim was to determine the prevalence and burden of coronary atherosclerosis and its association with risk scores and CAC. In this first article describing results from SCAPIS, Bergström et al report findings from 25 182 persons without a previous myocardial infarction or coronary intervention who had a valid measurement of CAC and an interpretable CCTA (Figure). They report several important observations. First, silent coronary atherosclerosis is common in the general population with 4 of 10 persons having any atheroma. The prevalence was 2-fold higher in men than in women and increased with age. Coronary atherosclerosis was considered significant (>50% stenoses) in 1 of 20 persons, and severe involving the left main stem, proximal left anterior descending artery, or all 3 territories

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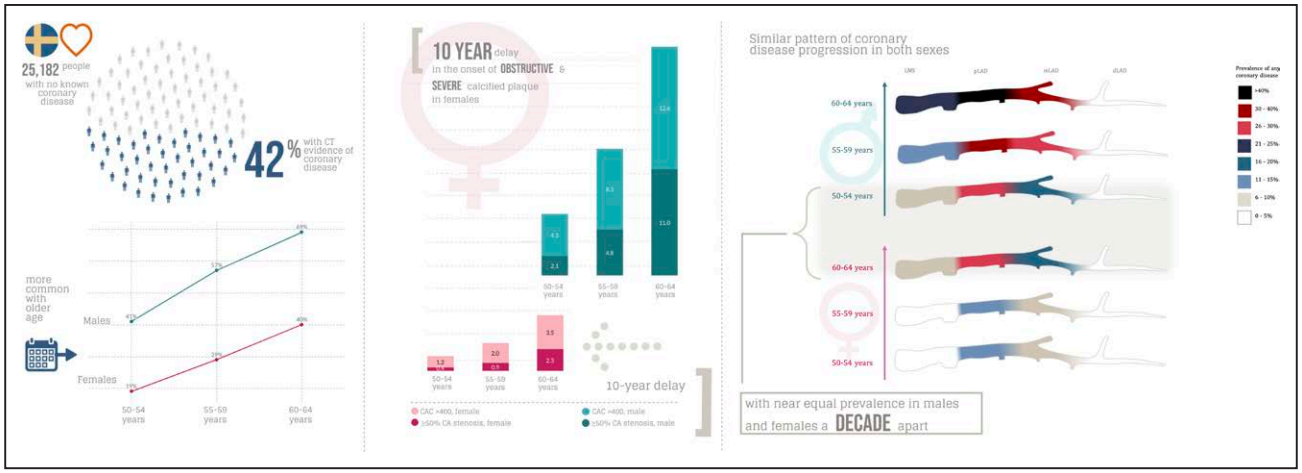

Figure. Prevalence of coronary artery disease in middle-aged men and women without previous myocardial infarction or coronary intervention.

SCAPIS (Swedish Cardiopulmonary Bioimage Study) enrolled 25 182 men and women 50 to 64 years of age without previous infarction or coronary intervention randomly selected from the general population. Coronary computed tomography angiography identified any coronary atherosclerosis in 42% (**Left**), which was significant with ≥50% stenoses or a coronary artery calcification (CAC) score >400 in 5.2% and 3.5%, respectively (**Middle**), with the prevalence of both increasing by age and was twice as common in men as in women. Although the onset of coronary atherosclerosis was delayed by 10 years in women, the distribution and pattern of disease were similar in both sexes (**Right**). CA indicates coronary artery; and CT, computed tomography.

in 1 of 50 persons. Second, the onset of coronary atherosclerosis was delayed by 10 years in women, but the distribution and pattern of disease was identical in both sexes. Third, although there were associations between coronary atherosclerosis, risk scores, and CAC, important subgroups were identified where atheroma burden was not accurately represented by either risk scores or CAC.

Do estimates of the prevalence of coronary atherosclerosis in the SCAPIS cohort reflect the wider population? The prevalence identified by CCTA in SCAPIS was slightly higher than previous estimates that have relied on CAC alone,[8] as is to be expected given that CCTA provides a more detailed assessment. It is plausible that selection bias could overestimate prevalence, but the investigators ensured that their findings were representative by identifying potential participants at random using a population census. They enrolled an impressive 50.3% of those invited to participate with no differences in enrollment by age or sex. Furthermore, they used a national sociodemographic register and inverse probability for participation weighting to adjust for any differences in the recruited population from the age-matched population in Sweden, and the prevalence of coronary atherosclerosis was largely unchanged.

Sex-based differences in the pattern of coronary artery disease in symptomatic persons are well established,[9,10] but these observations are susceptible to selection bias with women less commonly enrolled or referred for coronary imaging. In support of this concern, in patients with ST-segment–elevation myocardial infarction, where coronary angiography is ubiquitous and decisions are made before hospitalization, the pattern of disease and plaque characteristics are identical in men and women.[11] Although Bergström et al demonstrate that the prevalence of coronary atherosclerosis was 2-fold higher in men than in women in middle age, the distribution and burden of disease were identical, but the onset was delayed by 10 years in women. Thus, Bergström et al provide further support for the theory that coronary atherosclerosis is the same in women and men but presents at a later stage in women. The reasons for this are poorly understood but are likely to reflect the protective or harmful effects of sex hormones on atherosclerosis or other yet unknown factors.

Could CCTA improve the targeting of preventative therapies compared with probabilistic risk scores and CAC scoring in the general population? Although risk scores have been externally validated in large cohorts and perform well at predicting coronary events at a population level,[12] there are inherent limitations when applying these in individuals. They are well known to systematically overestimate and underestimate risk in certain ethnic groups, by socioeconomic status, and in those with comorbidities such as chronic inflammatory diseases.[13,14] Furthermore, many patients are classified as borderline or intermediate risk, in whom the benefit of preventative therapy is uncertain.

The SCAPIS investigators observed a good correlation between the prevalence of coronary atherosclerosis and risk categories using the Systematic Coronary Risk Estimation and the Pooled Cohort Equation.[7] Those participants classified as high risk had a 2.1-fold (95% CI, 2.0–2.2) and 2.9-fold (95% CI, 2.8–3.0) higher prevalence of coronary atherosclerosis than did those classified as low risk by Systematic Coronary Risk Estimation and the Pooled Cohort Equation, respectively. However, in

those classified as low risk by both scores, as many as 1 of 3 men and 1 of 4 women were found to have coronary atherosclerosis. Furthermore, in women, the prevalence of coronary atherosclerosis was similar whether they were classified as moderate or high risk by the Systematic Coronary Risk Estimation, suggesting that discrimination in those who are higher risk could also be improved. Although CAC scoring is recommended by guidelines in persons who are borderline or intermediate risk using the Pooled Cohort Equation,[12] 5.5% and 81.9% of participants with zero or very low[1–10] CAC scores had evidence of atherosclerosis on CCTA. For those who use CAC scoring in their practice, SCAPIS also provides insights into the prevalence of severe coronary atherosclerosis stratified by CAC score. In asymptomatic persons with a high CAC score (>400), it was remarkable that 1 of 5 had ≥50% stenosis in the left main stem, proximal left anterior descending artery, or all 3 coronary arteries.

There are several potential explanations for these discordant findings. Probabilistic risk scores were developed in older populations and designed to predict myocardial infarction, stroke, or cardiovascular death at 10 years. In contrast, the SCAPIS cohort is relatively young (median, 57.4±4.3 years) and most of the coronary atherosclerosis identified by CCTA was mild. It is therefore possible that the progression from early coronary atherosclerosis to acute coronary events will take >10 years. Nevertheless, the high prevalence of subclinical coronary atherosclerosis raises the question as to whether CCTA could help identify persons more precisely who would benefit from the early initiation of preventative therapies to treat the underlying atherosclerotic disease process and reduce their lifetime risk of coronary events.

Long-term follow-up of the SCAPIS cohort will inform whether measures of coronary atherosclerosis are superior to risk score estimates with or without CAC testing for the prediction of coronary events. Future analyses should evaluate alternative measures of coronary atherosclerosis burden including functional measurements of stenosis severity and quantification of plaque characteristics that have been shown to identify those at high risk in those with symptoms.[15] CCTA is not uniformly available in all health care systems, and, even where testing is routinely performed, a significant expansion in capacity would be needed to establish high-risk population screening programs. In this context, the SCAPIS investigators should explore the potential for novel blood and imaging biomarkers to identify those persons who are most likely to have subclinical coronary atherosclerosis.

Evidence from randomized controlled trials will ultimately be needed to determine whether targeting preventative therapy using CCTA is superior to our current practice of estimating risk using probabilistic risk scores. This question is currently being addressed in individuals with ≥1 cardiovascular risk factors enrolled in the SCOT-HEART 2 trial (Computed Tomography Coronary Angiography for the Prevention of Myocardial Infarction; URL: http://www.clinicaltrials.gov. Unique identifier: NCT03920176), which will determine whether screening with CCTA is associated with a reduction in the rate of fatal or nonfatal myocardial infarction in comparison with a risk score approach. In the meantime, the search for novel bioimaging markers of coronary atherosclerosis continues, and the SCAPIS investigators are well placed to lead these discoveries and to design novel approaches that may reduce the burden of coronary heart disease on our communities.

ARTICLE INFORMATION

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