**BACKGROUND** Despite advances in therapeutic strategies, atherosclerotic coronary artery disease (CAD) remains the commonest worldwide cause of morbidity and mortality. DNA damage and repair have been identified as important in atherogenesis. DNA ligase is crucial in single/double stranded DNA break repair by catalyzing phosphodiester bond formation. It is uncertain if DNA damage is associated with increased oxidative stress, defective DNA repair or a combination of both. We sought to examine the association of DNA repair activity and plaque stability in patients with stable CAD.

**METHODS** We recruited 12 patients with stable angina undergoing frequency domain optical coherence tomography (FD-OCT) guided percutaneous coronary intervention (PCI) along with 12 healthy controls. We isolated peripheral blood mononuclear cells (PBMC) and measured DNA repair activity using a novel microplate assay. Subjects with diabetes, renal impairment, left ventricular impairment, bleeding diathesis, contraindication to antiplatelets, malignancy, active inflammatory disease and prior coronary revascularization were excluded. Blood was drawn from a peripheral vein and the PBMC were isolated from whole blood with a flotation strategy using Optiprep (Sigma-Aldrich) to create a density barrier.

**RESULTS** A strong correlation existed between DNA ligase and gap-filling activity. By observing no substantial effect on gap-filling activity (measuring both DNA polymerase and DNA ligase activity) after spiking samples with excess DNA polymerase, and a dramatic enhancement of apparent gap-filling activity with the addition of extra DNA ligase, we deduced that the DNA ligase was rate-limiting in the gap-filling assay. Subsequent analysis of the DNA ligase assay demonstrated significantly lower activity in patients with stable angina undergoing PCI versus healthy controls (889 units/well vs 1483; p = 0.03). Furthermore, in a stable angina cohort, we found that DNA ligase activity is positively correlated with culprit fibrous plaque thickness (Pearson correlation analysis r = −0.62; p = 0.02). There was, however, no correlation between DNA ligase activity and arcs of lipid or calcification.
frequently presented with ST-elevation myocardial infarction (STEMI; 45.7%, 40.0%, 22.9%, p=0.030) and with TIMI flow <3 (32.9%, 20.0%, 17.1%, p=0.042). According to the ratio of upstream and downstream RG, 69.5% of lesions were classified as upstream-dominant lesions and 30.5%, as downstream-dominant lesions. Among the 66 upstream-dominant lesions, 65 cases (98.5%) had upstream rupture and the RG ratio (RGupstream/RGdownstream) was an independent predictor for upstream rupture (OR 1.481, 95% CI 1.035-2.120, p=0.032). Upstream-dominant lesions more frequently presented with STEMI than downstream-dominant lesions (48.5% vs. 24.1%, p=0.026). In the idealized model and CFD analysis, axial plaque stress in the upstream segment was higher than in the downstream segment (10,968 dyne/cm² vs. 5,651 dyne/cm²) in upstream-dominant lesions. The inverse was also true for downstream-dominant lesions (7,667 dyne/cm² vs. 12,312 dyne/cm²).

CONCLUSIONS Both clinical presentation and degree of flow limitation were associated with the location of plaque rupture. Longitudinal lesion asymmetry assessed by RG, which can affect regional distribution of hemodynamic stress, was associated with the location of rupture as well as clinical presentation.

CATEGORIES IMAGING: Cath Lab of the Future

KEYWORDS Coronary artery disease, Plaque rupture, Plaque, vulnerable

TCT-315
Variation in Collagen in the Caps of Human Coronary Lipid-core Plaque Autopsy Specimens: A Possible Measure of Cap Weakness

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BACKGROUND The cap over a coronary lipid core plaque (LCP) protects the plaque from rupture and causation of a coronary event. Cap thickness has been considered the primary measure of likelihood of plaque rupture. However, caps of equal thickness may contain different amounts of collagen and be at various risks of rupture. Collagen depletion at sites of LCP may provide additional valuable information regarding plaque vulnerability. This study assessed the correlation of dimensional cap thickness vs. a semi-quantitative measure of collagen in human coronary autopsy specimens.

METHODS Seven coronary segments from 5 human autopsy hearts were used in this study. Arterial segments were fixed and divided into a total of thirty-two 2mm blocks for picrosirius red (PR) and Movat’s (MP) staining. Pathological contouring of the lipid was performed on the unpolarized PR stain, using the MP as a histology reference. Cap thickness was assessed in the regions of histology-verified LCPs in 1 increments from the lumen center. Collagen was quantified in the same locations using co-registered polarized PR images. The data collected in this study are a part of a larger autopsy study of 40 hearts (n=103 artery segments) designed to build an algorithm for detecting weak LCP caps in patients using a commercial intravascular NIRS-IVUS catheter.

RESULTS A modest correlation (r=0.49) was found between caps <200µm and associated collagen content. However, for lipid-rich necrotic cores with much thicker caps (i.e. >200µm), the amount of collagen in the fibrous cap was not well correlated to its thickness, as measured on MP images. The correlation in 200µm ranges (e.g. 200-400µm) was no better than r=0.23, and as poor as r=0.18. Large caps were found to have variable collagen content and, often a non-uniform distribution throughout the cap (Figure 1D vs 1B).

CONCLUSIONS Caps of equal thickness can contain markedly different amounts of collagen. A thick cap may be low in collagen suggesting possible cap weakness. Poor correlation between cap thickness and collagen for caps above 200µm suggests that the clinical relevance of a dimensional measurement of cap thickness for detecting vulnerable plaques might be enhanced by assessing the amount of collagen in the plaque cap. Application of the aforementioned algorithm to patients in ongoing prospective clinical trials could increase the accuracy of vulnerable plaque detection.

CATEGORIES IMAGING: Vulnerable Plaque

KEYWORDS Collagen, Fibrous cap thickness, Histological analysis

TCT-316
Characteristics Of Culprit Lesions Vs. Non-Culprit Lesions In Patients With ST-Elevation Myocardial Infarction – An Optical Coherence Tomography Study. On Behalf Of The TOTAL-OCT Investigators

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BACKGROUND Autopsy and imaging studies have demonstrated that most ST-elevation myocardial infarctions (STEMI) are caused by plaque rupture of thin cap fibroatheroma. However, lesions with intact fibrous cap are also common as culprit lesions (CL) in myocardial infarction, suggesting that a thin fibrous cap may not be the only marker of vulnerable plaque. We compared OCT imaging findings between CL vs. non-culprit lesions (NCL) in the culprit vessel of patients undergoing primary percutaneous coronary intervention for STEMI.

METHODS We analyzed images from 65 patients recruited in the TOTAL-OCT substudy (ThrOmbecTomy versus PCI ALone) who had OCT imaging performed after thrombectomy and a plaque rupture or