Comparison of Coronary Plaque Morphology in Patients with Stable Coronary Artery Disease and Non-ST Myocardial Infarction Using Dual-Source CT

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Purpose

Acute coronary syndrome (ACS) is the leading cause of death in the western world.

Plaque rupture and plaque erosion of so-called vulnerable plaques are considered to be the most important cause of ACS. It has been demonstrated that the specific compositional characteristics of vulnerable plaques rather than the severity of an actual stenosis predict the risk of plaque rupture and subsequent complications of ACS. Therefore, in-vivo detection of potentially vulnerable plaques could play an important role for the prevention of severe cardiovascular events and offers opportunities for secondary prevention, especially in patients at high cardiovascular risk.

Virtual histology intravascular ultrasound (VH-IVUS) is the accepted reference standard to measure and characterize coronary atherosclerotic plaques. However, VH-IVUS due to its invasive nature is not appropriate in all patients. Moreover, VH-IVUS is cost and time consuming limiting its capability as a screening method.

Due to technological advances, coronary CT angiography (cCTA) has emerged as a promising tool for non-invasive plaque characterization over the past decade. Nevertheless, the small dimensions and the physiologic motion of the coronary arteries make the visualization of plaques by CT challenging.

The aim of this study was to assess the accuracy of dual-source CT (DSCT) to differentiate coronary atherosclerotic plaques in patients with non-ST myocardial infarction (NSTEMI) and patients with stable coronary artery disease (CAD) using VH-IVUS as the reference standard. Furthermore, also potential differences in plaque composition between culprit lesions of patients with NSTEMI and all non-culprit plaques were investigated.
Methods and Materials

This prospective single-center study was approved by the Federal Office for Radiation Protection (BfS) and institutional ethics committee. 59 consecutive patients (inclusion and exclusion criteria on page ) who had given their informed consent underwent contrast-enhanced ECG-triggered cCTA using a first-generation 64-channel dual-source CT system (SOMATOM Definition, Siemens Healthcare Sector, Forchheim, Germany) using the following imaging protocol:

- tube voltage 120 kV
- reference tube current 320 mAs
- detector collimation 64×0.6 mm
- gantry rotation time 0.33 s
- start of data acquisition by bolus-triggering ascending aorta
- 80 ml of Imeron 400® (Bracco, Italy)

Attenuation-based plaque characterization was performed semi-automatically with syngo Circulation Plaque Analysis (Siemens Healthcare, Forchheim, Germany).

Within 24 hours cCTA was followed by the VH-IVUS examination during invasive coronary angiography in 48 (81%) patients. 11 patients didn’t get the additional VH-IVUS examination and were excluded from the study (due to complete vessel occlusion (9), non-diagnostic CT-image quality (1) in-stent stenosis (1)).

Technical specifications of VH-IVUS (Volcano s5, Volcano Corporation, Rancho Cordova, CA.):

- 20-MHz ultrasonic probe
- 3.5 French catheter
- motorized pull-back of 0.5mm/s

Plaque analysis was performed semi-automatically with Volcano Image Analysis Software VIAS 3.0 (Volcano Corporation, Rancho Cordova, CA.).

cCTA and VH-IVUS datasets were analyzed with regard to plaque composition quantifying the extent of fatty, fibrous and calcified plaque components, degree of stenosis, plaque volume and plaque length.

Out of the 48 patients who were examined by both techniques, relevant CAD could be ruled out in 9 (19%) patients. Another 17 (35%) VH-IVUS datasets had to be excluded
because of non-diagnostic image quality (e.g. due to severe calcifications) or subtotal stenosis causing trapping of the catheter during automatic pullback.

In the remaining 22 patients (16 (73%) men; mean age 71 (+/-10) years; 12 (55%) with NSTEMI and 10 (45%) with stable CAD) 27 matched atherosclerotic lesions (8 (30%) culprit lesions and 19 (70%) non-culprit lesions) were analyzed.

For intermodality comparison of the amount of fatty tissue the VH-IVUS components "necrotic core" and "fatty-fibrous" tissue were grouped since cCTA only allows discrimination between fatty, fibrous and calcified plaque.

Statistical analysis was performed with SAS JMP8.0® statistical software (SAS Institute, Cary, NC). Continuous variables are presented as mean (standard deviation) and median (interquartile range).

Categorical variables are presented as counts (percentages).

Shapiro-Wilk-Test has been performed to test for normal distribution of the data, Bland-Altman analysis was used to calculate the bias of the tools' measurement. Correlation between cCTA and VH-IVUS values is depicted by Pearson's correlation coefficient.

A p-value of 0.05 indicates statistical significance.
Results

All cCTA and VH-IVUS studies were successfully completed and considered of diagnostic image quality.

Bland-Altman bias analysis revealed a significant overestimation of calcified tissue (p=0.001), fibrous tissue (p=0.01) and significant underestimation of fatty tissue (p=0.002) within coronary atherosclerotic plaques by cCTA when compared to VH-IVUS.

No bias was calculated for the assessment of all non-calcified plaque components, the overall plaque volume, vessel area stenosis and the length of the lesions between cCTA and VH-IVUS.

Regression analysis showed a good correlation between cCTA and VH-IVUS regarding area stenosis (r=0.66, p=0.0002) and length (r=0.45, p=0.02). No correlation was found between the entire plaque volume and single plaque components (all p> 0.05).

VH-IVUS measured significant differences in percent-area stenosis between culprit lesions and non-culprit lesions (71.9 (7.3)% vs. 60.5 (7.5)%, p=0.001), whereas cCTA measured no significant differences (69.5(10.1)% vs. 61.3(11.3)%, p=0.091).

No differences in the percent-area stenosis were found between patients with NSTEMI and patients with stable CAD neither with VH-IVUS nor with cCTA.

Non-culprit lesions measured significantly longer than culprit lesions using cCTA (17.6(5.9) mm vs. 12.7(2.9) mm, p=0.035) whereas VH-IVUS showed no significant differences. Comparison of all analyzed plaques between patients with NSTEMI and stable CAD showed no significant differences in length neither with cCTA nor with VH-IVUS.

No significant differences in the overall plaque volume was found between coronary plaques of patients with NSTEMI and patients with stable CAD, neither with VH-IVUS nor with cCTA. The same was true for the analysis of culprit lesions and non-culprit lesions and subanalysis of different plaque components.
Conclusion

We show that cCTA correlates well with VH-IVUS for the assessment of area stenosis on page and lesion length on page, whereas the correlation between both modalities for the quantitative assessment of different plaque components and overall plaque burden was poor.

In our relatively small cohort, we found no differences between plaque morphology between patients with NSTEMI and patients with stable CAD neither using cCTA nor using VH-IVUS.

In addition, we found no differences in the plaque composition when comparing culprit lesions and non-culprit lesions.

Larger patient cohorts are needed to validate these findings.

The systematic overestimation of calcified plaque components by cCTA found in this study is in accordance to a previous study by Brodoefel et al. who reported that differences between both modalities are most likely due to missed calcification because of acoustic shadowing in VH-IVUS-analysis and due to "blooming" artefacts in cCTA.

The systematic underestimation of fatty tissue assessed by cCTA could be based on the limited ability of VH-IVUS to differentiate accurately between thrombotic and fibro-fatty tissue and to assess areas of acoustic shadowing caused by calcification falsely as necrotic core.

Artefacts caused by even small amount of calcification can lead to inaccurate determination of plaque component and entire plaque burden in VH-IVUS and cCTA. The resulting necessity of manual correction of lumen and vessel borders leads to high subjectivity and variability of the data.

A limitation of cCTA in comparison to VH-IVUS is the limited capability to distinguish between fatty and necrotic tissue.


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Personal Information

Sonja Sudarski is a medical student in her fourth year at the Medical Faculty Mannheim, University of Heidelberg.

She is working on her doctoral thesis within the International Research Training Group Graduiertenkolleg 880/3: "Vascular Medicine", which is funded by the DFG.

The subject of her thesis is the assessment of plaque morphology and vulnerability by means of Dual Source CT, intravascular ultrasound and biomarkers in patients with stable coronary artery disease and acute coronary syndrome.

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