



Coronary calcification on invasive angiography and the Agatston score—a single-center experience

Zafraan Zathar^{1*} , Manish Pandit², Anne Karunatileke³, Alp Notghi², Vinoda Sharma^{1,4}

¹Department of Cardiology, City Hospital, Sandwell and West Birmingham Hospital NHS Trust, B18 7QH Birmingham, UK

²Department of Nuclear Medicine, Birmingham City Hospital, Sandwell and West Birmingham Hospital NHS Trust, B18 7Q Birmingham, UK

³General Practice, St Helen's & Knowsley Teaching Hospitals, L35 5DR Prescot, UK

⁴Institute of Cardiovascular Sciences, University of Birmingham, B15 2SQ Birmingham, UK

***Correspondence:** Zafraan Zathar, Department of Cardiology, City Hospital, Sandwell and West Birmingham Hospital NHS Trust, Dudley Road, B18 7QH Birmingham, UK. Zafraan.zathar2@nhs.net

Academic Editor: Antonello D'Andrea, University of Campania Luigi Vanvitelli, Italy

Received: November 28, 2023 **Accepted:** March 1, 2024 **Published:** April 15, 2024

Cite this article: Zathar Z, Pandit M, Karunatileke A, Notghi A, Sharma V. Coronary calcification on invasive angiography and the Agatston score—a single-center experience. *Explor Cardiol.* 2024;2:67–78. <https://doi.org/10.37349/ec.2024.00022>

Abstract

Aim: The pattern and severity of coronary artery calcification (CAC) can influence prognosis and outcome in percutaneous coronary intervention. An objective assessment of CAC during invasive angiography may provide additional prognostic information. This study aimed to assess the correlation between the angiographic Birmingham calcium score (BCS) and the Agatston coronary calcium score (CCS) performed as part of single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI).

Methods: In this retrospective observational study, patients undergoing SPECT-MPI and invasive coronary angiography as part of their routine management were included. BCS was calculated by reviewing angiography images in retrospect by an observer blinded to the SPECT-MPI calcium score. Spearman's correlation was used to analyze the correlation between BCS and SPECT-MPI. Receiver operating characteristic curve was used to detect cut-off for BCS that would detect clinically significant CAC [> 400 Agatston units (AU)]. Kaplan-Meier was used to report on outcomes at 5 years follow-up.

Results: In this cohort of 151 patients, there was a positive correlation between BCS and CCS [Spearman correlation coefficient (r) = 0.558, $P < 0.001$]. Cumulative BCS of 1 was able to identify clinically significant CAC [area under the curve 0.788, 95% confidence interval (CI) 0.714–0.863]. Cumulative BCS ≥ 3 was associated with major adverse outcomes at 5 years follow-up (log rank $P = 0.013$).

Conclusion: BCS correlates well with established higher CCS. Application of BCS during invasive coronary angiography will aid risk stratification, management, and follow-up with no extra patient involvement, radiation, or costs.

Keywords

Coronary artery calcification, Birmingham calcium score, invasive angiogram, calcium scoring



Introduction

Coronary artery calcification (CAC) can lead to poor cardiovascular outcomes [1, 2]. The two recognised types of coronary calcification are intimal and medial calcification. Renal dysfunction, hypercalcemia, hyperphosphatemia, parathyroid hormone abnormalities, and duration of dialysis are associated with medial calcification [3]. Intimal calcification is seen in advanced age, diabetes mellitus, dyslipidemia, hypertension, male gender, cigarette smoking, and renal disease.

Invasive coronary angiography has a restricted ability to detect and localise coronary calcification [4, 5]. Yet CAC is both a marker for significant coronary artery disease (CAD) and a major determinant of the success of percutaneous coronary intervention (PCI) [6, 7]. It is an independent predictor of mortality and future cardiac events [8–11]. An appreciation of calcium burden during angiography can allow calcium modification tools to be used improving the success of PCI. Indeed, in a prospective multicentre global investigational device exemption study (Disrupt CAD III), authors relied on invasive coronary angiography to identify severely calcified lesions to enable the use of intravascular lithotripsy to improve procedure success and post-procedure complications [12]. There is no recognized classification system for grading calcium burden in a coronary lesion during invasive angiography and it is unclear if this will correlate well with established and validated tools for coronary calcium scoring.

Myocardial perfusion scintigraphy (MPS) single-photon emission computed tomography (SPECT) is a well-recognized non-invasive technique in detecting myocardial ischemia and evaluating prognosis. This imaging modality shows great ability in the detection of lesions with flow restriction [13, 14]. MPS is helpful in identifying low and high-risk groups among heterogeneous populations of both symptomatic and asymptomatic patients [15, 16]. With the widely available nuclear medicine hybrid cameras, the SPECT myocardial perfusion imaging (SPECT-MPI) can be combined with low-dose calcium score computed tomography (CT) for a more complete evaluation of coronary arteries.

To date, no study has reported on the direct comparison between objective assessment of invasive angiographic calcification and coronary calcification on SPECT-MPI. Appreciation of calcium burden during invasive angiography can aid in risk stratification, management, and future follow-up. Therefore, the Birmingham calcium score (BCS) was used to assess angiographic calcification in an objective manner (Figure 1) [17, 18].

The aim of this study was to evaluate the correlation of coronary calcium score (CCS, performed during MPS study) with coronary angiographic calcium by BCS.

Materials and methods

This is a single-center retrospective analysis of patients who underwent invasive coronary angiography, where indicated, as part of their standard care, after a diagnostic SPECT-MPI between 2015 and 2016. All patients ≥ 18 years who underwent SPECT-MPI with CCS and invasive angiography were included. This study was approved by the local audit committee and conducted as a local service improvement project (approval number 2040). This study adhered to the principles of the Declaration of Helsinki and “Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies” [19, 20].

Protocol for SPECT-MPI with calcium scoring

During MPS patients underwent a gated SPECT (17 min duration) followed by attenuation correction CT (no breath-hold, non-diagnostic images with extremely low radiation) and then a breath-hold gated CT for calcium scoring (diagnostic quality with ultra-low dose radiation lasting 20 s in duration). The MPS, attenuation correction CT, and calcium score CT were performed in quick succession which minimized additional procedure time with relatively small additional radiation, with mean additional estimated radiation dose (ED) of 0.92 mSv (dose length product = 54 mGy*cm) for calcium scoring. Discovery NM/CT 670 GE hybrid camera with BrightSpeed Elite 16 slices CT scanner (GE healthcare, Milwaukee, Wisconsin,

USA) was used for myocardial perfusion imaging (MPI)/CT. Total coronary artery calcium score [Agatston units (AU)] was measured using corridor-4DM (Michigan University) software.

Protocol for BCS

Angiographic scoring of calcium was calculated by retrospective review of coronary angiograms and classified according to the BCS (Figure 1), score 0: vessel wall calcification only; score 1: spiculated calcium within the lesion; score 2: focal calcium within the lesion, < 50% of lumen diameter; score 3: focal calcium within the lumen, > 50% of lumen diameter.

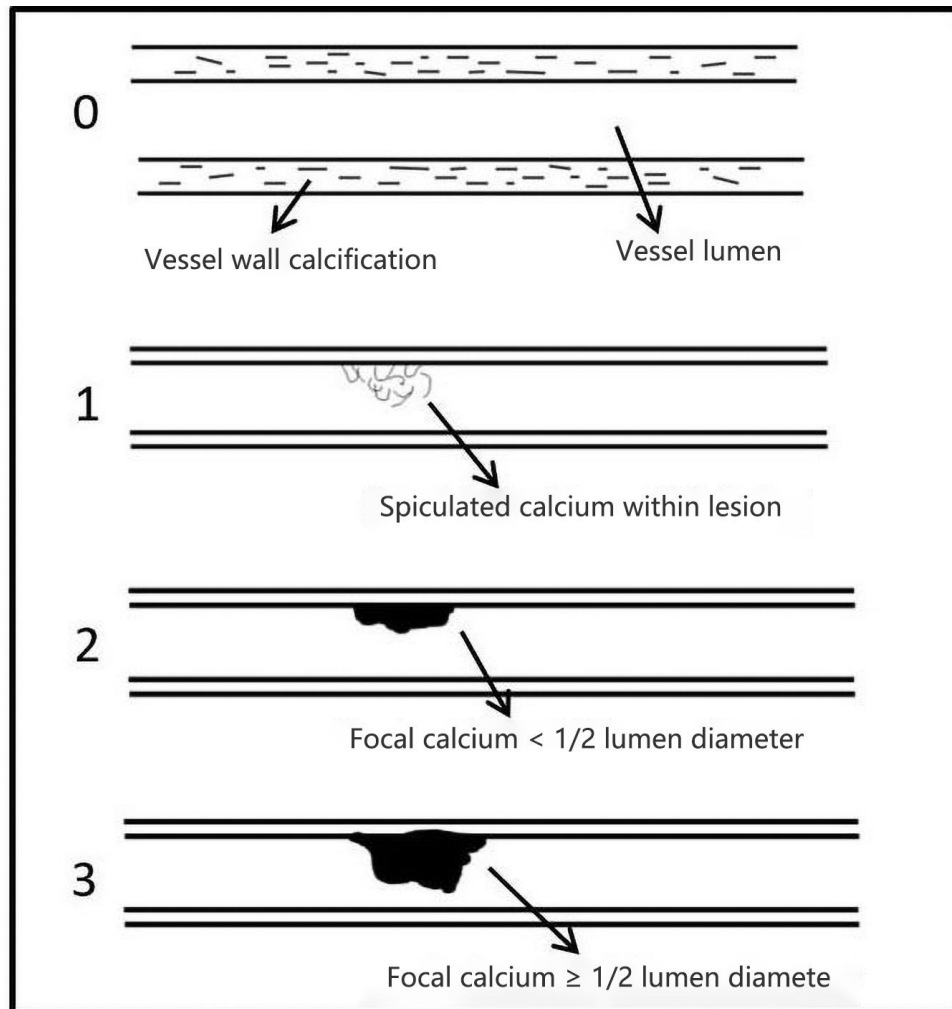


Figure 1. BCS

Note. Adapted with permission from “37 Coronary calcification on coronary angiography versus agatston score - does it matter?” by Zathar Z, Pandit M, Notghi A, Sharma V, Karunatileke A. *Heart*. 2023;109:A42–3 (https://heart.bmj.com/content/109/Suppl_3/A42). © 2023 BMJ Publishing Group Ltd & British Cardiovascular Society.

All coronary angiography was reviewed by an observer who was blinded to the CT calcium score along with all demographic data. In case of doubt or discrepancy, a second observer (senior cardiologist) reviewed the angiographic images and a consensus was reached. Interobserver variability for BCS in a proportion of the coronary angiograms was assessed by Cohen’s kappa to ensure the reproducibility of the BCS [21]. Each of the major coronary vessels was given a BCS which was then aggregated to obtain the cumulative BCS for all three coronary arteries (Figure 2). In cases of calcification in multiple segments, the highest BCS was used. The various calcium scores were analyzed with regard to their demographic and clinical characteristics. The presence or absence of cardiovascular risk factors such as diabetes, hypertension, hypercholesterolemia, smoking status, family history, and prior cardiovascular events were recorded and compared between 3 groups: cumulative BCS 0–1, BCS 2–3, and BCS > 3.

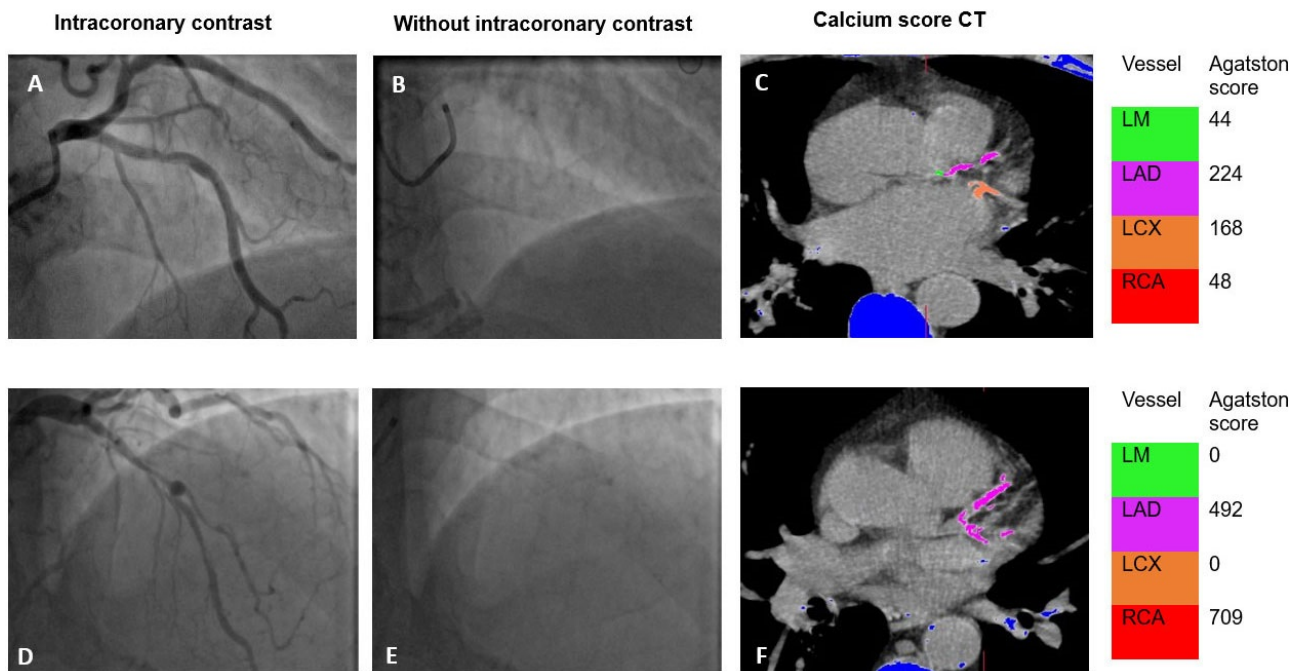


Figure 2. BCS and CCS on CT. Example of (A–C) BCS 2 and (D–F) BCS 3 depicting coronary calcification on invasive angiography along with Agatston score on CT. Blue areas in figures C and F represent calcification outside the coronary arteries. LM: left mainstem; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery

Table 1. Baseline characteristic

Variables	Total (n)	Percentage (%)
Age in years		
≤ 50	0	0
51–60	9	6
61–70	28	19
≥ 70	114	75
Gender		
Male	90	60
Female	61	40
Diabetes mellitus present	65	43
Hypertension present	94	62
Hypercholesterolemia present	62	41
Smoking status		
Current smoker	17	11
Ex-smoker	25	17
Non-smoker	109	72
Family history of CAD	21	14
Previous myocardial infarction	20	13
Previous PCI	10	7
Previous cerebral vascular accident	16	11
PVD	8	5

Statistical analysis

All data was analyzed using Statistical Package for Social Sciences for Windows (SPSS version 26). Continuous variables are presented as mean (\pm standard deviation) and categorical variables are presented as percentages. Comparison of categorical variables was done using Fisher's or χ^2 test. Spearman's correlation was used to assess the correlation between BCS and CT CCS. Receiver operating characteristic

(ROC) curve analysis was performed to detect cut-off BCS that would predict significant CAC (defined as coronary calcium > 400 AU [22]). Kaplan–Meier estimator was used to report on 5 years major adverse outcomes. Interobserver variability was assessed by Cohen’s kappa as discussed above. Confidence interval (CI) for significance was set at 95% with $P < 0.05$.

The primary outcome measure was to find the correlation between the BCS and CT CCS. The other outcome measures were to correlate BCS with traditional cardiovascular risk factors and report on the correlation between BCS and major adverse endpoints (readmission, revascularisation, myocardial infarction, and all-cause mortality).

Results

Of the 151 patients included in the study, 90 (60%) were male and 61 (40%) were female (Table 1). Mean age of the population was 76 years (± 9 years). Hypertension was the most common risk factor. Aside from peripheral vascular disease (PVD), all patient demographics were similar in the three BCS groups (Table 2).

Table 2. Cumulative BCS and risk factors

Variables	BCS 0–1 n (%)	BCS 2–3 n (%)	BCS > 3 n (%)	P-value
Age in years				0.874 ^a
≤ 50	0 (0)	0 (0)	0 (0)	
51–60	6 (4)	2 (1)	1 (1)	
61–70	21 (14)	5 (3)	2 (1)	
≥ 70	78 (52)	28 (19)	8 (5)	
Gender				0.109 ^b
Male	57 (38)	26 (17)	7 (5)	
Female	48 (32)	9 (6)	4 (3)	
Diabetes mellitus present	41 (27)	20 (13)	4 (3)	0.156 ^b
Hypertension present	65 (43)	24 (16)	5 (3)	0.383 ^b
Hypercholesterolemia present	47 (31)	9 (6)	6 (4)	0.090 ^b
Smoking history	29 (19)	6 (4)	7 (5)	0.011 ^b
Family history	14 (9)	5 (3)	2 (1)	0.855 ^a
Previous myocardial infarction	14 (9)	5 (3)	1 (1)	0.905 ^b
Previous PCI	10 (7)	0 (0)	0 (0)	0.100 ^a
Previous cerebral vascular accident	12 (8)	2 (1)	2 (1)	0.396 ^a
PVD	1 (1)	4 (3)	3 (2)	< 0.001 ^a

^a Fisher’s exact test was used; ^b χ^2 test was used

A large proportion of participants had clinically significant high calcium, defined ≥ 400 AU [22], as noted on CT (Table 3). Majority of the patients had ischemia on reversibility testing, however, those without reversible ischemia (28.5%, $n = 43$) on the SPECT-MPS who underwent invasive angiography had ongoing symptoms and/or very high calcium score ($1,159 \text{ AU} \pm 1,535 \text{ AU}$) to warrant invasive testing. There was a positive correlation between cumulative BCS and total Agatston score [Spearman correlation coefficient (r) = 0.558, $P < 0.001$]. Using cumulative BCS ≥ 1 as cut off, it was possible to detect clinically significant calcium burden (> 400 AU) (Figure 3). Cumulative BCS ≥ 1 had a statistically significant correlation with > 400 AU ($r = 0.408$, $P = 0.002$). BCS < 1 also had a statistically significant correlation with < 400 AU ($r = 0.555$, $P < 0.001$). ROC curve identified BCS of 1 as cut off for identifying significant coronary calcification (> 400 AU) with sensitivity of 60% and specificity of 77% (area under the curve 0.788, 95% CI 0.714–0.863). Cohen’s kappa for the cumulative BCS was 0.412 (Cohen’s kappa 0.41–0.60 = moderate agreement). No differences in BCS scores were observed between the sexes ($P = 0.27$).

Table 3. Cumulative BCS vs. cumulative Agatston score

AU	BCS < 1 n (%)	BCS ≥ 1 n (%)	P-value
0–200	32 (38.6)	7 (10.3)	< 0.0001 ^b
201–400	16 (19.3)	7 (10.3)	
401–999	16 (19.3)	22 (32.4)	
≥ 1,000	19 (22.9)	32 (47.1)	
Total	83 (100)	68 (100)	

^b χ^2 test was used

Note. Adapted with permission from “37 Coronary calcification on coronary angiography versus agatston score - does it matter?” by Zathar Z, Pandit M, Notghi A, Sharma V, Karunatileke A. Heart. 2023;109:A42–3 (https://heart.bmj.com/content/109/Suppl_3/A42). © 2023 BMJ Publishing Group Ltd & British Cardiovascular Society.

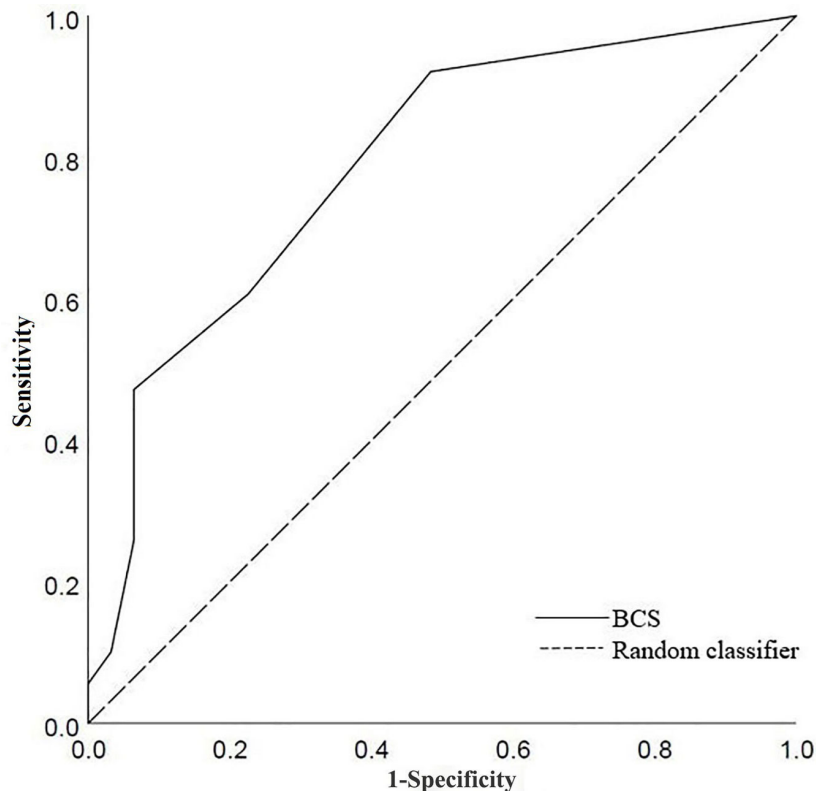


Figure 3. ROC curve for BCS to detect significant calcium (> 400 AU). Area under curve 0.788 (95% CI 0.71–0.863)

In this cohort, 70/151 (46%) patients undergoing invasive angiography had PCI performed. Majority of these patients had a successful procedure ($n = 65$, 93%). As expected, higher BCS scores were associated with the use of calcium modification tools during angiography ($r = 0.285$, $P = 0.02$). Patients with unsuccessful procedures ($n = 5$), on average, had higher cumulative BCS scores (mean BCS 3) compared to successful procedures (mean BCS 1). Of those with unsuccessful procedures, one represented with chest pain, and two patients died during the follow-up period. Issues that lead to procedural failure include chronic total occlusion ($n = 3$), coronary artery tortuosity ($n = 1$), and dissection ($n = 1$). Patients that had no coronary intervention performed 81/151 (54%) had either mild non-obstructive CAD ($n = 65$) or were referred to coronary artery bypass grafting due to their severe disease ($n = 16$).

With respect to long-term outcomes, cumulative BCS of ≥ 3 was associated with poor outcomes at 5 years follow-up. Kaplan–Meier analysis showed that the incidence of major adverse outcomes (re-admission, revascularisation, myocardial infarction, and all-cause mortality) differed between the cumulative BCS ≥ 3 and BCS < 3 cohorts (log rank $P = 0.013$) (Figure 4).

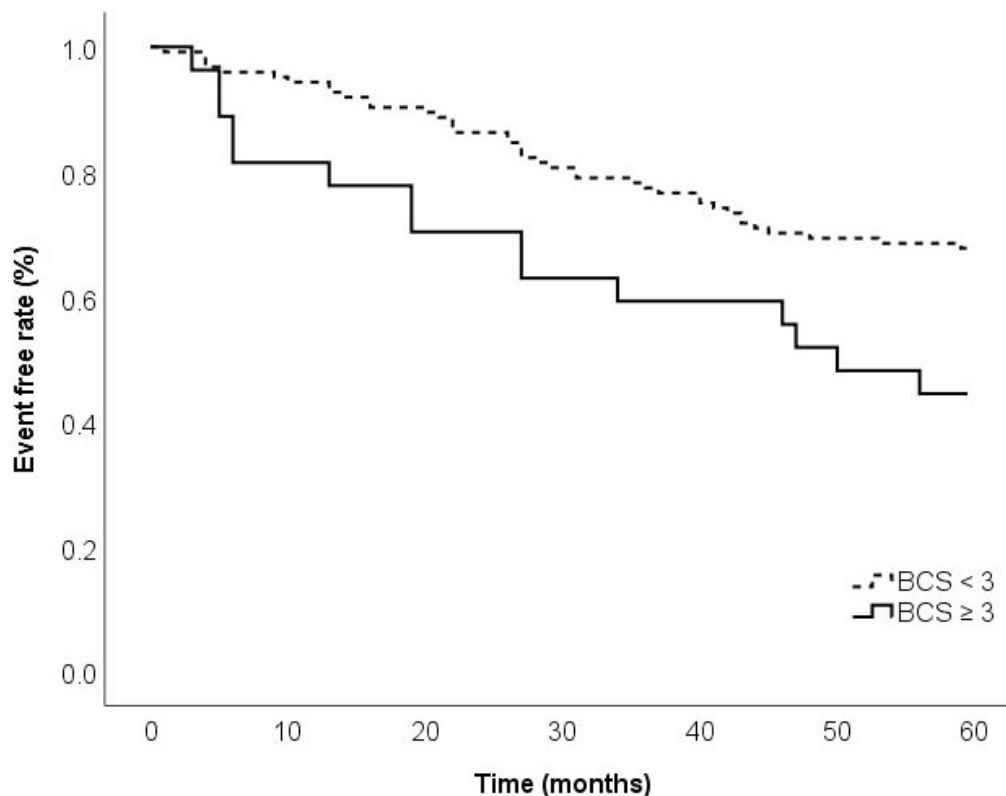


Figure 4. Kaplan–Meier curves comparing major adverse outcomes (re-admission, myocardial infarction, and all-cause mortality) among patients with BCS ≥ 3 vs. BCS < 3 at 5 years follow up. Log rank $P = 0.013$

Note. Reprinted with permission from “37 Coronary calcification on coronary angiography versus agatston score - does it matter?” by Zathar Z, Pandit M, Notghi A, Sharma V, Karunatileke A. *Heart*. 2023;109:A42–3 (https://heart.bmj.com/content/109/Suppl_3/A42). © 2023 BMJ Publishing Group Ltd & British Cardiovascular Society.

Discussion

This single-center, retrospective study, has demonstrated that BCS is a useful tool that correlates well with established calcium scoring in the form of CT. In patients whose cumulative BCS ≥ 1 , the calcium burden is likely to be very high. Cumulative BCS score of 1 can be used as a useful cut-off to estimate the likelihood of clinically significant coronary calcium (> 400 AU). Furthermore, cumulative BCS ≥ 3 can identify patients most at risk from major adverse outcomes in the next 5 years.

The European Society of Cardiology (ESC) recognizes that CAC scoring can contribute to pre-test probability in the assessment of obstructive CAD [23]. The American Heart Association (AHA) advises that CAC scoring can be used to inform treatment decision-making if risk-based treatment decision is uncertain [24]. However, CAC score ≥ 400 AU can make CT imaging difficult, as such, the National Institute for Health and Care Excellence (NICE) recommends invasive coronary angiography in this population, if considered clinically appropriate.

As established elsewhere in the literature, CAC score closely correlates with coronary stenosis in invasive coronary angiography [25–27]. Rosen et al. [28] assessed CAC score and the severity of coronary stenosis in coronary angiography during follow-up- they noted that the CAC scores predicted the severity of coronary stenosis as well as the extent and distribution of CAD in patients who underwent clinically driven coronary angiography. Furthermore, they noted that 66% of patients with CAC score < 100 AU did not have significant coronary stenosis whilst 13% of patients with CAC score > 400 AU had no coronary stenosis. In this study, a CAC cut-off of > 400 AU was chosen as this was highly predictive of significant CAC and stenosis as reported elsewhere in the literature [28–32]. Ho et al. [31] specifically correlated CAC score with the degree of coronary artery obstruction and noted CAC score 1–400 AU was consistent with minimal to moderate atherosclerosis and $< 10\%$ rate of obstructive stenosis. However, CAC score of > 400 AU was consistent with severe atherosclerosis and obstructive lesions > 2 times the frequency of those with CAC < 400 AU.

Although observational studies have demonstrated an increased risk of future cardiovascular events with higher calcium scores, a recent meta-analysis from Nerlekar et al. [33] would suggest that calcified plaque has a weak association with major adverse outcomes compared to non-calcified plaque. This would suggest that the pattern of coronary calcium and plaque morphology are important determinants of major adverse outcomes. In this study, 35/80 (39%) of patients with CAC > 400 AU received a BCS score < 1. In this subgroup, 28/35 (80%) received a BCS score of 0 suggesting vessel wall calcification as opposed to no calcium. The differences in major adverse outcomes observed at 5 years follow-up (Figure 4) further support the current evidence base that the pattern of calcium is more important than the total amount of calcium (AU). Spotty calcification is a commonly observed high-risk plaque feature that could double adverse event rates [33–35]. It can be a marker of plaque vulnerability which differs from the pattern of calcium seen in patients with stable CAD [36]. As BCS allows an objective assessment of calcified lesions, it can provide additional clinical information to aid aggressive preventative pharmacotherapy and regular follow-up.

In this study, cumulative BCS ≥ 1 had a statistically significant positive correlation with an Agatston score of ≥ 400 AU. This can provide an additional prognostic marker in patients who can then benefit from aggressive cardiovascular risk management. As CAC score of > 400 AU is considered high with 10-year coronary heart disease events exceeding 20%, prompt identification of these patients during invasive angiography may help clinicians risk stratify their patients [37].

BCS can be readily calculated during invasive angiography or shortly after the procedure in retrospect to inform further decision-making. BCS was not affected by the majority of the patient's cardiovascular risk factors (Table 2). A statistically significant difference was observed between the BCS outcomes for patients with PVD; a larger proportion of patients with BCS ≥ 2 had a history of PVD. Vascular calcification is commonly associated with PVD and it possible that this group of patients are also having higher coronary calcifications through the same pathophysiological mechanisms [38, 39]. Although it is well established that PVD is an indicator of underlying CAD, due to the small sample size we cannot draw any reliable conclusions between PVD and BCS.

Data from a large population observational study by Peng et al. [40] noted that patients with very high calcium ($\geq 1,000$ AU) had a higher risk for major adverse outcomes in the form of CAD and all-cause mortality. This study has established that a cumulative BCS of ≥ 3 was associated with adverse outcomes at 5 years follow-up relating to re-admission, revascularisation, myocardial infarction, and all-cause mortality (Kaplan–Meier log rank $P = 0.013$). Prompt identification of these high-risk patients during angiography can guide management strategy including aggressive preventative pharmacotherapy and regular follow-up.

CAC can pose a challenge to successful PCI due to suboptimal stent placement, higher stent failure rates, and longer procedure time [41, 42]. This has, to some extent, been overcome by intracoronary imaging and calcium modification techniques such as cutting balloons and intravascular lithotripsy. However, the severity of calcification in coronary targets may predict outcome and success [42]. As BCS can correlate well with coronary calcium burden, it may have utility in management and procedure planning.

Limitations

This was a single-center study with a cohort of 151 patients that could be subject to selection bias. It is recognized that there could be a subjective element to the BCS classification based on experience; however, this tool is designed for use by the interventional cardiologist who will have prior experience in recognizing coronary calcification. The retrospective observational nature of the study is also a limitation. Although the angiography images were reviewed in retrospect, the application of the scoring system is unlikely to lengthen the overall procedure duration. This study did not look at the correlation between BCS and percutaneous intervention procedure duration or complications, this could be a focus of future work. More importantly, data regarding intracoronary imaging was unavailable which may have helped further quantify the correlation between MPS CAC, BCS, and intracoronary imaging.

In conclusion, this is the first study to report on the direct correlation between an objective assessment of calcium during invasive angiography (BCS) and an established tool for coronary calcium assessment (CT). This study assessed the correlation of CAC (performed during MPS study) with coronary angiographic calcium BCS in order to assess the potential added value of BSC during routine angiography. The proposed cut-off of cumulative BCS ≥ 1 can identify patients who are likely to have a significant calcium burden. Also, a cumulative BCS ≥ 3 is associated with significantly worse major adverse outcomes at 5 years. Therefore, it can identify high-risk patients who would benefit from aggressive lifestyle risk modification and pharmacological prophylaxis. A large prospective cohort study may allow the BCS to be validated for independent use.

Abbreviations

AU: Agatston units

BCS: Birmingham calcium score

CAC: coronary artery calcification

CAD: coronary artery disease

CCS: coronary calcium score

CI: confidence interval

CT: computed tomography

MPS: myocardial perfusion scintigraphy

PCI: percutaneous coronary intervention

PVD: peripheral vascular disease

r: Spearman correlation coefficient

ROC: receiver operating characteristic

SPECT: single-photon emission computed tomography

SPECT-MPI: single-photon emission computed tomography myocardial perfusion imaging

Declarations

Author contributions

ZZ: Conceptualization, Methodology, Data curation, Formal analysis, Writing—original draft. MP: Methodology, Resources, Writing—review & editing. AK: Data curation, Resources. AN: Methodology, Resources, Writing—review & editing. VS: Conceptualization, Methodology, Formal analysis, Writing—review & editing, Supervision. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

This study was approved by the local audit committee and conducted as a local service improvement project (approval number 2040, Sandwell General Hospital, West Bromwich). This study adhered to the principles of the Declaration of Helsinki and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.

Consent to participate

Consent from participants is waived as the project is a retrospective study undertaken as an audit with local governance.

Consent to publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Funding

Not applicable.

Copyright

© The Author(s) 2024.

References

1. Detrano R, Hsiai T, Wang S, Puentes G, Fallavollita J, Shields P, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. *J Am Coll Cardiol.* 1996;27:285–90.
2. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med.* 2008;358:1336–45.
3. Goodman WG, London G, Amann K, Block GA, Giachelli C, Hruska KA, et al.; Vascular Calcification Work Group. Vascular calcification in chronic kidney disease. *Am J Kidney Dis.* 2004;43:527–9.
4. Mintz GS, Douek P, Pichard AD, Kent KM, Satler LF, Popma JJ, et al. Target lesion calcification in coronary artery disease: an intravascular ultrasound study. *J Am Coll Cardiol.* 1992;20:1149–55.
5. Mintz GS. Intravascular imaging of coronary calcification and its clinical implications. *JACC Cardiovasc Imaging.* 2015;8:461–71.
6. Lee MS, Shah N. The impact and pathophysiologic consequences of coronary artery calcium deposition in percutaneous coronary interventions. *J Invasive Cardiol.* 2016;28:160–7.
7. Sheikh AS, Connolly DL, Sharma V. Acute coronary syndrome associated with calcified coronary lesions. *Int J Cardiovasc Dis Diagn.* 2021;6:025–33.
8. Sharma V, Mughal L, Dimitropoulos G, Sheikh A, Griffin M, Moss A, et al. The additive prognostic value of coronary calcium score (CCS) to single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI)-real world data from a single center. *J Nucl Cardiol.* 2021;28:2086–96.
9. Budoff MJ, Shaw LJ, Liu ST, Weinstein SR, Tseng PH, Flores FR, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J Am Coll Cardiol.* 2007;49:1860–70.
10. Criqui MH, Denenberg JO, Ix JH, McClelland RL, Wassel CL, Rifkin DE, et al. Calcium density of coronary artery plaque and risk of incident cardiovascular events. *JAMA.* 2014;311:271–8.
11. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with framingham score for risk prediction in asymptomatic individuals. *JAMA.* 2004;291:210–5.
12. Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ, et al. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. *J Am Coll Cardiol.* 2020;76:2635–46.
13. Parker MW, Iskandar A, Limone B, Perugini A, Kim H, Jones C, et al. Diagnostic accuracy of cardiac positron emission tomography versus single photon emission computed tomography for coronary artery disease: a bivariate meta-analysis. *Circ Cardiovasc Imaging.* 2012;5:700–7.
14. George RT, Mehra VC, Chen MY, Kitagawa K, Arbab-Zadeh A, Miller JM, et al. Myocardial CT perfusion imaging and SPECT for the diagnosis of coronary artery disease: a head-to-head comparison from the CORE320 multicenter diagnostic performance study. *Radiology.* 2014;727:407–16.

15. Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusion SPECT. *J Nucl Cardiol*. 2004; 11:171–85.
16. Blumenthal RS, Becker DM, Moy TF, Coresh J, Wilder LB, Becker LC. Exercise thallium tomography predicts future clinically manifest coronary heart disease in a high-risk asymptomatic population. *Circulation*. 1996;93:915–23.
17. Sharma V, Rahman M, Elangovan SK, Yuan M, O’Kane P, Talwar S, et al. Rotashock therapy: an observational study. *J Cardiol Clin Res*. 2021;9:1169.
18. Sharma V, Abdul F, Haider ST, Din J, Talwar S, O’Kane P, et al. Rotablation in the very elderly – safer than we think? *Cardiovasc Revasc Med*. 2021:36–41.
19. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147:573–7. Erratum in: *Ann Intern Med*. 2008;148:168.
20. World Medical Association. World Medical Association declaration of Helsinki: ethical principles for medical research involving human subjects. *J Am Med Assoc*. 2013;310:2191–4.
21. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977; 33:159–74.
22. Rumberger JA, Brundage BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. *Mayo Clin Proc*. 1999;74: 243–52.
23. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). *Russ J Cardiol*. 2020;25:3757. Russian.
24. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D’Agostino RB, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of cardiology/ American heart association task force on practice guidelines. *Circulation*. 2014;29:S49–73.
25. Budoff MJ, Georgiou D, Brody A, Agatston AS, Kennedy J, Wolfkiel C, et al. Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease: a multicenter study. *Circulation*. 1996;93:898–904.
26. Budoff MJ, Diamond GA, Raggi P, Arad Y, Guerci AD, Callister TQ, et al. Continuous probabilistic prediction of angiographically significant coronary artery disease using electron beam tomography. *Circulation*. 2002;105:1791–6.
27. Rumberger JA, Sheedy PF 3rd, Breen JF, Schwartz RS. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effect of patient’s sex on diagnosis. *Circulation*. 1995;91:1363–7.
28. Rosen BD, Fernandes V, McClelland RL, Carr JJ, Detrano R, Bluemke DA, et al. Relationship between baseline coronary calcium score and demonstration of coronary artery stenoses during follow-up: MESA (multi-ethnic study of atherosclerosis). *JACC Cardiovasc Imaging*. 2009;2:1175–83.
29. Schmermund A, Möhlenkamp S, Baumgart D, Kriener P, Pump H, Grönemeyer D, et al. Usefulness of topography of coronary calcium by electron-beam computed tomography in predicting the natural history of coronary atherosclerosis. *Am J Cardiol*. 2000;86:127–32.
30. Lau GT, Ridley LJ, Schieb MC, Brieger DB, Freedman SB, Wong LA, et al. Coronary artery stenoses: detection with calcium scoring, CT angiography, and both methods combined. *Radiology*. 2005;235: 415–22.
31. Ho JS, FitzGerald SJ, Stolfus LL, Wade WA, Reinhardt DB, Barlow CE, et al. Relation of a coronary artery calcium score higher than 400 to coronary stenoses detected using multidetector computed tomography and to traditional cardiovascular risk factors. *Am J Cardiol*. 2008;101:1444–7.

32. Berman DS, Wong ND, Gransar H, Miranda-Peats R, Dahlbeck J, Hayes SW, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. *J Am Coll Cardiol.* 2004;44:923–30.
33. Nerlekar N, Ha FJ, Cheshire C, Rashid H, Cameron JD, Wong DT, et al. Computed tomographic coronary angiography–derived plaque characteristics predict major adverse cardiovascular events: a systematic review and meta-analysis. *Circ Cardiovasc Imaging.* 2018;11:e006973.
34. Puchner SB, Liu T, Mayrhofer T, Truong QA, Lee H, Fleg JL, et al. High-risk plaque detected on coronary CT angiography predicts acute coronary syndromes independent of significant stenosis in acute chest pain: results from the ROMICAT-II trial. *J Am Coll Cardiol.* 2014;64:684–92.
35. Hu MK, Yuan M, James S, Lee HP, Abdul F, Yousif A, et al. Positive remodelling of coronary arteries on computed tomography coronary angiogram: an observational study. *AsiaIntervention.* 2022;8:110–5.
36. van Velzen JE, de Graaf FR, de Graaf MA, Schuijf JD, Kroft LJ, de Roos A, et al. Comprehensive assessment of spotty calcifications on computed tomography angiography: comparison to plaque characteristics on intravascular ultrasound with radiofrequency backscatter analysis. *J Nucl Cardiol.* 2011;18:893–903.
37. Hecht HS. Coronary artery calcium scanning: past, present, and future. *JACC Cardiovasc Imaging.* 2015;8:579–96.
38. Rocha-Singh KJ, Zeller T, Jaff MR. Peripheral arterial calcification: prevalence, mechanism, detection, and clinical implications. *Catheter Cardiovasc Interv.* 2014;83:E212–20.
39. Zettervall SL, Marshall AP, Fleser P, Guzman RJ. Association of arterial calcification with chronic limb ischemia in patients with peripheral artery disease. *J Vasc Surg.* 2018;67:507–13.
40. Peng AW, Dardari ZA, Blumenthal RS, Dzaye O, Obisesan OH, Iftekhar Uddin SM, et al. Very high coronary artery calcium (≥ 1000) and association with cardiovascular disease events, non-cardiovascular disease outcomes, and mortality. *Circulation.* 2021;143:1571–83.
41. De Maria GL, Scarsini R, Banning AP. Management of calcific coronary artery lesions: is it time to change our interventional therapeutic approach? *JACC Cardiovasc Interv.* 2019;12:1465–78.
42. Abazid RM, Obadah Kattea M, Smettei OA, Beshir Y, Sakr H. Impact of coronary artery calcification on percutaneous coronary intervention and postprocedural complications. *J Saudi Heart Assoc.* 2017;29:15–22.