Comparison of Visual Scoring of Coronary Artery Calcium (CAC) on Coronary Computed Tomography Angiogram (CCTA) to Agatston Score

Sushilkumar K. Sonavane*, Nina Terry1, Naomi Fineberg2 and Hrudaya Nath3

1 Cardiopulmonary Section-Department of Radiology, University of Alabama in Birmingham, 619 19th ST S JTN 370, Birmingham AL 35294 USA
2 Department of Biostatistics, University of Alabama in Birmingham 619 19th ST S JTN 370, Birmingham AL 35294 USA
3 Department of Radiology/Cardiopulmonary Section, University of Alabama in Birmingham, 619 19th ST S JTN 370, Birmingham AL 35294 USA

Abstract

Purpose: Detection and quantification of coronary artery calcium (CAC) has a prognostic value for future cardiovascular events, beyond that accrued from other cardiovascular risk factors. CAC is conventionally measured as an Agatston score from an EKG-gated non-contrast CT of the heart using special software. The predominant indication for coronary CT angiography (CCTA) in clinical practice is to evaluate obstructive coronary artery disease (CAD) in a low to intermediate pretest probability population. At present there is no commercially available software for CAC measurement on CCTA scans. The purposes of this study were twofold. First, the study examines the correlation of estimated CAC from CCTA, using a novel method of visual scoring on the CCTA exam and comparing with the measured Agatston score from a non-contrast CAC score scan. Second, the study evaluates the performance of such estimation of CAC across radiologists with varying degrees of experience.

Methods: Two cardiac radiologists and a chest radiologist, with varying degrees of experience, evaluated 100 coronary CT angiograms for visual scoring of CAC. The three major coronary vascular segments; left anterior descending artery (LAD) including left main coronary artery (LM), left circumflex coronary artery (LCX) and right coronary artery (RCA) were examined and scored for linear extent (0-4) as well as thickness (0-3). The linear and thickness scores for each segment was multiplied to get a vessel score (0-12) and total CAC score was derived as thickness (0-3). The linear and thickness scores for each segment was multiplied to get a vessel score (0-12) and total CAC score was derived by adding all the vessel scores (0-36). Statistical analysis was performed using Kappa statistic and Spearman Rank Correlation for the agreement with the Agatston scores from non-contrast EKG gated calcium score CT scans performed at the same time as the CCTA. The scores of the senior cardiac radiologist with 30 years of experience were used for the primary analysis and the readings from the other two radiologists were used to calculate the inter-reader variability.

Results: Overall, 59 % and 57 % of patients had CAC detected by Agatston score and visual score respectively. CAC by visual score on CCTA strongly correlated with the Agatston score (Spearman correlation coefficient 0.86; P < 0.001). In 7 cases visual scoring failed to detect minimal CAC with low Agatston CAC score (mean 4.1, range 1-13). Visual score of > 7 identified CAC > 100 with an area under the curve of 0.96, sensitivity of 0.88 and a specificity of 0.92. A visual score of > 12 identified CAC > 300 with an area under the curve of 0.97, sensitivity of 0.95 and specificity of 0.90. The inter-reader agreement with the other cardiac and chest radiologist was high, with Spearman correlation coefficients of 0.90 & 0.91 (p < 0.001).

Conclusion: The visual estimation and stratification of CAC on CCTA is feasible and correlates well with the Agatston score and shows good inter-reader correlation. This additional information from CCTA will be useful for cardiovascular risk stratification and management.

Keywords: Coronary artery calcium; Agatston score; Visual score; Coronary CT angiography

Abbreviations: Computed Tomography (CT), Coronary CT Angiography (CCTA), Coronary Artery Calcium (CAC), Coronary Artery Disease (CAD), Left Main Coronary artery (LM), Left Anterior Descending Coronary Artery (LAD), Left Circumflex Coronary Artery (LCX), Right Coronary Artery (RCA)

Introduction

Cardiovascular disease is the leading cause of mortality worldwide and coronary artery disease accounts for half of those cardiovascular deaths [1,2]. Conventional risk factor assessment can only predict up to 65-80% of future cardiovascular events [1,2]. CT scan detected CAC score has gained increasing interest over the past decade and there is sufficient evidence to date showing correlation with histologically measured plaque burden as well as incremental risk prediction over models such as the Framingham score [3]. Recent evidence from a Multiethnic Study of Atherosclerosis (MESA) suggests that an Agatston score > 300 is associated with significant increase in the incidence of major adverse cardiac events compared with that derived from the Framingham risk score alone [4].

The CAC scoring is conventionally performed using the Agatston method on an EKG gated non-contrast cardiac CT. When combined with CCTA this additional scan typically precedes the CT coronary angiography [5]. The software utilizes the threshold of 130 Hounsfield units (H.U.) on the non-contrast study to determine a density as calcification. Attempts to separate calcium from the contrast filled vessel lumen on CCTA have been made in the past using different techniques [6-11]. These methods are time consuming and reproducibility of the results is low. However, these attempts attest the desire to assess CAC in addition to non-calcified plaque detection from CCTA.

Unlike the computer relying on density measurements, the human eye can differentiate calcification in the vessel wall from the intraluminal iodinated contrast. Recent investigations have demonstrated the feasibility of visual scoring of CAC from non-contrast CT scans, and good correlations with traditional Agatston scoring [12,13]. The aims of this retrospective study were first, to assess the correlation between Agatston score derived from EKG-gated non-contrast CT and a visual CAC scoring method (internally developed and validated) performed on CCTA images and second, to evaluate the inter-reader variation of the visual CAC score between readers with varying degrees of cardiac imaging experience.

Materials and Methods

The institutional Internal Review Board (IRB) approved our retrospective study. One hundred CCTA examinations that had
clinically indicated CCTA as well as calcium score CT at the same time were used in this study. Our group of 100 patients had 58 women and 42 men with an age range of 21-81 years (mean 59.6 ± 12.1 years, median 61 years). The majority of the indications were to assess for obstructive CAD in patients with atypical chest pain and normal or equivocal myocardial perfusion imaging or stable angina. The younger subjects were being evaluated for a suspected anomalous coronary artery.

**Imaging and Interpretation of Images**

These studies were performed on 64-128 slice scanners from various vendors. Prospective EKG-gated non-contrast scans with a slice thickness of 2.5 mm, tube potential of 120 kVp and tube current (mAs) adjusted according to the patient body habitus were obtained through the heart for assessment of CAC with Agatston score. The Agatston score analysis was performed by experienced cardiac CT technologists on a PC-based workstation utilizing commercially available software (Aquarius, Terarecon). The CCTA studies were performed with tube potential of 120 kVp and tube current (mAs) adjusted according to the patient body habitus with a slice thickness range between 0.63 to 0.75 mm. The radiologist performing the scan determined the choice of prospective versus retrospective EKG-gating. The reconstructed slice thickness of the CCTA images stored in the PACS ranged from 0.63 – 3.0 mm (mean 1.31 ± 0.94, median 0.9). For CCTA studies, image reconstructions between 70-80% R-R intervals were used for assessment of visual CAC score.

A cardiac radiologist with 30 years of experience, another cardiac radiologist with 5 years of experience and a non-cardiac chest radiologist with 20 years of radiology experience reviewed the CCTA scans independently. The visual scoring was performed only from axial images. The readers were blinded to the results of Agatston scores as well as demographic and clinical data. While interpreting these studies, each reader individually adjusted the image display parameters such as magnification, window level and width for viewing as required.

**Visual Scale for CAC Scoring**

The axial images were reviewed for the linear extent and thickness of calcium along three vascular segments (LAD including LM, LCX and RCA with their respective branches). Ramus Intermedius (RI), if present, was considered a part of the circumflex artery. Linear extent was scored as follows: 0 = No visible calcification; 1 = 1-3 images with calcification; 2 = 4-5 images with calcification; 3 = 6-10 images with calcification; 4 = > 10 images with calcification. The visual thickness was scored as follows: 0 = No visible calcification; 1 = any calcification < 25% of vessel diameter; 2 = 1-3 images with 25% or more of the vessel calcified; 3 = > 3 images with 25% or more of vessel calcified. The scoring scale is shown in Tables 1, 2, with representative images shown in Figure 1. The individual vessel score was calculated as the product of the linear extent and thickness (ranging from 0-12). The total score was calculated as the sum of the three vessel scores (ranging from 0-36).

**Statistical Methods and Results**

Data are given as mean (±) standard deviation, median and range. The agreement between Agatston scores and visual scores for binary variables is measured with a Kappa statistic and percent agreement. The agreement on values greater than zero is measured with a Spearman Rank correlation coefficient using all cases where either the Agatston Score or visual score, or both, are greater than zero. Inter-observer variability is measured with the Kappa statistic and percent agreement.

| Number of axial CT images showing CAC | Score |
|--------------------------------------|-------|
| 0                                    | 0     |
| 1 - 3                                | 1     |
| 4 - 5                                | 2     |
| 6 - 10                               | 3     |
| > 10                                 | 4     |

**Table 1:** Visual scoring scale for linear extent of coronary artery calcium (CAC).

| Thickness extent of CAC | Score |
|-------------------------|-------|
| No calcium visible      | 0     |
| Any CAC, < 25% vessel diameter | 1 |
| 1 – 3 image with CAC > 25% vessel diameter | 2 |
| > 3 images with CAC > 25% vessel diameter | 3 |

**Table 2:** Visual scoring scale for thickness extent of coronary artery calcium (CAC).

Figure 1: Axial CCTA images showing examples of thickness extent of CAC. No calcification (a), calcification < 25% of vessel diameter in RCA (b), LAD (c), calcification > 25% of vessel diameter in LAD (d).

The total CAC score was used for the analysis. Our group of 100 patients had 58 women and 42 men with an age range of 21-81 years (mean 59.6 ± 12.1 years, median 61 years). Overall, 59% and 57% of patients had CAC detected by Agatston score and visual score respectively. Whereas 51% patients had CAC detected with both of the methods. Figure 2 shows the distribution of total Agatston CACs plotted against the visual score with a Spearman’s correlation coefficient of 0.88 (P < 0.001). Further distribution of total Agatston CACs up to 1000 and up to 400 were plotted against the visual score and are shown in Figures 3 and 4 respectively. The distribution of patients with total Agatston CACs is as follows: 0 (n=40), 1-100 (n=26), 101-300 (n=13), > 301 (n=19) (Table 3). In general the mean total visual CAC score increased with increasing Agatston score. Absence of CAC on CCTA by visual score was noted in 7 cases that were associated with very low Agatston CAC score (mean 4.1, range 1-13).
The receiver operating characteristic (ROC) curve for patients with Agatston score > 100 demonstrates the area under the curve was 0.965 (Figure 5). The visual score cut off point of > 7 predicted CAC > 100 with sensitivity of 88%, specificity of 92%, positive predictive value of 85% and negative predictive value of 94%. The ROC curve for patients with Agatston score > 300 show that the area under the curve was 0.970 (Figure 6). The visual score cut off point of >12 predicted a CAC > 300 with sensitivity of 95%, specificity of 90%, positive predictive value of 69 % and negative predictive value of 99%.

The inter-observer agreement between the senior radiologist and another cardiac and a non-cardiac chest radiologist was excellent with Spearman correlation coefficients of 0.90 & 0.91 (p < 0.001).

**Discussion**

The results of our investigation show a good correlation...
between visual scoring of CAC on CCTA and Agatston score performed on EKG-gated non-contrast scans. The visual scores of > 7 and > 12 were associated with the Agatston scores of > 100 and > 300 respectively. Further, there was strong inter-reader agreement even with a varying degree of cardiac imaging experience.

In our clinical practice, the non-contrast CAC scan is not routinely performed in all CCTA examinations. Most of the patients undergoing the CCTA for coronary artery evaluation are low to intermediate risk and the majority lack significant coronary stenosis. However, the CAC score in such patients will be helpful for risk stratification and thus impact patient management in terms of lifestyle modification or medications. The data from this study show that visual scoring of CAC performed on a CCTA with our method correlates well with the Agatston score categories and achieves good agreement among readers with varying degrees of experience. However, a larger scale study needs to be performed to further validate these results. With the use of dual energy CT scanners, virtual unenhanced images obtained without an additional scan may serve as an alternative to the conventional non-contrast scan in the near future.

Conventionally, the measurement of CAC is performed from an EKG-gated, non-contrast CT of the heart. The images are post processed on a dedicated workstation with appropriate software that automatically detects calcium with an attenuation threshold value of 130 HU or greater when present in two or more adjacent pixels. This calcium score scan is not routinely performed as a part of CCTA evaluation for obstructive CAD. This may partly be due to additional scan, radiation, effort and time on part of technologists as well as radiologist, non-reimbursement of this service. A few studies, which have shown that calcium score estimation is possible from CCTA, used higher intensity thresholds and demonstrated a good correlation with the conventional Agatston score [6-9]. Ebersberger, et al. [10] used an adaptive intensity distribution model that creates a normal vessel cross section attenuation map on CCTA and detects calcium as significant attenuation deviation on all axial images and adds them up to give a total calcium score. Though automated segmentation was performed, manual adjustment of contours was still required in most cases; making these methods time consuming [7-9]. The sample sizes of these studies were small and larger studies will be required to prove their efficacy. A recent study used automated software to create virtual unenhanced images using multiple parameters from CCTA and applied the Agatston score that showed strong correlation with the conventional Agatston score from non-contrast CT [11]. However, at present there is no software program approved for clinical practice that can perform CAC scoring on a CCTA study. Nonetheless there is potential CAC information on the CCTA scan that will be of clinical importance. Since the human eye can visualize the coronary artery wall calcification separately from the luminal contrast on CT angiogram, we wanted to investigate if our visual scoring method that has been validated to estimate CAC from non-contrast chest CT examinations would be equally effective when applied to CCTA [13]. To the best of our knowledge there are no prior descriptions of a visual estimate of CAC from CCTA compared to Agatston scores from an EKG-gated non-contrast CT.

At least two other visual scoring systems are described in the literature for estimates of CAC on non-contrast CT scans [12, 14]. The method by Shemesh, et al. [14] takes into consideration the linear extent of coronary calcification and showed a good correlation with all-cause mortality. Another method by Kirsch, et al. [12] relies on the densest calcification involving coronary arteries and its blooming artifact and showed good correlation with the Agatston score in a small cohort. We believe that our method is a better reflection of CAC since it looks at both the linear extent and thickness of the calcification. Blooming artifact as used for scoring in the method by Kirsch et al may be difficult to evaluate in a CCTA, as opposed to a non-contrast CT. Also these other methods score LM as a separate segment that may sometimes be difficult to distinguish from LAD on axial images, especially on non-contrast studies and therefore, we try to eliminate the error by scoring the LM and LAD segments together.

The visual method failed to detect calcifications in seven patients that had very low Agatston scores (mean 4.1, median 0, range 0-13). However, studies in asymptomatic patients have shown 2-3 fold-increased risks of future cardiovascular events with low Agatston score (1-10) compared to Agatston score (0) [15,16]. Since most of our patients were symptomatic and getting evaluated for obstructive CAD, the difference between 0 and very low CAC may not have significantly influenced the future cardiovascular risk prediction. Though we did not assess the role of curved MPR reconstructions in visual detection of CAC, their use could potentially decreases the odds of missing minimal CAC. Since most patients referred for CCTA have some risk factors for coronary artery disease, whether the potentially missed minimal CAC confers significantly added risk is unknown. However, if such determination is deemed important in a given patient then, performing a gated calcium score scan would be indicated.

**Limitations**

We acknowledge a few limitations of the present study. Apart from inherent bias of a retrospective study, it is a small sample size. Our method of visual CAC scoring appears to be complex and time consuming in the beginning. Though we did not keep a note of the actual time taken for reading the CCTA scans for visual scoring, the readers felt that it was quicker after they were used to scoring the initial cases. However, we believe that our method is a better reflection of CAC since it looks at both the linear extent and thickness of the calcification compared to other methods. The contrast in the coronary arteries on good quality CCTA studies can reach up to 300 HU and small calcifications may not be recognized separately from the luminal contrast in the axial images even after...
changing the window width/level settings, thus underestimating the score (Figure 7). This may explain the seven cases scored as no visual CAC, which had minimal CAC on Agatston score. The contrast in region of acute bends in the vessels may appear dense and lead to CAC overestimation on visual scoring (Figure 8). It may be possible to avoid these errors if visual scoring is performed using curved MPR images. However, visual scoring of CAC from such images has not been studied so far. Out of 100 cases, 71 patients had sub millimetre slice thickness whereas 29 patients had slice thickness greater than 1 mm for CCTA. We do not think that this variability affected our results as studies have shown that varying slice thickness between 1.5 mm versus 3 mm does not have significant affect on Agatston scoring in vitro on phantom [17] as well as in vivo [18].

Conclusion

Since non-contrast CAC score scans are not always performed as a part of CCTA for evaluation of obstructive coronary artery disease, there is a potential for capturing important information about the presence and magnitude of CAC from the CCTA images using a semi quantitative visual scoring method that may help the clinician in risk stratification of these patients.

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD et al. (2014) American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2014 update—a report from the American Heart Association. Circulation 129: e28-e292.

2. Fuster V, Voute J, Hunn M, Smith SC Jr (2007) Low priority of cardiovascular and chronic diseases on the global health agenda: a cause for concern. Circulation 116: 1966–1970.

3. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC (2004) Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 291: 210–215.

4. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, et al. (2008) Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med 358:1336-1345.

5. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, et al. (1990) Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 15:827–832.

6. Moselewski F, Ferencik M, Achenbach S, Abbara S, Curry RC, et al. (2006) Threshold dependent variability of coronary artery calcification measurements—implications for contrast-enhanced multi-detector row computed tomography. Eur J Radiol 57: 390–395.

7. Gladny B, Helmel B, Trieb T, Schenk C, Taferner B, et al. (2009) A method for calcium quantification by means of CT coronary angiography using 64+ multidetector CT: very high correlation with Agatston and volume scores. J Am Coll Cardiol 53:1661–1668.

8. Van der Bijl N, Joemai RM, Geleijns J, Bax JJ, Schuijf JD, et al. (2010) Assessment of Agatston coronary artery calcium score using contrast-enhanced CT coronary angiography. AFR Am J Roentgenol 195: 1299-1305.

9. Otton J, Länborg J, Bosshell D, Feneley M, Hayen A, et al. (2012) A method for coronary artery calcium scoring using contrast-enhanced computed tomography. J Cardiovasc Comput Tomogr 6: 37–44.

10. Ebersberger U, Eliot D, Goldberg R, Lev A, Spears JR, et al. (2013) Fully automated derivation of coronary artery calcium scores and cardiovascular risk assessment from contrast medium-enhanced coronary CT angiography studies. Eur Radiol 23: 650-657.

11. Rabinstein R, Halon DA, Gaspar T, Lewis BS, Peled N (2014) Automatic assessment of coronary artery score from contrast –enhanced 256-row coronary computed tomography angiography. Am J Cardiol 113: 7-11.

12. Kirsch J, Buttrago I, Mohammed TL, Gao T, Asher CR, et al. (2012) Detection of coronary calcium during standard chest computed tomography correlates with multi-detector computed tomography coronary artery calcium score. Int J Cardiovasc Imaging 28: 1249-1256.

13. Watts JR, Daniel J Dauer, Fineberg N, Budoff M, Nath H (2014) Correlation between Measured and Visual Scoring of Coronary Calcium. International Journal of Cardiovascular and Cerebrovascular Disease 2: 11-17.

14. Shemesh J, Henschke CI, Shaham D, Yip R, Faroqui AO, et al. (2010) Ordinal scoring of coronary arterial calcifications on low-dose CT scans of the chest is predictive of death from cardiovascular disease. Radiology 257: 541-548.

15. Blaha M, Budhoff MJ, Shaw LJ, Khosa F, Rumberger JA, et al. (2009) Absence of coronary artery calcification and all-cause mortality. JACC Cardiovascular Imaging 2: 69-700.

16. Budhoff MJ, McClelland RL, Nasir K, Greenland P, Kronmal RA, et al. (2009) Cardiovascular events with absent or minimal coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). Am Heart J 158: 554-561.

17. Mao S, Child J, Carson S, Liu SC, Oudiz RJ, et al. (2003) Sensitivity to detect small coronary artery calcium lesions with varying slice thickness using electron beam tomography. Invest Radiol 38: 183-137.

18. Sabour S, Rutten A, van der Schouw YT, Atsma F, Grobbee DE, et al. (2007) Inter-scan reproducibility of coronary calcium measurement using Multi- Detector-Row Computed Tomography (MDCT). Eur J Epidemiol 22: 235-243.