Evaluation of clinical applicability of coronary artery calcium assessment on non-gated chest computed tomography compared with the classic Agatston score on cardiac computed tomography

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Evaluation of Clinical Applicability of Coronary Artery Calcium Assessment on Non−Gated Chest Computed Tomography, Compared With the Classic Agatston Score on Cardiac Computed Tomography

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Given current pretest probability (PTP) estimations tend to overestimate patients' risk for obstructive coronary artery disease, evaluation of patients' coronary artery calcium (CAC) is more precise. The value of CAC assessment with the Agatston score on cardiac computed tomography (CT) for risk estimation has been well indicated in patients with stable chest pain. CAC can be equally well assessed on routine non−gated chest CT, which is often available. This study aims to determine the clinical applicability of CAC assessment on non−gated CT in patients with stable chest pain compared with the classic Agatston score on gated CT. Consecutive patients referred for evaluation of the Agatston score, who had a previously performed non−gated chest CT for evaluation of noncardiac diseases, were included. CAC on non−gated CT was ordinally scored. Subsequently, patients were stratified according to CAC severity and PTP. The agreement and correlation between the classic Agatston score and CAC on non−gated CT were evaluated. The discriminative power for risk reclassification of both CAC assessment methods was assessed. Invasive coronary angiography was used as the gold standard, when available. A total of 140 patients aged between 30 and 88 years were included. The agreement between ordinally scored CAC and the Agatston score was excellent (κ = 0.82) and the correlation strong (r = 0.94). Most patients (80%) with an intermediate PTP had no or mild CAC on non−gated CT. They were reclassified at low risk with 100% accuracy compared with invasive coronary angiography. Similarly, 86% of patients had an Agatston score <300. These patients were reclassified with 98% accuracy. In patients with high PTP, the accuracy remained substantial and comparable, 94% and 89%, respectively. In conclusion, we believe this is the first study to assess the clinical applicability of CAC on non−gated CT in patients with stable chest pain, compared with the classic Agatston score. The agreement between methods was excellent and the correlation strong. Furthermore, CAC assessment on non−gated CT could reclassify patients' risk for obstructive coronary artery disease as accurately as could the classic Agatston score. **(Am J Cardiol 2023;208:92−100)**

Keywords: coronary artery disease, coronary calcium, non−gated computed tomography

Currently applied methods to determine patients' pretest likelihood of obstructive coronary artery disease (CAD)[1] tend to overestimate patients' actual risk. This overestimation causes an essential overuse of noninvasive diagnostic tests. With large healthcare expenditures for diagnosing CAD[2,3] and the current economic strain on healthcare systems, there is increasing interest in using simple, clinically available information on cardiac risk factors to optimize patient selection for additional imaging. Guidelines recommend assessing patients' coronary artery calcium (CAC).[4] Patients' CAC is classically assessed on electrocardiogram (ECG)-gated cardiac computed tomography (CT) with the Agatston score.

Coincidentally, CAC can be equally well assessed on non−gated chest CT performed for evaluation of noncardiac disease, such as pulmonary embolism.[5−8] This simple visual method correlates well with the Agatston score on gated CT.[9−11] Whether it can be applied as an additional tool for risk classification in patients with stable chest pain has yet to be determined. This study aims to evaluate the clinical applicability of CAC to non−gated CT in patients with stable chest pain, compared with the Agatston score in gated CT.

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See page 99 for Declaration of Competing Interest.

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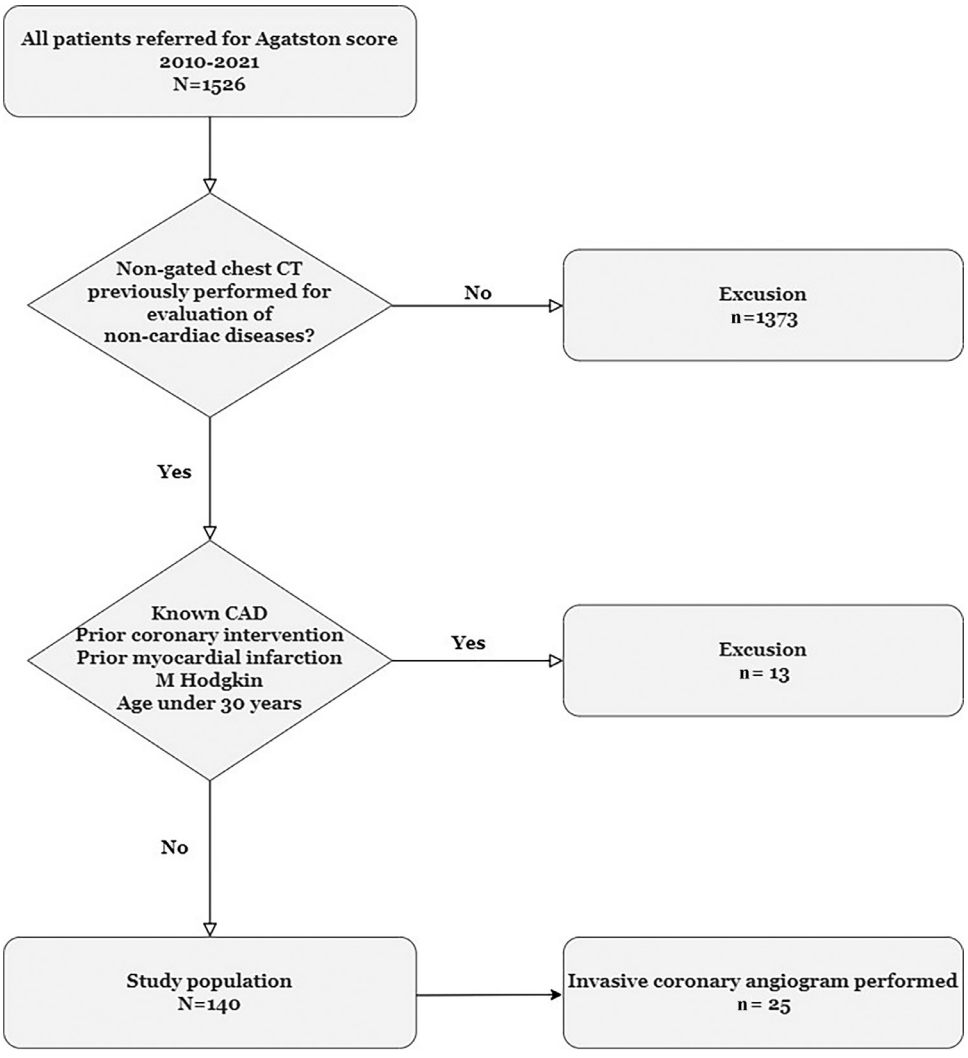

Figure 1. Selection of study population.

Methods

This retrospective study comprises patients presenting with stable chest pain at the outpatient cardiology clinic of the Leiden University Medical Center, who were referred for CAC assessment with the Agatston score. Between 2010 and 2021, 1,526 patients were referred for evaluation of the Agatston score. We selected all patients in whom a non−gated chest CT was previously performed for the evaluation of noncardiac diseases (n = 153, 10% of 1,526).

The patient selection is depicted in Figure 1. Subsequently, we excluded all patients with known CAD, percutaneous coronary intervention, coronary artery bypass graft, Morbus Hodgkin, or age <30 years. Ultimately, the remaining 140 patients formed the final study population. Of interest, all patients had a non−gated chest CT performed within 10 years of their first presentation at the outpatient clinic.

Furthermore, we determined each patient's pretest probability (PTP) of obstructive CAD following the European Society of Cardiology guidelines of 2019.[1] Subsequently, the patients were stratified according to PTP categories, defined as "low" (PTP of ≤5%), "intermediate" (PTP of 6% to 15%), or "high" (PTP of >15%), and analyzed accordingly. In addition, the patients' medical records were screened for presence of cardiovascular risk factors, such as diabetes mellitus and smoking.

The hospital's ethical review board waived the need for informed consent.

The Agatston score was performed on ECG-gated cardiac CT, using 320-slice scanners (Canon Medical Systems, Amstelveen, The Netherlands). A voltage of 120 kV and axial slices of 3 mm were used. Imaging software computed the Agatston score on the basis of the area of calcification per slice and the density of the calcification, as previously described by Agatston et al.[12]

Non−gated chest CT was performed as part of routine noncardiac care or as a follow-up of other diseases (e.g., lung nodules), before the patients' referral for CAC assessment. The specific scan protocol was different per indication (Canon Medical Systems); these protocols are described in Supplementary Table 1. CAC assessment on both nonenhanced and contrast-enhanced scans has been proved accurate.[13] The patients' CAC was assessed on standard dose scans with 1-mm axial slices. Recent literature describes a variety of methods for CAC assessment on

non−gated chest CT.[10,14,15] The studies revealed that simple visual assessment of CAC with severity quantified on an ordinal scale could accurately predict patients' CAD burden.[16,17] Furthermore, this method had excellent agreement with the classic Agatston score.[7,16] Ultimately, it appeared most time-efficient in comparison with other methods because CAC severity could be determined in <1 minute.[15] For these reasons, this previously described method[6,16,18] was used for CAC assessment in this study.

In brief, CAC is quantified on an ordinal scale ranging from 0 to 12, based on the extent of CAC in 4 coronary arteries (right coronary artery, left main, left anterior descending, left ramus circumflex), including secondary branches (e.g., diagonal, marginal). Subsequently, the patient's total CAC score is categorized on the basis of increasing severity: no (CAC 0), mild (CAC 1 to 3), and severe (CAC 4 to 12). These categories were used to evaluate the influence of risk factors and gender on the agreement with the following Agatston score categories: no (0), mild (1 to 299), and severe (≥300).[8,10,19] Gender is defined as a set of biologic attributes that are associated with physical and physiologic features (e.g., chromosomal genotype, hormonal levels, internal and external anatomy).

To compare the discriminative power of ordinally scored CAC with that of the classic Agatston score, invasive coronary angiography (ICA) was used as the gold standard, when available. Obstructive CAD on ICA was defined as a stenosis grade of ≥70%. Performance of fractional flow reserve was at the discretion of the operator, and a fractional flow reserve cut-off value of <0.80 was used as significant obstructive CAD. Patients were classified as not having obstructive CAD when no ICA was performed or when no obstructive CAD was observed on ICA. Conversely, when patients showed obstructive CAD on ICA, they were classified as having obstructive CAD. Ultimately, the medical records of all patients were screened for the occurrence of myocardial infarction and subsequent revascularization during follow-up.

Statistical analyses were performed using IBM SPSS, Chicago, Illinois version 25.0. Dichotomous variables were described as numbers (%), and continuous variables were reported as mean ± SD or median (interquartile range [IQR]). CAC severity groups were compared using a 1-way analysis of variance or a Kruskal-Wallis test for numerical outcomes and a chi-square test for dichotomous outcomes.

Fleiss' kappa statistic was used to assess the agreement between ordinally scored CAC on non−gated CT and the classic Agatston score. Stratified analyses were performed for gender and risk factors. The agreement was classified as poor with κ <0, as slight with κ = 0.01 to 0.20, as fair with κ = 0.21 to 0.40, as moderate with κ = 0.41 to 0.60, as good with κ = 0.61 to 0.80, and as excellent with κ = 0.81 to 1.00. Furthermore, a Spearman correlation was performed to assess the correlation between ordinally scored CAC and the classic Agatston score.

Results

Patient characteristics are described in Table 1. The mean age was 57 ± 11 years and was significantly different among the CAC severity groups (p <0.01). Of the 140 patients, 44% were male. More than 1/3 of patients (39%) had a history of hypertension; 19% had a history of hypercholesterolemia, and only 11% had diabetes mellitus. Gender and the presence of these risk factors did not differ significantly among the CAC groups. The median Agatston score of the entire study population was 3 (IQR 0 to 87). The Agatston score

Table 1
Baseline characteristics of study population, N=140

	All (n=140)	*None (n=74)*	*Mild (n=43)*	*Severe (n=23)*	*P-value*
Age, years	57 ±11	52±11	62 ±9	66 ±11	**<0.01**
Sex, men, %	61 (44%)	26 (35%)	24 (55%)	11 (48%)	0.09
BMI, kg/m^2	26 ±5	26 ±6	26 ±4	27 ±4	0.56
Comorbidities					
Hypertension* (%)	54 (39%)	22 (30%)	21 (48%)	12 (52%)	0.07
Diabetes, %	15 (11%)	6 (8%)	6 (14%)	3 (13%)	0.57
Hypercholesterolemia* (%)	27 (19%)	11 (15%)	11 (24%)	5 (22%)	0.35
ESRD/CKD (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	n/a
History of					
Cardiovascular disease (%)					
AF/AFI	9 (6%)	6 (8%)	2 (4%)	1 (4%)	0.56
CVA/TIA	8 (6%)	4 (5%)	3 (7%)	2 (9%)	0.87
History of smoking (%)					
Yes	49 (36%)	20 (27%)	20 (48%)	9 (39%)	0.08
Agatston score	3 (0-87)	0 (0-0)	51 (14-102)	367 (266-1073)	**<0.01**
Male					
Median	11 (0-113)	0 (0-0)	39 (9-98)	338 (255-1073)	**<0.01**
Female					
Median	0 (0-0)	0 (0-0)	62 (19-114)	407 (290-1023)	**<0.01**

All data are presented as mean ±SD, median (IQR) or as number (%).

* Hypertension: a systolic blood pressure >130 mmHg or a diastolic blood pressure >80 mmHg or taking medication for hypertension, Hypercholesterolemia: total cholesterol >200 mg/dL or ratio greater than 5 to 1.

AF = atrial fibrillation; AFI = atrial flutter; Abn = abnormalities; BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; CVA/TIA = cerebrovascular accident/transient ischemic attack; ESRD = end-stage renal disease; PE = pulmonary embolism.

Table 2
Agreement between ordinal coronary artery calcium and the Agatston score

AGREEMENT	Yes	No
Hypertension	0.80	0.83
Hypercholesterolemia	0.70	0.85
Diabetes	0.83	0.79
Smoking	0.84	0.80
Male sex	0.76	0.86

increased per ordinal CAC category and was significantly different among the CAC groups ($p < 0.01$).

Half of the patients (n = 69) were initially classified at intermediate risk of having obstructive CAD (i.e., had an intermediate PTP); 21% (n = 30) had low risk, and 29% (n = 41) had high risk of obstructive CAD.

Most non−gated chest CTs (68%) were performed within 1 year before presentation at the outpatient cardiology clinic. The median time interval was 0 (0 to 3) years.

The agreement of ordinally scored CAC and the Agatston score is listed in Table 2 and depicted in Figure 2. The overall agreement for the entire study population was excellent ($\kappa = 0.82$), and 93% of patients were categorized in the same risk category according to CAC severity. When patients were stratified according to risk factors, a similar agreement was seen in patients with hypertension ($\kappa = 0.80$) and without hypertension ($\kappa = 0.83$). The agreement decreased slightly in patients without versus those with diabetes mellitus ($\kappa = 0.79$ and $\kappa = 0.83$, respectively) yet remained good. In patients with hypercholesterolemia, the agreement was excellent ($\kappa = 0.85$), versus good ($\kappa = 0.70$) in patients without hypercholesterolemia. The agreement for smokers versus nonsmokers was similar ($\kappa = 0.84$ and $\kappa = 0.80$, respectively). In terms of gender, the agreement was slightly better in female than in male patients ($\kappa = 0.86$ and $\kappa = 0.76$, respectively), as depicted in Figure 2. Furthermore, a strong correlation was observed between ordinally scored CAC on non−gated CT and the classic Agatston score, with r = 0.94.

Of interest, an ordinal CAC score of 0 corresponded with a median Agatston score of 0 (IQR 0 to 0). Of the 74 patients with an ordinal CAC score of 0, 66 had an Agatston score of 0, yielding an accuracy of 89%. The remaining 8 had a median Agatston score of 9 (IQR 2 to 21). A mild

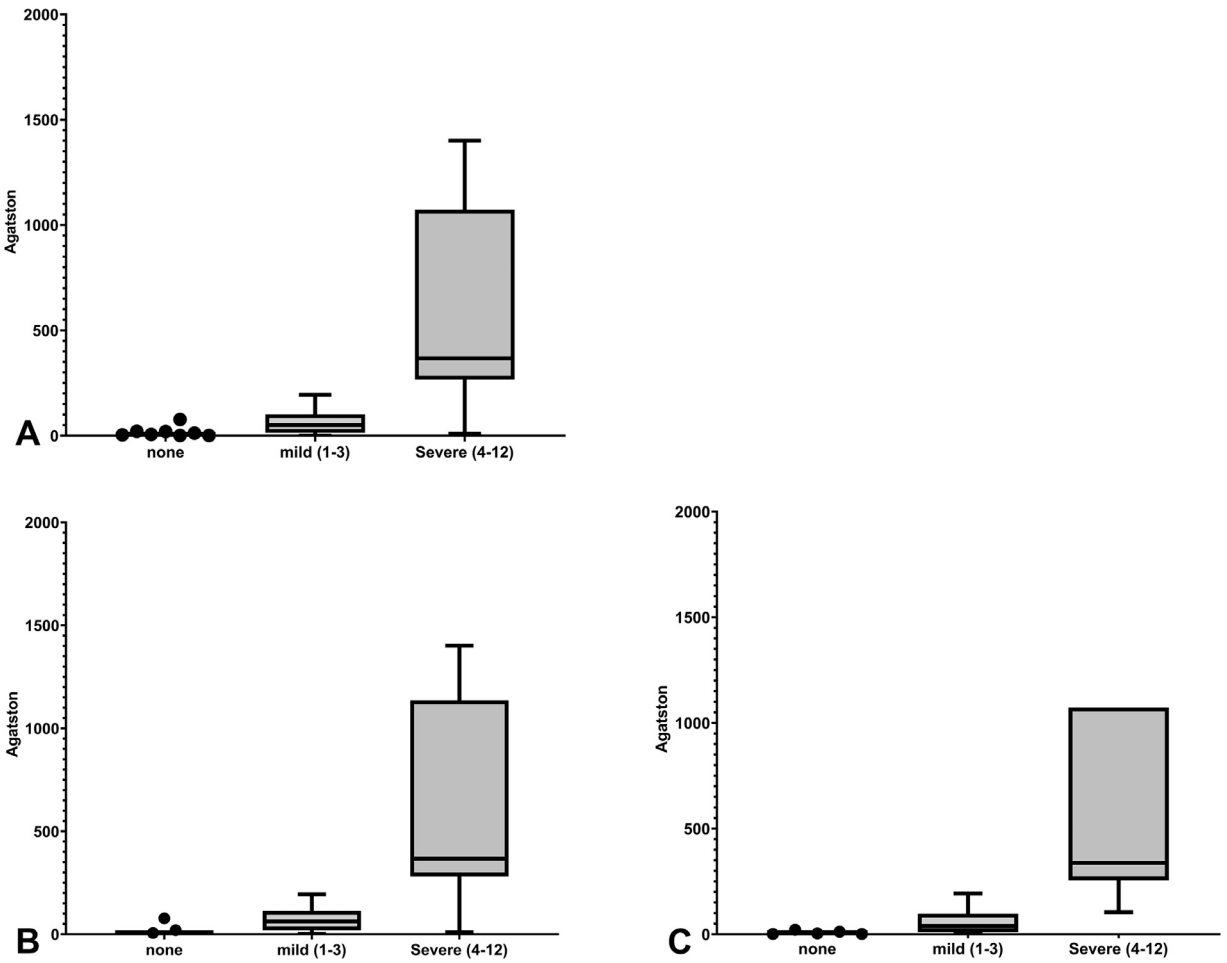

Figure 2. Corresponding Agatston score for ordinal CAC categories. (*A*) Corresponding Agatston scores for ordinal CAC categories in entire study population. (*B*) Corresponding Agatston scores for ordinal CAC categories in female patients. (*C*) Corresponding Agatston scores for ordinal CAC categories in male patients.

ordinal CAC score corresponded with an Agatston score 51 (IQR 14 to 102), and a severe ordinal CAC score corresponded with Agatston 367 (IQR 266 to 1,073). Similar trends were found for male and female patients.

The patients were stratified on the basis of their PTP in 3 groups (i.e., low, intermediate, and high). In each PTP group, patients were reclassified according to their ordinal CAC score, and ICA was performed in 25 of the 140 patients. The patients in whom no ICA was performed were classified as having absence of obstructive CAD. Of these patients, only 1 patient (<1%) received revascularization a year later, after presenting with acute coronary syndrome.

The patients' initial risk (i.e., intermediate or high) of obstructive CAD was "down"-classified to a low risk, when they had no or mild CAC (i.e., CAC ≤3). Severe CAC might have indicated a high(er) risk of obstructive CAD in patients with initially a low risk of obstructive CAD. However, in none of the patients with low PTP (n = 30) was severe CAC observed. Coincidentally, none of these patients had obstructive CAD. The same analyses were performed on the basis of the patients' Agatston score to compare the discriminative power of both CAC evaluation methods; patients' initial risk (i.e., intermediate or high) of obstructive CAD was down-classified to low risk when they had an Agatston score of <300. An Agatston score of ≥300 might have indicated a high(er) risk of obstructive CAD in patients who initially had a low risk. However, none of the patients with low PTP had an Agatston score of ≥300. Coincidentally, none of these patients had obstructive CAD.

Firstly, patients with intermediate PTP were reclassified on the basis of ordinal CAC, as is depicted in Figure 3. In this patient group (n = 69), 36 patients showed no CAC, and 19 showed mild CAC on non−gated chest CT. These 55 patients (80%), that is, patients with an intermediate PTP and CAC ≤3, were reclassified to a low risk. None of the 55 patients had obstructive CAD. Therefore, an ordinal CAC score of ≤3 could reclassify 80% of patients (55 of 69) at initially an intermediate risk, to a low risk with 100% accuracy (55 of 55). In the remaining 14 patients with intermediate PTP, severe CAC was observed. These patients could not be reclassified to a lower risk for obstructive CAD on the basis of their ordinal CAC score.

Secondly, the reclassification of patients with intermediate PTP based on the classic Agatston score is depicted in Figure 4. Most patients (n = 59) had an Agatston score of <300 and were reclassified to a low risk for obstructive CAD. Only 1 of these 59 patients had obstructive CAD. The remaining 58 patients had no obstructive CAD. Therefore, an Agatston score of <300 could reclassify 86% of patients (59 of 69) at initially an intermediate risk, with 98% accuracy (58 of 59). The remaining 10 patients with an intermediate PTP had an Agatston score of ≥300. These patients could not be reclassified to a low risk for obstructive CAD on the basis of their Agatston score.

Thirdly, patients with a high PTP were reclassified on the basis of ordinal CAC, as is depicted in Figure 5. Most patients (78%) with a high PTP showed no or mild CAC on non−gated chest CT (i.e., CAC ≤3). Of these patients, 2 showed obstructive CAD on ICA. The first patient was re-evaluated 2 years after CAC assessment owing to persistence of chest pain symptoms. Obstructive CAD was observed, and subsequent revascularization was performed. The second patient had an Agatston score of 188 and showed significant stenosis on coronary CT angiography (CCTA). Subsequent ICA was performed, and the patient was revascularized. The remaining 30 patients did not have obstructive CAD. Therefore, an ordinal CAC score of ≤3 could reclassify 78% of patients (32 of 41) at initially a high risk for obstructive CAD, to a low risk, with 94% accuracy (30 of 32). The remaining 9 patients with a high PTP had severe ordinal CAC and could not be reclassified.

Finally, reclassification according to the Agatston score is depicted in Figure 6. In 85% of patients with a high PTP, an Agatston score of <300 was observed. Subsequently, these patients were reclassified to a low risk for obstructive

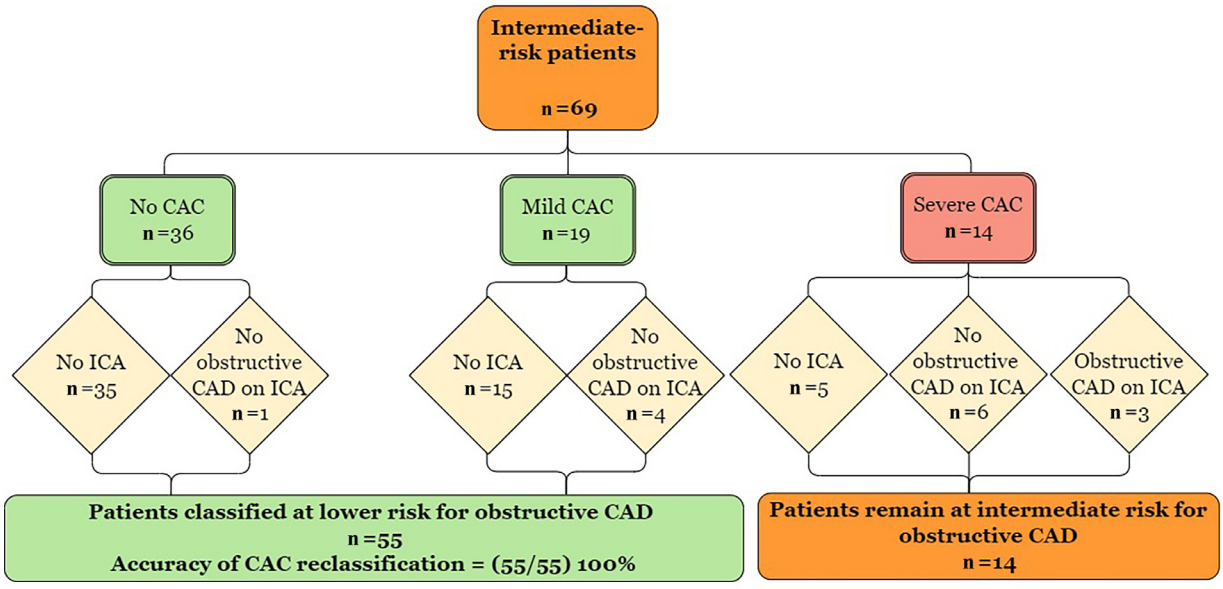

Figure 3. Reclassification of patients with intermediate PTP according to ordinal CAC.

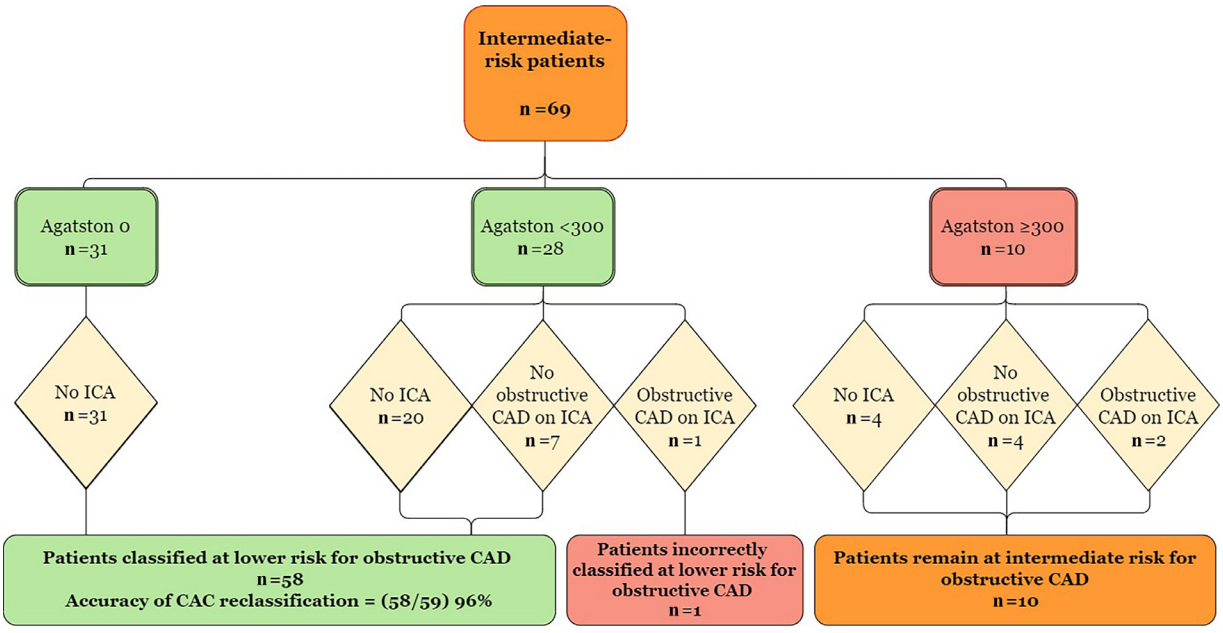

Figure 4. Reclassification of patients with intermediate PTP according to the Agatston score.

CAD. Only 4 of these patients showed obstructive CAD on ICA. The remaining 31 patients did not have obstructive CAD. An Agatston score of <300 could therefore reclassify 85% of patients (35 of 41) at initially high risk, to low risk with 89% accuracy (31 of 35). A total of 6 patients with a high PTP had a severe Agatston score of ≥300 and could not be reclassified at low risk for obstructive CAD.

As previously shown, on the basis of visual CAC assessment, additional noninvasive diagnostic testing could have been avoided in 84% of patients (117 of 140) with a previously performed CT. Incorporating missed diagnosis, additional imaging could have effectively been withheld in 82% of patients with a previously performed non−gated CT (10% of all patients with stable chest pain). Therefore, if 1,000 patients were to be referred to for CAD evaluation, the expenses for downstream testing could be reduced by 8% by incorporating this strategy.

Discussion

To further validate the accuracy of visually assessed CAC on non−gated CT, the present study analyzed the influence of risk factors and gender on the agreement with the classic Agatston score on ECG-gated cardiac CT. Furthermore, to

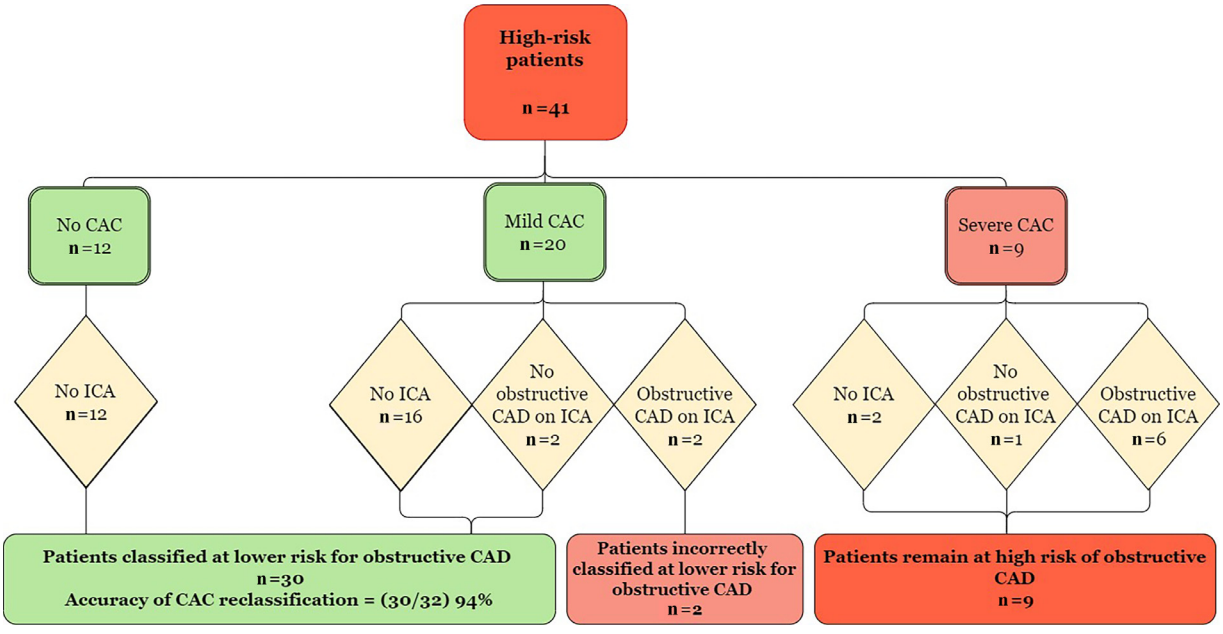

Figure 5. Reclassification of patients with high PTP according to ordinal CAC.

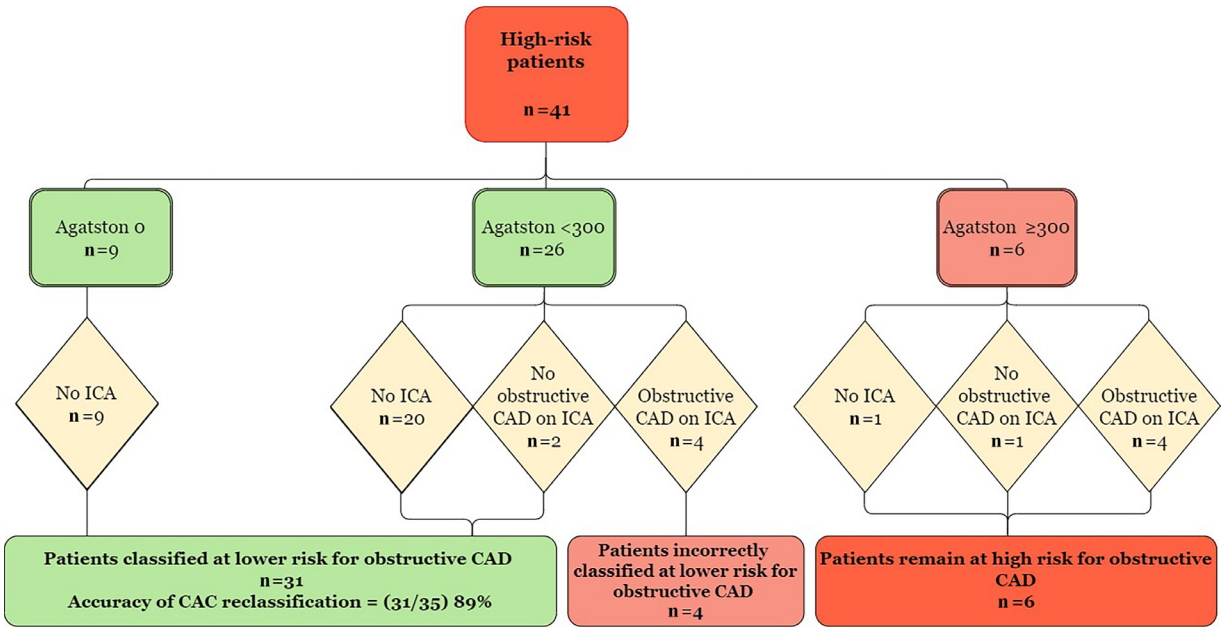

Figure 6. Reclassification of patients with high PTP according to the Agatston score.

the best of our knowledge, this study is the first to evaluate the discriminative power of CAC on non−gated CT for reclassification of patients' risk of obstructive CAD, as opposed to PTP estimations based on gender, age, and type of symptoms. The overall agreement between scoring methods was excellent (κ = 0.82). When patients with and those without cardiovascular risk factors were compared, the agreement between ordinal CAC on non−gated CT and the Agatston score on gated CT remained good (κ = 0.7 to 0.9). The observed correlation between ordinal CAC and the Agatston score was strong (r = 0.94). In addition, we showed that an ordinal CAC score of ≤3 on non−gated CT could efficiently reclassify patients with an initial intermediate and high risk of obstructive CAD. The impact and accuracy of reclassification based on ordinal CAC on non−gated CT were similar to those of the Agatston score on gated CT.

Several studies have assessed the agreement and correlation of the ordinal CAC score incorporated in this study and the classic Agatston score. Firstly, Azour et al[16] evaluated the agreement between ordinally assessed CAC and the Agatston score in 221 subjects without symptoms, living in the community. As in our study, most patients (>60%) had no CAC, and only a few had severe CAC (8%). The authors found an excellent agreement for the absence of CAC with (κ = 0.96). Furthermore, they revealed that severe ordinal CAC, that is, ≥4, corresponded with a median Agatston of 350, similarly to our study results. Chiles et al[20] reported an overall agreement of k = 0.75 between the 2 methods, analyzed in 1,442 patients of the National Lung Screening Trial. The agreement of ordinal CAC and the classic Agatston score in the abovementioned studies was comparable with ours (i.e., κ = 0.82). Two studies[7,17] reported a good-to-excellent correlation of the methods, with r ranging from 0.72 to 0.86. In our study, we observed a similar correlation (r = 0.94).

In terms of prognostic value, a study by Blair et al[17] compared the association of both methods with cardiovascular event (e.g., cardiac death). They reported that the Agatston score and ordinal CAC had a similar association with the occurrence of cardiovascular events, with odds ratio of 1.57 and 1.66, respectively. A study by Shao et al[21] compared the negative predictive value of no visible CAC with that of an Agatston score of 0 in 410 patients without symptoms who were referred by a respirologist. They showed a similar event-free survival rate for both visual CAC 0 on non−gated CT and an Agatston score of 0, 96.1% and 95.9%, respectively. Therefore, both methods could down-classify patients' risk for cardiovascular events.

Two studies[22,23] compared CAC-guided risk stratification with other risk estimation methods (e.g., PROspective Multicenter Imaging Study for Evaluation of chest pain [PROMISE] Risk Tool). They investigated which method of risk estimation could effectively defer patients at low risk for obstructive CAD. CAC-guided risk estimation yielded the highest specificity and negative predictive value among the risk models. To the best of our knowledge, no studies have previously described CAC on non−gated CT for risk reclassification.

A complementary benefit of incorporating CAC assessment in risk stratification for obstructive CAD is the reduced costs of not performed additional noninvasive diagnostic tests; no or mild CAC can accurately defer patients for noninvasive additional imaging, and a high CAC score could indicate immediate performance of functional tests (e.g., magnetic resonance imaging perfusion) rather than nondiagnostic anatomical tests (i.e., CCTA) first. A recent study by Gomes et al[24] described a cost-effective analysis of CAC evaluated on ECG-gated CT in patients with a PTP <15%. The authors analyzed the costs and benefits for 3 different strategies of patient evaluation. For the first strategy, no additional imaging was performed. For the second strategy, further testing was withheld when CAC was absent. When CAC was observed, a subsequent CCTA was

performed. For the third strategy, CCTA was performed immediately in all patients. They found that the costs of the first strategy were lowest; however, this strategy yielded too many missed diagnoses (10%). The second strategy could reduce the use of CCTA by 50%, at the expense of ~1% of patients being misdiagnosed for not having obstructive CAD. This yielded a total cost reduction of 8.8%. Incorporation of CAC evaluation in non−gated CT would reduce the costs of additional imaging by 8.2% (in 10% of patients with a non−gated CT). A combined strategy, with visual CAC evaluation on nongated CT and the Agatston score, might reduce the use and expenses of CCTA even more, given evaluation of CAC assessment on previously performed CT is both accurate and free of costs. The implementation of this inexpensive and additive method for risk classification would especially be relevant in low-resource healthcare settings.

The time interval between patients' non−gated CT and their first cardiology consultation could influence the predictability of CAC for obstructive CAD. Currently, no warranty for visually assessed CAC has been described. However, according to some studies,[25−28] the warranty of CAC on ECG-gated CT ranges from 5 to 15 years. The first study, by Dzaye et al,[26] indicated that the time to conversion of CAC 0 to CAC >0 would be 3 to 7 years, depending on age, gender, and risk factors. However, Valenti et al[27] described a warranty period for CAC 0 defined as <1% annual mortality rate. They showed a warranty period of 15 years for patients with low-to-intermediate risk, independent of age and gender. In our study, all patients had a previous CT performed within 10 years before their first presentation of chest pain. It would be interesting to validate the warranty of CAC assessed on previously performed non−gated CT.

Our study population is relatively small; nevertheless, we believe this is the first study to investigate the clinical value of CAC evaluation on non−gated CT in patients without symptoms. Previous studies have only described this method in an asymptomatic population. The present study provides a proof of concept for the application in patients with symptoms. For future perspectives, a larger (multicenter) study cohort could increase the study population and validate the predictive value of ordinal CAC. In addition, a prospective evaluation incorporating this method in standard care could be of interest for further investigation.

As stated earlier, ICA was performed in only 25 patients in this study. However, this is reasonable, given performance of ICA would be futile in patients with no or mild CAC.

The present study aimed to investigate the clinical applicability of CAC on non−gated CT in patients with stable chest pain. An excellent agreement of ordinally quantified CAC on non−gated CT and the Agatston score on ECG-gated CT was revealed, which was limitedly influenced by risk factors or gender. Overall, the correlation between methods was strong (r = 0.94). Furthermore, the discriminative power of CAC on non−gated CT for risk reclassification of patients with symptoms was evaluated and compared with the discriminative power of the Agatston score on gated CT. CAC assessment on non−gated CT could accurately defer patients who were essentially at low risk for obstructive CAD, and had equal discriminative power to that of the Agatston score on ECG-gated CT. Thus, when available, CAC on non−gated chest CT can be used as an additional tool for clinical evaluation of patients presenting with stable chest pain. We therefore recommend physicians to check whether previous imaging is available and incorporate the available data. When no non−gated CT has been performed, the Agatston score on ECG-gated cardiac CT remains the modality of choice. Ultimately, incorporating cost-free CAC assessment on non−gated CT as a gatekeeper for downstream testing in patients with stable chest pain could effectively reduce expenses.

Declaration of Competing Interest

The authors have no competing interests to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.08.186.

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