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Research paper

Non-invasive assessment of coronary artery geometry using coronary CTA

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A R T I C L E I N F O

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A B S T R A C T

Aim: To assess the association of coronary artery geometry with the severity of coronary artery disease (CAD).
Methods: 73 asymptomatic individuals at increased risk of CAD due to peripheral vascular disease (18 women, mean age 63.5 ± 8.2 years) underwent coronary computed tomography angiography (coronary CTA) using first generation dual-source CT. Curvature and tortuosity of the coronary arteries were quantified using semi-automatically generated centerlines. Measurements were performed for individual segments and for the entire artery. Coronary segments were labeled according to the presence of significant stenosis, defined as > 70% luminal narrowing, and the presence of plaque. Comparisons were made by segment and by artery, using linear mixed models.
Results: Overall, median curvature and tortuosity were, respectively, 0.094 [0.071; 0.120] and 1.080 [1.040; 1.120] on a per-segment level, and 0.096 [0.078; 0.118] and 1.175 [1.090; 1.420] on a per-artery level. Curvature was associated with significant stenosis at a per-segment ($p < 0.001$) and per-artery level ($p = 0.002$). Curvature was 16.7% higher for segments with stenosis, and 13.8% higher for arteries with stenosis. Tortuosity was associated with significant stenosis only at the per-segment level ($p = 0.002$). Curvature was related to the presence of plaque at the per-segment ($p < 0.001$) and per-artery level ($p < 0.001$), tortuosity was only related to plaque at the per-segment level ($p < 0.001$).
Conclusion: Coronary artery geometry as derived from coronary CTA is related to the presence of plaque and significant stenosis.

1. Introduction

Atherosclerotic plaques evolve over time, and can cause narrowing of coronary arteries with subsequently reduced downstream blood flow. Development and progression of plaque is complex and not yet fully understood. One of the mechanical factors affecting the plaque process is wall shear stress.[1–3] *In-vivo* studies have shown that low shear stress is predominantly present in the inner curvature of the vessel. Atherosclerotic plaque distribution is reported to be associated with the vessel curvature, as well as with vessel bifurcations.[1,4] The methods used to obtain these data were invasive techniques that can only be applied in symptomatic patients with clinical indication for invasive coronary angiography, resulting in biased samples. However, gaining insight in the relationship between three-dimensional vessel geometry and plaque development could be of importance to allow early detection of individuals at increased risk of developing CAD. Using coronary computed tomography angiography (coronary CTA), we investigated the relationship between coronary curvature and tortuosity on one hand and the presence and extent of CAD on the other.

2. Methods

2.1. Patients and cardiac CT protocol

The current study is a sub-study of the GROUND-2 study, which evaluated the presence of silent CAD in cardiac asymptomatic patients with known extra-cardiac arterial disease.[5] The medical ethical committee waived the need for additional approval for this retrospective analysis. From GROUND-2 participants with coronary CTA data (n = 75), only those with reconstructions at end-diastolic phase were

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Abbreviations and acronyms

AHA	American Heart Association
CAD	coronary artery disease
CI	confidence interval
CT	computed tomography
cCTA	coronary computed tomography angiography
ECG	electrocardiographic
ICA	invasive coronary angiography
ICC	intra-class correlation coefficient
IVUS	intravascular ultrasound
LAD	left anterior descending
LM	left main
LCX	left circumflex
MPR	multi planar reformat
RCA	right coronary artery
SD	standard deviation
WSS	wall shear stress

included (n = 73, 97.3%), to enable comparison of curvature and tortuosity based on the same phase in the cardiac cycle.

CT scans were performed on a dual-source CT scanner (SOMATOM Definition, Siemens, Erlangen, Germany). Coronary CTA was performed in spiral mode, using retrospective electrocardiographic gating, the common approach for coronary CTA acquisition at time of inclusion.

During the GROUND-2 study, attending radiologists with (coronary CTA experience from 5 to > 10 years) evaluated CT data sets for the presence and severity of CAD[5] per segment, according to the 15-segment modified American Heart Association classification.[6] More than 70% luminal narrowing was interpreted as significant stenosis. Detailed information on the inclusion, the CT scan/evaluation protocol and the population characteristics can be found in the previous publication.[5]

2.2. Assessment of coronary artery geometry

Geometry assessment was performed using dedicated software (Aquarius iNtuition Ver.4.4.11, Terarecon, San Mateo, USA). Following automatic ribcage removal, appropriate cardiac workflow steps were selected for detailed inspection of the main coronary arteries (right coronary artery (RCA) (segment 1–3), left main (LM) (5), left anterior descending artery (LAD) (6–9), and left circumflex artery (LCX) (11,13)). The coronary arteries could be selected on the transverse slices or on the volume-rendered reconstruction, resulting in a curved multi-planar reformat reconstruction (cMPR) of the selected vessel with automatic centerline extraction. Curvature and tortuosity measurements were performed based on the centerline of the coronary artery selected in the three-dimensional view (Fig. 1). Selected arteries were stretched in the cMPR for determination of the start and end points of the segments (Fig. 2). Each segment was marked manually (Fig. 2) followed by curvature and tortuosity measurements of the marked region based on the three-dimensional course of the centerline. If needed, centerlines were manually corrected. Measurements were performed for each segment (Fig. 2a), and for the entire vessel (Fig. 2b). Segments with an average diameter of less than 1.5 mm were excluded, to ensure reproducibility. Initially segments 1–3, 5–9, 11, and 13 were assessed (730 segments). Due to the high exclusion rate (71.2%), segment 9 was excluded.

Local curvature was calculated between a selected point, a point 5 mm before and a point 5 mm beyond on the centerline, at every 5 mm using Menger's curvature.[7] The scale of the interval was decided after testing intervals from 1 mm to 20 mm with 1 mm increment, as it is known that smaller scales lead to fluctuation, whereas larger scales become less sensitive to sharp local bends. The average of the local curvatures on the selected range was expressed in mm^{-1} and constituted the result of the curvature measurement. Tortuosity was defined as the total length of the centerline divided by the straight distance between start and endpoint of the indicated range on the centerline.[8,9] Intra-reader agreement for geometry measures was assessed for all scans by having one experienced reader perform all measurements twice at a three-week interval. To assess inter-reader agreement, a second reader independently evaluated 20 randomly selected scans.

2.3. Statistical analysis

Intra-class correlation coefficients (ICC) were calculated to assess the reproducibility.[10] Systematic intra- and inter-reader differences were assessed by Bland-Altman analysis.

To investigate the association between a significant stenosis and curvature or tortuosity, a linear mixed model was applied for curvature and tortuosity separately. The analyses were performed at the segment level and at the artery level (RCA, LM, LAD, and LCX). Association and interaction analyses were corrected for age, sex and hypertension. All statistical tests were two-sided. Statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics version 20.0.0.1 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Study characteristics

Seventy-three participants (76.3% males, mean age 64.8 ± 8.1 years) with an available coronary CTA data set reconstructed at an end-diastolic phase could be included in this sub-study. Characteristics of the participants are shown in Table 1. The prevalence of cardiovascular risk factors was high. For the total population of the GROUND-2 study, the prevalence of significant CAD was 56.8%. Median curvature and tortuosity were respectively 0.094 [0.071; 0.120] and 1.080 [1.040; 1.120] on segment level, and 0.096 [0.078; 0.118] and 1.175 [1.090; 1.420] on artery level.

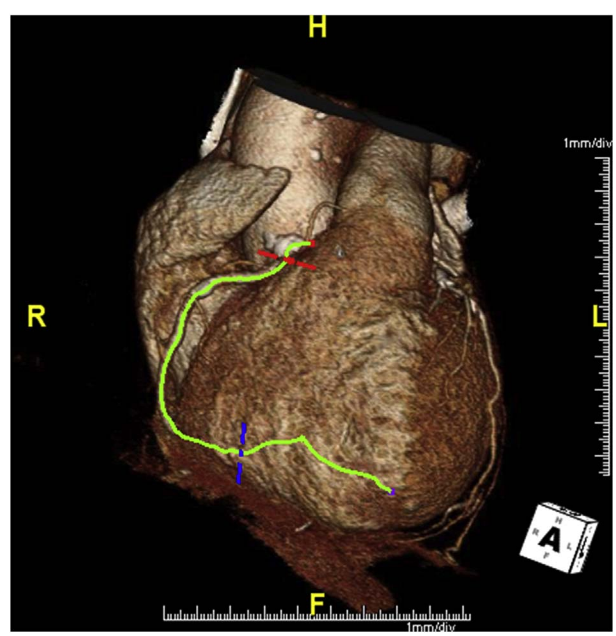

Fig. 1. Volume rendered computed tomography image of a segmented right coronary artery.

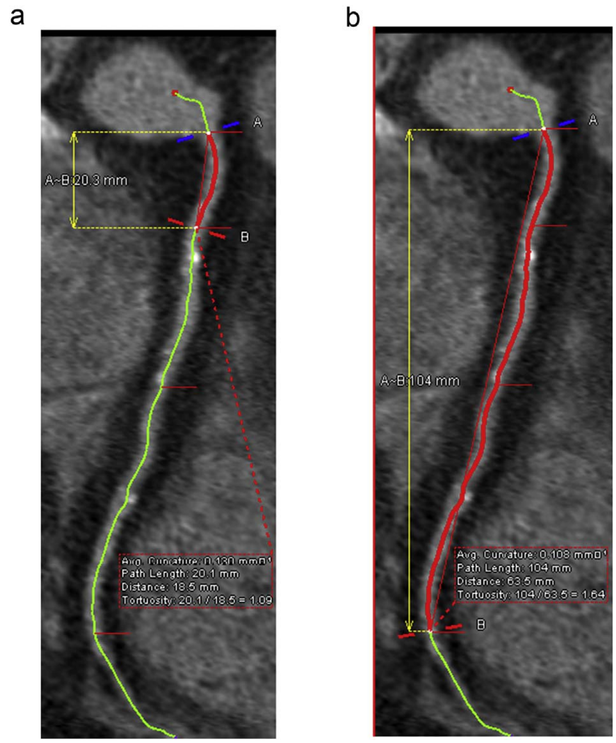

Fig. 2. Example of the right coronary artery in curved multiplanar reformat reconstructions. Segments are separated by the red markers. Curvature and tortuosity are measured for (a) segment 1, and (b) whole vessel. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Clinical characteristics of the study population.

	All patients (N = 73)
Age (years)	64.8 ± 8.1
Male gender (%)	76.7
Body mass index (kg/m^2)	26.2 ± 3.8
Systolic blood pressure (mmHg)	140 ± 24
Diastolic blood pressure (mmHg)	79 ± 9
Hypertension (%)	82.2
Cholesterol (mmol/L)	4.7 ± 1.2
Triglyceride (mmol/L)	2.02 ± 1.8
HDL cholesterol (mmol/L)	1.2 ± 0.4
LDL cholesterol (mmol/L)	2.9 ± 0.9
Dyslipidemia (%)	93.2
Glucose (mmol/L)	5.8 ± 1.1
Diabetes mellitus (%)	9.6
Smoking (%)	32.9
Significant stenosis prevalence (%)	46.6
Plaque prevalence (%)	82.2

Continuous variables are expressed as mean ± standard deviation or median (25th, 75th percentile), dichotomous variables are expressed as percentages. HDL: high density lipoprotein; LDL: low density lipoprotein.

3.2. Reproducibility and reader agreement

The overall ICC showed excellent intra-reader agreement (ICC > 0.80) for tortuosity and curvature measurements. Inter-reader agreement was found to be good for curvature (ICC = 0.73) and excellent for tortuosity (ICC = 0.92)(Supplementary data, Table S1).

Bland-Altman analysis showed a mean intra-reader difference for curvature and tortuosity of −0.0013 (95% CI:-0.0398, 0.0425) mm^{-1} and 0.0011 (95% CI:-0.1755,0.1734), respectively. Mean inter-reader differences for curvature and tortuosity were 0.0036 (95% CI: −0.0513, 0.0585) mm^{-1} and 0.0236 (95% CI:-0.1606, 0.2078), respectively (Supplementary data, Figs. S1–S4).

3.3. Association between vessel geometry and stenosis

A significant association was observed between curvature and significant stenosis both on a per-segment level ($p < 0.001$) and a per-artery level ($p = 0.002$) (Table 2). Patients with a significant stenosis had 16.7% and 13.8% higher curvature at the per-segment and per-artery level, respectively, than patients without stenosis.

There was an association between tortuosity and significant stenosis at the per-segment level ($p = 0.002$). There was interaction for tortuosity at the per-segment level ($p = 0.041$), indicating that the relationship between tortuosity and significant stenosis is not the same across segments.

3.4. Association between vessel geometry and presence of plaque

A significant association was observed between curvature and plaque presence at both the segment ($p < 0.001$) and artery level ($p < 0.001$) (Table 3). For instance, segments with plaque had 17.6% higher curvature than segments without coronary plaque. There was also an association between tortuosity and plaque presence at the per-segment level ($p < 0.001$). On average, segments with plaque were 30.8% more tortuous. The interaction of tortuosity and plaque presence indicated that the association was not the same across segments ($p = 0.013$).

4. Conclusion

Measures of coronary artery curvature and tortuosity can be derived reproducibly based on semi-automatic analysis of coronary CTA. Curvature of the coronary arteries was more closely related to the presence of significant stenosis and plaque than tortuosity. Our findings provide a preliminary indication that more pronounced curvature of the vessels may indicate sites that are prone to plaque development, which should be studied in follow-up studies. In conclusion, coronary artery geometry measures are potential imaging biomarkers for future risk assessment of CAD, based on coronary CTA examinations.

Conflicts of interest

The authors have no conflicts of interest to report on the work as presented in this paper.

Table 2
Association of curvature and tortuosity with significant stenosis, corrected for age, sex, and hypertension.

Measure	Analysis on segment level			Analysis on artery level		
	Estimate	P-value		Estimate	P-value	
		Association	Interaction		Association	Interaction
Curvature	1.167 [1.088; 1.251]	< 0.001	0.421	1.138 [1.049; 1.235]	0.002	0.106
Tortuosity	1.279 [1.097; 1.491]	0.002	0.041	1.105 [0.964; 1.267]	0.149	0.056

Table 3
Association presence of plaque with curvature and tortuosity corrected for age, sex, and hypertension.

Measure	Analysis on segment level			Analysis on artery level		
	Estimate	P-value		Estimate	P-value	
		Association	Interaction		Association	Interaction
Curvature	1.176 [1.106; 1.251]	< 0.001	0.066	1.161 [1.078; 1.250]	< 0.001	0.136
Tortuosity	1.308 [1.142; 1.498]	< 0.001	0.013	1.096 [0.969; 1.241]	0.145	0.237

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jcct.2018.02.003.

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