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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

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