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**Title**: Clinical applications of non-invasive imaging techniques in suspected coronary artery disease and in acute myocardial infarction  
**Issue Date**: 2015-04-02
Part I

RISK STRATIFICATION WITH MDCT
Chapter 2

Coronary Artery Calcium Scoring in Cardiovascular Risk Assessment

Gaetano Nucifora, Jeroen J. Bax, Jacob M. van Werkhoven, Mark J. Boogers, Joanne D. Schuijf

Cardiovasc Ther 2011;29:e43-53
ABSTRACT

Identification of patients at risk of future coronary artery disease (CAD) events traditionally relies on scoring tools that take demographic and clinical characteristics into account (e.g., the Framingham risk score in the United States and the Heart Score in Europe). Although these scoring tools have been shown to have a good predictive value, they may still fail to recognize a proportion of patients with coronary atherosclerosis at risk for future CAD events. In order to improve risk stratification, direct visualization of subclinical atherosclerosis has been advocated. Electron-beam computed tomography and multislice computed tomography provide a direct estimation of coronary calcium, a marker of coronary atherosclerosis. A large amount of data is available supporting the clinical value of the noninvasive assessment of coronary artery calcium score (CACS) with these techniques and its incremental prognostic information over traditional risk stratification. Aim of this review is to provide an overview of the literature regarding the prognostic value of CACS assessment. In addition, potential other applications of CACS assessment as well as the limitations of the technique are discussed.
INTRODUCTION

Identification of patients at risk of developing coronary artery disease (CAD) events is one of the most challenging issues in clinical cardiology. Indeed, in a large proportion of individuals, the initial presentation of CAD is acute myocardial infarction (AMI) or sudden cardiac death. The risk of CAD events in subjects without known CAD is related to the presence of coronary risk factors (i.e., age, gender, diabetes mellitus, systolic blood pressure, total cholesterol and high-density lipoprotein cholesterol level, and smoking history). For this reason, scoring tools that take demographic and clinical characteristics into account (e.g., the Framingham risk score (FRS) in the United States and the Heart Score in Europe) have been developed and are frequently used in clinical practice to predict the 10-year risk of hard CAD events. Accordingly, these algorithms allow stratification of individuals into low-, intermediate- and high-risk categories, in order to determine the need and intensity of risk-modifying interventions. However, these scoring tools have several limitations that reduce their ability to provide accurate risk stratification.

In particular, cardiovascular risk may not be adequately recognized in certain subset of patients including young individuals and nondiabetic women below the age of 70 years. In addition, a variation in CAD severity for each level of risk factor exposure has been observed, likely related to the duration of exposure, genetic susceptibility and other biochemical and environmental risk factors.

Several biomarkers and noninvasive imaging techniques have been advocated to refine the traditional risk assessment of CAD events. Among the available noninvasive imaging techniques, coronary artery calcium score (CACS) assessment with electron-beam computed tomography (EBCT) or multislice computed tomography (MSCT) may represent a practical approach since it provides a direct noninvasive estimate of atherosclerotic plaque burden in the coronary arteries. The aim of this review is to provide an overview of the literature regarding the prognostic
value of CACS assessment. In addition, potential other applications of CACS assessment as well as the limitations of the technique are discussed.

**EBCT AND MSCT FOR CORONARY ARTERY CALCIUM ASSESSMENT**

EBCT and MSCT have been previously validated as sensitive techniques for the detection of coronary calcium, a marker of coronary atherosclerosis.\(^\text{10}\) EBCT was introduced in the early 1980s specifically for cardiac imaging. The use of nonmechanical X-ray source allows for prospective ECG-triggered image acquisition with high temporal resolution (50–100 ms), thereby limiting respiratory and cardiac motion artifacts. Usually, 30–40 nonoverlapping slices of 3 mm thickness are obtained during a single 20-to 30-second breath hold to include the whole heart and the entire coronary artery tree.\(^\text{11}\) Coronary calcifications are defined as hyperattenuating lesions >130 Hounsfield units with an area of three or more adjacent pixels (at least 1 mm\(^2\)).\(^\text{11}\) To quantify the extent of coronary calcium, a score has been developed by Agatston et al.\(^\text{12}\) Using 3-mm slice thickness images, the CACS is defined as the product of the area of calcification per coronary segment and a factor rated 1 through 4 determined by the maximum calcium CT density within that segment. To express the extent of detected coronary calcium, CACS is commonly classified into four categories: 0, 1–99, 100–399, and ≥400, indicating no calcific deposits, mild, moderate, and severe coronary calcifications, respectively.\(^\text{13}\) The presence of coronary calcifications and the extent of CACS has been found to be also gender- and age-related; in particular, a rapid increase in CACS is present in men after age 45 and in women after age 55.\(^\text{14}\) These data have been used to derive nomogram tables, in order to compare CACS of asymptomatic subjects with the expected normal values (Table 1).\(^\text{14}\) A CACS ≥75th percentile for age- and gender-matched individuals is usually considered as an indicator of elevated coronary calcium burden.\(^\text{15-17}\) Several studies have recently demonstrated that
CACS obtained using newer generation MSCT scanners (with higher number of detectors and faster X-ray gantry rotation time) are comparable to those obtained with EBCT.\textsuperscript{18-20} However, it should be acknowledged that MSCT has still lower interscan and interreader reproducibility than EBCT.\textsuperscript{21} Examples of patients with and without coronary calcium, as detected by MSCT, are shown in Figure 1.

**Table 1.** Coronary artery calcium scores (CACS) by percentile, gender and age in a large asymptomatic population (N* = 21265) screened with electron-beam computed tomography. Adapted from Wong et al.\textsuperscript{14} with permission.

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Figure 1. **Panel A.** 47-year-old asymptomatic female at intermediate risk for future coronary artery disease (CAD) events. Coronary artery calcium score (CACS) assessment by MSCT reveals the absence of coronary calcium. **Panel B.** 55-year-old asymptomatic male patient at intermediate risk for future CAD events. Evaluation of CACS by MSCT reveals the presence of coronary calcium in the left anterior descending coronary artery. Total CACS was >400.

**CORONARY ARTERY CALCIFICATIONS AND Atherosclerosis**

Calcifications of the coronary arteries are strictly related to the process of atherosclerotic plaque formation and evolution.\(^{22}\) Previous studies have consistently demonstrated that vascular deposition of mineral calcium is not simply a passive precipitation of calcium phosphate crystals in damaged tissues.\(^{23,24}\) Instead, it is an organized and regulated process similar to bone formation that typically occurs in areas of atherosclerotic lipid accumulation.\(^{23,24}\) Consequently, the presence of calcific deposits in coronary arteries is considered to be pathognomonic of coronary atherosclerosis. In addition, histopathological and intravascular ultrasound studies found a good correlation between CACS measured using EBCT and the volume of coronary artery atherosclerosis, leading to the concept that CACS may be considered a surrogate of total atherosclerotic plaque burden.\(^{10,25-27}\) In this regard, however, two main drawbacks of CACS assessment should be acknowledged. Firstly, a large part of the total plaque volume is due to noncalcified tissue, which is not detected. As a result, CACS may underestimate total coronary atherosclerotic plaque burden, particularly in younger individuals.\(^{10}\) Secondly, the relation of
coronary calcification and the presence of significant stenosis is more variable.\textsuperscript{22} Even though a positive relation exists between the amount of CACS and the likelihood of significant luminal narrowing, obstructive plaques can occur at sites with limited calcium, while extensive calcific deposits without stenosis can be observed.\textsuperscript{28-32}

**RISK STRATIFICATION OF ASYMPTOMATIC SUBJECTS**

Numerous studies have previously demonstrated the ability of CACS to predict cardiac events in asymptomatic subjects, with significant incremental value over conventional risk factor assessment. In a retrospective study of 5635 asymptomatic adults at low-intermediate risk (mean age 51±9 years), Kondos et al.\textsuperscript{17} observed that CACS >170 measured with EBCT was associated with a relative risk of cardiac events of 7.2 (95% CI 2.0–26.2), after a mean follow-up of 37 months. The prognostic information obtained from CACS assessment was incremental to conventional risk stratification. Similar findings were reported by Shaw and colleagues in a retrospective analysis of 10,377 asymptomatic patients (40% women), with a mean of 5 years follow-up after EBCT evaluation.\textsuperscript{33} CACS was an independent predictor of death after adjustment for Framingham risk factors (p <0.001), with an increase of risk that was proportional to the increase of CACS (risk-factor adjusted relative risk of 1.6, 1.7, 2.5, and 4 for CACS 11–100, 101–400, 401–1000, and >1000, respectively). The incremental value of CACS to FRS was illustrated by a significant increase of the area under the ROC curves, from 0.72 for FRS to 0.78 with the addition of CACS (p <0.001). Further follow-up in a large cohort of 25,253 asymptomatic subjects confirmed these data, showing increasing mortality rates after a mean follow-up of 6.8 years with increasing baseline CACS (Figure 2).\textsuperscript{34}
Figure 2. Cumulative survival by coronary artery calcium score (CACS) after adjustment for coronary risk factors (age, hypercholesterolemia, diabetes mellitus, smoking, hypertension, and family history of premature coronary heart disease). Increasing CACS was associated with increased risk of all-cause mortality. DM: diabetes mellitus; HTN: hypertension. Adapted from Budoff et al.\textsuperscript{34} with permission.

Prospective studies have confirmed these observations reinforcing the concept that CACS assessment may be of clinical value to refine traditional risk stratification.\textsuperscript{35–37} In a prospective observational population-based study, Greenland et al.\textsuperscript{35} used EBCT to screen 1029 asymptomatic nondiabetic subjects older than 45 years with at least one coronary risk factor. After a median follow-up of 7 years, a CACS >300 predicted the risk of AMI or cardiac death (hazard ratio 3.9; 95% CI 2.1–7.3; \( p < 0.001 \)) compared with a CACS of zero. Across FRS categories, CACS was predictive of risk among subjects with intermediate and high FRS, but not among subjects with low FRS. Figure 3 shows the predicted 7-year event rates (AMI or cardiac death) across FRS and CACS categories.
Figure 3. Predicted 7-year event rates for categories of FRS and CACS. Pairwise analyses compared the highest CACS level (>300) with each of the lower levels of CACS within each FRS group. A statistically significant difference between CACS >300 and each of the other three CACS groups was observed for FRS >10% (p <0.001) and between CACS >300 and CACS zero for FRS <10% (p = 0.01). From Greenland et al.\textsuperscript{35} with permission.

More recently, in the St. Francis Heart Study,\textsuperscript{36} screening for CAD by EBCT was performed in 4903 asymptomatic individuals. In the subgroup of 1357 subjects in whom risk factors were measured, CACS was superior in the prediction of CAD events (cardiac death, AMI, surgical, or percutaneous coronary revascularization procedures) after a mean follow-up of 4.3 years as compared to the FRS. Area under the ROC curve for CACS was 0.79 as compared to 0.68 for FRS (p <0.001). In addition, CACS significantly improved the risk stratification based on FRS (p <0.001 for trend).

On the basis of these previous studies, a consensus document from the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) has been recently published, providing
recommendations on the use of CACS assessment for risk stratification of asymptomatic subjects. In particular, individuals at intermediate FRS risk are considered to represent potential candidates for evaluation of CACS. In this group, the presence of \( \text{CACS} \geq 400 \) would allow reclassification of individuals to a higher risk category, thereby altering clinical decision-making. Conversely, CACS screening is not recommended in subjects at either low or high FRS. In patients at low risk, the presence of a high CACS would not elevate the individual's risk above the threshold to initiate medical therapy. Conversely, in the latter category, a high risk of CAD events is a priori anticipated on the basis of the high-risk profile, and aggressive medical therapy is already required. Moreover, Blaha et al. recently showed that, after a mean follow-up of 5.6 years, asymptomatic subjects at high risk (in particular diabetic patients and smokers) even in the absence of coronary calcifications, experience more CAD events, as compared to patients at low risk. Accordingly, the ACCF/AHA consensus document does not support the concept that absence of CACS would lower the risk status of individuals with high FRS.

Of note, in opposition to ACCF/AHA consensus document, the US Preventive Services Task Force (USPSTF) did not recommend the use of CACS for risk stratification of asymptomatic subjects. In particular, the USPSTF pointed out that only poor- to fair-quality evidence indicates that higher CACS predicts CAD events independent of Framingham risk factors, on the basis of a systematic review of eight cohort studies. However, it is important to remark that USPSTF did not include in its analysis the results of important large prospective, population-based studies clearly demonstrating the incremental prognostic value of CACS over conventional risk factor assessment. Inclusion of these studies may possibly lead the USPSTF to revise its recommendation.
RISK STRATIFICATION OF SYMPTOMATIC PATIENTS

Most of the available data regarding the clinical value of CACS assessment have been obtained in asymptomatic individuals. However, several studies have shown the utility of CACS for risk stratification also in symptomatic subjects. In a prospective, multicenter study of 491 symptomatic patients (mean age 55±12 years) who underwent both invasive coronary angiography and EBCT, Detrano and colleagues observed a strong association between CACS and the occurrence of CAD events.\(^{41}\) Patients with CACS higher than the median value (75.3) had a six times higher probability of CAD events after a mean follow-up of 30±13 months, as compared to patients with CACS below the median value. Interestingly, at multivariate analysis, log CACS, but not the number of significantly diseased segments at invasive coronary angiography, was selected as an independent predictor of CAD events, suggesting that global plaque burden rather than the degree of stenosis mainly determines the prognosis of CAD.

Keelan et al.\(^ {42}\) further confirmed these preliminary observations. A total of 288 symptomatic subjects who underwent invasive angiography and EBCT were followed-up for 6.9 years. Univariate analysis showed that CACS ≥100 was significantly related to the occurrence of hard CAD events (unadjusted relative risk 3.2, 95% CI 1.17–8.71; \(p = 0.023\)). At multivariate analysis, besides increasing age, CACS was the most powerful predictor of future hard CAD events. Conversely, none of the conventional coronary risk factors (except age) nor angiographic stenosis was related to the occurrence of CAD events, supporting the results of Detrano and colleagues. In another study, Georgiu et al.\(^ {43}\) screened, by EBCT, 192 patients admitted in the emergency department because of chest pain. A graded relation between increasing CACS values and the incidence of cardiovascular events after a mean follow-up of 50±10 months was observed. In particular, the annualized event rate was 0.6% for the patients without coronary calcium as compared with 13.9% per
year for the patients with CACS >400 (p <0.001). At multivariate analysis, CACS and age- and gender-matched calcium percentiles were the strongest predictors of future events. The results of these studies demonstrate that CACS assessment also in symptomatic subjects may provide valuable prognostic information.

**SELECTION OF PATIENTS REQUIRING TREATMENT**

On the basis of the prognostic data previously described, CACS has been proposed to refine medical decision-making. Indeed, the National Cholesterol Education Program’s Adult Treatment Panel III guidelines state that the presence of a high CACS (defined as CACS at or above the 75th percentile for age and gender) in subjects at intermediate risk of CAD events identifies advanced coronary atherosclerosis. In these patients, more intensive lipid-lowering therapy is recommended in order to achieve a low-density lipoprotein cholesterol target of less than 100 mg/dl. However, thus far, only few data on the outcome of medical therapy based on CACS are available. In the St. Francis Heart Study, 1005 asymptomatic subjects (mean age 59±6 years) with CACS at or above the 80th percentile for age and gender were randomized to receive atorvastatin 20 mg daily, vitamin C 1 g daily, and vitamin E (alpha-tocopherol) 1000 U daily or placebo. All subjects received aspirin 81 mg daily. Mean duration of treatment was 4.3 years. Treatment significantly reduced total cholesterol by 26.5–30.4% (p <0.0001), low-density lipoprotein cholesterol by 39% (p <0.001), and triglycerides by 11% (p = 0.02). Nevertheless, no significant reduction in atherosclerotic cardiovascular disease event rate was achieved by treatment. Interestingly, however, subanalysis revealed that treatment did reduce event rates in individuals with baseline CACS >400 (8.7% vs. 15.0%, 42% reduction, p <0.046).

More recently, McCullough and Chinnaiyan systematically reviewed five prospective randomized trials evaluating the change in CACS as a
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surrogate endpoint for treatment effect in patients at risk for or with CAD and could not demonstrate any consistent treatment effect on CACS progression at 1 year of follow-up.\textsuperscript{46} Further randomized studies are therefore needed to clarify whether clinical management based on CACS may positively impact outcome.

**SELECTION OF FURTHER DIAGNOSTIC TESTS**

CACS provides a relatively simple method for early identification of atherosclerosis. Accordingly, the technique may be used to identify patients that may benefit from further evaluation by means of functional testing. In comparative studies between CACS and myocardial perfusion imaging a relationship has been observed between the presence and extent of calcifications and the presence of ischemia.\textsuperscript{47–62} In one of the first comparative studies by He et al.\textsuperscript{47} in predominantly asymptomatic individuals, abnormal perfusion was observed in 0% of individuals with a CACS \(<10\), in 2.6% of individuals with a CACS \(11–100\), in 11.3% of individuals with a CACS \(101–400\), and in 46% of individuals with a CACS \(>400\). Similar increases in the prevalence of ischemia with increasingly higher CACS have been observed in other studies.\textsuperscript{48–52,54–61} Importantly, a CACS above 400 has consistently been shown to imply a high likelihood of ischemia. Accordingly, further evaluation by means of myocardial perfusion imaging in patients with CACS exceeding 400 has been deemed appropriate.\textsuperscript{63} Since a CACS \(>400\) is observed in only approximately 10% of asymptomatic individuals,\textsuperscript{34} only a small proportion of patients referred for CACS will need further evaluation with ischemia testing. Conversely, in asymptomatic individuals with a CACS \(<100\), further testing using myocardial perfusion imaging may not be needed as the prevalence of ischemia in patients with a CACS \(<100\) is generally very low (\(<10\%).\textsuperscript{47,48,50,58,63,64} Although this notion may be valid for the general asymptomatic population, some studies have reported a higher prevalence of ischemia in
patients with low CACS. Most likely, the observed discrepancies may reflect differences in study populations.\textsuperscript{49,54,56,60} In a large study in asymptomatic patients with diabetes, a higher prevalence of myocardial perfusion defects (18\%) was observed in patients with a low CACS between 11 and 100.\textsuperscript{53} In a further evaluation by Scholte et al.\textsuperscript{60} in asymptomatic diabetics, the prevalence of ischemia in patients with a low CACS <100 was 21\%. These observations indicate that CACS should be treated with caution in patients with diabetes, as a low CACS may not invariably rule out the presence of ischemia. Also in symptomatic patients, a higher prevalence of ischemia (exceeding 10\%) has been observed in individuals with a low CACS <100; furthermore, the increased prevalence of ischemia has been linked to the severity of symptoms and the pretest likelihood of CAD.\textsuperscript{55,57–59} As compared to patients with minor symptoms or a low pretest likelihood, a higher proportion of patients with more severe symptoms or a higher pretest likelihood appear to have ischemia despite low CACS.\textsuperscript{58} In symptomatic patients therefore, CACS may only serve as a reliable gatekeeper for myocardial perfusion imaging in patients with relatively minor symptoms and a low pretest likelihood for CAD.

\textbf{EVALUATION OF TREATMENT}

Serial assessment of CACS has been previously proposed to evaluate the efficacy of treatment with lipid-lowering drugs. Callister and colleagues retrospectively studied 149 asymptomatic patients (age range 32–75 years, 61\% men) who underwent two consecutive EBCT examinations for CACS evaluation at least 12 months apart.\textsuperscript{65} Patients treated with HMG-CoA reductase inhibitors with a final low-density lipoprotein cholesterol level of less than 120 mg/dl had a significant reduction in CACS (mean change $-7 \pm 23\%$; $p = 0.01$) whereas a significant increase in CACS (mean change $+25 \pm 22\%$, $p < 0.001$) was observed in treated patients with a final low-density lipoprotein cholesterol level of at least 120 mg/dl.
An even larger increase in CACS was observed in untreated patients who had a final low-density lipoprotein cholesterol level of at least 120 mg/dl; in these subjects, a mean change of $+52 \pm 36\%$ in CACS was observed at follow-up ($p < 0.001$).

Similar results were observed by Budoff et al.\textsuperscript{66} and Achenbach et al.\textsuperscript{67} Budoff et al.\textsuperscript{66} studied 299 asymptomatic subjects (mean age 58±10 years, 76\% men) who underwent baseline EBCT for CACS evaluation and follow-up assessment after a minimum of 12 months. The observed mean change in CACS in the study population was $33.2 \pm 9.2\%$ per year. The increase in CACS among patients receiving statin therapy was significantly lower, as compared to nontreated patients ($15 \pm 8\%$ per year vs. $39 \pm 12\%$ per year; $p < 0.001$) (Figure 4).

![Figure 4](image)

**Figure 4.** Effect of statin therapy on the progression of coronary calcifications in 299 asymptomatic subjects with high cholesterol levels. The progression of coronary calcifications in the study population was $33.2 \pm 9.2\%$ per year (right). The progression of coronary calcifications among patients receiving statins (left) was significantly lower, as compared to nontreated patients (middle). From Budoff et al.\textsuperscript{66} with permission.

Achenbach et al.\textsuperscript{67} studied 66 asymptomatic subjects with low-density lipoprotein cholesterol level higher than 130 mg/dl, no lipid-lowering treatment and a prior EBCT scan with evidence of coronary calcium (CACS
A second EBCT scan was performed after a mean interval of 14 months (untreated period) and a third EBCT scan was repeated after 12 months of therapy with cerivastatin (treatment period). During the untreated period, the median annual relative increase in CACS was significantly higher (25%) as compared to the median annual relative increase in CACS during the treatment period (8.8%, \( p < 0.001 \)).

Assessment of CACS progression during statin treatment may be also useful to improve the identification of patients at risk of future CAD events. Raggi and colleagues [68] studied 495 asymptomatic subjects (57 ± 8 years) in whom an initial EBCT study had revealed evidence of coronary calcium (CACS ≥ 30). After the baseline EBCT study, statin therapy was started and, after a mean interval of 1.9 ± 1 years, the EBCT examination was repeated. During a mean follow-up of 3.2 ± 0.7 years, AMI was observed in 41 patients. Interestingly, CACS progression was significantly higher among patients experiencing AMI as compared to event-free subjects (42 ± 23% per year vs. 17 ± 25% per year; \( p < 0.001 \)). At multivariate analysis, besides CACS at follow-up, CACS progression >15% per year was the most powerful predictor of future AMI (\( p < 0.001 \)).

However, more recent randomized trials failed to confirm these preliminary results. In particular, the St. Francis Heart Study failed to demonstrate that atorvastatin 20 mg daily (together with vitamin C 1 g daily, and vitamin E 1000 U daily) was able to reduce the progression of coronary calcifications in 1005 asymptomatic subjects.\(^{45}\) Similarly, the BELLES study showed that intensive statin therapy (i.e., atorvastatin 80 mg daily) compared to moderate statin therapy (i.e., pravastatin 40 mg daily) did not reduce the progression of coronary calcifications in 615 hyperlipidemic, postmenopausal women.\(^{69}\) Consequently, on the basis of these contradictory data, serial CACS scanning to evaluate the efficacy of treatment with lipid-lowering drugs and the progression of coronary calcification cannot be currently advised.
LIMITATIONS OF CALCIUM SCORING

Despite the large amount of data supporting its value as noninvasive marker of coronary atherosclerosis and its clinical utility, some limitations of CACS assessment need to be acknowledged. CACS assessment does not provide information on the degree of coronary stenosis. Previous studies showed that the specificity for obstructive CAD is about 40%. Accordingly, in symptomatic patients, in whom the clinical goal is to determine the cause of symptoms and thus assess the presence of lesions potentially requiring revascularization, the value of CACS assessment may be limited. Moreover, CACS assessment only visualizes calcified plaques, and consequently patients with exclusively noncalcified plaques are not identified. This issue appears to be relevant especially in the setting of diabetes mellitus and (acute) chest pain syndromes. Scholte et al. for instance, using MSCT coronary angiography, showed that in asymptomatic patients with type 2 diabetes a nonnegligible proportion of coronary plaques (41%) are noncalcified. Among patients with acute and long-term chest pain syndrome, Rubinshtein and colleagues showed that a low or zero CACS was not able to exclude the presence of obstructive CAD. Use of MSCT coronary angiography revealed single-vessel CAD in all patients with zero CACS, while multivessel CAD was identified in 50% of patients with low CACS (defined as CACS <100). More recently, Gottlieb et al. observed that a nonnegligible proportion (19%) of patients with zero CACS clinically referred for conventional angiography had indeed ≥1 obstructive coronary lesion; of note, 12.5% of patients with zero CACS underwent coronary revascularization within 30 days. Similar results were reported by Henneman et al. and Marwan et al. In these studies, a high prevalence of obstructive CAD in the absence of coronary calcifications was observed among patients with acute coronary syndromes.
Figure 5. Panel A. Coronary artery calcium score (CACS) has a significant incremental prognostic value (depicted by χ² value on the y-axis) over age and gender (#). Obstructive CAD (50% stenosis) on multislice computed tomography coronary angiography (MSCTA) and plaque burden (i.e., number of diseased segments or segments with obstructive CAD on MSCTA) have a further incremental prognostic value over age, gender, and CACS (*). Panel B. CACS has a significant incremental prognostic value (depicted by χ² value on the y-axis) over age and gender (#). MSCTA plaque composition has a further incremental prognostic value over age, gender, and CACS (*). Adapted from van Werkhoven et al.76 with permission.
On the basis of these data, noninvasive assessment of coronary atherosclerosis by means of MSCT coronary angiography may further improve identification of high-risk patients. Recently, van Werkhoven et al.\textsuperscript{76} demonstrated indeed that evidence of obstructive CAD as well as the number of diseased segments, obstructive segments, and noncalcified plaques at MSCT coronary angiography have significant incremental prognostic value over CACS in symptomatic patients with suspected CAD (Figure 5).

**CONCLUSIONS**

A large amount of data supports the use of CACS assessment to improve risk stratification as compared to conventional risk assessment. CACS may be particularly valuable in asymptomatic individuals at intermediate risk. In these patients, the information provided by CACS assessment could significantly alter the clinical decision-making.

**REFERENCES**


52. Ramakrishna G, Breen JF, Mulvagh SL, et al. Relationship between coronary artery calcification detected by electron-beam computed tomography and


