TCT-310

Peripheral pressure wire measurement of the below-the knee arteries in critical limb ischemia: validation with angiography and Laser Doppler measurements

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BACKGROUND The aim of the study was to assess the correlation between non-invasively versus invasively measured parameters by pressure wire during rest and after maximal hyperemia (peripheral fractional flow reserve (pFFR)) before and after below-the-knee angioplasty.

METHODS We have enrolled 31 patients in a prospective study with below-the-knee stenosis in critical limb ischemia. Inclusion criteria were: chronic critical limb ischemia (Rutherford 4-6), angiographically proven significant lesion of the distal lower limb (DS > 69%). Exclusion criteria were chronic total occlusion to the wound that makes pFFR measurement impossible or unacceptably risky, diabetic foot syndrome and non-viable distal lower limb. Routine quantitative angiography, pressure wire (pressure gradient, resting and stress FFR), laser Doppler (Perfusion unit (DPU), transcutaneous oxygen (TcO2)) and duplex ultrasound measurements were performed before and after angioplasty. The intervention was done by routine angiographic guidance.

RESULTS The intervention was performed with good angiographic result in all patients. Diameter stenosis improved from 85.3 ± 14.8 % to 17.1 ± 12.9 % ($p<0.01$). Resting systolic gradient was 51.4 ± 28.5 mm Hg before and 21.3 ± 17.9 mm Hg after intervention ($p<0.01$). Rest FFR improved from 0.7 ± 0.2 to 0.9± 0.1 ($p<0.01$). pFFR improved from 0.56 ± 0.2 to 0.74 ± 0.1 ($p<0.01$). Resting and stress Doppler perfusion units before the intervention were 28.2 ± 17.5 at rest and 136.1 ± 76.2 after provocation and 28.9 ± 18.8 (p=ns.) at rest and 160.1 ± 86.1 ($p<0.05$.) after intervention. The percentage change in DPU improved from 510.6 ± 424.5 to 652.1 ± 572.5 ($p<0.05$). Resting and stress TcO2 before intervention was 28 ± 17.8 and 99 ± 99.6 and after intervention it was 27.5 ± 14.9 (p=ns.) and 106.9 ± 105.8 ($p<0.05$). The percentage change in TcpO2 was 214.2 ±203.5 before and 237 ± 213 after intervention ($p<0.05$). Significant correlation was found between diameter stenosis, pressure gradient and pFFR values ($p<0.05$) and between Tc PU % and TcO2 percentage change and Dp, rest FFR, stress FFR ($P<0.05$). Toe pressures also correlated significantly with distal invasive pressures. The limb survival at one month follow up was 100%.

CONCLUSIONS Diameter stenosis, toe pressure, laser Doppler perfusion unit and TcO2 change during stress shows significant correlation with invasively assessed resting gradient and pFFR values. All invasive parameters improved after successful intervention. Further and larger patient series are necessary to clarify the real benefit of the direct pressure measurement during BTK interventions.

CATEGORIES IMAGING: FFR and Physiologic Lesion Assessment

KEYWORDS Critical limb ischemia, Fractional flow reserve

TCT-311

The comparison of myocardial perfusion imaging with fractional flow reserve to detect ischemic territory for patients with multi-vessel disease

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BACKGROUND The role of myocardial perfusion imaging (MPI) in patients with multi-vessel disease is uncertain because the accuracy of MPI to identify myocardial ischemia is limited in the multi-vessel settings. The aim of this study was to assess the ability of stress MPI to detect myocardial ischemia in patients with multi-vessel disease from two different points of view: 1) MPI for revascularization decision-making, and 2) MPI for screening ischemia-positive patients.

METHODS We analyzed 102 patients with angiographically multivessel disease who underwent both stress MPI and three vessel FFR measurements to evaluate the accuracy of stress MPI in identifying myocardial ischemia using FFR < 0.75 as the gold standard. We tested 1) whether MPI findings were completely concordant with FFR in every perfusion territory (complete concordance investigation for revascularization decision-making), and 2) whether MPI could identify a patient with any FFR positive lesions (partial concordance investigation for screening ischemia-positive lesions).

RESULTS There was a poor concordance between MPI and FFR in the complete concordance investigation ($\kappa = 0.153$, $p = 0.054$) with 53% accuracy, while there was a good concordance between MPI and FFR in the partial concordance investigation ($\kappa = 0.658$, $p < 0.001$) with 84% accuracy.

CONCLUSIONS MPI often failed to identify all perfusion territory with myocardial ischemia in patients with multi-vessel disease, whereas it could identify a patient with myocardial ischemia with high accuracy even in multi-vessel settings. These results suggested that MPI was inappropriate in deciding which lesion should be treated, but could be a good help in deciding which patient should be delivered to further diagnostic test.

CATEGORIES IMAGING: FFR and Physiologic Lesion Assessment

KEYWORDS Fractional flow reserve, Multivessel disease, SPECT

TCT-312

Effects of Dobutamine and Glyceryl Trinitrate on coronary blood flow and the coronary wave intensity profile

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BACKGROUND Coronary blood flow (CBF) is uniquely dependent upon central aortic blood pressure (CBP) and myocardial microvascular resistance but the underlying mechanisms are ill-defined. Coronary wave intensity (CWI) permits aortic and myocardial forces acting on CBF to be resolved. CWI has identified two major accelerative waves - the systolic forward travelling compression wave (sFCW) generated by aortic pressure rise and the diastolic backward travelling expansion wave (dBEW) attributed to the suction effect induced by diastolic microvascular recoil. The systolic backward travelling compression wave (sBCW) generated by myocardial microvascular compression during systole coincides with the sFCW and attenuates its effects on CBF. The effects of varying ventricular contractility, heart rate and blood pressure on the CWI profile are unknown.

METHODS Intracoronary pressure and CBF velocity waveforms were acquired in 21 patients with near normal (<20% luminal stenosis) epicardial coronary arteries. A dual pressure and Doppler flow velocity transducer tipped coronary guidewire was positioned in the proximal left anterior descending coronary artery. Intraventricular pressure measurements were also obtained to enable calculation of the time constant of isovolumic pressure decline (tau) and the maximal rate of systolic pressure increase (dP/dT). Measurements were taken at rest, with dobutamine 10 μg/kg/min or sublingual GTN 400mcg. CWI profiles were generated and cumulative intensities of the sFCW, dBEW and sBCW calculated.

RESULTS Heart rate, diastolic blood pressure and maximum left ventricular (dP/dT) increased with dobutamine whilst tau decreased (see Table). CBF increased with dobutamine and decreased with GTN. The cumulative intensity of all three waves increased with dobutamine and either decreased or remained stable following GTN. Dobutamine resulted in increased sFCW cumulative intensity but this increase was counterbalanced by increased sBCW intensity, thereby attenuating any change in systolic flow. The cumulative intensity of the dBEW also increased with dobutamine and this primarily accounted for increased CBF. Conversely, GTN resulted in significantly decreased systolic blood pressure, CBF and cumulative intensity of the sFCW with a trend to decrease for sBCW and dBEW intensity.

	Baseline Mean (SEM)	Post Dobutamine Mean (SEM)	P-Value
Systolic Blood Pressure (mmHg)	137.9 (4.5)	132.9 (6.2)	0.41
Diastolic Blood Pressure (mmHg)	76.3 (3.2)	66.2 (4.1)	0.003
Heart Rate (bpm)	66.9 (4.1)	86.0 (6.4)	0.001
Tau (ms)	47 (2.9)	37 (2.7)	0.002
dP/dT (mmHg/s)	1450 (82.9)	2761 (197.2)	<0.001
Mean Systolic Flow velocity (cm/s)	11.3 (0.9)	16.6 (2.5)	0.002
Mean Diastolic Flow velocity (cm/s)	22.5 (3.5)	32.5 (5.3)	0.001
	Baseline Mean (SEM)	**Post GTN Mean (SEM)**	**P-Value**
Systolic Blood Pressure (mmHg)	135.7 (7.9)	118.6 (5.4)	0.01
Diastolic Blood Pressure (mmHg)	72.3 (3.1)	70.8 (2.4)	0.73
Heart Rate (bpm)	66.1 (3.5)	65.7 (3.0)	0.91
Tau (ms)	57 (3.5)	53 (4.9)	0.25
dP/dT (mmHg/s)	1451 (109)	1403 (123)	0.65
Mean Systolic Flow velocity (cm/s)	16.9 (2.5)	11.5 (1.4)	0.002
Mean Diastolic Flow velocity (cm/s)	28.2 (3.1)	22.2 (2.3)	0.004

CONCLUSIONS Augmented diastolic suction wave intensity induced by enhanced lusitropy is the principal driver of increased CBF with dobutamine despite larger increases in systolic compression wave intensity. Conversely, GTN administration results in decreased coronary blood flow through a reductions in both systolic and diastolic accelerative wave intensity.

CATEGORIES IMAGING: FFR and Physiologic Lesion Assessment

KEYWORDS Coronary flow, Coronary microcirculation, Coronary Physiology

VULNERABLE PLAQUE

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TCT-313

DNA repair activity determines atherosclerotic plaque stability in patients with stable coronary artery disease

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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 facilitating the joining of DNA strands 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 the 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.

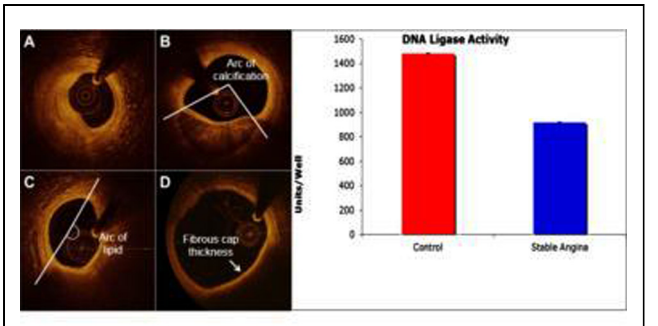

Figure 1: Examples of atherosclerotic plaques visualised by optical coherence tomography. Panel of four optical coherence tomography images showing a fibrotic plaque (**A**), fibrocalcific plaque (**B**), lipid-rich fibroatheroma (**C**) and a thin-cap (arrow) fibroatheroma (**D**). Lipid/calcification arcs and fibrous cap thickness are marked.

Figure 2: Comparison of DNA ligase activity between healthy volunteers and patients with stable angina undergoing FD-OCT guided PCI (p=0.03)

CONCLUSIONS DNA repair activity is reduced in patients with stable angina compared to healthy controls and may be a key determinant of atherosclerotic plaque stability.

CATEGORIES OTHER: Genomics / Proteomics

KEYWORDS Atherosclerosis, coronary, OCT

TCT-314

Impact of Longitudinal Lesion Geometry on Location of Plaque Rupture and Clinical Presentations

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BACKGROUND The relationship among lesion geometry, external hemodynamic forces acting on the plaque, location of plaque rupture, and clinical presentation has not been comprehensively investigated. We sought to investigate the impact of longitudinal lesion geometry on the location of plaque rupture and clinical presentation and its mechanism.

METHODS 125 patients with documented plaque rupture by intravascular ultrasound (IVUS) were enrolled. Longitudinal locations of plaque rupture were identified and categorized by IVUS. Patient's clinical presentations and TIMI flow grade in initial angiogram were compared according to the location of plaque rupture. Longitudinal lesion asymmetry was quantitatively assessed by the luminal radius change over the segment length (radius gradient, RG). Lesions with steeper radius change in upstream compared with downstream segment (RGupstream>RGdownstream) were defined as upstream-dominant lesions.

RESULTS On the basis of the site of maximum aperture, 56.0%, 16.0%, and 28.0% of the patients had upstream, MLA, and downstream rupture, respectively. Patients with upstream rupture more