Effect of intracycle motion correction algorithm on image quality and diagnostic performance of computed tomography coronary angiography in patients with suspected coronary artery disease

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Abstract

Rationale and objectives: We sought to explore the impact of intracycle motion correction algorithms (MCA) in the interpretability and diagnostic accuracy of computed tomography coronary angiography (CTCA) performed in patients suspected of coronary artery disease (CAD) referred to invasive coronary angiography.

Materials and methods: Patients with suspected CAD referred for invasive coronary angiography previously underwent CTCA. Patients under rate-control medications were advised to withhold for the previous 24 hours. The primary endpoint of the study was to evaluate image interpretability and diagnostic performance of MCA compared to conventional reconstructions in patients referred to invasive angiography due to suspected CAD.

Results: Thirty-five patients were prospectively included in the study protocol. The mean age was 61.4±9.4 years. Twenty-seven (77 %) patients were male. A total of 533 coronary segments were evaluated using conventional and MCA reconstructions. MCA reconstructions were associated to higher interpretability rates (525/533; 98.5% vs. 515/533; 96.6 %, p<0.001) and image quality scores (3.88±0.54 vs. 3.78±0.76, p<0.0001) compared to conventional reconstructions. Although only mild, a significant difference was observed regarding the diagnostic performance between reconstruction modes, with an area under the curve of 0.90 (0.87-0.92) vs. 0.89 (0.86-0.92), respectively, for MCA and conventional reconstructions (p=0.0447).

Conclusions: In this pilot investigation, MCA reconstructions performed in patients with suspected CAD were associated to higher interpretability rates and image quality scores compared to conventional reconstructions, although only mild differences were observed regarding the diagnostic performance between reconstruction modes.

Keywords: imaging; beta blockers, interpretability, multidetector

Introduction

During the past decade, computed tomography coronary angiography (CTCA) has gained a role in a number of diagnostic algorithms as a validated non-invasive diagnostic tool aimed at evaluating symptomatic patients at intermediate risk of coronary artery disease (CAD). This position has been obtained mainly on the basis of a high sensitivity and an excellent negative predictive value.[1-3] Nevertheless, the positive predictive value of CTCA has yielded considerably lower results, particularly in patients with intermediate to high probability of CAD, driven by a larger prevalence of false positive findings in such populations. Indeed, although CTCA has shown a high diagnostic accuracy in most clinical scenarios, it does not provide a significant incremental value over functional tests in patients with high pretest probability.[4] Most false positive findings in CTCA are associated to diffuse coronary calcification and/or motion artifacts.[5] So far, the development of newer generations of CT scanners has failed to provide major improvements in the evaluation of diffusely calcified lesions. In turn, several hardware and software-based approaches have demonstrated, with different success rates, to improve temporal resolution in order to diminish motion artifacts associated to high or irregular heart rates.[6] Recently, intracycle motion correction algorithms (MCA) that use information from adjacent cardiac phases to compensate for coronary motion have been proposed as a potential means to scan patients with high or irregular heart rates without using rate-control medications.[7] We therefore sought to explore the impact of MCA in the interpretability and diagnostic accuracy of CTCA performed in patients suspected of CAD referred to invasive coronary angiography.

Methods

Study population

The present was a single-center, investigator driven, prospective study, that involved patients with suspected CAD referred for invasive coronary angiography. All patients included were more than 18 years old, in sinus rhythm, able to maintain a breath-hold for 15 seconds; without a history of contrast related allergy, renal failure, or hemodynamic instability. Additional exclusion criteria comprised a history of previous myocardial infarction within the previous 30 days, previous percutaneous coronary revascularization or coronary bypass graft surgery, or chronic heart failure. Patients under rate-control medications were advised to withhold for the previous 24 hours. Coronary risk factors and clinical status were recorded at the time of the CT scan, and clinical variables were defined as indicated by the Framingham risk score assessment. No rate-control medications were administrated prior to the scan.

The primary endpoint of the study was to evaluate image interpretability and diagnostic performance of MCA compared to conventional reconstructions in patients referred to invasive angiography due to suspected CAD. For this purpose, we prospectively enrolled consecutive patients with suspected CAD to undergo CTCA before the invasive procedure.

Image acquisition

Patients were scanned using a 64-slice high definition scanner (Discovery HD 750, GE Healthcare, Milwaukee, USA), after intravenous administration of iodinated contrast (iobitridol, Xenetix 350^{TM}, Guerbet, France) through an antecubital vein. A total of 60-80 ml of iodinated contrast was injected using a three-phase injection protocol, as follows. Phase 1: 80 % of the total iodinated contrast volume being injected undiluted at a rate of 4.5 to 5.0 mL/sec; phase 2: the other 20 % of the contrast medium mixed at a 50 % saline dilution, injected at a rate of 4.5 to 5.0 mL/sec; and phase 3: a 30 to 40 mL saline chasing bolus at a rate of 4.5 to 5.0 mL/sec. A bolus tracking technique was used to synchronize the arrival of contrast at the level of the coronary arteries with the start of the scan. Image acquisition was performed after sublingual administration of 2.5-5 mg of isosorbide dinitrate.

The decision to perform retrospective or prospective acquisitions was left at discretion of the investigators, based on the body mass index and the heart rate prior to the scan. Briefly, in patients with a heart rate lower than 65 bpm, a prospective ECG-triggered acquisition was performed using a 100 msec padding centered at 75 % of the cardiac cycle; in patients with high or irregular heart rates a retrospective acquisition was performed with dose modulation to reduce tube output during systole. Other scanner-related parameters were a collimation width of 0.625 mm and a slice interval of 0.625 mm. Maximum tube voltage and current was adjusted according to the acquisition mode (prospective or retrospective) and body habitus (100 kV or 120 kV for patients with body mass index < 30 kg/m2 or larger, respectively).

Image analyses

CTCA image analyses were performed off-line on a dedicated workstation, using a commercially available dedicated software tool (AW 4.6, GE Healthcare) by consensus of two experienced level 3–certified coronary CTCA observers (PC, AD), blinded to the clinical data and to the reconstruction mode. The same observers were randomly assigned MCA or conventional reconstructions of each patient, with at least a 2-week window period between paired examinations. Briefly, the MCA multi-phase reconstruction (Snapshot Freeze, GE Healthcare, Milwaukee, USA) algorithm, after automated coronary vessel tracking, utilizes information from adjacent cardiac phases within a single cardiac cycle to characterize vessel motion (vessel path and velocity) in order to determine the actual vessel position at the pre-specified target phase and adaptively compensate for any residual motion at that phase. The time required for MCA reconstruction to be completed is 27 seconds, whereas conventional reconstructions entail 9 seconds.

Iterative reconstruction algorithms were applied in all cases at 40% ASIR (adaptive statistical iterative reconstruction). Axial planes, curved multiplanar reconstructions, and maximum intensity projections were used at 1-5 mm slice thickness, according to the previously reported American Heart Association 17-segment model. Images were evaluated on a per segment basis and per territory basis. Segments with a reference diameter lower than 1.5 mm were not included in the analysis. Each segment was graded as follows: normal; non-significant stenosis (< 50 %); significant stenosis (≥ 50 %); or uninterpretable. Uninterpretable segments due to motion artifacts or severe calcification were assumed as positive for the diagnostic performance analysis.

Quantitative image quality assessment was performed using a 4-point Likert scale, as follows: 1) Non-diagnostic, impaired image quality due to motion artifacts or severe calcification that precluded appropriate assessment; 2) Sufficient but suboptimal, reduced image quality due to motion artifacts, image noise or low contrast attenuation, but sufficient to rule out obstructive disease; 3) Good, presence of mild motion artifacts, image noise, coronary calcifications or low contrast, but preserved ability to evaluate the presence of stenosis as well as to identify the presence mild atherosclerosis; and 4) Excellent, absence of motion artifacts, high intraluminal attenuation and clear delineation of vessel walls, with the ability to evaluate both the presence of obstructive disease and mild atherosclerosis.

CT effective radiation dose was derived by multiplying the dose-length product with the weighting (*k*) value of 0.014 mSv/mGy/cm for chest examinations, as suggested by the Society of Cardiovascular Computed Tomography.[8]

Invasive angiography acquisition and analyses

All procedures were performed in accordance to standard techniques. Coronary angiograms were obtained in multiple projections after administration of intracoronary nitrates. Quantitative coronary angiography analysis was performed by an independent observer blinded to the CTCA data (AG). The catheter tip was cleared of contrast for accurate calibration. Lesion measurements were performed using the "worst" view of an end-diastolic frame.

The institutional review board approved the study protocol, which complied with the Declaration of Helsinki, and written informed consent was obtained from all patients.

Statistical analysis

Discrete variables are presented as counts and percentages. Continuous variables are presented as means ± SD, or median (interquartile range), as indicated. Comparisons among groups were performed using paired samples t-test, and one-way analysis of variance, with Bonferroni tests being performed for multiple comparisons. To determine the accuracy of MCA versus conventional reconstructions for the detection of stenoses ≥ 50 % by invasive angiography, we calculated the sensitivity, specificity, negative predictive value, positive predictive value, and likelihood ratios, accounting for potential non-uniform distribution (95 % confidence intervals). Receiver-operating characteristic (ROC) curve analyses were also performed to evaluate the diagnostic performance of the two reconstruction approaches using specific software for ROC analysis (MedCalc Software, Ostend, Belgium). The difference between the two areas under the curve was tested with the z test. Differences in the parameters a and b of two ROC curves are tested using the bivariate chi-square test, as previously described.[9, 10] All other statistical analyses were performed using SPSS software, version 13.0 (Chicago, Illinois, USA). A two-sided p value of less than 0.05 indicated statistical significance.

Results

Thirty-five patients were prospectively included in the study protocol. All patients enrolled underwent CTCA and invasive angiography. The mean age was 61.4±9.4 years. Twenty-seven (77 %) patients were male. Seven patients (20 %) had diabetes, thirty two (91 %) had hypertension, and twenty one (60 %) had hypercholesteromia as coronary risk factors. Other demographical characteristics are depicted in Table 1. Median heart rate during the CT scan was 62.0 (50.0-68.0) bpm. The median effective radiation dose related to CTCA was 4.7 (4.1-10.2) mSv. The prevalence of stenosis greater than 50 % on a per patient basis by means of invasive angiography was 74 % (26/35).

A total of 533 coronary segments were evaluated using conventional and MCA reconstructions. MCA reconstruction improved image quality in 34/533 segments (6.4 %). In three (0.6 %) segments, image quality was deemed inferior with MCA compared to conventional reconstructions. Overall, MCA reconstructions were associated to higher interpretability rates (525/533; 98.5% vs. 515/533; 96.6 %, $p<0.001$) and image quality scores (3.88±0.54 vs. 3.78±0.76, $p<0.0001$) compared to conventional reconstructions (Figures 1 and 2). Image quality scores according to each coronary territory are depicted in Table 2, showing a larger effect among the right coronary artery. Image quality scores were not significantly reduced in patients with higher heart rates within the MCA group, whereas a significant drop in image quality was observed in patients with higher heart rates within the conventional reconstruction group (Table 3).

On a per segment basis, although only mild, a significant difference was observed regarding the diagnostic performance between reconstruction modes, with an area under the curve of 0.90 (0.87-0.92) vs. 0.89 (0.86-0.92), respectively, for MCA and conventional reconstructions ($p=0.0447$). No significant differences were identified on a per patient basis in this regard (area under the curve of 0.83 (0.64-1.0) vs. 0.83 (0.64-1.0), respectively, for MCA and conventional reconstructions ($p=1.0$). All other diagnostic measures are depicted in Table 4. Analyses discriminated according to heart rate tertiles did not reveal further differences in this regard (Table 5).

Discussion

In spite of the development and incorporation of newer CT generation scanners, the high sensitivity and negative predictive value of CTCA has remained relatively unaffected through the past decade.[11] In turn, newer scanners have achieved higher specificity and positive predictive value levels, reflecting a reduction in the number of false positives attributed to diffusely calcified vessels and motion artifacts related to high and/or irregular heart rates.[5] Notwithstanding, even with the incorporation of dual source CT scanners provided with a temporal resolution of approximately 83 milliseconds, although image quality has significantly improved, this has not been visibly translated into higher a diagnostic performance. Indeed, such temporal resolution remains insufficient predominantly for the evaluation of the mid right coronary artery among patients with high heart rates, since the period of minimal cardiac motion is inversely related to heart rate and approaches to zero above heart rates of 91 bpm for the circumflex artery and above 78 bpm for the right coronary artery.[12, 13] In parallel, beam hardening artifacts (BHA) originated by the polychromatic nature of x-rays and the energy dependency of x-ray attenuation, are commonly aggravated by motion and could therefore potentially be minimized with the application of MCA.[14]

There is therefore a persistent need for improvements in the ability to reduce motion artifacts related to CTCA acquisitions and, as aforementioned, even dual source systems might benefit from further improvements in temporal resolution in order to achieve heart rate independent motion-free imaging. Motion artifacts can be reduced by lowering heart rate sufficiently in order to attain a temporal window of at least the temporal resolution of the technique. This cannot be routinely accomplished due to a number of diverse clinical scenarios, namely contraindications for beta-blockers or calcium-channel antagonists, heart failure, or tachycardia in the context of acute chest pain triage. Furthermore, dual-source scanners are not widely available thus the development of post-processing techniques that enable motion correction with 64-detector scanners are warranted.

To the best of our knowledge, our investigation is the first to explore the effect of motion correction algorithms (MCA) in the interpretability and diagnostic accuracy of patients suspected of CAD referred to invasive angiography. Our findings can be summarized as follows: 1) MCA reconstructions were associated to higher interpretability rates and image quality scores compared to conventional reconstructions; 2) only mild differences were observed regarding the diagnostic performance between reconstruction modes.

As previously described, by using automated coronary vessel tracking and information from a minimum of 2 adjacent phases within a single cardiac cycle, MCA allow motion artifacts compensation both using prospective and retrospectively gated acquisitions. In contrast to multisector reconstructions techniques, MCA aims at coronary-specific motion; and it is less vulnerable to beat-to-beat variability.[15]

In our study, MCA were associated to higher image quality scores compared to conventional reconstructions, being this more evident within the analysis of the right coronary artery, that has been recognized as the epicardial artery with the fastest motion velocity.[16] Notwithstanding, only mild differences were observed regarding the diagnostic performance, being this potentially attributed to the relatively low heart rate of the patients included. To perceive this with a closer insight, it should be emphasized that the duration of the period with minimal cardiac motion at a heart rate of 62 bpm is generally larger than the temporal resolution of conventional reconstructions.[13] Furthermore, image quality scores were not significantly reduced in patients with higher heart rates within the MCA group, possibly reflecting an attenuation of motion artifacts with MCA reconstructions. In turn, a significant drop in image quality was observed in patients with higher heart rates among conventional reconstructions. These findings are in line with the study of Brodoefel et al, that reported a heart-rate independent image quality using dual source CT scanners.[5]

A recent investigation reported the effect of the current vendor-specific MCA reconstruction. Nevertheless, this study was performed in an entirely different population such as octogenarians with severe aortic stenosis and indication of transcatheter aortic valve replacement, and only retrospectively gated acquisitions were performed. Furthermore, as expected from such population, 14 % of those patients were not in sinus rhythm, and heart rate was significantly higher.[7] Our study included patients suspected of CAD referred to invasive angiography, a population more representative of the patients routinely referred to undergo CTCA. Moreover, we evaluated the effect of MCA including both prospective and retrospective acquisitions.

It has been previously reported that CTCA might lead to an increased number of subsequent functional and/or invasive studies, at least partly being attributed to inconclusive findings in patients with motion artifacts or diffuse calcification.[17] Our findings suggest that post-processing techniques such as MCA might result in an attenuation of motion artifacts observed in 64-slice CTCA, thus potentially leading to a decrease in the number of non-assessable or inconclusive studies.

Our study has some limitations that should be acknowledged. The relatively small sample size might lead to selection bias. Likewise and for the same reason, analyses on a per patient basis should be considered with caution. The mild effect observed of MCA reconstructions in terms of diagnostic performance might have been influenced by the relatively low heart rates of the patients included, given that a large percent of patients were under treatment for hypertension. Given the relatively low median heart rate found in our study, conventional reconstructions showed high interpretability rates and image quality scores, potentially explaining the similar diagnostic performance between conventional and MCA reconstructions. Further studies including larger populations with higher heart rates would be expected to demonstrate a greater impact of MCA reconstructions in terms of diagnostic performance. Finally, we did not include patients with atrial fibrillation, thus our results should not be extrapolated to such population.

Conclusions

In this pilot investigation, vendor-specific MCA reconstructions performed in patients with suspected CAD were associated to higher interpretability rates and image quality scores compared to conventional reconstructions, although only mild differences were observed regarding the diagnostic performance between reconstruction modes.

References

1. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, Nieman K, van Werkhoven JM, Pundziute G, Weustink AC, de Vos AM, Pugliese F, Rensing B, Jukema JW, Bax JJ, Prokop M, Doevendans PA, Hunink MG, Krestin GP, de Feyter PJ. Diagnostic accuracy of 64-slice computed tomography coronary angiography: A prospective, multicenter, multivendor study. *Journal of the American College of Cardiology*. 2008;52:2135-2144
2. Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de Roos A, Cox C, Brinker J, Lima JA. Diagnostic performance of coronary angiography by 64-row ct. *The New England journal of medicine*. 2008;359:2324-2336
3. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *Journal of the American College of Cardiology*. 2005;46:552-557

4. Meijboom WB, van Mieghem CA, Mollet NR, Pugliese F, Weustink AC, van Pelt N, Cademartiri F, Nieman K, Boersma E, de Jaegere P, Krestin GP, de Feyter PJ. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. *Journal of the American College of Cardiology*. 2007;50:1469-1475
5. Brodoefel H, Burgstahler C, Tsiflikas I, Reimann A, Schroeder S, Claussen CD, Heuschmid M, Kopp AF. Dual-source ct: Effect of heart rate, heart rate variability, and calcification on image quality and diagnostic accuracy. *Radiology*. 2008;247:346-355
6. Hassan A, Nazir SA, Alkadhi H. Technical challenges of coronary ct angiography: Today and tomorrow. *European journal of radiology*. 2011;79:161-171
7. Leipsic J, Labounty TM, Hague CJ, Mancini GB, O'Brien JM, Wood DA, Taylor CM, Cury RC, Earls JP, Heilbron BG, Ajlan AM, Feuchtner G, Min JK. Effect of a novel vendor-specific motion-correction algorithm on image quality and diagnostic accuracy in persons undergoing coronary ct angiography without rate-control medications. *Journal of cardiovascular computed tomography*. 2012;6:164-171
8. Halliburton SS, Abbara S, Chen MY, Gentry R, Mahesh M, Raff GL, Shaw LJ, Hausleiter J, Society of Cardiovascular Computed T. Scct guidelines on radiation dose and dose-optimization strategies in cardiovascular ct. *Journal of cardiovascular computed tomography*. 2011;5:198-224
9. Park SH, Goo JM, Jo CH. Receiver operating characteristic (roc) curve: Practical review for radiologists. *Korean journal of radiology : official journal of the Korean Radiological Society*. 2004;5:11-18
10. Metz CE. Some practical issues of experimental design and data analysis in radiological roc studies. *Investigative radiology*. 1989;24:234-245
11. Hamon M, Morello R, Riddell JW, Hamon M. Coronary arteries: Diagnostic performance of 16- versus 64-section spiral ct compared with invasive coronary angiography--meta-analysis. *Radiology*. 2007;245:720-731
12. Ohashi K, Ichikawa K, Hara M, Kawai T, Kunitomo H, Higashide R, Shibamoto Y. Examination of the optimal temporal resolution required for computed tomography coronary angiography. *Radiological physics and technology*. 2013;6:453-460
13. Otton JM, Phan J, Feneley M, Yu CY, Sammel N, McCrohon J. Defining the mid-diastolic imaging period for cardiac ct - lessons from tissue doppler echocardiography. *BMC medical imaging*. 2013;13:5
14. Choi HS, Choi BW, Choe KO, Choi D, Yoo KJ, Kim MI, Kim J. Pitfalls, artifacts, and remedies in multi- detector row ct coronary angiography. *Radiographics : a review publication of the Radiological Society of North America, Inc*. 2004;24:787-800
15. Min JK, Arsanjani R, Kurabayashi S, Andreini D, Pontone G, Choi BW, Chang HJ, Lu B, Narula J, Karimi A, Roobottom C, Gomez M, Berman DS, Cury RC, Villines T, Kang J, Leipsic J. Rationale and design of the victory (validation of an intracycle ct motion correction algorithm for diagnostic accuracy) trial. *Journal of cardiovascular computed tomography*. 2013;7:200-206
16. Achenbach S, Ropers D, Holle J, Muschiol G, Daniel WG, Moshage W. In-plane coronary arterial motion velocity: Measurement with electron-beam ct. *Radiology*. 2000;216:457-463
17. Shreibati JB, Baker LC, Hlatky MA. Association of coronary ct angiography or stress testing with subsequent utilization and spending among medicare beneficiaries. *JAMA : the journal of the American Medical Association*. 2011;306:2128-2136

Figure legends:

Figure 1. Non-diagnostic computed tomography coronary angiography in a 63 year-old male using conventional reconstruction. A prospective scan was performed at 75 % of the cardiac cycle with a 100 ms padding (heart rate 64 bpm). Severe motion artifacts are observed at the mid right coronary artery (*) that preclude the assessment. After application of motion correction algorithm (panel B) the vessel is clearly depicted, with mild mixed irregularities are confirmed at invasive angiography (panel C).

Figure 2. Mild motion artifacts observed at the mid right coronary artery of a 55 year old asymptomatic male with abnormal functional test using conventional reconstruction (panel A). A prospective scan was performed at 75 % of the cardiac cycle with a 100 ms padding (heart rate 63 bpm). A calcified plaque is observed at the mid segment, although vessel and plaque edges are relatively blurred. After application of motion correction algorithm, image quality is enhanced (panel B). Invasive angiography confirms the absence of significant stenosis (panel C).