Supplementary Online Content


eMethods.

**eFigure 1.** High-risk plaque features in culprit vs. non-culprit lesions and vs. highest-grade stenosis lesions of matched control patients.

**eFigure 2.** PCAT CT attenuation in culprit vs. non-culprit lesions and vs. highest-grade stenosis lesions of matched control patients

**eFigure 3.** 3D Quantification of PCAT CT attenuation in the mid LAD

This supplementary material has been provided by the authors to give readers additional information about their work.
eMETHODS

Patients

In this retrospective study with a matched case control design we analyzed consecutive patients presenting with a first ACS (n=19) who underwent CTA as part of their initial workup, which was followed by invasive angiography.7 The CTA of the ACS group was compared to controls with stable CAD, matched by age decile, gender and risk factors, who also underwent coronary CTA similarly followed by invasive coronary angiography because of the detection of at least one coronary stenosis ≥50 %. ACS included non-ST-segment elevation myocardial infarction (NSTEMI) or unstable angina defined by the latest guidelines of the American Heart Association or American College of Cardiology. In patients with ACS the culprit lesion was identified by an experienced independent interventional cardiologist (S.A.) blinded to findings of CTA using a combination of electrocardiography, echocardiography, and angiographic lesion morphology.7 Controls were matched to patients with ACS by age decile, gender and risk factors from consecutive patients with stable coronary artery disease (CAD), who underwent coronary CTA followed by invasive coronary angiography within a period of 14 days at the University of Erlangen.7 Stable CAD was defined by the presence of stable exercise-induced symptoms and no suspicion for ACS when coronary CTA was performed. Patients with previous myocardial infarction, revascularization by coronary bypass surgery or stenting, hemodynamic or clinical instability, atrial fibrillation, contraindications to iodinated contrast agents, and impaired renal function (creatinine level >1.4 mg/dL) were excluded.7 The study was performed according to the guidelines of the institutional review board and all patients provided written informed consent for use of their data.

CT imaging protocol

CTA was performed using a first-generation dual-source CT scanner (SOMATOM Definition; Siemens Healthcare, Forchheim, Germany); the acquisition protocol has been previously described. Briefly, beta-blockade was administered to reduce heart rate to ≤ 60 beats/min. Iodinated contrast (60 to 90 ml, 350-mg iodine per mL [iomeprol]) was injected at a flow rate of 6 mL/s.7 The scan parameters were as follows: section collimation of 0.6 mm with z-flying focal spot, 330 ms gantry rotation time, reference tube current of 400 mAs per rotation, and a tube voltage of 120 kVp. All coronary CTA were performed using electrocardiography-gated helical acquisition with tube current modulation. Transverse images were reconstructed using filtered back projection with 0.75-mm slice thickness, 0.4 mm increment, and a medium-soft convolution kernel (B26f).7 Motion-free data sets, typically in mid-diastole, were collected for analysis and transferred to an off-line standard Windows workstation.

Analysis of coronary plaque

The analysis of coronary arteries was performed per-segment using the model of the Society of Cardiovascular Computed Tomography. All CTA data sets were visually assessed for the presence of coronary plaque by an experienced independent reader using multiplanar coronary CTA images.

All coronary segments with a lumen diameter ≥2 mm were analyzed by semi-automated software Autoplaque (Autoplaque version 2.0, Cedars-Sinai Medical Center, Los Angeles, USA). Quantitative plaque assessment and plaque characterization were performed on a per coronary lesion basis. Coronary plaque measurements included absolute volumes (in mm³) and corresponding burden (plaque volume x100%/vessel volume) of calcified plaque (CP) and noncalcified plaque (NCP) as well as remodeling index, plaque length, contrast density difference (CDD) and diameter stenosis.

An experienced independent reader, who was blinded to patient characteristics and clinical data, identified all lesions and marked the proximal and distal ends of each lesion. A low intra- and inter-observer variability for coronary plaque assessment using Autoplaque has been reported previously.14

As described and validated previously, scan-specific thresholds for NCP and CP were automatically generated.15 NCP was further divided into its components low- (-30 to 30 HU), intermediate- (31-130 HU) and high-attenuation NCP (131-350 HU) volumes, and the corresponding plaque component burden was computed by Autoplaque.

Quantitative percent stenosis was calculated as ratio of the narrowest lumen diameter and the mean of two non-diseased reference points.16 Vessel remodeling index was determined as the ratio of maximum vessel area to that at the proximal normal reference point.17 Positive remodeling was defined by remodeling index >1.1.18 Plaque length (in mm) was defined as the length of the diseased vessel. CDD across the lesion was computed as follows: the luminal contrast density, defined as attenuation per unit area, similar to area gradient, was computed over 1-mm cross sections.19 The CDD is the maximum percent difference in measured contrast density with respect to the proximal normal reference cross section.19 Manual adjustments of vessel contours and plaque were made by the expert reader if necessary.
Depending on the image quality and number of coronary lesions, the per-patient processing time ranged between 30-45 minutes for complete plaque analysis of the coronary tree. The per-lesion processing time ranged between 3-7 minutes, depending on coronary plaque features such as location, length and burden.

**Analysis of pericoronary adipose tissue**

Following plaque analysis, CT measurement of PCAT measurement for each lesion was fully automated. For each lesion, PCAT was sampled in three-dimensional layers, moving radially outwards from the outer vessel wall in 1 mm increments. Adipose tissue was defined as all voxels with attenuation between -190 and -30 HU and the PCAT CT attenuation was defined as the average CT attenuation in HU of the adipose tissue within the defined volume of interest (Figure 1, eFigure 4).\(^6\) Quantification of coronary plaque and PCAT CT attenuation was exported for each examined lesion along with the plaque characteristics (19 culprit lesions of ACS patients and 105 non-culprit lesions in the ACS and control group). Depending on the lesion length and the defined volume of interest the processing time of the fully-automated quantification of PCAT CT attenuation was <1 minute. From the exported data, we considered the PCAT CT attenuation (HU) within an outer radial distance from the vessel wall equal to the average diameter of the lesion, as described recently (Figure 1, eFigure 4)\(^6\); the average diameter was typically 3 mm.

The measurement of the PCAT gradient or as introduced by Antonopoulos et al. as volumetric perivascular characterization index (VPCI) might be a promising novel approach to indirectly quantify the cholesterol efflux in fat cell as a result of adjacent coronary inflammation.\(^6\) Briefly, VPCI was measured by Antonopoulos et al. as the ratio in CT attenuation (HU) between the PCAT (3D cylindrical layer within a diameter equal to the average diameter of the lesion) and non-PCAT (3D cylindrical layer with 1 mm diameter 20 mm away from the vessel wall of the lesion).\(^6\) In accordance to Antonopoulos et al. we defined PCAT CT attenuation as the average CT attenuation in HU of the adipose tissue within the defined volume of interest and considered the PCAT CT attenuation within an outer radial distance from the vessel wall equal to the average diameter of the lesion. In some parts of the LAD and LCX because of confounding non-fatty structures such as coronary side branches, fibrous tissue or myocardium or/and the presence of too small amounts of adipose tissue, the quantification of non-PCAT 20 mm away from the vessel wall was not possible. Thus, in the present study we focused on the measurement of the PCAT instead of the PCAT gradient.

**Online-Only References**


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