Computed tomography coronary angiography : from quantification of coronary atherosclerosis to risk stratification of patients

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Chapter 9

Feasibility of automated quantitative assessment of serial computed tomography angiography to detect changes in coronary atherosclerosis

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Abstract

Purpose: The aim of this study was to evaluate the feasibility of quantitative computed tomography angiography (QCT) for the assessment of coronary atherosclerosis changes over time on serial coronary computed tomography angiography (CTA) in patients with stable chest pain.

Methods: The patient population consists of 53 patients clinically referred for the evaluation of chest pain who underwent a coronary CTA. After a minimum of 2 years CTA was repeated to evaluate changes in coronary atherosclerosis over time. For accurate and reproducible assessment of coronary artery disease (CAD) changes, all CTAs were quantitatively analysed using QAngioCT. All parameters of dimension and composition of CAD were compared between patients to assess possible regression and progression of CAD.

Results: Of the 53 patients, 32(60%) showed regression of coronary total atheroma volume (TAV) whereas 21(40%) showed progression of coronary atheroma. In patients with progression of coronary atheroma, median $TAV_{indexed}$ increase was 117.73(56.76; 236.01)mm^3 compared to -82.49(-114.17; -42.58)mm^3 for patients with regression. Patients with progression of coronary atheroma had progression of all four plaque types. However, patients with regression demonstrated a regression of all plaque components except for dense calcium, for which progression was observed.

Conclusion: The assessment of changes in CAD with QCT is feasible. In patients with stable chest pain syndrome both regression and progression of coronary atheroma is observed. Potentially QCT could be applied to assess the efficacy of anti-atherosclerotic therapy.

Introduction

Progression of coronary atherosclerosis is of clinical importance. Serial intravascular ultrasound (IVUS) or invasive coronary angiography (ICA) studies have been used to assess progression of atherosclerosis over time, mostly as part of an evaluation on the efficacy of anti-atherosclerotic therapy.[1] However, these methods are invasive, time consuming and expensive. Computed tomography coronary angiography (CTA) is a suitable method for non-invasive assessment of coronary atherosclerosis. Its value in clinical practice has been extensively established.[2, 3] For accurate and robust assessment of coronary atherosclerosis, novel quantitative computed tomography (QCT) algorithms are available which allow quantification of coronary atherosclerosis dimensions and composition.[4, 5] The accuracy and reproducibility of these tools have been previously validated.[6] Potentially, these algorithms can be applied to quantify coronary atherosclerosis in serial CTA studies. Therefore, the aim of this study was to evaluate the feasibility of QCT for the assessment of coronary atherosclerosis changes over time on serial coronary CTA in patients with stable chest pain.

Methods

Patients

This prospective study included 137 patients clinically referred for the evaluation of chest pain to the Rijnland Hospital between July 2009 and June 2011. Patients underwent a non-contrast computed tomography (CT) scan for coronary artery calcium (CAC) score and coronary CTA. By protocol, after a minimum of 2 years CAC-score and CTA were repeated to evaluate changes in coronary atherosclerosis over time. Patients who had undergone prior, myocardial infarction, percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) were excluded. The clinical data were prospectively entered into the hospital's electronic patient file and retrospectively analysed. The Institutional Review Board approved this clinical study. Informed consent was obtained in all patients.

CTA acquisition

All patients underwent a non-contrast and contrast coronary CTA. Contra-indications for CTA were, 1) impaired renal function (glomerular filtration rate <30 ml/min/1.73m^2), 2) pregnancy, 3) (supra-) ventricular arrhythmias, 4) known allergy to contrast agent, 5) severe claustrophobia. CTA was performed according to standard clinical practice using a Philips Brilliance 64-slice CT scanner. Prior to CTA examination, beta-blocking medication was administered if the heart rate was ≥65 beats

per minute, unless contra-indicated. Scan parameters were as follows: tube voltage 120kV, automated tube current modulation 250–400mA, pitch 0.2–0.3, collimation 64 × 0.625mm, and gantry rotation time 420ms. Images were acquired prospectively and reconstructed at 75% and at the best phase of the R-R interval. All data were stored for offline analysis. The CAC-score was calculated by the Agatston approach. Contrast CTA image quality was classified as: (1) good image quality (scans without motion artefacts), (2) moderate image quality (scans with motion artefacts or increased image noise) and (3) poor image quality (non-diagnostic scans); the last were excluded from the analysis.

Quantitative CTA

For accurate and reproducible assessment of CAD changes, all CTAs were quantitatively analysed using QAngioCT Research Edition version 1.3.6 (Medis medical imaging systems, Leiden, The Netherlands). This software allows for quantitative assessment of both dimension and composition of coronary atherosclerosis. QCT was performed as previously described.[4] In brief, the following automatic processing steps were performed. The 3-dimensional coronary tree was automatically extracted from the coronary CTA dataset. Using an automatic tree labelling algorithm, the segments of the coronary tree were automatically labelled according to the American Heart Association (AHA) 17-segment model. The extracted and labelled coronary tree was verified by an experienced observer. Next, of each coronary, multiplanar reformations (MPRs) were constructed based on the centrelines of the detected coronaries. Thereafter, the lumen and vessel wall were automatically segmented using a previously validated software tool and coronary artery atherosclerosis dimension quantified.[5] If necessary, limited manual input was used to improve the automatic processing steps. With the help of a dedicated tissue characterization algorithm, coronary plaque composition was determined. This algorithm allows differentiating the detected coronary plaque into four different plaque types: fibrotic (FI) plaque, fibro-fatty (FF) plaque, necrotic core (NC) and dense calcium (DC). For the present study, a previously validated method using adaptive HU thresholds was used.[5]

The four major coronaries were studied (i.e. right coronary artery (RCA), left main (LM) artery, left anterior descending (LAD) artery and left circumflex (LCx) artery). Moreover, segments with cross-sectional lumen areas (<1.5mm^2) were excluded as well as segments shorter than 10 mm. The reproducibility of this algorithm has been previously addressed.[6] The reported inter-observer concordance correlation coefficient was 0.96 for plaque burden and plaque area.

Quantitative CTA atherosclerosis parameters

Figure 1 depicts the definitions of the quantitative derived CTA parameters of atherosclerosis dimensions and composition used in this study. For all four plaque types (i.e. FI, FF, NC, DC0 volumes and percentages were derived from the software. All parameters were indexed to the mean segment length of the total population to account for different segment lengths per patient and per scan providing the possibility to compare these parameters over time.[1] This was performed by calculating:

$$\text{Total volume}_{\text{indexed(i)}} = \frac{\text{total volume}}{\text{total segment length}} \times \text{mean segment length population}$$

To compare patients with regression and progression of coronary atheroma, ΔTAV_i was calculated by subtracting $TAV_{i\ baseline}$ from $TAV_{i\ follow\text{-}up}$. There is limited data in the literature to serve as a cut-off to define progression or regression of coronary atheroma volume on coronary CTA. To be as sensitive and accurate as possible, we prospectively determined that any change in ΔTAV_i was considered as a change in coronary atheroma volume. Thus, $\Delta TAV_i < 0\ mm^3$ was classified as regression and $\Delta TAV_i > 0\ mm^3$ as progression of coronary atheroma volume. Subsequently, the change over time in volume of the different coronary plaque types in relation to ΔTAV_i was established.

Statistical analysis

For reasons of clarity, all continuous parameters are reported as mean ± SD and median (interquartile range (IQR)). Categorical data are presented as absolute numbers and percentages. All analyses were performed on a patient-basis. First, both baseline and follow-up plaque characteristics were described. Moreover, the changes over time in these parameters were assessed. Second, a comparison was made between patients with progression or regression of coronary atheroma volume. The change over time in the different atherosclerosis parameters (dimension and composition)

Parameter	Definition
Segment length (mm)	Total distance between the proximal and distal point of the extracted segment.
Lumen volume (mm^3)	Total volume of the vessel lumen of the extracted segment
Vessel wall volume (mm^3)	Total volume of the vessel wall of the extracted segment
Total atheroma volume (TAV_i) (mm^3)	Total vessel volume – total lumen volume.
Percentage atheroma volume (PAV) (%)	[(Total vessel volume – total lumen volume) / total vessel volume] x 100%.
Total (FI/FF/NC/DC)volume(mm^3)	Total volume per plaque type
Percentage (FI/FF/NC/DC) (%)	[(Volume of plaque type – plaque volume) / total plaque volume] x 100%

Figure 1. Definitions of QCT plaque parameters.

was compared between patients with regression or progression of coronary atheroma volume. The baseline patient characteristics were compared between patients with regression or progression of coronary atheroma volume. Lastly, the difference in baseline plaque characteristics was compared between patients with regression or progression of coronary atheroma volume. All statistical tests were two-sided and a P-value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS software (Version 20.0, SPSS Inc., Chicago, Illinois).

Results

Patient population

For this study, 137 consecutive patients were included with diagnostic qualitative CTA images. The flow diagram in Figure 2 illustrates the selection of patients eligible for inclusion as well as the reasons for exclusion. Of these patients, 65 did not have a follow-up appointment scheduled for logistic reasons or were lost to follow-up. Moreover, 7 patients only had a CAC-score at baseline. The remaining 65 patients completed the study with a CTA scan at baseline and follow-up. In 10 of the 65 patients, the CTA image quality was insufficient. Furthermore, 2 of the remaining 55 patients underwent revascularization between the two studies and were also excluded. In total, 53 patients with 377 segments were analysed. The median time between baseline and follow-up CTA was 25 (IQR 24-26) months. The patient characteristics at baseline and follow-up are listed in Table 1. Mean age was 54 ± 8.7 years and 28 (52.8%) of the patients were male. At baseline, 30% of patients received

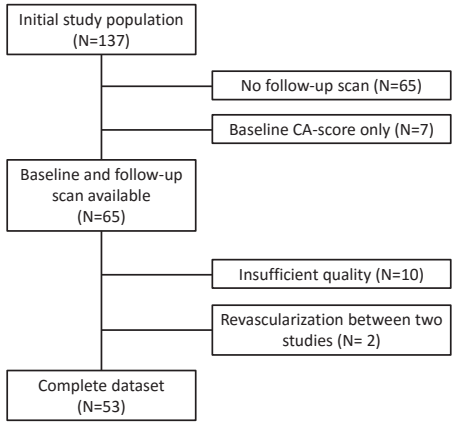

Figure 2. Flowchart of the study population.

Table 1. Patient characteristics.

Patient characteristics (n=53)	Baseline	Follow-up
Age (yrs.)	54 ± 8.7	N/A
Gender (% male)	28 (52%)	N/A
Non AP complaints	8 (15%)	9 (17%)
AP Complaints	45 (85%)	44 (83%)
Atypical AP complaints	32 (60%)	29 (55%)
Typical AP complaints	12 (22%)	14 (26%)
Typical and Atypical AP complaints	1 (2%)	1 (2%)
Cardiovascular risk factors		
Hypertension†	18 (34%)	17 (32%)
Hypercholesterolemia ‡	6 (11%)	6 (11%)
Diabetes Mellitus	4 (8%)	5 (9%)
Family history of CAD*	37 (70%)	N/A
Current Smoking	12 (23%)	12 (23%)
Ex-Smoker	9 (17%)	9 (17%)
Obesity (BMI ≥ 30 kg/m^2)	2 (4%)	2 (4%)
Medication		
ACE/ATII	8 (15%)	8 (15%)
Calcium channel blockers	4 (8%)	7(13%)
NTG	7 (13%)	9 (17%)
Bèta blockers	20 (38%)	16 (30%)
Diuretics	7 (13%)	7 (13%)
Asprin	19 (36%)	20 (38%)
Statines	16 (30%)	22 (42%)
Triglycerides	1.31 ± 0.59	1.20 ± 0.50
Cholesterol	5.53 ± 0.84	5.02 ± 1.38
HDL Cholesterol	1.61 ± 0.57	1.54 ± 0.61
LDL Cholesterol	3.44 ± 0.80	2.90 ± 1.04
VLDL Cholesterol	0.44 ± 0.50	0.42 ± 0.50
Creatinine	82.54 ± 13.03	79.58 ± 16.72
Agatston CAC score	35 ± 60 1.00 (IQR 0 – 51)	51 ± 77 18 (0 – 73)
Increase in Agatston CAC score		15 ± 25 5 (0 – 20)

Data are represented as mean ± SD, median (interquartile range) or as number and percentages of patients.
†Defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or treatment for hypertension
‡Serum total cholesterol ≥230 mg/dL or serum triglycerides ≥200 mg/dL or treatment with lipid lowering drugs.
*Defined as the presence of coronary artery disease in first-degree family members at <55 years in men and <65 years in women.
Abbreviations: ACE: Angiotensin Converting Enzyme, AP: Angina pectoris, BMI: body mass index, CAC: coronary artery calcium, IQR: Interquartile Range, NTG: Nitro-glycerine

statins, compared to 42% at follow-up. The mean Agatston CAC-score at baseline was 35 ± 60 compared to 51 ± 77 at follow-up.

Comparison of QCT parameters between baseline and follow-up

Both baseline and follow-up coronary artery plaque characteristics were reported on a patient-basis (Table 2). The percentage atheroma volume (PAV) was 34.6(32.6-39.3)% at baseline and 36.1(32.5-41.2)% at follow-up, (P=0.241). The TAV_i significantly increased from 737.6(629.1-901.5)mm^3 at baseline, to 812.7(687.9-951.6)mm^3 at follow-up (P=0.043). Overall, the median increase in TAV_i was 5.10(-6.32-16.71)%. Overall both NC_i and DC_i were significantly increased at follow-up. NC_i had increased from 20.33(6.45-41.30)mm^3 to 29.66(11.45-49.09)mm^3, DC_i had increased from 5.36(2.07-12.75)mm^3 to 9.63(2.79-24.00)mm^3. Figure 3 presents a case example with progression of atherosclerosis.

Table 2. QCT plaque characteristics.

Baseline and follow-up plaque quantitative parameters	Baseline	Follow-Up	Change	P-Value
Percent atheroma volume (PAV) (%)				
Mean ± SD	36.0 ± 5.31	37.1 ± 5.51	1.10 ± 4.52	
Median (IQR)	34.6 (32.6-39.3)	36.1 (32.5-41.2)	0.33 (-1.97-3.63)	0.241
Total atheroma volume (TAV_i) (mm^3)				
Mean ± SD	768.1 ± 182.8	832.8 ± 237.4	64.78 ± 208.65	
Median (IQR)	737.6 (629.1-901.5)	812.7 (687.9-951.6)	34.80 (-58.95-175.91)	<0.043
% Change in total atheroma volume				
Mean ± SD			8.49 ± 22.08	
Median (IQR)			5.10 (-6.32-16.71)	
Total fibrotic tissue volume (FI_i) (mm^3)				
Mean ± SD	285.18 ± 89.07	308.25 ± 109.57	23.07 ± 85.60	
Median (IQR)	270.81 (222.68-332.13)	303.19 (227.81-367.70)	17.80 (-41.42-77.25)	0.079
Total fibro-fatty tissue volume (FF_i) (mm^3)				
Mean ± SD	89.32 ± 48.96	100.49 ± 50.60	11.17 ± 49.98	
Median (IQR)	69.23 (47.16-128.50)	94.56 (57.10-128.46)	5.66 (-14.70-22.12)	0.186
Total necrotic core volume (NC_i) (mm^3)				
Mean ± SD	24.75 ± 19.38	36.18 ± 35.43	11.42 ± 36.15	

Table 2. (Continued)

Baseline and follow-up plaque quantitative parameters	Baseline	Follow-Up	Change	P-Value
Median (IQR)	20.33. (6.45-41.30)	29.66 (11.45-49.09)	5.08 (-0.14-14.14)	<0.001
Total dense calcium volume (DC_i) (mm^3)				
Mean ± SD	10.51 ± 11.59	17.25 ± 22.40	6.74 ± 13.73	
Median (IQR)	5.36 (2.07-12.75)	9.63 (2.79-24.00)	2.23 (-0.29-9.99)	<0.001
% fibrotic tissue				
Mean ± SD	36.77 ± 4.33	36.53 ± 4.38	-0.25 ± 4.22	
Median (IQR)	36.10 (34.20-39.65)	36.49 (33.58-39.35)	0.06 (-3.58-2.95)	0.821
% fibro-fatty tissue				
Mean ± SD	11.00 ± 4.13	11.59 ± 3.39	0.59 ± 3.87	
Median (IQR)	10.06 (7.67-14.60)	12.10 (8.27-14.59)	-0.01 (-1.49-1.58)	0.767
% necrotic core				
Mean ± SD	2.95 ± 1.99	3.93 ± 2.61	0.98 ± 2.65	
Median (IQR)	2.69 (1.03-4.63)	3.79 (1.93-5.17)	0.57 (-0.09-1.79)	<0.001
% dense calcium				
Mean ± SD	1.34 ± 1.34	2.04± 2.36	0.70 ± 1.44	
Median (IQR)	0.90 (0.29-1.93)	1.27 (0.34-2.63)	0.28 (-0.22-1.07)	<0.001

Patients with regression vs. progression of coronary atheroma volume

Of the 53 patients, 32(60%) showed regression of coronary atheroma volume (ΔTAV_i <0 mm^3) whereas 21(40%) showed progression of coronary atheroma volume (ΔTAV_i >0 mm^3). In 29 (55%) patients an increase in PAV was observed, whereas 24 (45%) patients showed a decrease in PAV. Moreover, 26 (49%) patients had an increase in PAV >1%, which is considered a relevant threshold for significant change under intensive lipid-lowering therapy in clinical studies.[7, 8] A decrease in PAV >1% was observed in 22 (42%) patients. As depicted in Table 3, in patients with progression of coronary atheroma volume, median TAV_i increase was 117.73(56.76; 236.01)mm^3. Patients with regression of coronary atheroma volume presented with a median decrease in TAV_i of -82.49(-114.17; -42.58) mm^3. Of particular interest, in patients with regression of coronary atheroma volume an increase in total DC_i volume was observed 0.42(-0.96; 5.50) mm^3 The other plaque types showed regression in these patients. In contrast, patients with progression of coronary atheroma volume,

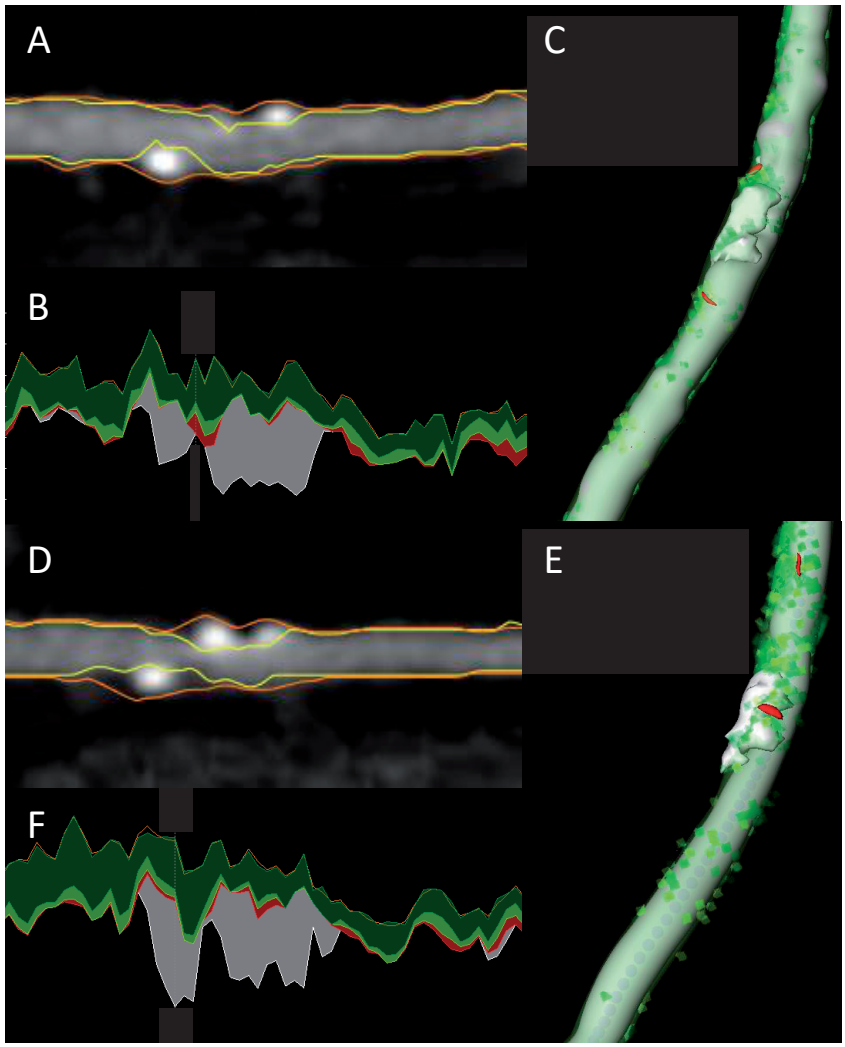

Figure 3. Case example of a case with progression of coronary atherosclerosis.
Example of a the left anterior descending (LAD) artery of 48 years old female with stable angina. Panel A show the multiplanar reformation (MPR) of the LAD at baseline. Panel B demonstrated the corresponding quantitative computed tomography data; the lower part of the graphs represents the lumen cross-sectional area, the upper part the vessel wall cores sectional area. The part between the graphs represents the plaque area. Dark-green represent fibrotic plaque, the light-green represent fibro-fatty plaque, red marks necrotic core and white marks dense calcium. Panel C shows a 3D-representation of the coronary vessel with the same color coding. Panel D-F represent the same vessel but after two year follow-up. Overall, progression of atherosclerosis is observed, specifically of calcified plaque.

Table 3. Comparison of change in coronary plaque dimension and composition over timebetween patients with regression vs. progression of coronary atheroma volume.

Change in plaque quantitative parameters	Regression of coronary atheroma volume (n=21)	Progression of coronary atheroma volume (n=32)	P-Value
Change in PAV			
Mean ± SD	-2.63 ± 1.88	4.19 ± 3.63	
Median (IQR)	-2.18 (-3.60; -1.10)	3.08 (1.08; 7.81)	NA
Change TAV_i			
Mean ± SD	-104.81 ± 101.12	176.07 ± 184.82	
Median (IQR)	-82.49 (-114.17; -42.58)	117.73 (56.76; 236.01)	NA
Change in total fibrotic tissue volume (FI_i) (mm^3)			
Mean ± SD	-46.00 ± 49.07	68.40 ± H73.38	
Median (IQR)	-49.09 (-64.74; -10.48)	59.11 (24.60; 107.86)	NA
Change in total fibro-fatty tissue volume (FF_i) (mm^3)			
Mean ± SD	-20.35 ± 33.06	31.86 ± 48.68	
Median (IQR)	-15.68 (-28.43; 2.20)	14.13 (2.08; 47.13)	NA
Change in total necrotic core volume (NC_i) (mm^3)			
Mean ± SD	-4.92 ± 17.69	22.15 ± 41.11	
Median (IQR)	0.53 (-8.12; 6.50)	10.55 (3.68; 26.55)	NA
Change in dense calcium volume (DC_i) (mm^3)			
Mean ± SD	3.29 ± 14.27	9.00 ± 13.10	
Median (IQR)	0.42 (-0.96; 5.50)	6.29 (0.41; 14.72)	NA

showed an increase in in volume of all four plaque types. The differences in baseline characteristics between patients with regression and patients with progression of coronary atheroma volume were assessed. Besides hypercholesterolemia, there were no significant differences between the two patients groups. Worth mentioning, there was no difference in increase in CAC-score between patients with regression or progression of coronary atheroma volume. Table 4 demonstrates the difference in baseline coronary atherosclerosis dimensions and composition between patients with regression or progression of coronary atheroma volume. Patients with regression of coronary atheroma had significantly higher baseline PAV compared to patients with progression of disease (36.64% (33.72; 40.62) vs 33.44% (31.50; 37.58), P=0.040). Both groups had comparable baseline composition of coronary atherosclerosis.

Table 4. Comparison of baseline coronary plaque dimensions and composition between patients with regression vs. progression of coronary atheroma volume.

Baseline plaque quantitative parameters	Regression of coronary atheroma volume (n=21)	Progression of coronary atheroma volume (n=32)	P-Value
Baseline PAV (N)			
Mean ± SD	37.80 ± 5.88	34.76 ± 4.60	
Median (IQR)	36.64 (33.72; 40.62)	33.44 (31.50; 37.68)	0.040
Baseline TAV_i (N)			
Mean ± SD	801.09 ± 132.59	746.38 ± 208.59	
Median (IQR)	810.78 (697.84; 905.59)	695.04 (570.18; 856.84)	0.102
Baseline % fibrotic tissue (FI)			
Mean ± SD	69.88 ± 8.38	72.13 ± 9.80	
Median (IQR)	69.69 (64.00; 76.20)	73.82 (63.28; 78.11)	0.536
Baseline % fibro-fatty tissue (FF)			
Mean ± SD	21.83 ± 5.16	20.02 ± 7.07	
Median (IQR)	21.70 (17.51; 25.81)	18.77 (15.46; 25.54)	0.335
Baseline % necrotic core (NC)			
Mean ± SD	5.96 ± 3.34	5.10 ± 3.55	
Median (IQR)	5.97 (2.92; 8.06)	3.75 (2.08; 8.49)	0.383
Baseline % dense calcium (DC)			
Mean ± SD	2.32 ± 2.71	2.75 ± 2.52	
Median (IQR)	1.21 (0.38; 2.83)	2.16 (0.85; 4.04)	0.317

Discussion

The present study addressed the feasibility of a novel CTA quantification tool to assess changes of coronary atherosclerosis in a CTA population evaluated for stable chest pain. In addition to the assessment of progression of coronary atheroma volume, the change in specific coronary plaque components was assessed. In 40% of the patients progression of coronary atheroma volume was observed, whereas 60% showed regression of atheroma volume. Patients with progression of coronary atheroma had progression of all four plaque types. However, patients with regression of atheroma demonstrated a regression of all plaque components except for dense calcium, for which progression was observed.

Assessments of coronary atherosclerosis progression

Currently, the standard for evaluating coronary atherosclerosis changes is IVUS. This method allows evaluation of lumen and vessel wall dimensions as well as assessment of coronary atheroma volume. By applying radiofrequency backscatter analysis, IVUS Virtual Histology (VH) allows for assessment of coronary plaque components. IVUS VH has been validated against histopathology.[9] Both IVUS and IVUS VH are often used in studies assessing coronary atherosclerosis progression or regression.[1, 10-13] However, since IVUS is an invasive and costly method, new research has focused on the value of CTA for the assessment of coronary atherosclerosis progression. By applying novel imaging quantification tools, coronary atherosclerosis dimension can be quantified on CTA and used to follow-up changes of atherosclerosis in patients.[4, 6] The validity of these tools has been established and QCT has become accepted as a research tool. More recently, using a Hounsfield Unit (HU) threshold, different plaque components can be individually assessed and quantified using QCT.[5] This allows for a more advanced assessment of coronary atherosclerosis, similar to IVUS VH. Especially with decreasing radiation exposures for CTA, QCT techniques become more available for serial evaluation of coronary atherosclerosis. Another advantage of CTA over IVUS is that CTA allows for visualization of the entire coronary artery tree, whereas IVUS only allows assessment of large coronaries in which a catheter can be introduced. However, a major advantage of IVUS is the higher spatial resolution as compared to CTA. This allows for assessment of more subtle changes in coronary atherosclerosis.[14]

Quantification of CAD progression on CTA

Previous studies have focussed on the validity of quantifying CAD progression with CTA and quantification software. Papadopoulou *et al.* studied the natural history of coronary atherosclerosis in 32 patients with acute coronary syndrome.[8] Patients were serially scanned with a mean interval of 39 months. Overall, the mean change in TAV was 6.7% and 34% of the patients demonstrated regression of coronary atherosclerosis, whereas 44% showed progression of disease. More recent investigations have addressed the feasibility of CTA to study plaque progression or regression as influenced by statin therapy. Hoffman *et al.* performed a second CTA in 63 patients who had 18-36 month earlier been clinically referred to CTA.[15] Using commercially available software coronary atherosclerosis was quantified in a volumetric approach. It was demonstrated that statin therapy induced a decrease in the growth rate of non-calcified plaque but not of plaques containing calcium (i.e. mixed or calcified plaque). Similarly, Zeb *et al.* included 100 patients who underwent serial CTA with a mean interval of 13 months.[16] In statin users, total plaque progression was significantly reduced compared to non-statin users (33.3 mm^3 ±90.5 vs. 31.0 mm^3 ± 84.5).

Moreover, a significantly larger reduction in non-calcified plaque was observed in statin users compared to non-statin users. However, in both groups an increase in calcium was noted on the CTA. It seems that anti-atherosclerotic therapy leads to a reduction of non-calcified plaque without affecting the growth-rate of calcified plaque. Similarly, in the present study, in patients with regression of coronary atheroma volume over time, an increase in calcium volume was observed. This has previously been shown in several IVUS VH studies that investigated the change in coronary plaque composition over time influenced by statin therapy.[10-13] In the majority of these studies, the volume and relative percentage of NC, FI or FF changed over time in patients receiving statin therapy. However, in none of the studies a significant change in DC was noted neither in patients receiving statin therapy, nor in the control cases.

Limitations

The study is hampered by some limitations. First, the study included a limited number of patients. Therefore the lack of significant differences in baseline characteristics between patient groups should be considered with care. Second, the patients were relatively disease free (mean CAC-score 35) and the results cannot be extrapolated to a population with a higher disease burden. Moreover, in current literature there is limited evidence for standard procedures for serial plaque imaging on coronary CTA. We have used a very sensitive parameter to define regression or progression of coronary atherosclerosis, namely any change in TAV. However, establishing standard procedures for assessing changes on CTA is needed. Additionally there was no reference data to compare the quantification results with (i.e. no IVUS or ICA); therefore the present study should be seen as a feasibility study.

Conclusion

The assessment of changes in CAD with QCT is feasible. In patients with stable chest pain both regression and progression of coronary atheroma is observed. Potentially QCT could be applied to assess the efficacy of anti-atherosclerotic therapy.

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