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Research paper

Reproducibility of semi-automatic coronary plaque quantification in coronary CT angiography with sub-mSv radiation dose

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ABSTRACT

Introduction: Coronary computed tomographic angiography (CTA) can characterize coronary atherosclerotic plaque components as calcified and non-calcified. Quantitative measurements of coronary plaque burden by coronary CTA may play a role in serial studies to determine disease progression or response to medical therapies. The reproducibility from repeated assessment of such quantitative measurements from low-radiation dose coronary CTA has not been previously assessed.
Purpose: To evaluate the interscan, interobserver and intraobserver reproducibility for coronary plaque volume assessment using semi-automatic plaque analyses algorithm in low radiation dose coronary CTA.
Methods: In 50 consecutive patients undergoing two 128-slice dual source CT scans within 12 days with a mean radiation dose of 0.7 mSv per coronary CTA, the interscan, interobserver and intraobserver reproducibility of coronary plaque assessment using validated software (AutoPlaq) were evaluated.
Results: Interscan, interobserver and intraobserver agreement for non-calcified and calcified plaque volumes were excellent (Spearman rho 0.87–0.99). Interscan mean percentage difference in non-calcified and calcified plaque volumes were 0.1% ($p = 0.8$) and 1.9% ($p = 0.19$) with limits of agreement of ±11% and ±48.5%; per inter- and intraobserver mean percentage differences were 0.1% ($p = 0.25$) and 0.3% ($p = 0.001$), and 0.3% ($p = 0.33$) and 0.4% ($p = 0.59$) with limits of agreement of ±7% and ±32.9%, and ±6.6% and ±32.1%, respectively.
Conclusion: A semi-automatic plaque assessment algorithm in repeated low radiation dose coronary CTA allows for high reproducibility of coronary plaque characterization and quantification measures.

1. Introduction

Coronary computed tomographic angiography (CTA) allows for coronary artery visualization, permits detection and exclusion of significant coronary artery disease (CAD),[1] and may provide valuable prognostic information.[2–4] Non-invasive coronary plaque detection and characterization in terms of composition and stenosis severity, is part of contemporary practice when evaluating coronary CTA studies, and comport valuable diagnostic and prognostic information.[3,5–13] Quantitative assessment of coronary plaque burden by coronary CTA has the potential by serial assessment to determine disease progression or response to medical therapy. The reproducibility of identification and quantification of coronary plaques by coronary CTA have previously been investigated in few studies.[13,14] For manual coronary plaque assessment, interobserver variability has been reported to vary between 11% and 37%.[5,10,15] However, manual plaque quantification is time-consuming and tedious, thus reducing its applicability in clinical practice. Semi-automatic plaque assessment using dedicated software may introduce easier, faster and higher reproducible plaque quantification compared to manual tracing. Studies evaluating semi-automatic plaque assessment algorithms have, in selected patients, provided promising results for plaque characterization and quantification using standard coronary CTA protocols.[14,16,17]

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Although the radiation exposure related to a standard coronary CTA protocol is reasonably low, any additional scanning and radiation exposure is of concern, a good interscan, inter- and intra-observer reproducibility for visual coronary plaque identification have previously been demonstrated using a low radiation dose scan protocol,[18] however the interscan reproducibility of volumetric plaque quantification from low dose coronary CTA is not known. Rapid and reproducible coronary plaque burden quantification with low radiation dose exposure may potentially permit serial assessment of disease progression or response to therapy with possible future clinical implications.

The objective of this study was to evaluate the interscan, interobserver, and intraobserver reproducibility of coronary plaque quantification and characterization using a semi-automated plaque analysis algorithm in low radiation dose high-pitch spiral acquisition coronary CTA.

2. Materials and methods

2.1. Patients

Consecutive patients with chest pain and intermediate pre-test likelihood of CAD, without known CAD, age ≥40 years, regular heart rate <60 beats per minute (bpm), body weight <90 kg and body mass index (BMI) ≤27 kg/m^2, undergoing clinical low dose coronary CTA with 100 kV and high-pitch spiral acquisition mode were eligible for study inclusion. Patients were included if willing to undergo a second coronary CTA within two weeks of the initial scan. A 30–80% pre-test likelihood of significant CAD (≥50% coronary artery lumen reduction) based on age, gender and symptoms was considered intermediate.[19] Traditional cardiovascular risk factors were categorized as previously reported.[20] Symptoms were categorized into typical, atypical angina or non-anginal pain.[21] Left ventricular ejection fraction was evaluated by 2-dimensional echocardiography. Patients were pre-medicated with 100 mg atenolol >1 h before the scanning, with additional intravenous metoprolol in doses of 5–20 mg if necessary. All patients received 0.8 mg nitroglycerin sublingually prior to scanning. The study complies with the declaration of Helsinki and was approved by the regional Ethical Committee. All patients gave written informed consent.

2.2. Coronary CTA

Coronary CTA was performed with identical protocols for scan 1 and 2 using a dual source CT (DSCT) scanner (Somatom Flash, Siemens Medical Solution, Forchheim, Germany). A prospective electrocardiogram-gated sequential non-enhanced scan was acquired at 55% of the RR interval, and 3 mm slices were reconstructed to obtain an Agatston score using dedicated software (Syngo Calcium scoring, Siemens Medical Solutions).[22] Contrast transit time was determined by injecting a contrast test bolus of 10 ml 350 mg I/ml (Iomeron, Bracco, Italy) followed by a 50 ml saline chaser both at flow rates of 5 ml/s, measuring the peak enhancement in the ascending aorta. Coronary CTA was performed with 100 kV tube voltage, adaptive tube current with a reference of 370 mAs, 2 × 128 × 0.6 slice collimation, z-flying focal spot, gantry rotation time 280 ms, pitch 3.4. For coronary CTA, 60 ml 350 mg I/ml were injected followed by 60 ml saline chaser both at flow rates of 5 ml/s. Image acquisition was prospectively electrocardiogram triggered at 60% of the RR interval. Images were reconstructed with a slice thickness of 0.6 mm and a 0.3 mm slice increment using a medium sharp kernel (B26f). Window level and width were adjusted for optimal visualization at the discretion of the observer. Coronary CTA studies were randomly and independently assessed by two experienced observers (more than 5 years experience with coronary CTA), using axial images and multiplanar reconstructions on separate workstations blinded to patient characteristics. A coronary plaque was defined as a visual entity >1 mm^2 within the vessel wall, and clearly distinctive from tissue surrounding the vessel.

Plaque quantification from CTA was performed in all segments >1.5 mm using previously described and validated analysis software (AutoPlaq, version 9.5, Cedars-Sinai Medical Center, Los Angeles).[14,16] In brief, for plaque assessment, coronary CTA images were examined in multiplanar reformats, and a circular region of interest was placed in the aorta to define the "normal reference bloodpool." The proximal and distal limits of each lesion were identified and marked by the reader. The software then automatically tracked the centreline of the coronary artery. Plaque quantification was automated and utilized adaptive scan-specific plaque thresholds, and based on lesion length and enhancement, estimated the coronary plaque characteristics including non-calcified and calcified plaque volumes (Fig. 1).[14,16] Coronary plaque composition and volumetry was assessed quantitatively on a per segment-basis using an 18-segment model[6] as well as on a per patient-level. In order to evaluate the intraobserver reproducibility, 20 coronary CTA studies were reanalysed >1 week (10–30 days) after the first evaluation by one observer. Image noise was measured with SD of CT attenuation values in a circular region of interest in the aortic root at the level of the left main coronary artery in the coronary CTA dataset. Radiation exposure was estimated from the recorded dose length product multiplied by the conversion factor for chest region (0.014 mSv mGy^{-1} cm^{-1}).[23]

2.3. Statistics

Continuous normally distributed data are presented as means (±standard deviation, SD), whereas non-normally distributed continuous data are presented as median values (interquartile range; range). Categorical data are presented as numbers (proportions). Interscan, interobserver and intraobserver reproducibility estimates were analysed using the Paired *t*-test, Spearman's rho correlation, coefficient of reproducibility (2 × SD) and Bland Altman analyses estimating 95% limits of agreement. A *p*-value <0.05 was considered statistically significant. Data analyses were performed using STATA\IC 10 statistical software (StataCorp, Texas, USA).

3. Results

Of 222 consecutive patients with suspected CAD evaluated by coronary CTA through April to September 2010, 66 (30%) met the inclusion criteria; 156 patients did not meet the study inclusion criteria because of a different CT scan mode or tube voltage, primarily due to higher heart rates and body sizes. Sixteen patients were not enrolled because of inability to undergo a repeated scan within 2 weeks ($n = 10$) or lack of consent ($n = 6$). Patient and scan characteristics are presented in Tables 1 and 2, respectively. The median (interquartile range, range) individual heart rate difference between scan 1 and 2 was 0 (−2 to 3, −20 to 15, $p = 0.78$). The scan heart rate was >60 bpm in one of the scans in 6 patients (61–74 bpm). The mean attenuation in the ascending aorta was 500.5 ± 86 HU, with a corresponding mean image noise of 30.6 ± 5.0 HU. In 50 patients, 88 segments were non-evaluable (48 segments <1.5 mm and 40 segments with motion artefacts) and 627 segments were evaluable by both observers. No evidence of CAD was observed in 18 patients, non-obstructive CAD in 27 patients, a 50–70% stenosis in 4 and >70% stenosis in 1 patient. Coronary artery plaques were present in 72 segments, with non-