In Vivo Measurement of Plaque Neovascularization and Thermal Heterogeneity in Intermediate Lesions of Human Carotids

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Abstract: Purpose: Both plaque angiogenesis and inflammation contribute to the development and progression of atherosclerosis. Contrast-enhanced ultrasound (CEUS) allows direct visualization of the adventitia vasa vasorum. Microwave Radiometry (MWR) is a special technology, which quantifies internal temperature of tissues, reflecting their inflammatory status. In the present study we aimed to evaluate in human carotid arteries, whether atherosclerotic plaque temperature, measured by MWR, is associated with plaque neovascularization assessed by CEUS. Methods: For this purpose, 48 consecutive patients with significant coronary artery disease and carotid plaques in at least one carotid were included in the analysis .All patients underwent basic ultrasound carotid imaging, neovascularization evaluation through CEUS and temperature measurements through MWR. Results: Plaques with vulnerable characteristics showed both higher temperatures and contrast uptake. There was a positive correlation between temperature and CEUS measurements. Conclusions: In vivo non-invasive assessment of the functional characteristics of carotid artery atherosclerotic plaques is feasible, promising and may serve as an additional screening tool to identify 'high risk' patients for future cerebrovascular events.

1 INTRODUCTION

Both plaque angiogenesis and inflammation contribute to the development and progression of atherosclerosis. Contrast-enhanced ultrasound (CEUS) provides direct visualization of the adventitial vasa vasorum and intraplaque neovascularization. Microwave radiometry (MWR) is a new non-invasive method, which detects radiation transmitted from internal tissues in microwave frequencies and converts these signals into temperature measurements. It allows this way the in vivo measurement of internal temperature of tissues, reflecting inflammatory activation. The aim of the current study is to assess whether carotid plaque temperature, measured by MWR, is associated with plaque neovascularization assessed by CEUS.

2 METHODS

2.1 Study Population

Consecutive patients undergoing coronary angiography for stable angina or acute coronary syndrome were prospective enrolled in the study. Patients with significant coronary artery disease (stenosis≥50% in at least one major epicardial artery) were evaluated with standard carotid ultrasound. Only patients with carotid plaques in at least one carotid artery (defined as intima-medial thickening of at least 1.2mm) were finally included in the study. Exclusion criteria included previous cerebrovascular event, vasculitis, intermittent inflammatory or neoplastic conditions.

2.2 Standard Carotid Ultrasound

Extracranial (common, internal, external) carotid arteries were examined with a high resolution B-

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mode ultrasound unit (Philips iEE33 ultrasound machine, Philips, Bothell, Washington), using the 7.5-MHz linear probe L9-3. All carotid plaques were characterized according to their surface contour (regular, irregular), echogenicity (homogeneous, heterogeneous) and texture (fatty, mixed, calcified), according to predefined criteria.

2.3 Contrast Enhanced Ultrasound (CEUS)

All CEUS examinations were performed with the commercially available contrast agent, SonoVue (Bracco Imaging, Milan). The contrast agent was infused intravenously via an infusion pump at a rate of 0.8 ml/min. Contrast enhancement (CE) was quantified using dedicated software. CE was defined as the percentage of signal intensity difference, prior and post contrast infusion.

2.4 Microwave Radiometry Measurements (MWR)

The MWR measurements were performed with the RTM 01 RES microwave computer based system (Bolton, UK) that measures temperature from internal tissues at microwave frequencies. Briefly, MWR is based on the measurement of the electromagnetic thermal noise that is emitted by lossy materials in the microwave frequency range. All media with absolute temperature $T>0^{o}K$ emit electromagnetic radiation towards their surroundings. Microwave radiation is capable of penetrating human tissue and therefore the emission provides information related to subcutaneous conditions within the body. The depth of penetration of microwave radiation depends on the wavelength, the dielectric properties, and the water content of the tissue. The signal which is recorded by the sensor is given by the equation $P=k\ T\ \Delta F$, where K is Bolzmann coefficient, T absolute temperature and ΔF the receivers bandwidth.

The sensor of the antenna of the device measures with an accuracy of 0.20°C the 'volume under investigation' as a rectangular area of 3 cm in width, 2 cm in length, and 3–7 cm in depth depending on the water content of the body. Temperature measurements were performed along each carotid artery over segments 2cm of length. Thermal heterogeneity (ΔT) was assigned as maximal temperature along the carotid artery minus minimum.

3 RESULTS

Eighty-six carotid arteries of 48 patients were included in the analysis. Fatty plaques (n=9) had higher CE% compared to mixed (n=55) and calcified plaques (n=22) (21.4±2.70 versus 17.11±5.23 versus 8.55±2.42%, $p<0.01$). Heterogeneous plaques (n=9) had higher CE% compared to homogenous (n=77) (21.44±2.7 versus 14.66±6.02% $p<0.01$). Plaques with irregular surface (n=32) had higher CE% compared to plaques with regular surfaces (n=54) (18.29±5.09 versus 13.64±6.06%, $p<0.01$). Fatty plaques (n=9) had higher ΔT compared to mixed (n=55) and calcified plaques (n=22) (1.13±0.27 versus 0.96±0.34 versus 0.53±0.26°C $p<0.01$). Plaques with irregular surface (n=32) had higher ΔT compared to plaques with regular surfaces (n=54) (1.05±0.32 versus 0.75±0.36°C, $p<0.01$). Heterogeneous plaques (n=9) had higher ΔT compared to homogenous (n=77) (1.13±0.27 versus 0.83±0.37°C $p<0.01$). There was a positive correlation between mean ΔT and CE ($R=0.60$, $p<0.001$).

4 CONCLUSIONS

In the present study a significant correlation between two vulnerable plaque characteristics, inflammation and neoangiogenesis, was shown. The prognostic significance of the evaluation of those characteristics in clinical practice warrants further studies.