Impact of low/no-charge coronary artery calcium scoring on statin eligibility and outcomes in women: The CLARIFY study

Sadeer Al-Kindi a,b, Nour Tashtish a,b, Imran Rashid a,b, Claire Sullivan a,b, Ian J Neeland a,b, Monique Robinson a,b, Ewa M. Gross a,b, Leslee Shaw c, Miguel Cainzos-Achirica d, Khurram Nasir d, Catherine Kreatsoulas e, Robert Gilkeson b,c, Daniel I Simon a,b, Sanjay Rajagopalan a,b,*

a Harrington Heart and Vascular Institute, University Hospitals, 11100 Euclid Ave, Cleveland, OH 44106, United States
b Case Western Reserve University School of Medicine, Cleveland, OH 44106, United States
c Weill Cornell Medicine/NewYork-Presbyterian Hospital, New York, NY 10065, United States
d Center for Outcomes Research and Division of Cardiovascular Prevention and Wellness, Department of Cardiology, Houston Methodist DeBakey Heart & Vascular Center, Houston, TX 77030, United States
e Department of Health Policy and Management, Harvard T.H. Chan School of Public Health, Boston, MA 02115, United States

**Corresponding author at: University Hospitals Harrington Heart and Vascular Institute, 11100 Euclid Ave, Cleveland, OH 44106, United States.
E-mail addresses: sadeer.al-kindi@uhhospitals.org (S. Al-Kindi), Sanjay.rajagopalan@uhhospitals.org (S. Rajagopalan).**

**ARTICLE INFO**

**Keywords:**
Coronary artery calcium scoring
Women
Sex disparities
Cardiovascular prevention
Statin eligibility

**ABSTRACT**

**Background:** Prior studies have suggested significant underutilization of statins in women and worse cardiovascular outcomes. Data examining the impact of real-world coronary artery calcium (CAC) scoring to improve utilization of preventive therapies and outcomes is limited.

**Methods:** In a prospective registry study of low cost or no-cost CAC scoring between 2014 and 19 (CLARIFY Study, Clinicaltrials.gov NCT04075162), we sought to study the association of CAC scoring on statin utilization, blood lipids (LDL, total cholesterol, triglycerides), downstream ischemic testing (coronary angiography and stress testing), coronary revascularization and outcomes (MI, stroke, death) in women compared with men.

**Eligibility for statin initiation was defined as atherosclerotic cardiovascular disease pooled cohort equation (ASCVD-PCE) ≥ 7.5% and CAC ≥ 75th percentile.**

**Results:** A total of 52,151 patients (26,336 women and 25,815 men) were enrolled. Women were more likely to have CAC 0 (51% vs 30%, P < 0.001). Among patients not eligible for statin by PCE, CAC reclassified statin eligibility in a smaller proportion of women than men (25.4% vs 30%, P < 0.001), while among patients eligible...
1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in the US in both men and women [1]. Although randomized trials of statins in primary and secondary prevention have demonstrated no heterogeneity of benefit in men compared with women, real-world studies have suggested significant underutilization of statins and other preventive therapies in women, leading to poorer cardiovascular outcomes [2,3]. The current approach for use of preventive therapies such as anti-hypertensive therapy and cholesterol lowering agents is based on the use of pooled cohort equation to guide cholesterol lowering therapies [2,3] and blood pressure management [4]. While the reasons for this are likely multifactorial, imprecision in risk assignment in women when using probabilistic risk scores that are more suited to population level studies has been raised [5,6]. This on the one hand may result in undertreatment of women in primary prevention but may also have the unintended consequence of committing too many women to unnecessary treatment.

Coronary artery calcium (CAC) scoring allows individual risk assessment and may improve risk stratification to a greater extent in women than men [7]. CAC score regardless of sex has also been shown to improve adherence and facilitate lifestyle modifications to improve cardiovascular risk profile[8,9]. Despite robust evidence for the role of CAC in risk stratification and endorsement by guidelines at least for patients with low to intermediate ASCVD risk, CAC is not reimbursed by many payors in the United States, thereby limiting our ability to understand real-world sex-related disparities in CAC utilization and outcomes. We have previously shown that removing cost burden improves CAC utilization, particularly among women [10]. In this work, we sought to explore sex-related differences in statin therapy and downstream procedural utilization and outcomes, when cost barriers to use of CAC scoring are eliminated.

2. Methods

Setting: University Hospitals Health System (UHHS) is one of northeast Ohio’s largest health providers and is one of Ohio’s largest health care networks. UHHS is comprised of 11 large hospitals and >31 Health Centers. Given that Medicare does not reimburse CAC testing in the state of Ohio, and to allow patients to benefit from this testing, UHHS started a system-wide low-charge CAC program ($99 per test) in 2014 and piloted the impact of a no charge CAC temporarily in June 2015, followed by full implementation starting in January 2017.

Criteria for CAC Screening: CAC scoring was offered to all men 45 or older and women age 55 or older, with no history of cardiovascular disease, and with one or more risk factors for heart disease, including: dyslipidemia, hypertension, smoking, diabetes, family history of coronary artery disease (at age 55 or younger in men and 65 or younger in women). The test was also made available for men and women age 40 or older who are diagnosed with a chronic inflammatory condition (e.g., inflammatory bowel disease, lupus, rheumatoid arthritis, ankylosing spondylitis, psoriasis). CAC testing was offered at 21 radiology locations within the system, geographically distributed throughout northeast Ohio. For the present study, we included all patients who entered into the CAC program at University Hospitals Health System (UHHS) from January 1st, 2014 through November 4th, 2020. Patient data were captured using electronic medical records and were maintained in a prospective registry, the Community Calcium Scoring Assessment for Cardiovascular Risk Stratification (CLARIFY, ClinicalTrials.gov NCT04075162). Informed consent was waived by the University Hospitals institutional review board for entry into the registry. The cost of offering no-charge CAC screening was offset by scheduling patients in CT scanners across the health system (18 total CT scanners), when they were not being utilized for other studies, thereby enhancing efficiency for a fixed cost (maintenance and upkeep of CT scanners and personnel time).

Coronary Artery Calcium Scoring: The coronary artery calcium score was assessed using standardized protocols with Multi-Detector CT (MDCT) scanners with either 64 or 256 detectors. The protocols for CAC acquisition were standardized across the system and followed protocols recommended by Society for Cardiovascular Computed Tomography (SCCT) [9]. The scans procured by various system CT scanner locations were sent to a centralized reading facility for quantification, which was performed on a workstation with dedicated software for calcium scoring (Heartbeat-CS, EBW, Philips Medical Systems, Cleveland, OH). All regions with a density over 130 Hounsfield units were identified as a potential calcification. The CAC results were communicated with referring provider using electronic medical record system, using a structured report. CAC report templates included a calcium score per vessel and total calcium score, and the 10-year cardiovascular risk by group (0, 1–99, 100–399, 400 or above) using data by McClelland et al. [11]. Patients had access to CAC reports using an online secure patient portal.

Outcomes: We tested sex-stratified difference in patient characteristics, CAC results, metabolic health parameters before and after CAC scoring. Additionally, we explored the impact of CAC on downstream cardiovascular procedures. Specifically, outcomes included caridiometabolic variables and medication use (ASCVD risk by pooled-cohort equation, low density lipoprotein levels, total cholesterol levels, triglycerides, statin and aspirin utilization prior to and within 1 year of CAC); downstream cardiovascular procedures within 12 months of CAC including stress testing, coronary CT angiography, coronary angiograms, percutaneous coronary interventions, and coronary artery bypass grafting procedures. Hard cardiovascular events were also followed and included myocardial infarction, stroke (using international classification of diseases, version 10 codes), and all-cause mortality following CAC (via linkage with the Ohio death index).

Data were extracted from the electronic medical records at UHHS. Race/ethnicity was self-reported. The timing of laboratory values (LDL, total cholesterol, HDL, triglycerides) was defined as follows: “Before CAC” refers to the most recent value within the 365 days prior to CAC up to 1-month post CAC, and “After CAC” refers to values nearest to 365 days, provided they were measured between 180 and 730 days. For analyses of medication prescription, the denominator was all patients who had at least one physician visit in the electronic medical record prior to CAC. All deaths in our electronic medical records are linked with the death certificates from Ohio department of health. Cardiovascular events (myocardial infarction, stroke) were identified using specific international classification of diseases, version 10. Patients who were lost to follow-up were censored at the last follow-up date.

Statistical Analysis: Categorical variables are presented as number and proportion, and continuous variables are presented as mean with
standard deviations or median and 25th-75th percentiles as appropriate. Analyses throughout the manuscript refer to categories of CAC result (0, 1–99, 100–399, ≥400). Comparisons were done using chi square (for categorical variables), t-test (for normally distributed continuous variables) and Mann-Whitney U test (for non-normally-distributed continuous variables) as appropriate. These analyses included only patients who have baseline and follow-up values of metabolic health parameters. For post-CAC prescriptions, procedures, and events, we estimated the cumulative incidence using Kaplan-Meier (with comparisons done using Mantel-Cox test) to allow for attrition, as some patients did not receive care (other than CAC) at UHHS. Hazard ratios were estimated using Cox-proportional hazard models. Two-sided P ≤ 0.05 was considered statistically significant. We additionally used penalized smoothed splines to visualize the association between CAC (as a continuous variable) and MACE events. R 4.0.0 and Statistical Package for Social Sciences version 21 (IBM, NY) was used for analyses.

3. Results

A total of 52,151 patients (26,336 women and 25,815 men) were enrolled. Compared with the low-charge phase, no-charge phase increased CAC referral in women (46.3% vs 51.0%, P < 0.001), Fig. 1. Compared with men, women were slightly older (61 vs 58 years), more likely to be Black (9.9% vs 6.6%), had lower 10-year predicted ASCVD risk (9.4% vs 14%, P < 0.0001), and have higher LDL (126 vs 117 mg/dL, P < 0.001), CAC ≥400 (OR 0.33 [0.30–0.36], P < 0.001) compared to one-third of men (51.4% vs 30.3%). When comparing men vs. women for the subgroups, CAC ≥7.5% had CAC ≥100 (OR 0.76 [0.72–0.80], P < 0.001), CAC ≥100 had CAC ≥399, and 6.8% vs 17.5% [CAC ≥100, respectively [P < 0.001 for all]. Prevalence of any coronary calcification (CAC>0) across the age spectrum is shown in Fig. 2. At all age groups, men had higher prevalence of CAC, with a decreasing gap with increasing age (women vs men: 11% vs 22% [age 30–39 years] to 84% vs 96% [age 80–89 years]). Even after adjusting for age and 10-year predicted PCE risk, women had lower risk of CAC>0 (OR 0.36 [0.34–0.38], P < 0.001), CAC>100 (OR 0.36 [0.34–0.39], P < 0.001), and CAC≥400 (OR 0.33 [0.30–0.36], P < 0.001).

CAC significantly reclassified risk from the 10-year predicted risk by PCE in both women and men. Among women with low to borderline predicted 10-year risk (<7.5%), 9% had CAC≥100, compared with 17% in men. Conversely, among patients with high 10-year predicted risk by PCE (>20%), 54% of women and 36% of men had CAC<100, with 22% of women and 10% of men having CAC=0. Fig. 3 shows the categories of CAC by PCE in men and women. Assuming statin threshold CAC≥100 and 10-year predicted risk of ≥7.5%, CAC reclassified statin eligibility in 31% total (28% of women and 35% of men). CAC upgraded statin eligibility (ineligible by PCE to eligible by CAC) in 5.6% of women and 5.5% of men, and downgraded statin eligibility (eligible by PCE but ineligible by CAC) in 28% of women and 35% of men.

Table 1

| Baseline Characteristics of Women and Men who underwent CAC in CLARIFY. |
|-----------------|-----------------|-----------------|
|                  | Women           | Men             | P value |
| n                | 26,336          | 25,815          |         |
| Age, years       | 61±9            | 58±10           | <0.001  |
| Race             |                 |                 |         |
| White            | 22,753 (86%)    | 22,761 (88%)    |         |
| Black            | 2597 (9.9%)     | 1696 (6.6%)     |         |
| Other            | 457 (1.7%)      | 544 (2.1%)      |         |
| Unknown          | 529 (2%)        | 816 (3.2%)      |         |
| 10-year ASCVD risk by PCE | 9.4 ± 9.7 | 14±11 | <0.001  |
| ASCVD risk Categories (PCE) |            |                 | <0.001  |
| ≤7.5%            | 7451 (58%)      | 3824 (33%)      |         |
| 7.5-20%          | 3989 (30%)      | 5234 (45%)      |         |
| ≥20%             | 1544 (12%)      | 2618 (22%)      | <0.001  |
| CAC              |                 |                 | <0.001  |
| 0                | 13,536 (51%)    | 7829 (30%)      |         |
| 1–99             | 7674 (29%)      | 8504 (33%)      |         |
| 100–399          | 3330 (13%)      | 4973 (19%)      |         |
| ≥400             | 1796 (6.8%)     | 4509 (18%)      |         |
| Blood pressure   |                 |                 |         |
| Systolic BP      | 128±16          | 130±15          | <0.001  |
| Diastolic BP     | 77±10           | 80±10           | <0.001  |
| Total Cholesterol| 212±44          | 193±43          | <0.001  |
| HDL-C            | 60±16           | 48±13           | <0.001  |
| LDL-C            | 126±39          | 117±38          | <0.001  |
| Triglycerides    | 128±78          | 145±116         | <0.001  |
| Statin           | 8473 (32%)      | 8719 (34%)      | <0.001  |
| High intensity statin | 1958 (7.4%) | 2506 (9.7%) | <0.001  |
| Aspirin          | 5877 (22%)      | 5868 (23%)      | 0.26    |
| Household income ($) | 68,028 | 70,887 ± 23,193 |         |
| No Charge CAC    | 23,769 (90%)    | 22,841 (89%)    | <0.001  |

Fig. 1. Impact of reducing charge burden on sex distribution (A) proportion of men vs women in the no-charge vs low-charge CAC period (B) relative change in proportion by sex and race between no charge and low charge CAC periods. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).
Among patients not eligible for statin by PCE, CAC facilitated statin eligibility, but in a smaller percentage of women than men (10% vs 17%, \( P < 0.001 \)), while among patients eligible for statin by PCE, CAC was more likely to downgrade risk/statin eligibility in women than men (66% vs 52%, \( P < 0.001 \)). Comparing statin eligibility based on PCE (10-year risk \( \geq 7.5\% \)) vs CAC scoring (CAC \( \geq 100 \) or \( \geq 75\text{th percentile} \)), CAC reclassified eligibility by 14.4% (non-eligible to eligible) and 25.5% (eligible to non-eligible) in women. Conversely, CAC reclassified eligibility by 8.9% (non-eligible to eligible) and 34.1% (eligible to non-eligible) in men.

Among patients who did not receive statin at baseline, one-year cumulative rates of statin prescription were not different between men and women when stratified by CAC score (women vs men: 6.3% vs 7% [CAC=0], 22.3% vs 23.6% [CAC 1–99], 56.9% vs 56.3% [CAC 100–399], and 72.6% vs 70.6% [CAC \( \geq 400 \)], Fig. 4 and Table 2. However, overall rates of high-intensity statin were lower in women vs men (women vs men: 1.2% vs 1.8% [CAC=0], 4.4% vs 5.4% [CAC 1–99], 11% vs 14.8% [CAC 100–399], and 23.2% vs 28.3% [CAC \( \geq 400 \)]), Table 2. After adjusting for CAC group, women were 24% less likely to receive high intensity statin compared with men (HR 0.76 [0.70–0.83], \( P < 0.001 \)). Interestingly, there were no difference in aspirin prescriptions between men and women, Table 2.

At one year, there was a significant decrease in total cholesterol in both women and men (women vs men median difference: −5 vs −9 mg/dL, \( P < 0.001 \) compared to baseline), LDL-C (women vs men median difference: −4 vs −8 mg/dL, \( P < 0.001 \)) and triglycerides (women vs men median difference: −1 vs −6 mg/dL, \( P < 0.001 \)). When stratified by CAC, there were no differences in lipid profile changes between men and women with few exceptions (Table 3). For example, among patients with CAC \( \geq 400 \), women had smaller reduction in total cholesterol (−17 vs −23 mg/dL, \( P = 0.045 \)), and smaller reduction in triglycerides (−6 vs −11 mg/dL, \( P = 0.014 \)).

Stress testing or coronary CT angiography were utilized slightly less frequently within the year after CAC in women vs men with CAC \( \geq 400 \) (44% vs 47%, \( P = 0.018 \)). Overall invasive coronary angiography and revascularization were low. While invasive angiography did not differ significantly between women and men, it was lower among patients CAC 100–399. Revascularization rates were consistently lower in women vs
Table 2
Preventive medication prescription at one-year post CAC by sex and CAC.

|                      | Women | Men | P Value |
|----------------------|-------|-----|---------|
| Any Statin           |       |     |         |
| CAC 0                | 6.3%  | 7.0%| 0.10    |
| CAC >0               | 36.1% | 42.2%| <0.001 |
| CAC 1–99             | 22.3% | 23.6%| 0.16    |
| CAC 100–399          | 56.9% | 56.3%| 0.94    |
| CAC ≥400             | 72.6% | 70.6%| 0.72    |
| High-Intensity Statin|       |     |         |
| CAC 0                | 1.2%  | 1.8%| 0.007   |
| CAC >0               | 8.7%  | 13.6%| <0.001 |
| CAC 1–99             | 4.4%  | 5.4%| 0.021   |
| CAC 100–399          | 11.0% | 14.8%| <0.001 |
| CAC ≥400             | 22.2% | 28.3%| 0.001   |
| Aspirin              |       |     |         |
| CAC 0                | 5.0%  | 5.1%| 0.96    |
| CAC >0               | 21.4% | 26.3%| <0.001 |
| CAC 1–99             | 12.0% | 12.6%| 0.08    |
| CAC 100–399          | 29.5% | 30.8%| 0.50    |
| CAC ≥400             | 51.5% | 50.6%| 0.82    |

4. Discussion

In this pragmatic study of no-charge/low charge CAC, meant to eliminate barriers to testing, we demonstrate (1) increased CAC utilization by women, (2) although most women with lower predicted risk by PCE, had lower CAC scores, a fraction of women were misclassified and were high risk (3) CAC significantly reclassified/downgraded risk among women who are at high predicted risk compared with men, (4) while CAC-guided statin utilization was similar between men and women, women were less likely to receive high intensity statin.

Several studies have shown that statins and other preventive therapies are underutilized in women compared with men. In a recent systematic review of 43 studies (2000–2019) reporting sex-related utilization of cardiovascular medications in >2 million patients in primary care (28% women), women were 10% less likely to receive statin and 19% less likely to receive aspirin, compared with men [12]. CAC may facilitate prescription of appropriate statins [9] and may reduce the sex-related gap in statin utilization.

We show that women who had elevated CAC were more likely to receive statin and experience significant reduction in LDL-C. CAC has been shown to lead to statin initiation [8, 13, 14] and result in improved adherence and lifestyle changes [13, 14]. In the Early Identification of Subclinical Atherosclerosis Using Non-Invasive Imaging Research (EISNER) trial (47.5% women), CAC led to improvement in risk factor profile [8]. In this study, the median LDL-C reduction in women with CAC ≥ 400 was −17 mg/dL, which is equivalent to approximately 10% risk reduction of major adverse cardiovascular events [15] which may have saved 100 women from events in this study.

This study shows that removing cost barrier (going from 99$ to 0$) and eliminating cost altogether can significantly increase CAC utilization in women. There was a 10% relative increase in representation of women during the no-charge phase, resulting in more women than men in the registry. This is in contrast with prior studies that included lower percentage of women (approximately 30%–40%) [14, 16, 17]. The no-charge CAC strategy may also facilitate identification of at-risk women for enrollment in randomized trials of primary prevention, where women have been traditionally underrepresented [18]. This is especially true for Black women where there was a 52% relative increase in representation between the low-charge and no charge periods.

The use of probabilistic equations for risk ASCVD estimation is...
The association between CAC and cardiovascular risk seems to be consistent regardless of sex, and appears to be more predictive of risk in women compared to men [7]. In the current study, we show that CAC reclassified statin eligibility in 30% of women. Our findings are consistent with prior literature suggesting that CAC can be used to risk stratify women as well as facilitate shared decision making through one-year post CAC by sex and CAC.

Table 3
Changes in lipid profile between baseline and one-year after CAC by sex and CAC.

| Lipid Profile          | Women | Men | P Value* |
|------------------------|-------|-----|----------|
| Total Cholesterol (mg/dL) |       |     |          |
| CAC 0                  | –1 [19 to 14] | –1 [19 to 14] | 0.98 |
| CAC >0                 | 10 [39 to 10] | 13 [43 to 6] | <0.001 |
| CAC 1–99               | 6 [28 to 13] | 7 [30 to 10] | 0.06 |
| CAC 100–399            | 18 [55 to 6] | 15 [48 to 4] | 0.29 |
| CAC ≥400               | 17 [53 to 4] | 23 [56 to –1] | 0.045 |
| HDL-C (mg/dL)          |       |     |          |
| CAC 0                  | –1 [16 to 13] | –1 [17 to 13] | 0.42 |
| CAC >0                 | 8 [36 to 8] | 11 [38 to 5] | 0.002 |
| CAC 1–99               | 5 [25 to 10] | 6 [27 to 9] | 0.16 |
| CAC 100–399            | 16 [49 to 3] | 13 [42 to 4] | 0.065 |
| CAC ≥400               | 17 [47 to 1] | 20 [51 to –1] | 0.15 |
| Systolic blood pressure (mmHg) |       |     |          |
| CAC 0                  | 10 [10 to 10] | 10 [10 to 10] | 0.84 |
| CAC >0                 | 11 [10 to 10] | 10 [10 to 10] | 0.45 |
| CAC 1–99               | 10 [10 to 10] | 10 [10 to 10] | 0.90 |
| CAC 100–399            | 12 [10 to 10] | 10 [10 to 10] | 0.14 |
| CAC ≥400               | 15 [15 to 10] | 12 [10 to 10] | 0.09 |
| Dianortic blood pressure (mmHg) |       |     |          |
| CAC 0                  | 6 [6 to 6] | 7 [6 to 6] | 0.15 |
| CAC >0                 | 7 [6 to 6] | 8 [6 to 6] | 0.38 |
| CAC 1–99               | 6 [6 to 6] | 7 [6 to 6] | 0.28 |
| CAC 100–399            | 8 [8 to 6] | 8 [6 to 6] | 0.28 |
| CAC ≥400               | 8 [8 to 6] | 8 [8 to 6] | 0.66 |
| BMI (kg/m2)            |       |     |          |
| CAC 0                  | 0.06 [0.74 to 0.86] | 0.07 [0.81 to 0.86] | 0.23 |
| CAC >0                 | 0.08 [0.84 to 0.85] | 0.083 [0.73 to 0.73] | 0.10 |
| CAC 1–99               | 0.03 [0.77 to 0.76] | 0.074 [0.76 to 0.73] | 0.42 |
| CAC 100–399            | 0.09 [0.94 to 0.84] | 0.087 [0.68 to 0.75] | 0.56 |
| CAC ≥400               | 0.11 [1.11 to 0.87] | 0.097 [0.97 to 0.95] | 0.95 |

*aMann-Whitney U test comparing changes in men vs women.*

The significant CAC [19] has been shown to improve risk stratification beyond clinical risk factors in women, and may be a reasonable option to risk-stratify as well as facilitate shared decision making through one-year post CAC by sex and CAC. LaMonte et al. analyzed nearly 10,000 patients (36% women) undergoing CAC at cooper clinic in Dallas (1995–2000) and showed that CAC is associated with incident events in men and women [16]. Michos et al. studied 2447 women who underwent CAC and showed that Framingham risk equation classified the majority of women (84%) with significant CAC [19]. Shaw et al. analyzed >60,000 patients (32% women) undergoing CAC in the CAC consortium study, and showed that any detectable CAC was associated with 1.3 fold higher long-term (median follow-up of 12.6 years) mortality for women vs men [17]. The current study shows that the predictive power of CAC is equivalent in women vs men, though analysis is limited by short follow-up time. A longer duration of follow-up may be required to demonstrate outcome differences as a consequence of less intense statin therapy, lower reductions in LDL-C compared to men and finally lower rates of revascularizations.

This study has multiple limitations that need to be acknowledged. First, given that this was a pragmatic study of low-charge/no-charge CAC testing, some information may be missing, such as care received at outside facilities, death outside the state of Ohio, and laboratory results performed at other facilities. Secondly, not every patient had sufficient follow-up to ascertain changes in preventive measures, procedures and all outcomes. Third, the reasons for the changes in preventive parameters cannot be ascertained in this study and could relate to medications and/or lifestyle changes, although the fact the HDL-C did not change argues that changes in total cholesterol and HDL-C may not be related to lifestyle changes, but this is speculative. Additionally, the impact of such a strategy on quality of life and cost effectiveness was not ascertained. However, previous cost-effectiveness analyses are consistent with the concept that CAC testing represents a reasonable option to risk-stratify as well as facilitate shared decision making without any significant downstream adverse outcomes, loss of quality of life, and/or increased costs [20]. Further, depression and de-escalation of therapy based on CAC results was not available in our cohort due to difficulties with ascertainment from electronic medical records.

5. Conclusions

Removing cost burden increases utilization of CAC scoring by women. Women referred for CAC had lower cardiovascular risk compared with men, but CAC significantly reclassified statin eligibility compared with pooled cohort equations alone. Following CAC, women undergoing CAC scoring were less likely to be prescribed high-intensity statin but had similar CAC-guided reduction in LDL cholesterol compared with men. None of the authors have disclosures related to the

Table 4
Downstream non-invasive and invasive ischemic evaluation, and revascularization through one-year post CAC by sex and CAC.

| Outcome                  | Women | Men | P Value* |
|--------------------------|-------|-----|----------|
| Stress Testing/CCTA      |       |     |          |
| CAC 0                    | 4.3% | 4.8% | 0.15 |
| CAC >0                   | 16.5% | 22.1% | <0.001 |
| CAC 1–99                 | 6.8% | 7.5% | 0.15 |
| CAC 100–399              | 22.4% | 23.2% | 0.43 |
| CAC ≥400                 | 44.3% | 47.0% | 0.018 |
| Invasive coronary angiography |     |     |          |
| CAC 0                    | 0.2% | 0.2% | 0.79 |
| CAC >0                   | 1.3% | 2.7% | <0.001 |
| CAC 1–99                 | 0.4% | 0.5% | 0.44 |
| CAC 100–399              | 0.8% | 1.7% | 0.003 |
| CAC ≥400                 | 6.7% | 8.0% | 0.13 |
| Revascularization        |       |     |          |
| CAC 0                    | 0.7% | 2.3% | <0.001 |
| CAC 1–99                 | 0.2% | 0.4% | 0.027 |
| CAC 100–399              | 0.5% | 1.3% | 0.003 |
| CAC ≥400                 | 3.6% | 6.8% | <0.001 |

Removing cost burden increases utilization of CAC scoring by women. Women referred for CAC had lower cardiovascular risk compared with men, but CAC significantly reclassified statin eligibility compared with pooled cohort equations alone. Following CAC, women undergoing CAC scoring were less likely to be prescribed high-intensity statin but had similar CAC-guided reduction in LDL cholesterol compared with men. None of the authors have disclosures related to the

5. Conclusions

Removing cost burden increases utilization of CAC scoring by women. Women referred for CAC had lower cardiovascular risk compared with men, but CAC significantly reclassified statin eligibility compared with pooled cohort equations alone. Following CAC, women undergoing CAC scoring were less likely to be prescribed high-intensity statin but had similar CAC-guided reduction in LDL cholesterol compared with men. None of the authors have disclosures related to the

5. Conclusions

Removing cost burden increases utilization of CAC scoring by women. Women referred for CAC had lower cardiovascular risk compared with men, but CAC significantly reclassified statin eligibility compared with pooled cohort equations alone. Following CAC, women undergoing CAC scoring were less likely to be prescribed high-intensity statin but had similar CAC-guided reduction in LDL cholesterol compared with men. None of the authors have disclosures related to the
contents of this manuscript.
Clinical trial registration
Clinicaltrials.gov NCT04075162

Funding

This work was partly funded by the National Institute on Minority Health and Health Disparities Award # P50MD017351

CRediT authorship contribution statement

Sadeer Al-Kindi: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft. Nour Tashtish: Data curation, Formal analysis, Writing – review & editing, Writing – review & editing. Imran Rashid: Investigation, Writing – review & editing. Claire Sullivan: Investigation, Writing – review & editing. Ian J Neeland: Investigation, Writing – review & editing. Monique Robinson: Investigation, Writing – review & editing. Ewa M. Gross: Investigation, Writing – review & editing. Leslee Shaw: Investigation, Writing – review & editing. Miguel Cairoz-Achirica: Investigation, Writing – review & editing. Khurram Nasir: Investigation, Writing – review & editing. Catherine Kretsoaoulas: Investigation, Writing – review & editing. Robert Gilkeson: Investigation, Writing – review & editing. Daniel I Simon: Conceptualization, Investigation, Writing – review & editing. Sanjay Rajagopalan: Conceptualization, Investigation, Writing – review & editing, Supervision.

Disclosures

None of the authors have disclosures related to the contents of this manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpcr.2022.100392.

References

[1] Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation 2020;E139–596.
[2] Stone NJ, Robinson JG, Lichtenstein AH, Merz CNB, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889–934.
[3] Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberg ZD, Haba EJ, Himmelfarb CD, Khara A, Lloyd-Jones D, McEvoy JW. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;74:e177–232.
[4] Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018;71:e127–248.
[5] Mora S, Wengen NK, Cook NR, Liu J, Howard BV, Limacher MC, et al. Evaluation of the Pooled Cohort risk equations for cardiovascular risk prediction in a Multinational Cohort from the women’s health initiative. JAMA Intern Med 2016;176:1231–40.
[6] DeFilippis AP, Young R, Carrubba CJ, McEvoy JW, Budoff MJ, Blumenthal RS, Kronmal RA, McClelland RL, Nasir K, Blaha MJ. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. Ann Intern Med 2015;162:266–75.
[7] Raggi P, Shaw LJ, Berman DS, Callister TQ. Gender-based differences in the prognostic value of coronary calcification. J Women’s Health 2004;13:273–83.
[8] Rozanski A, Gransar H, Shaw LJ, Kim J, Miranda-Peatts L, Wong ND, Rana JS, Orakazi R, Hayes SW, Friedman JD, Thomson LE, Polk D, Min J, Budoff MJ, Berman DS. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. J Am Coll Cardiol 2011;57:1622–32.
[9] Gupta A, Lau E, Vashney R, Hulten EA, Cheezum M, Bittencourt MS, Blaha MJ, Wong ND, Blumenthal RS, Budoff MJ. The identification of calcified coronary plaque is associated with initiation and continuation of pharmacological and lifestyle preventive therapies: a systematic review and meta-analysis. JACC Cardiovasc Imaging 2017;10:833–42.
[10] Al-Kindi SG, Costa M, Tashtish N, Duriez J, Zidar D, Rashid I, et al. No-charge coronary artery calcium screening for cardiovascular risk assessment. J Am Coll Cardiol 2020;76:1259–62.
[11] McClelland RL, Jorgensen NW, Budoff M, Blaha MJ, Post WS, Kronmal RA, et al. 10-year coronary heart disease risk prediction using coronary artery calcium calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNIR (Heinz Nixdorf Recall) study and the DHS (Dallas Heart Study). J Am Coll Cardiol 2015;66:1643–53.
[12] Zhao M, Woodward M, Vaartjes I, Millett ERC, Kligstein-Grobusch K, Hyun K, et al. Sex differences in cardiovascular medication prescription in primary care: a systematic review and meta-analysis. J Am Heart Assoc 2020;9:e014742.
[13] Gupta A, Lau E, Vashney R, Hulten EA, Cheezum M, Bittencourt MS, et al. The identification of calcified coronary plaque is associated with initiation and continuation of pharmacological and lifestyle preventive therapies: a systematic review and meta-analysis. JACC Cardiovasc Imaging 2017;10:833–42.
[14] Nasir K, McClelland RL, Blumenthal RS, Goff DC, Hoffmann U, Pasy BM, Greenland P, Kronmal RA, Budoff MJ. Coronary artery calcium in relation to initiation and continuation of cardiovascular preventive medications the multi-ethnic study of Atherosclerosis (MESA). Circulation: Cardiovasc Qual Outcomes 2010;3:228–35.
[15] Collaboration C.T.T. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. 2015.
[16] LaMonte MJ, Fitzgerald SJ, Church TS, Barlow CE, Radford NB, Levine BD, Pippin JJ, Gibbons LW, Blair SN, Nichaman MZ. Coronary artery calcium score and coronary heart disease events in a large cohort of asymptomatic men and women. Am J Epidemiol 2005;162:421–9.
[17] Shaw LJ, Min JK, Nasir K, Xie JX, Berman DS, Miedema MD, Whelton SP, Dardari ZA, Rozanski A, Rumberger J, Bairey Merz CN, Al-Mallah MH, Budoff MJ, Blaha MJ. Sex differences in calcified plaque and long-term cardiovascular mortality: observations from the CAC Consortium. Eur Heart J 2018;39:3727–35.
[18] Melloni C, Berger JS, Wang TY, Gunas F, Stebbins A, Pieper KS, Dolor RJ, Douglas P5, Mork JB, Newby LK. Representation of women in randomized clinical trials of cardiovascular disease prevention. Circulation: Cardiovasc Qual Outcomes 2010;3:135–42.
[19] Michos ED, Nasir K, Braunstein JB, Rumberger JA, Budoff MJ, Post WS, Blumenthal RS. Framingham risk equation underestimates subclinical atherosclerosis risk in asymptomatic women. Atherosclerosis 2006;184:201–6.
[20] Hong JC, Blankstein R, Shaw LJ, Padula WV, Arrieta A, Fialkow JA, Blumenthal KS, Blaha MJ, Krumholz HM, Nasir K. Implications of coronary artery calcium testing for treatment decisions among statin candidates according to the ACC/AHA cholesterol management guidelines: a cost-effectiveness analysis. JACC Cardiovasc Imaging 2017;10:938–52.