Video Article

Identifying Coronary Artery Calcification on Non-gated Computed Tomography Scans

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Abstract

Coronary artery calcification (CAC) provides an objective measure of coronary artery disease and can readily be identified on non-gated computed tomography (CT) scans with a high correlation with gated cardiac CT scans. This standardized protocol takes a step-wise approach to not only optimizing an image for the identification of calcification but also to distinguishing CAC from other common causes of calcification in the cardiac silhouette. Recognition of CAC on non-gated CT scans helps to identify a very powerful prognostic factor that can influence therapeutic interventions or downstream diagnostic testing without requiring a gated cardiac scan. These non-gated CT scans are often acquired as part of the routine care of the patient, and this data is readily available without another dose of ionizing radiation. This protocol allows for the precise and accurate extraction of this data for the purposes of retrospective data analysis in clinical research studies, but also in the clinical evaluation and management of patients.

Video Link

The video component of this article can be found at https://www.jove.com/video/57918/

Introduction

Coronary artery disease is a predictor of major adverse cardiovascular events. CAC on CT scans provides objective evidence of coronary artery disease and may identify previously undiagnosed patients. In addition, CAC has a significant prognostic value. Specifically, the absence of CAC on gated cardiac CT scans identifies a patient population that has a low risk for subsequent cardiovascular events in many different subsets of patients, including patients presenting with cardiac symptoms, as well as asymptomatic patients[1,2]. With ~70 million CT scans performed in the United States and the usage rising, and approximately 11 - 12 million of those scans being CT scans of the chest, the potential for identification of CAC in a large number of patients remains high[3]. However, the majority of the CT scans of the chest performed in that analysis are not dedicated cardiac CT scans. Dedicated cardiac CT scans have standardized slice thickness, acquisition protocols, electrocardiographic (ECG) gating to minimize cardiac motion, and reconstruction protocols. There is also a standardized quantitation for gated cardiac CT scans using the Agatston score. The Agatston scoring system has been well validated and associated with clinical outcomes[1,2].

CAC can be readily identified on these non-gated CT scans but is often overlooked[4]. Good correlation has been demonstrated between CAC identified on non-gated CT scans and Agatston scores obtained from gated CT scans (> 90% in pooled analysis)[5,6,7,8,9,10]. In non-gated CT scans, the presence of CAC has been associated with worse clinical outcomes; whereas, the absence is linked to morbidity and mortality benefits[10,11,12,13,14,15].

While different studies have looked at the prognosis of CAC on non-gated studies, there has been limited published data on how best to identify CAC. There have been attempts to identify an automated approach to the identification of CAC in low-dose CT chests scans done for lung cancer screening purposes; however, the translation of this to other study protocols is extremely limited[16]. The introduction of differential CT scanners, protocols, and contrast (both timing and amount) limits the application of this automated approach. Attempts by the Society of Cardiovascular Computed Tomography and the Society of Thoracic Radiology to promote the standard reporting of CAC on all CT chests have been met with mixed results[17]. While offering a general framework in this guideline document, the specifics of the identification of coronary calcification, especially for providers who do not routinely visualize coronary anatomy, are limited. Also, strategies specific to abdominal CT scans, contrasted studies, and adjudicating challenging cases are not addressed. Many studies publish their own inter- and intra-observer reproducibility for the protocol they used; however, there is not a standard approach used across different studies.

The ability to consistently and reliably identify CAC on these non-gated CT scans allows for the retrospective and prospective observational investigation of CAC in predicting cardiovascular outcomes in many different conditions. However, there needs to be a standard approach taken

to identifying CAC on non-gated CT scans to ensure the reproducibility of the results, as well as a consistency in training to help in clinical practice.

Protocol

This protocol follows guidelines set forth by the Institutional Review Board and human subject research protocol of the University of Kentucky.

1. Opening the Image Viewer

1. Open the image viewer used at the institution where the research is being conducted. Double-click on the desktop icon to open the viewer.
2. Log in using an institutional username and password.

2. Identifying the Appropriate Patient

1. Click on the **Study List** icon in the toolbar.
2. Under the **Search Criteria** drop-down list, choose the option labeled **With Patient ID Equal To**.
3. Enter the patient's hospital identification number.
4. Under **Modalities**, click on **All Modalities** to unselect all the imaging modalities.
    1. Click on **CT** to select this modality.
5. Under **Body Regions**, leave the default to **All Body Regions**.
6. Then, click with the mouse on **Find**.

3. Identifying the Optimal Study

1. Click on **Performed on** to organize the list by the date of study.
2. Then, click on the study of interest.
   NOTE: The optimal study is a CT chest (either with or without contrast). When multiple studies are available, use the CT scan that can visualize the entire coronary tree closest to the index time point (for retrospective data analysis) or the most recent CT scan (for clinical purposes).

4. Identifying Optimal Image Series

1. Click with the mouse on the tile icon in the top-right corner of the screen and highlight a single tile. Click to make the screen a single pane.
2. Hover over the series icon on the top row of images to identify the series that has a 3 mm slice thickness (or the closest to 3 mm).
3. Click and hold the left mouse button, drag this icon to the center of the viewing screen, and release the left mouse button.
4. Use the center mouse scroll bar (or, alternatively, hold the left mouse button and drag to the right) to scroll through images and ensure an adequate visualization of the coronary tree.

5. Optimizing the Images to Highlight Calcification

1. Scroll through the images until an image where one of the coronary arteries is visualized.
2. Right-click and select the **Window/Level** option.
3. Click on **Interactive W/L**.
4. As a starting point, type in **500** in the W (window) field.
5. As a starting point, type in **150** in the L (level) field.
   NOTE: The goal of adjusting the window and level settings is to optimize the contrast between epicardial fat [usually the lowest Hounsfield unit (HU) in the cardiac silhouette], cardiac chambers, and calcification or metallic structures (usually the highest HU). CT scans with contrast that use lower kV often require the highest level (often > 250 HU) and the largest window (often > 1,000 HU). For "low-dose" CT scans (low mAs) without contrast, would use a slightly lower level (0 - 150 HU).
6. Manually adjust the window by holding down the left mouse button on the horizontal slide bar and moving it right and left (moving the scroll bar to the right increases the window).
7. Manually adjust the level by holding down the left mouse button on the vertical slide bar and moving it up and down (moving the scroll bar up increases the level).
   NOTE: The goal is to adjust the window and level to achieve the following: fat, including epicardial fat, should be dark gray to black; myocardium should be a slightly lighter gray; and calcium and metal should be white.
8. Click on **Close** to close the window and level box and begin viewing the images.

6. Identifying Coronary Artery Calcification

1. Use the center scroll ball on the mouse to scroll up and down the series of images, looking at one coronary at a time.
2. Mark (on a separate document, spreadsheet, *etc.*) whether coronary artery calcification is present or absent in each of the four major epicardial coronary arteries (**Figure 1**).
   NOTE: CAC is deemed as present in the left anterior descending artery (LAD), left circumflex artery (LCx), or right coronary artery (RCA) if it is seen in the vessel itself or in its branches.

7. Techniques for Identifying Subtle Areas of Calcification

1. Identify an area of questionable coronary artery calcification.
2. Right-click on the screen to bring up the menu.
3. Click on **Annotate**.
4. Then, click on **Elliptical ROI**.
5. Click and hold down the left mouse button on the area of calcification and move it down and to the right to create a circle or ellipse large enough to cover the area of calcification.
   NOTE: Make sure the region of interest (ROI) is large enough to cover the entire area of potential calcification and some epicardial fat, but small enough to not include other chambers (especially those with contrast). The software will then provide the minimum, maximum, and average HU in the area without the region of interest.
   1. Click and hold the left mouse button in the center of the region of interest to move it if necessary.
   2. Click and hold the left mouse button on the corners of the region of interest to adjust the size if necessary.
6. Repeat steps 7.5 - 7.5.2 to create another region of interest over the sternum, the bright bony structure at the top of the screen.
7. Repeat steps 7.5 - 7.5.2 to create another region of interest over the ascending aorta.
8. Compare the maximum HU in the area of potential calcification to the maximum HU in the ascending aorta and the sternum.
   NOTE: Classify an area as coronary artery calcification if it is more than 2 standard deviations away from the maximum HU in the ascending aorta. Coronary artery calcification should have a maximum HU closer to the maximum HU in the sternum than the maximum HU in the ascending aorta (**Figure 2**).

8. Distinguishing Coronary Artery Calcification from Other Sources of Calcification

1. To open the post-processing software, left click on Windows' start button and then click on the post-processing software. Now, log in using an institutional username and password.
2. To open the study and series, type in either the **Patient ID** or the **Patient Name** in the appropriate field in the search options at the top right of the screen. Then, uncheck **Date 1**.
   1. Now, click on **Update Study List** and then perform a single click on the desired study from the results list at the top left of the screen.
   2. In the **Series List** below, click on the series that has the 3 mm slice thickness in the label.
3. Click and hold the center mouse scroll bar on one of the images and move the mouse up to zoom in so the arteries can be visualized well.
4. Click and hold the left mouse button on the center of each of the crosshairs to move them over the center of the area of calcification in question.
5. Click and hold the left mouse button on the marker on the crosshairs to be able to rotate the other two images. Continue to watch the other two images until the adjacent structure of interest is well visualized.
   NOTE: The 3 areas that are most often confused for coronary artery calcification include aortic wall calcification as RCA or left main artery (LM) calcification, mitral annular calcification (mistaken for LCx calcification) or tricuspid annular calcification (mistaken for RCA calcification), and pericardial calcification. Coronary arteries are surrounded by epicardial fat, whereas these other adjacent structures are not.

Representative Results

Coronary anatomy is relatively predictable in most patients as described above. The typical locations to evaluate these vessels are also easily identified in most patients (**Figure 1**). Using the described methodology, the presence or absence of CAC could be reliably identified in 84% of the patients in a single cohort (267 of 317 possible patients)[15]. The vast majority of patients excluded did not have a CT scan in the designated time frame or had an abdominal CT scan in which the complete coronary vasculature was not seen, and no CAC was identified. In a single patient, a severe respiratory and cardiac motion artifact obscured the discrimination of CAC from mitral annular calcification and was not included in the analysis. The impact of a cardiac motion artifact can be mild or severe (**Figure 3**). This is one of the main reasons why the correlation between gated and non-gated CT scans is not perfect. However, as scanners become faster, the duration of breath holds and time to acquisition becomes shorter. This minimizes the impact of respiratory and cardiac motion on image quality and improves the temporal resolution of the image.

The degree and distribution of CAC on gated CT scans are independently associated with clinical outcomes but have not been as well assessed in non-gated studies[2,19]. While it is possible (and recommended, based on guideline documents) to assess the severity of CAC visually, this does require experience. In addition, it is difficult to standardize the visual estimates of severity for research purposes, and while reported inter- and intra-observer reproducibility within the study helps ensure internal validity, it does little to ensure that the correlation between studies is adequate. However, with the validation of some correlative non-gated and gated studies (with quantification) to train the reader and the use of standard protocols across studies, this may be possible to overcome (**Figure 4**). General considerations for identifying severity include the number of vessels involved, the number of plaques in each vessel, and the density of calcification in each plaque. Single plaques in one or two vessels are usually mild in severity. Multiple calcified plaques involving all 3 epicardial vessels, especially if they are densely calcified, are usually considered as severe CAC.

The distribution of CAC in non-gated studies is more readily identified, although the clinical significance of this in non-gated studies is less clear. Theoretically, multivessel CAC (or diffuse CAC) likely portends worse outcomes beyond the degree of CAC in non-gated studies as it does in gated studies, but this has not been validated. The classification of distribution is usually based on the four epicardial vessel territories (LM, LAD, LCx, and RCA). We have typically classified these as single vessels *versus* multi-vessel disease (> 1 vessel involved). Proposed quantifications derived from gated studies beyond this (*i.e.*, diffusivity indices) require a reliable CAC score, which is not reliably attainable in non-gated studies.

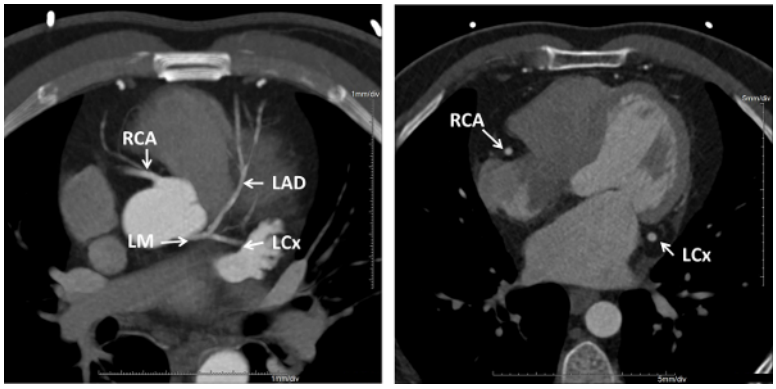

Figure 1: Normal anatomic position of major epicardial coronary arteries. (**A**) This panel is a more cranial axial slice (maximal intensity projection), close to the origin of the coronary arteries. (**B**) This panel is a more caudal axial slice, at the mid-ventricular level. The left main artery (LM) originates from the aorta more posteriorly before branching into the left anterior descending artery (LAD) and left circumflex artery (LCx). The LAD runs in the anterior interventricular groove. The LCx runs in the left atrioventricular groove around the mitral valve. The right coronary artery (RCA) originates from the aorta more anteriorly and runs in the right atrioventricular groove around the tricuspid valve. Please click here to view a larger version of this figure.

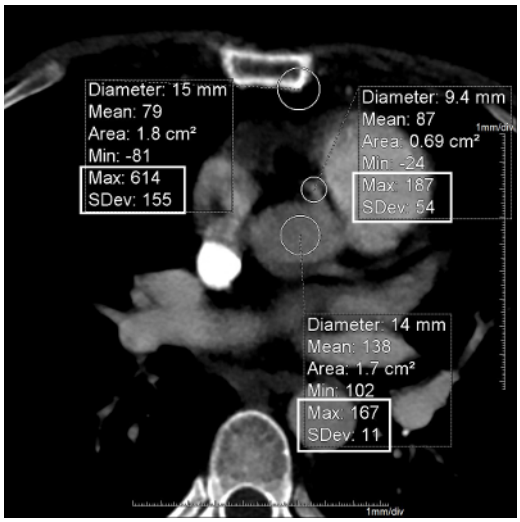

Figure 2: Identifying subtle areas of coronary artery calcification. This panel shows regions of interest (ROI) over the area of questionable calcification, the ascending aorta, and the sternum, to see the difference in signal intensity as measured by Hounsfield units (HU). The area in question in the RCA is not coronary artery calcification, and the maximal signal intensity is more consistent with the ascending aorta than it is with the sternum (white boxes). Please click here to view a larger version of this figure.

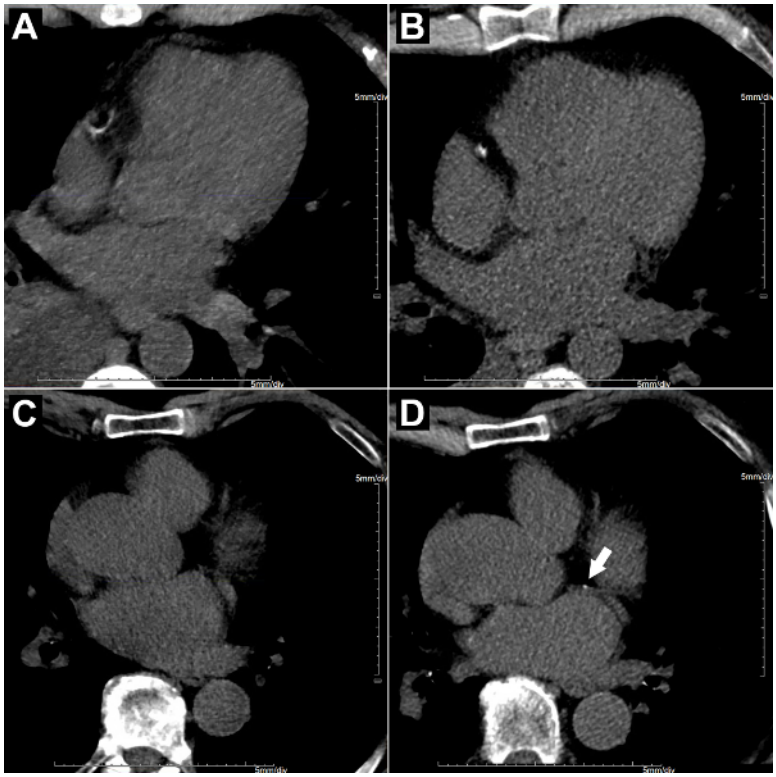

Figure 3: The impact of gating on the visualization of coronary calcium. The upper two panels show (**A**) a non-gated and (**B**) a gated CT chest scan on the same patient, where calcification in the right coronary artery (RCA) is still visualized. The lower two panels show (**C**) a non-gated and (**D**) a gated CT chest scan on a different patient showing cardiac motion obscuring the mild coronary calcification in the proximal left circumflex artery (white arrow). Please click here to view a larger version of this figure.

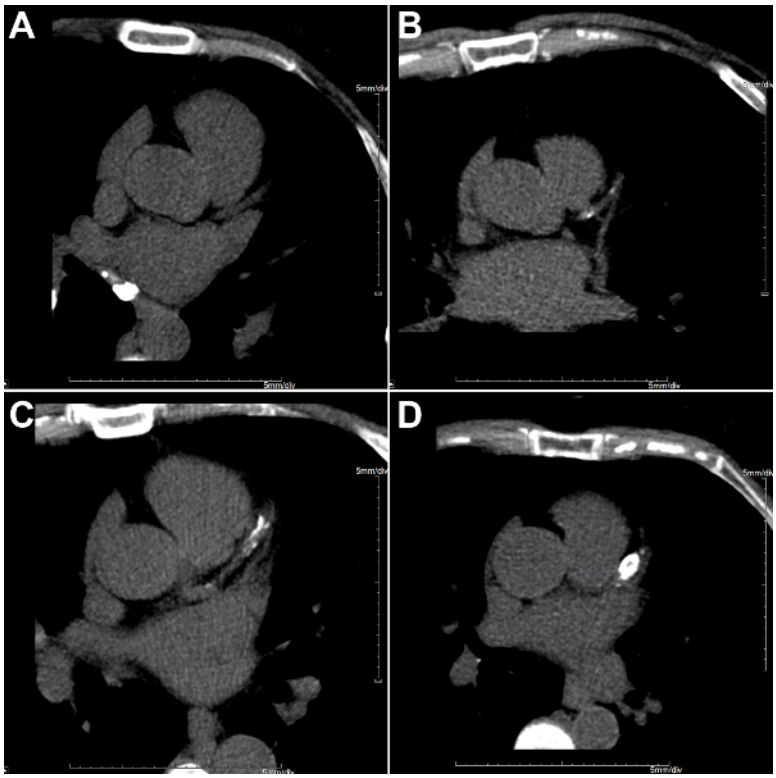

Figure 4: Different degrees of coronary calcification. These panels show axial non-contrast CT chest images of different patients showing (**A**) no calcification, (**B**) mild calcification, (**C**) moderate calcification, (**D**) and severe calcification of the left anterior descending artery. Please click here to view a larger version of this figure.

Discussion

The identification of CAC is an extremely powerful prognostic tool with an ever-growing body of literature supporting its use in many different clinical scenarios. The majority of the literature is focused on gated cardiac CT scans for the identification of CAC, but there is robust evidence of both the correlation of CAC on non-gated CT scans, as well as the prognostic ability of this finding. Given the CT scan utilization in the United States, as well as the ever-growing concerns about radiation exposure, the ability to extract CAC information from CT scans already acquired seems to offer additional value (*i.e.*, improved quality at minimal to no additional cost). This will continue to be important in the evolving healthcare environment. To do this meaningfully and reliably, standardized approaches to identifying CAC on non-gated CT scans are necessary, from a research perspective but also for the translation to clinical application.

Optimizing the sequence identification and performing an accurate window/leveling of the grayscale are the most critical steps of the described methodology. Maintaining an optimal slice thickness, radiation exposure (kV and mAs), and post-processing to mimic the well-validated gated cardiac CT scans allows for the best correlation. When possible, studies that maintain a 2 - 3 mm slice thickness and 120 kV are ideal to allow for the optimal identification of CAC[17]. Given that the goal of the methodology is to identify CAC in many different types of CT protocols, appropriate window and leveling is essential, especially in studies that are not acquired using the above protocols. Lowering kV is important to reduce radiation exposure at the expense of signal-to-noise. The impact of kV on window and leveling is dependent on whether it is a contrasted study or not. The higher the contrast concentration in the coronary arteries, the higher the level and the larger the window will need to be. This effect is augmented when lower kV is administered. Given that body habitus and reconstruction protocols may influence this, subtle adjustments will likely need to be made on a case-by-case basis. As a consistent reference, the optimal window and leveling is one that makes epicardial fat appear dark gray to black, soft tissue gray, and calcium very light gray to white.

After an optimal sequence identification and appropriate window and leveling, the next stage that warrants focus is differentiating CAC from other sources of calcification in the cardiac silhouette. This can be challenging in studies with a significant cardiac and respiratory motion artifact. The use of multi-planar reconstruction can help to identify CAC (usually seen within the epicardial fat) *versus* annular calcification (seen in the myocardium itself), pericardial calcification (seen outside of the epicardial fat) and aortic root/aortic valve calcification (seen in the aortic wall). On rare occasion, a severe cardiac and respiratory motion artifact degrades the image sufficiently to prevent differentiation, and these studies should be removed from any analysis.

Given the variance in patients, as well as in acquisition techniques, there is always the need for potential troubleshooting. In addition to patient-specific modifications in window and level, there are potential issues with identifying subtle areas of calcification and discriminating between coronary calcification and non-coronary calcification. Subtle areas of calcification can be difficult to identify, especially with contrast-enhanced studies. Using region of interest tools on any image post-processing software can help to compare HU in areas of calcification to HU in areas of contrast, as well as to HU in other areas of calcification (such as bone). Subtle areas of coronary calcification are likely to have similar HU as bone and should generally be higher than the HU of areas of contrast. Multi-planar reconstruction helps to distinguish coronary calcification (seen in the epicardial coronary arteries that sit in the epicardial fat) from other sources of calcification in the cardiac silhouette. Mitral annular calcification, aortic wall calcification, and pericardial calcification can all be seen independent of coronary artery calcification. Given their location in the mitral valve annulus, the aortic wall, and in the pericardium, respectively, the use of multi-planar reconstruction can help to reliably differentiate these from coronary artery calcification.

Given that the negative prognostic value of CAC is its more powerful asset, the simple presence or absence of CAC provides significant value in cardiovascular risk assessment. This proposed methodology does allow for a standardized approach to this. It also does allow for the identification of single-vessel *versus* multi-vessel CAD, which in gated CT scans has also been shown to have prognostic significance. However, this protocol limits the quantification of CAC, largely due to concerns about inter-and intra-observer reproducibility, especially amongst less experienced readers. Dedicated cardiac CT scans allow for more validated quantification and may help to provide a tiered risk model for cardiovascular events based on the Agatston score. However, this requires dedicated cardiac CT scans, local expertise, and dedicated post-processing software, with its associated costs and radiation exposure. Requiring gated cardiac CT scans also requires a prospective analysis for most conditions, and the application of CAC in certain disease states may not be validated enough to warrant this. Furthermore, in the current healthcare delivery model with its emphasis on value, the ability to identify CAC on CT scans already acquired has significant appeal for clinical translation. Hopefully, this methodology for identifying CAC in non-gated CT scans allows for such reproducible, value-added research and clinical applications. Future applications of this technique include creating semi-automated CAC detection software, as well as well as training modules for clinicians to be able to integrate into their practice[4].

Disclosures

The authors have nothing to disclose.

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