



Invited commentary

Quantification of aortic calcification – How and why should we do it?

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The identification and quantification of vascular calcification has garnered much research interest over the last two decades. The presence and extent of calcification in several vascular beds is independently associated with non-cardiovascular disease mortality, likely due to chronic inflammation [1]. Coronary artery calcification is an important factor associated with obstructive coronary artery disease and future cardiac events [2]. Thoracic aorta calcification is significantly associated with fatal and non-fatal cardiovascular disease and all-cause mortality, whereas abdominal aorta calcification is significantly associated with cardiovascular disease mortality [3–5]. The arch and the proximal descending aorta are the most prone segments of the thoracic aorta to demonstrate calcium by CT [3].

Coronary artery calcium is quantified using non-contrast ECG-gated CT scan-based Agatston score [2]. Aortic calcification score is calculated using a modified Agatston method, which is obtained by summing the product of the pixel area (mm²) and the density score (“1” if 130–199 HU, “2” if 200–299 HU, “3” if 300–399 HU, and “4” if > 400 HU) over each calcified lesion with a CT attenuation of 130 or greater. In contrast to coronary artery calcification, the quantification of aortic calcium can vary considerably [3,6,7] because the acquisition of the CT images is not standardized for this application,

thereby limiting known methods like the Agatston score to be translated from the coronary arteries to the aorta.

In the April 2015 issue of *Atherosclerosis*, Mori et al. described and validated a new volume-rendering approach to quantify aortic calcification using commercially available software [8]. Using a 130 HU threshold, the authors at first performed a validation study for assessing influence of slice thickness in aortic calcium analysis between a slice-by-slice pixel-based aorta calcium score and a voxel-based volumetric aorta calcium score using prospectively ECG-gated non-contrast cardiac CT scans in 60 patients reconstructed at 3 mm and 5 mm slice thickness. The study demonstrated an excellent agreement of the pixel-based aorta calcium score with volumetric aorta calcium score and noted that volume-based score was less influenced by slice thickness as compared to pixel-based score. Furthermore, the authors investigated the agreement between the volume-based calcium score and the proposed volume rendering generated aorta calcium volume using non-gated CT images of the thoracoabdominal aorta in 126 consecutive patients. The investigators found excellent agreement between the volumetric aorta calcium scores and the volume rendering aorta calcium volume since with the former technique the voxels were extracted from every slice while from the three dimensional volume in the volume rendering technique. The authors reported reasonably less time for the proposed volume rendering approach for aortic calcium quantification and concluded that CT-based volume-rendering is an easy, feasible and reproducible technique for 3D visualization and quantification of the aortic calcium burden in any part of the aorta. This work extends our understanding regarding the usefulness of the CT-based non-ECG gated volume rendering technique to overcome some of the limitations in Agatston scores-based methods (i.e. pixel-based and volume-based) for aortic calcium quantification (see Fig. 1).

Despite the potential clinical benefits of this method, a few cautionary notes should be considered. This study did not aim to quantify overall plaque burden, including non-calcified plaque. While aortic calcium can be quantified more rapidly than in the past, and this metric can be a potential tool for assessing response to anti-atherosclerotic therapy, there is little data regarding the clinical decision making related to calcium in the aorta. The location of calcified plaque may also have clinical importance in pre-

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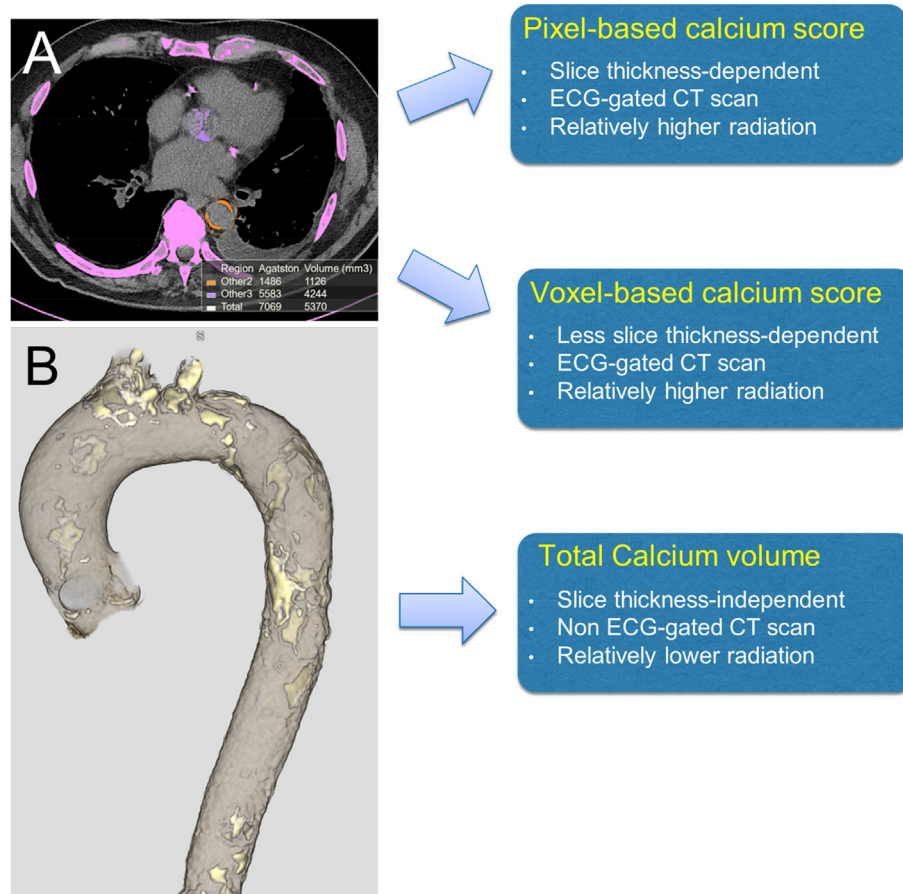


Fig. 1. CT-based techniques of measuring aorta calcium burden: A. Axial non-contrast CT image at the level of the left atrium used for pixel-based calcium score (Agatston score) or voxel-based calcium score calculation at the root of thoracic aorta and mid descending thoracic aorta. Calcification is denoted with orange color, B. 3D-volume rendered candy cane view of the thoracic aorta used for the visualization and quantification of total aorta calcium volume. Calcification is denoted with lighter yellow color. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

aortic surgical setting and require appropriate weighting to optimize risk stratification. In order to establish a new imaging “biomarker” for future cardiovascular events, large-scale population studies would have to positively correlate the proposed metric with future events. Another consideration is the fact that since there are multiple proprietary algorithms to arrive at a desired volume rendered image, the volume rendering software is important to identify. The Ziosoft platform is commonly used in Asia and Agatston calcium scoring with this software has been validated in a large cohort [9]. However, this software is less commonly used outside of Asia. The authors acknowledge that their protocol has been tested on two of the four CT hardware vendors. While this may be of some relevance, it is likely to be the case that the method of image reconstruction proves more important than the hardware platform itself. Typical volume rendered images utilize thinner slices with image reconstruction intervals of 1.5 mm or less overlap in the reconstructed images to generate smoother images [10]. Based on volume averaging principles, the calcium score is likely to increase with decreasing reconstruction thickness as demonstrated (Table 3 of the manuscript) in the comparison of 3 mm versus 5 mm reconstructed images. We also suggest that all methods under consideration be comprehensively assessed with a CT phantom of a calcified aorta. To our knowledge, such a phantom has not been used for aortic calcium scoring development and testing. However, one could be developed using 3D printing [10], but this model will require custom materials so that the soft tissue and calcium CT attenuation are physiologic and amenable for experimentation [11].

We believe that a full scale validation should be completed before considering clinical application of aortic calcification quantification. At this time, considerations should include the overall radiation risk profile of a screening study [12], and the tradeoff between fewer image artifacts from an ECG-gated acquisition versus the lower radiation profile from a non-ECG-gated acquisition.

Finally, if a new scoring system is to be developed, there appears to be an opportunity to move beyond the widely used Agatston-based methods. This method has served society well, but has some limitation related to the attenuation threshold dependent variability of the calcium quantification. More exact methods such as the mineral mass [13] have been proposed but have not received any traction in the past due to the large amount of available meaningful data using the Agatston method and due to lack of automation of the new methods. Since aortic calcium scoring is in the early development phase and relying on advanced automation, perhaps now is the time to re-consider more exact quantification metrics.

Disclosures

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