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Review

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Effects of Iterative Reconstruction on the Diagnostic Assessment of Coronary Calcium Scores

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ABSTRACT

Coronary Artery Calcium (CAC) score is a widely used indicator to determine disease severity and predict the risk of severe cardiac events. However, radiation dose associated with coronary CT scanning for CAC scoring raises concerns, especially for asymptomatic patients. Iterative Reconstruction (IR) technique represents a recently developed image processing approach for reduction of image noise and radiation dose, while improving diagnostic image quality. Despite these advantages over conventional filtered back projection technique, effects of IR techniques on CAC scores remain unclear. This review article aims to provide an overview of clinical applications of IR techniques in coronary CT angiography with a focus on the effects of different IR techniques on CAC score assessment.

KEYWORDS: Coronary calcium score; Coronary artery disease; Diagnosis; Calcified plaque; Image processing; Iterative reconstruction.

INTRODUCTION

Coronary Artery Calcium (CAC) scoring is considered a reliable, noninvasive technique for determining coronary plaque burden, risk stratification and reclassification of risk of coronary artery disease.[1] CAC scoring used to be performed by electron beam CT (EBCT), but has now been replaced by coronary CT angiography (CTA) due to rapid technical developments of multi slice CT scanners over the last 15 years.[2-4] The rationale behind CAC scoring is that coronary calcification represents atherosclerotic changes in the coronary arterial wall, thus, measurement of the amount of calcium is usually performed to estimate the amount of coronary atherosclerosis and consequently, the risk of coronary artery disease (CAD).[5] Although different calcium scoring techniques have been proposed and used in clinical practice, such as Agatston score, volume score and mass score, with each of them having strengths and limitations,[6] the Agatston score is the most widely used method for quantification of CAC in routine clinical practice during coronary CT imaging.

The extent of coronary calcification has been shown to be closely related to the risk of major adverse cardiac events; therefore, quantitative assessment of coronary calcifications by coronary CTA has become a risk stratification scheme for patients with suspected CAD. However, image quality of coronary CTA depends on image reconstruction process. In recent years, iterative reconstruction (IR) an alternative to conventional filtered back projection (FBP) has been increasingly used in coronary CTA due to the following advantages: reduce image noise and radiation dose, in particular, significant dose reduction by up to 80% compared to FBP, while still preserving diagnostic image quality.[7] A recent systematic review has shown that IR serves as a feasible alternative to the standard FBP in coronary CTA with significant lower radiation dose, improved image quality and high diagnostic value in the diagnosis of CAD.[8]

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Despite these promising results of using IR in coronary CTA for dose reduction and image quality improvement, the effect of IR on image appearance change compared to FBP reconstructions should not be ignored. There is concern that this effect may generate negative impact of coronary CTA on coronary plaque characterization, in particular, quantification of high CAC, or severely calcified plaques. While beneficial effects of IR in coronary CTA have been reported to reduce blooming artifacts in highly calcified plaques and coronary stents,[9-11] effects of IR on CAC scoring are contradictory and debatable. This review provides an overview of the clinical applications of IR in coronary CTA with regard to its effects on CAC score, with a focus on how IR techniques affect CAC scoring and patient stratification.

DIAGNOSTIC VALUE OF CORONARY CTA IN HEAVILY CALCIFIED PLAQUES

Coronary CTA has been widely accepted as a less invasive imaging modality with high diagnostic value in coronary artery disease. The very high negative predictive value (>95%) of coronary CTA allows it to serve as a gatekeeper for excluding patients with suspected CAD.[12-17] However, diagnostic value of coronary CTA is affected by presence of high calcification in the coronary artery disease, and this is manifested by the limited specificity and positive predictive value (PPV) due to high percentage of false positive rates.[18-21] These studies have shown that diagnostic performance of coronary CTA decreases significantly with the increase of CAC score. This is mainly because of the blooming artifacts from heavy calcification in coronary plaques which result in overestimation of coronary lumen stenosis; thus, leading to low specificity and PPV. Figure 1 is an example of coronary CTA in a patient with heavily calcified plaques in left coronary artery showing significant lumen stenosis but invasive coronary angiography confirms stenosis of less than 50%.

The limited diagnostic value of coronary CTA in the assessment of severely calcified plaques can be addressed by two methods: use of image post-processing to minimize or suppress the effect of heave calcification for improvement of coronary lumen visualization, and use of IR techniques in either raw data or image space for reduction of image noise. Although only a few studies are available in the literature, use of image post-processing algorithms in calcified coronary arteries has been shown to be effective with promising results reported. Tanaka et al studied 11 patients with inclusion of 55 calcified coronary segments by comparing subtracted images with coronary CTA images, with invasive coronary angiography as the standard method.[22] At per-segment level, specificity of subtracted coronary CTA was improved from 48.7% (from standard CTA) to 59%. The area under curve (AUC) by receiver-operating characteristic (ROC) was also increased from 0.741 to 0.905. We reported our early experience of using different image post processing methods for assessment of calcified coronary plaques with resultant improved visualization of coronary lumen when the image post-processing "sharpen" algorithm was used compared to other algorithms.[23] This technique has been further verified by our recent report in 50 patients with calcified coronary plaques.[24] All coronary CTA data were post processed with "sharpen" and smooth reconstruction algorithms in comparison with the original coronary CTA data with the aim of determining the effects of image post processing on reduction of blooming artifacts. Diagnostic value of coronary CTA in CAD was compared at per-vessel assessment with invasive coronary angiography as the reference method. While the sensitivity and negative predictive value of coronary CTA remain unchanged among these coronary CTA data, the specificity and PPV were 66% and 57% with application of "sharpen" algorithm to coronary CTA data, which were significantly higher than 33% and 41%, 44% and 44%, corresponding to the original and coronary CTA data with use of smooth algorithm, respectively (Figure 2). The AUC by ROC analysis also showed significant improvement for >50% coronary stenosis is assessment in the left anterior descending artery when compared to the other two approaches (Figure 3).

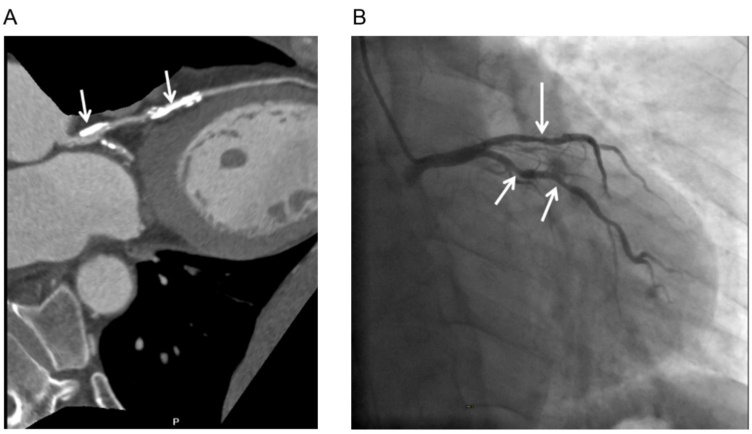

Figure 1: (A). Curved planar reformatted coronary CT angiography (CCTA) shows extensively calcified plaques (arrows) at the left anterior descending (LAD) coronary artery in a 55-year-old man. More than 50% and 90% stenosis was noticed at the proximal and mid-segments of LAD and about 50% stenosis at left circumflex (LCx) on CCTA. (B). Less than 50% stenosis was confirmed in LAD (short arrows) and LCx (long arrow) in invasive coronary angiography.

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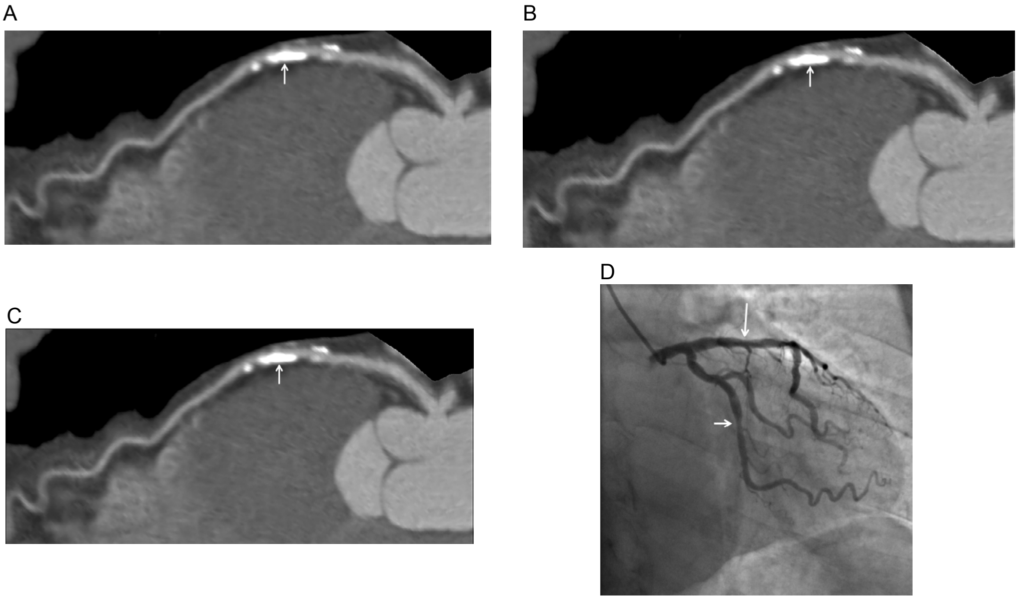

Figure 2: Curved planar reformatted coronary CT angiography (CCTA) shows multiple calcified plaques at the left anterior descending coronary artery (LAD) in a 59-year-old man. CCTA original data (CCTA_O) shows 69% stenosis in LAD due to the heavily calcified plaque, while CCTA with "sharpen" algorithm (CCTA_S) demonstrates 45% stenosis, and 68% stenosis as shown with CCTA with original data integrated with outcome of smoothed image subtracted from the original (CCTA_OS) (A-C). Invasive coronary angiography confirms mild stenosis of 28% at LAD and 44% stenosis at LCx (D). Long and short arrows refer to the stenosis at LAD and LCx, respectively. Reprinted under terms of Open Access article from reference.[24]

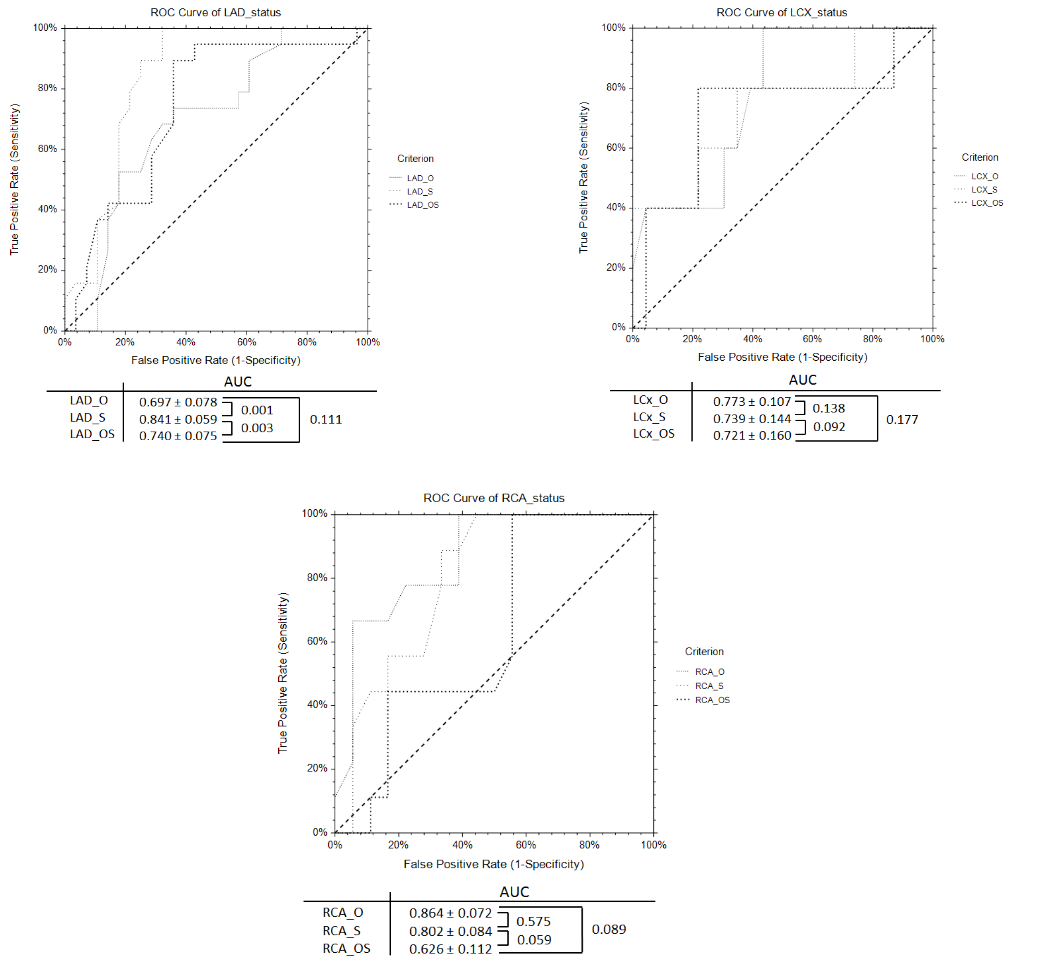

Figure 3: Areas under the curve by receiver-operating characteristic curve analysis demonstrate the diagnostic performance of coronary CT angiography (CCTA) original (CCTA_O), with use of image sharpen (CCTA_S) and smooth algorithms (CCTA_OS) in the detection of significant coronary stenosis when compared to invasive coronary angiography at left anterior descending (LAD), left circumflex (LCx) and right coronary artery (RCA) (A-C). Reprinted under terms of Open Access article from reference.[24]

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While image post-processing methods need to be confirmed by more studies, the current literature seems to favour the use of IR techniques in coronary CTA. The use of IR has become a common practice in latest multi slice CT scanners mainly because of significant dose reduction when compared to the conventional FBP. By the end of 2011, IR techniques are available in all four major CT vendors.[7] Although IR is widely accepted as an effective alternative to FBP for radiation dose reduction and image quality improvement, mixed results are reported in the literature with regard to its effect on the assessment of extensively calcified plaques in the coronary arteries. The following section will focus on detailed discussion of these studies in relation to the use of IR in coronary artery calcium assessment.

EFFECTS OF IR ON CORONARY CALCIUM SCORES

Extensive calcifications cause blooming artifacts which lead to over estimation of coronary stenosis, and this often results in unnecessary examinations such as invasive coronary angiography or myocardial perfusion imaging studies.[25,26] This inherent limitation in FBP image reconstruction can be overcome with use of IR techniques.

Renker et al in their prospective study compared IR with FBP reconstructions in 55 patients with an Agatston score of more than 400 (indicating severe calcification in the coronary arteries).[9] Specificity and PPV were significantly improved by using IR on a per-segment (91.2% and 61.1% for FBP, 95.8% and 76.9% for IR, $p<0.001$) and per-patient level (66.7% and 78.9% for FBP, 79.2% and 85.7% for IR, $p<0.05$) for diagnosis of significant coronary stenosis with invasive coronary angiography as the reference method. Their results also showed that IR enabled reclassification from false positive to true negative findings in 4% of coronary segments and 5.5% of patients, respectively. When compared with FBP, IR resulted in significantly lower calcium volumes.

The effects of IR on CAC scores are inconclusive according to the current literature, since some studies reported no effect, while others demonstrated significant impact which could change patient reclassification.[27-37] IR techniques include either image-based such as iterative reconstruction in image space (IRIS), or raw-data based such as Adaptive Statistical Iterative Reconstruction (ASIR) or sonogram-affirmed iterative reconstruction (SAFIRE), or hybrid approaches such as I-Dose.[7] While results of an *in vitro* phantom study showed mixed findings of using IR in relation to the corresponding effects on calcium measurements,[28,29] results of some *in vivo* studies showed no significantly reduced calcium score measurements.

Matsuura and colleagues compared hybrid IR with FBP in 77 patients with suspected CAD, and their results showed no significant effect of using IR on assessing the calcium score, with percentage difference between FBP and hybrid IR being 20.7%, 20.7% and 27.1%, respectively corresponding to the Agatston, volume and mass scores.[30] Hecht et al tested standard CAC scoring protocol using I-Dose level 3 and low-dose protocol of using I Dose level 7 in 102 consecutive patients. Agatston, volume and mass scores were measured and compared between these two protocols. There was excellent correlation in Agatston, volume and mass scores between the standard and low-dose protocols ($p<0.001$), with the mean differences in Agatston scores between these two protocols being 17.4±25.8. There were no significant differences in Agatston scores, except for the right coronary artery, or for aortic calcification.[31] These findings are further confirmed by a recent *in vitro* and *in vivo* study.[32] Schindler et al evaluated IRIS and SAFIRE techniques in a cardiac phantom and 110 patients for calcium scoring. Both IR techniques had excellent agreement with FBP for Agatston scores, while the patient's risk reclassification was less than 3%, indicating no significant effect on Agatston assessment.

Contrary to the above-mentioned studies, most of the recent reports support the statement that IR has significantly affected the CAC scores which could change patient's risk stratification.[33-39] These studies can be summarized into three groups based on the use of IR techniques: use of ASIR or SAFIRE for image reconstruction, use of I-Dose with different levels and use of iterative model reconstruction (IMR). A number of studies have reported the effects of using ASIR or SAFIRE on calcium score measurements with results showing significant reduction in Agatston score and volume scores.[33-36] These findings generally indicate that the mean calcium scores decreased with the use of IR or increased SAFIRE degrees, with up to one third of patients being reclassified to a lower risk category with IR in comparison with FBP. Furthermore, increased IR level such as high-grade SAFIRE has been shown to result in a negative calcium score as reported by Kurata et al.[34] Similarly, use of I-Dose levels leads to reduction in Agatston, volume and mass scores, with reclassification of patient risk up to 15%.[37,38] Szilveszter et al in their recent study applied IMR and hybrid IR techniques in 63 symptomatic patients and 504 asymptomatic individuals. Use of IR techniques resulted in significantly lower CAC score with the median values of CAC score being 147.7, 107 and 115.1 for FBP, hybrid IR and IMR, respectively. No significant difference in CAC score was found between these two IR techniques; however, the main difference was noticed between FBP and IMR reconstructions with difference of 7.3%. Authors found that the IMR led to 2.4% of individuals reclassified with modest effect on the actual risk classification.[39] These findings raised concerns about use of IR techniques in CAC scoring, although further larger prospective studies are needed to confirm these results.

SUMMARY AND CONCLUDING REMARKS

There is no doubt that IR techniques are replacing the conventional filtered back projection in coronary CT angiography due to significant image noise and radiation dose reduction and improvement of image quality. However, the effects of IR techniques on coronary calcium scores remain to be further clarified since these reported findings should be interpreted with caution. It should also be noted that CAC scoring not only depends on

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the use of imaging reconstruction techniques, but also relies on different vendors. Significantly different CAC scores were reported among different CT scanner types with resultant reclassification of patients in up to 6.5% of cases.[40] Further studies are warranted to assess the effects of different IR reconstruction techniques with use of different types of CT scanners in larger population groups.

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