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Research paper

Coronary computed tomography angiography derived risk score in predicting cardiac events

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ABSTRACT

Background: We evaluated the prognostic value of an integrated atherosclerosis risk score combining the markers of coronary plaque burden, location and composition as assessed by computed tomography angiography (CTA).
Methods: 922 consecutive patients underwent CTA for suspected coronary artery disease (CAD). Patients without atherosclerosis (n = 261) and in whom quantitative CTA analysis was not feasible due to image quality, step-artefacts or technical factors related to image acquisition or data storage (n = 153) were excluded. Thus, final study group consisted of 508 patients aged 63 ± 9 years. Coronary plaque location, severity and composition for each coronary segment were identified using automated CTA quantification software and integrated in a single CTA score (0–42). Adverse events (AE) including death, myocardial infarction (MI) and unstable angina (UA) were obtained from the national healthcare statistics.
Results: There were a total of 20 (4%) AE during a median follow-up of 3.6 years (9 deaths, 5 MI and 6 UA). The CTA risk score was divided into tertiles: 0–6.7, 6.8–14.8 and > 14.8, respectively. All MI (n = 5) and most of the other AE occurred in the highest risk score tertile (3 vs. 3 vs. 14, p = 0.002). After correction for age and gender, the CTA risk score remained independently associated with AE.
Conclusions: Comprehensive CTA risk score integrating the location, burden and composition of coronary atherosclerosis predicts future cardiac events in patients with suspected CAD.

1. Introduction

Coronary computed tomography angiography (CTA) is a non-invasive imaging modality for diagnosis of coronary artery disease (CAD). In addition to coronary artery stenosis severity, coronary CTA allows visualization of the extent and location of coronary atherosclerosis in all coronary artery branches. CTA can also further assess plaque composition as well as vessel remodelling.

Absence of atherosclerosis on coronary CTA confers excellent cardiovascular prognosis whereas severe obstructive CAD significantly increases cardiac risk.[1–10] In patients with CAD, proximal plaques are related to increased risk for future cardiac events compared to distal plaques.[1,3,4,8,11] Moreover, more extensive non-obstructive atherosclerosis has been associated with worse cardiovascular outcome.[1–10] Finally, the composition of coronary artery plaques has been shown to affect the probability of cardiac events. The presence of non-calcified or partially calcified plaques have been suggested as a marker of a thin-cap fibroatheroma and are associated with future acute coronary events.[4,8,9,11–16]

Using advanced atherosclerosis and plaque phenotyping CTA

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Abbreviations

AE	adverse event
CAD	coronary artery disease
CTA	computed tomography angiography
ECG	electrocardiogram
MPR	multiplanar reformation

has great potential to provide improved individualized risk stratification. However, a comprehensive risk assessment based on integrated and weighted risk components is needed. Therefore, we have previously proposed a novel risk score, integrating all the different components of coronary atherosclerosis on CTA (i.e. stenosis severity, plaque location and composition).[17] This score is based on a quantitative assessment of coronary atherosclerosis using a novel software algorithm and the feasibility of this score for cardiovascular risk prediction has been previously established.[17] The aim of the current study was to perform further, external validation of the prognostic value of this integrated risk score in a different population from a different medical centre. Our study included symptomatic patients with intermediate likelihood of obstructive CAD.

2. Methods

2.1. Study population

The study population consisted of 922 consecutive outpatients referred for CTA between 2007 and 2011. The patients were symptomatic and had intermediate pre-test likelihood of obstructive CAD.[18] Patients in whom quantitative CTA analysis was not feasible due to image quality, step-artefacts or technical factors related to image acquisition or data storage (n = 153) were not included. Of the 769 remaining patients, 261 had no atherosclerosis on visual assessment. Therefore, the final study group of patients with visually some degree of atherosclerosis consisted of 508 patients who underwent quantitative CTA analysis. The study was performed according to the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the Hospital District of South-West Finland and all patients gave informed consent.

2.2. CTA, acquisition

CTA was performed using a 64-row PET/CT scanner (GE Discovery VCT, General Electric Medical Systems, Waukesha, Wisconsin, USA). Intravenous metoprolol 0–30 mg was administered before the scan to reach a target heart rate of less than 60 bpm. Sublingual nitrate 800 μg was given before the scan. Iodinated contrast infusion (60–80 mL of 400 mg iodine/mL iomeprol at 4–4.5 mL/s) was followed by saline flush. The collimation was 64 × 0.625 mm, gantry rotation time was 350 ms, tube current was 600–750 mA, and voltage was 100–120 kV, depending on the patient's posture. To reduce radiation dose, prospectively triggered acquisition was applied whenever feasible.

2.3. CTA, analysis

All CTA scans were analyzed using a novel quantification software tool (QAngio CT Research Edition, version 1.3.6; Medis Medical Imaging Systems, Leiden, the Netherlands).[17] Using an automated algorithm all branches of the coronary tree were extracted from the coronary CTA data set and automatically labelled according to the American Heart Association 17-segment model.[11] Based on this coronary tree, multiplanar reformations (MPR) are created of each vessel and side branches. In these MPR images, the lumen and vessel wall were automatically segmented. Thereafter, all lesions in the coronary artery tree were detected by the algorithm. An experienced observer confirmed the detected coronary lesions. For each lesion, the software automatically identified stenosis location, stenosis severity and coronary plaque composition. Proximal lesions were defined as lesions in the left main artery, proximal left anterior descending coronary artery, proximal right coronary artery or proximal circumflex coronary artery. Coronary stenosis severity was defined as any atherosclerotic plaque (≥30% luminal stenosis), obstructive lesions (≥50% stenosis) or severe lesions (≥70% stenosis). For lesions in the left main coronary artery, a ≥30% stenosis was used as a cutoff to define an obstructive lesion. Coronary plaque composition was categorized as non-calcified plaque, calcified plaque or partially calcified plaque using a previously described automatic CTA plaque characterization algorithm.[17,19] The assessment of coronary vessel dominance was based on visual analysis. Chronic total occlusion was also visually identified and thereafter quantified using a dedicated algorithm.

The same CTA risk score as previously reported, was implemented in the current analysis.[17] Information about severity, location and composition of coronary artery plaques in each coronary artery segment was integrated into the CTA risk score as depicted in Fig. 1. The CTA risk score consists of three components:

1) The location of each coronary artery plaque is represented by a segment weight factor based on the Leaman score.[20,21] A different weight factor was used for a left- and right-dominant coronary artery system.

2) The severity of each coronary stenosis is represented by a stenosis weight factor of 1.4 for each obstructive lesion. This weight factor was derived from a previous meta-analysis reporting a hazard ratio of 1.35 for each coronary artery segment with a significant stenosis.[4]

3) A weight factor for each plaque composition was also derived from a previous study[8] and translated in the CTA risk score by a weight factor of 1.2 for calcified, 1.6 for partially calcified, and 1.7 for non-calcified plaques.

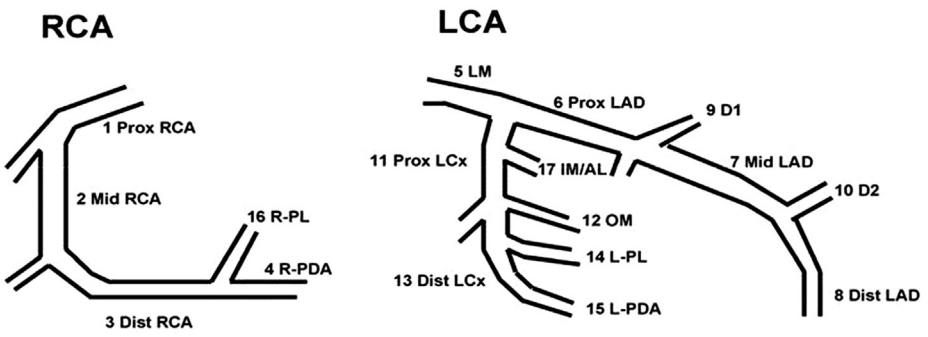
For each segment, a score is calculated by multiplying the location weight factor with the stenosis weight factor and the plaque weight factor. If plaque is absent, the score is zero. The total score is calculated by adding the individual segment scores (0–42).

2.4. Follow-up

Follow-up data on cardiac events was obtained from the national health statistics. Death, myocardial infarction (MI) and unstable angina (UA) requiring hospitalization were considered as adverse events (AE). Myocardial infarction was diagnosed based on clinical presentation, ECG and cardiac enzymes. Unstable angina was defined as acute chest pain with or without the presence of ECG abnormalities, and negative cardiac enzyme levels according to current guidelines with proven obstructive CAD on invasive coronary angiography.[22] Following CTA, patients were treated according to the clinical judgment of the referring cardiologist with lifestyle modifications, medical therapy or were referred for invasive angiography with subsequent revascularization when indicated.

2.5. Statistical analysis

Categorical variables are presented as frequencies and



Segment Weight Factor

Segment	Right Dominant	Left Dominant
LM	5	6
Prox LAD	3.5	3.5
Mid LAD	2.5	2.5
Dist LAD	1	1
D1	1	1
D2	0.5	0.5
Prox LCx	1.5	2.5
Dist LCx	1	1.5
AL/IM	1	1
OM	1	1
L-PL	0.5	0.5
L-PDA	0	1
Prox RCA	1	0
Mid RCA	1	0
Dist RCA	1	0
R-PL	0.5	0
R-PDA	1	0

Stenosis Weight Factor

<50%	1
≥50%	1.4

Plaque Weight Factor

Calcified	1.2
Partially Calcified	1.6
Non-Calcified	1.7

Segement(n) Score =

Plaque Weight Factor
X
Stenosis Weight Factor
X
Segment (n) Weigt Factor

CTA Risk Score = Σ Segment (1-17) Score

Fig. 1. Schematic overview of the computed tomography angiography derived risk score.[17] Risk score is calculated by the summation of the individual segment scores obtained by multiplying the segment specific weight factor, the stenosis weight factor, and the plaque weight factor. Reprinted with permission from de Graaf et al.[17] AL = anterolateral segment; D1 = diagonal 1; D2 = diagonal 2; Dist = distal; IM = intermediate segment; LAD = left anterior descending artery; LCA = left coronary artery; LCx = left circumflex artery; LM = left main segment; L-PDA = left posterior descending artery; L-PL = left posterolateral segment; OM = obtuse marginal segment; Prox = proximal; RCA = right coronary artery; R-PDA = right posterior descending artery; R-PL = right posterolateral segment.

percentages and were compared with the Chi-square test. For reasons of uniformity, all continuous variables are presented as mean and standard deviation and 95% confidence intervals (CI) were calculated when appropriate. Normally distributed variables were compared using the independent Student's T-test and non-normally distributed variables with the non-parametric Mann–Whitney *U* test. Baseline clinical characteristics and quantitative CTA variables were compared between patients with and without AE during follow-up. Next, the distribution of events across the groups of tertiles of the CTA risk score was assessed. Patients were classified in the lowest, middle or highest CTA risk score tertile. Thereafter, survival analyses were performed for the 3 tertiles. Event rates were estimated by the Kaplan-Meier method. Univariate and multivariate Cox proportional hazard models were used to assess the association of baseline clinical and CTA variables and the CTA risk score with the occurrence of AE at follow-up. All variables with a p-value <0.1 in the univariate analyses were introduced to further multivariate analysis. Two-tailed p-values of <0.05 were considered statistically significant. Statistical analyses were performed using SPSS (SPSS version 22, Inc., Chicago, IL, USA).

3. Results

The clinical characteristics and the relationship between CAD risk factors and cardiac events are shown in Table 1. The mean age of patients was 63 ± 9 years and 54% were male. A total of 20 (4%) AE were recorded in 508 patients during a median follow-up of 3.6 years (interquartile range of 2.7–4.8 years). Ten patients died, 5 experienced an acute MI and 6 had UA. One of the patients who had UA also died. Patients with AE were older than patients without events (68 ± 8 vs. 63 ± 8 years, p = 0.008). Conventional risk factors for CAD including gender, hypertension, diabetes, dyslipidaemia, obesity, smoking and a family history of CAD were comparable between patients with or without AE. The Agatston coronary artery

Table 1
Baseline characteristics according to the presence of adverse events (AE) during follow-up.

Variable	All patients (N = 508)	No AE (N = 488)	AE (N = 20)	p-value
Risk factors:				
Age, years	63 ± 9	63 ± 8	68 ± 8	0.008
Male	275 (54)	260 (53)	15 (75)	0.06
Diabetes	90 (18)	85 (17)	5 (25)	0.38
Hypertension	398 (78)	381 (78)	17 (85)	0.46
Dyslipidaemia	369 (73)	357 (73)	12 (60)	0.20
Obesity	109 (31)	101 (30)	8 (47)	0.14
Smoking	71 (14)	69 (14)	2 (10)	0.60
Family history of CAD	226 (45)	217 (45)	9 (45)	0.96
Calcium score	354 ± 575	331 ± 531	1053 ± 1205	0.03
Medications:				
Statin	255 (58)	247 (58)	8 (50)	0.50
Aspirin	305 (69)	292 (69)	13 (81)	0.28
Beta-blocker	260 (58)	247 (58)	13 (81)	0.06
Nitrate	64 (15)	59 (15)	5 (31)	0.07
Diuretic	109 (25)	103 (25)	6 (38)	0.19
ACE inhibitor	108 (25)	101 (24)	7 (47)	0.048
Angiotensin II receptor blocker	88 (21)	85 (21)	3 (19)	0.86
Calcium channel blocker	85 (20)	80 (19)	5 (31)	0.24
Interventional treatment:				
Revascularization*	81 (16)	73 (15)	8 (40)	0.03
PCI*	66 (13)	59 (12)	7 (35)	0.03
CABG*	17 (3)	15 (3)	2 (10)	0.09

Values are mean ± SD or n (%). * within 6 months of CTA. ACE = angiotensin converting enzyme inhibitor; CAD = coronary artery disease; CABG = Coronary artery bypass graft; PCI = Percutaneus coronary intervention.

calcium score was higher in patients with AE (1053 ± 1205 vs. 331 ± 531, p = 0.03).

The association between AE and baseline characteristics of coronary atherosclerosis as assessed by quantitative CTA are shown in Table 2. Patients with AE during follow-up more often presented with any atherosclerotic plaques (≥30%) compared to event-free patients (number of plaques 5.3 ± 2.6 vs. 3.0 ± 2.2, p < 0.001). Moreover, in patients with AE, a larger number of obstructive lesions (≥50%) were observed (number of plaques 3.8 ± 2.6 vs. 1.6 ± 1.7, p < 0.001). Similarly, the number of severe lesions (≥70%) was higher in patients with AE compared to event-free patients (number of plaques 1.9 ± 1.8 vs. 0.6 ± 1.0, p < 0.001). The mean number of calcified plaques per patient was higher in patients with AE (number of plaques 3.7 ± 2.7 vs. 1.7 ± 1.9, p < 0.001). However, the number of partially calcified or non-calcified plaques per patient were comparable between patients with and without AE (number of plaques 0.8 ± 1.0 vs. 0.6 ± 0.9, p = 0.36 and 0.6 ± 0.8 vs. 0.5 ± 0.7, p = 0.37, respectively). In addition, patients with AE had a higher number of proximal obstructive lesions (≥50%) (number of plaques 2.0 ± 1.5 vs. 0.8 ± 1.0, p < 0.001) and more often presented with left main disease (40% vs. 18%, p = 0.01).

In the entire population, the CTA risk score was 11.7 ± 7.8 (95% CI 4.0–10.8). In the patients with AE, the CTA risk score was significantly higher as compared to event-free patients (18.8 ± 9.1 vs. 11.4 ± 7.6, p < 0.001, 95% CI 14.5–23.1 and 10.7–12.1, respectively). The lowest tertile of CTA risk score ranged from 0 to 6.7, the middle from 6.8 to 14.8 and the highest tertile included patients with a CTA risk score >14.8. The distribution of cardiac events within the tertiles of the CTA risk score is shown in Table 3. The majority (70%) of AE occurred in the highest tertile (p = 0.002). All patients with MI (n = 5) were in the highest tertile (p = 0.006). The Kaplan Meier survival curve for the different CTA risk score tertiles is shown in Fig. 2. Patients in highest CTA risk score tertile had lower event-free survival rate compared to other tertiles (84 ± 5% versus 97 ± 2% and 98 ± 1%, p = 0.002).

The univariate and multivariate Cox survival analyses for the association between CTA risk score, baseline clinical risk factors and AE are shown in Table 4. In the univariate Cox regression analysis age and gender were significantly associated with AE. The presence of atherosclerotic plaques, both the overall number of plaques and the presence of obstructive lesions were significantly correlated with outcome. Similarly, the number of calcified plaques significantly predicted events. After correction for age and gender, the CTA risk score remained independently associated with the occurrence of AE.

4. Discussion

The present study performed evaluated previously described CTA derived risk score that integrates coronary atherosclerosis extent, location, degree of obstruction and plaque composition into a single score for prediction of prognosis.[17] The risk score was obtained using a novel, automated quantification software tool which allows effective quantitative assessment of coronary atherosclerosis on CTA.[17] The CTA risk score was significantly elevated in patients with AE compared to event-free patients and provided independent predictive value over age and gender.

As there are numerous different CTA markers associated with cardiovascular risk, it can be assumed that for accurate risk assessment a comprehensive score would be useful. The extent of atherosclerotic changes in the coronary vasculature is an important prognostic indicator.[1–10] Non-obstructive atherosclerosis was associated with elevated mortality (hazard ratio 1.6) in the CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter registry) registry compared to patients with normal coronary arteries.[10] Similarly, Ostrom et al. demonstrated that three-vessel, non-obstructive atherosclerosis is linked with increased mortality (HR 1.7).[6] Thus, non-obstructive atherosclerosis cannot be considered as a truly benign phenomenon. Although the number of obstructed coronary arteries is a well-known predictor of prognostic severity of CAD,[1–10] Bittencourt et al. demonstrated in their study that the annual event-rate of extensive coronary atherosclerosis is comparable to localized obstructive CAD.[4] The highest event rate was observed in patients with both extensive atherosclerosis and obstructive CAD which underlines the importance of further characterization of atherosclerotic

Table 2
Quantitative coronary computed tomography angiography results according to the presence of adverse events (AE) during follow-up.

Variable	All patients (N = 508)	No AE (N = 488)	AE (N = 20)	p-value
Any atherosclerotic plaques (≥30%)	3.1 ± 2.1 (2.9–3.3)	3.0 ± 2.2 (2.8–3.2)	5.3 ± 2.6 (4.1–6.5)	<0.001
Obstructive lesions (≥50%)	1.6 ± 1.8 (1.5–1.8)	1.6 ± 1.7 (1.4–1.7)	3.8 ± 2.6 (2.5–5.0)	<0.001
Severe lesions (≥70%)	0.6 ± 1.1 (0.5–0.7)	0.6 ± 1.0 (0.5–0.6)	1.9 ± 1.8 (1.0–2.7)	<0.001
Proximal obstructive lesions (≥50%)	0.9 ± 1.1 (0.8–1.0)	0.8 ± 1.0 (0.7–0.9)	2.0 ± 1.5 (1.3–2.7)	<0.001
Non-calcified plaques (≥30%)	0.5 ± 0.7 (0.4–0.5)	0.5 ± 0.7 (0.4–0.5)	0.6 ± 0.8 (0.2–1.0)	0.37
Partially calcified plaques (≥30%)	0.6 ± 0.9 (0.5–0.7)	0.6 ± 0.9 (0.5–0.6)	0.8 ± 1.0 (0.3–1.2)	0.36
Calcified plaques (≥30%)	1.8 ± 2.0 (1.6–2.0)	1.7 ± 1.9 (1.5–1.9)	3.7 ± 2.7 (2.4–5.0)	<0.001
Patients with left main lesion (≥30%)	94 (19)	86 (18)	8 (40)	0.01
Patients with chronic total occlusions[a]	30 (6)	28 (6)	2 (10)	0.43
Left or co-dominant coronary systems[a]	45 (9)	45 (9)	0 (0)	0.15

Data are presented as mean ± SD (CI) or number (percentage).
CTA = computed tomography angiography.
[a] Based on visual analysis.

Table 3
Clinical events during follow-up according to CTA risk score tertiles.

Variable	CTA Risk score			p-value
	Lowest tertile 0–6.7 (N = 170)	Middle tertile 6.8–14.8 (N = 169)	Highest tertile >14.8 (N = 169)	
Adverse event	3 (15)	3 (15)	14 (70)	0.002
Death	1 (10)	2 (20)	7 (70)	0.04
Unstable angina	2 (33)	2 (33)	2 (33)	1
Acute myocardial infarction	0 (0)	0 (0)	5 (100)	0.006

Data are presented as number (%).
CTA = computed tomography angiography.

coronary arteries. Moreover, the composition of coronary plaques is strongly related to the risk of acute coronary syndrome.[4,8,9,11–16] In a previous meta-analysis, the presence of non-calcified plaque was associated with a 1.3-fold increase in cardiac events.[4] The presence of other vulnerable plaque features such as positive remodelling, spotty calcification and napkin-ring sign increases the risk even further.[14–16] In addition, proximal coronary atherosclerosis is independently related to worse outcome in multiple studies[1,3,4,8,11] and rupture of a proximal plaque will induce a large area of myocardial ischemia. Interestingly, vulnerable plaques are also associated with a more proximal location in the coronary tree.[1,12]

Similarly to previous studies, there were multiple individual CTA findings that were associated with future adverse events. As previously observed, the number of obstructive (>50%) and severe (>70%) stenoses was higher in patients with AE.[1–10] Patients with AE also had a greater total atherosclerotic burden and lesions were located more proximally. Stenosis of the left main coronary artery was significantly more prevalent in patients with AE (40 vs. 18%). Number of atherosclerotic plaques was the strongest component of the CTA score in the prediction of AE and provided incremental value over age and gender. This is in agreement with Bittencourt et al. who observed that extensive non-obstructive atherosclerosis is just as strongly associated with cardiac events as focal obstructive coronary lesion.[5] Of interest, the number of non-calcified and partly calcified plaques was not significantly increased in patients with AE. This could be explained by the fact that we did not further characterize the spotty calcification phenotype or other vulnerable plaque features. Furthermore, the link between vulnerable plaque, fibrous cap rupture and myocardial infarction is complex and requires, for example, pro-thrombotic blood for the formation of thrombus. Fibrous cap rupture could be also be prevented by various interventions that cause plaque stabilisation during follow-up. Moreover, one third of MI are not caused by fibrous cap rupture

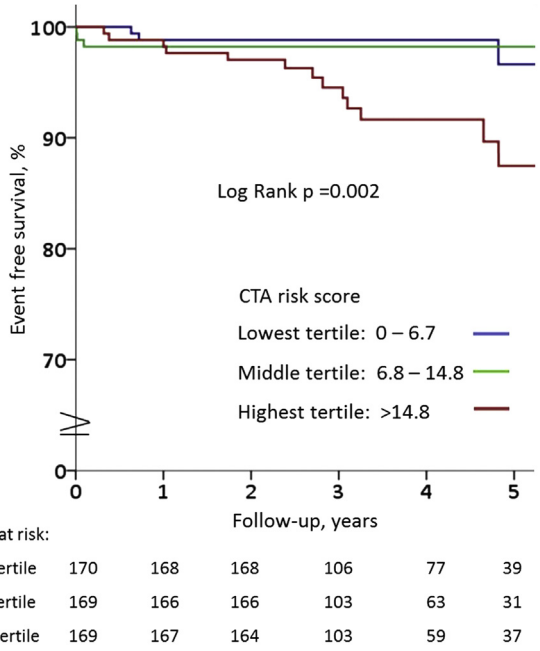


Fig. 2. Kaplan-Meier survival curves according to coronary computed tomography angiography (CTA) risk score tertiles. Patients in the highest risk score tertile (red) had significantly worse event-free survival from adverse events (death, myocardial infarction or unstable angina) during median of 3.6 years of follow-up. In comparison patients in the low (blue) or intermediate (green) risk score tertiles had good cardiovascular prognosis. The p-value was derived by log-rank test. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 4
Cox-regression survival analysis for the association of clinical factors and coronary computed tomography angiography derived risk factors with adverse events.

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Baseline characteristics						
Age, years	1.08	1.02–1.14	0.005	1.08	1.02–1.14	0.008
Male gender	2.43	0.88–6.70	0.09	2.32	0.82–6.59	0.112
Diabetes	1.51	0.55–4.17	0.42			
Hypertension	1.67	0.49–5.70	0.41			
Dyslipidaemia	0.55	0.22–1.35	0.19			
Obesity	2.21	0.85–5.74	0.11			
Smoking	0.70	0.16–3.01	0.63			
Family history of CAD	1.03	0.43–2.49	0.94			
CTA parameters						
No. of atherosclerotic plaques (≥30%)	1.44	1.21–1.72	<0.001			
No. of obstructive lesions (≥50%)	1.48	1.25–1.74	<0.001			
No. of severe lesions (≥70%)	1.67	1.34–2.09	<0.001			
No. of prox. obstructive lesions (≥50%)	2.10	1.52–2.91	<0.001			
No. of non-calcified plaques (≥30%)	1.35	0.77–2.36	0.304			
No. of part. calcified plaques (≥30%)	1.15	0.77–1.71	0.505			
No. of calcified plaques (≥30%)	1.41	1.19–1.68	<0.001			
CTA risk score	1.11	1.06–1.18	<0.001	1.09	1.03–1.16	0.002

CI = confidence interval, CTA = computed tomography angiography, HR = hazard ratio.

but intimal erosion which might partly explain the lack of a relationship between soft and fibrous plaques and AE in our study.[12]

A comprehensive CTA derived risk score for the evaluation of atherosclerosis correctly stratified patients with future adverse events. All patients with MI were correctly classified as high risk individuals, as well as the majority of patients who died during follow-up (70%). CTA based risk score provided incremental prognostic value to baseline risk factors. In previous studies, CTA based scores were used that were based on segment involvement score (number of plaques) or summed stenosis score (number and severity of stenoses) which demonstrated good prognostic value[2,3,10,23]; the score in our study however, provides a more complete assessment of the different parameters that each have been demonstrated to have prognostic value. Similarly to our study, Mushtaq et al. recently validated a CTA adapted Leaman score for integrated assessment of atherosclerosis severity, location, extent and plaque composition.[24] The adapted Leaman score was superior (hazard ration 5.4) to segment involvement score (hazard ration 3.1) and segment stenosis score (hazard ratio 4.4) in the prediction of future cardiac events. This further underlines the clinical importance of integrating stenosis severity with other parameters such as stenosis location, but also plaque composition. However, manual assessment of multiple segment scores is cumbersome for clinical practise. The developed automated software for quantitative analysis of CTA enables faster characterization of atherosclerosis and easier risk score calculation. In our study, such scoring algorithm was demonstrated to classify patients adequately into low and high risk groups.

Although an elevated CTA derived risk score correctly stratified all patients with myocardial infarction and most of the AE, patients with unstable angina were evenly distributed among risk score tertiles. In addition, we used all-cause-mortality instead of cardiac deaths. This was justified since the precise diagnosis of death is often uncertain. However, we acknowledge this as a possible confounder and a limitation in our study. Moreover, in the present study the number of cardiac events during follow-up was relatively small which might be explained by the fact that patients received optimized medical therapy, and that significant CAD was treated as clinically appropriate at baseline. Furthermore, the current CTA score does not take into account some of the novel, less established CTA markers of plaque vulnerability. Including these features could further enhance the predictive value of the score.

5. Conclusions

A comprehensive CTA risk score integrating the atherosclerotic burden, plaque severity, location and composition provides advanced risk stratification and adequate prediction of future cardiac events in patients who are clinically evaluated for suspicion of coronary artery disease. Extent of atherosclerosis was the strongest CTA risk score component in the prediction of adverse events.

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