**PS510 | BEDSIDE**

Relation of peri-procedural plasma matrix metalloproteinase-8 and -9 levels to microvascular obstruction after primary percutaneous coronary intervention

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**Purpose:** Reperfusion injury is central to the pathophysiology of microvascular obstruction (MVO) after primary percutaneous coronary intervention (p-PCI). Matrix metalloproteinases (MMPs) do not only regulate the release of pro-inflammatory cytokines and the expression of adhesion molecules but also facilitate leukocyte transmigration across the endothelium during an inflammatory response. The aim of this study was to investigate the relation of peri-procedural plasma MMP-8 and -9 levels to MVO after p-PCI in patients with acute ST segment elevation myocardial infarction (STEMI).

**Methods:** Forty-two patients with acute STEMI who underwent p-PCI within 12 hours of the onset of symptoms were prospectively enrolled. Plasma samples for MMP-8 and -9 analysis were obtained on admission and at post-PCI 6th and 24th hours. MVO was assessed and quantified by the index of microcirculatory resistance (IMR) measured with the use of a guidewire tipped with pressure and temperature sensors on post-PCI day 4 to 5.

**Results:** When we categorized the patients according to the mean value of IMR (30 U) and define MVO as IMR>30 U, baseline MMP 8 (21.1±18.8 vs 8.1±4.3, p=0.001) and baseline MMP 9 (108.8±76.4 vs 71.9±59.9, p=0.013) levels were significantly higher in patients with MVO. However, there was no difference between the two groups with respect to the MMP levels at the 6th and 24th hours (Figure 1). Plasma MMP-8 and -9 levels on admission were positively correlated with IMR (r=0.56 vs p=0.001 and r=0.34 vs p=0.03, respectively). However, magnitude of change (in percentages) in plasma MMP-8 and -9 levels between admission and post-PCI 6th hour was negatively correlated with IMR (r=0.38 vs p=0.01 and r=0.34 vs p=0.03, respectively). In addition to MMP-8 and -9, D-dimer (r=0.46, p=0.016) and BNP (r=0.43, p=0.003) levels on admission, peak troponin level (r=0.27, p=0.07) and age (r=0.28, p=0.07) were also found to be significantly correlated with IMR. Multiple linear regression analysis revealed that MMP-8 level on admission (β=0.026, p=0.025) and BNP level on admission (β=0.006, p=0.038) were independently associated with IMR.

**Conclusions:** Plasma MMP-8 level on admission is related to microvascular obstruction after p-PCI and significantly correlated with IMR. Furthermore, the presence of MVO seems to influence the dynamic nature of the MMPs after p-PCI. MMP inhibitors may be targets for future studies investigating alternative strategies for prevention of MVO.

**PS511 | BENCH**

The anti-interleukin-1beta monoclonal antibody, gevokizumab, reduces hs-crp in subjects with type 2 diabetes mellitus

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The new anti-interleukin-1 (IL-1) monoclonal antibody, gevokizumab, was evaluated in patients with type 2 diabetes mellitus (T2DM) not adequately controlled on stable metformin treatment. In a parallel-group, double-blind, placebo-controlled phase II trial, 421 patients were randomized to monthly subcutaneous injections of placebo or gevokizumab at doses of 0.01, 0.03, 0.1, or 0.3 mg/kg for 6 months. The primary objective in terms of reduction of hemoglobin A1c was not reached. By contrast 6 months’ treatment with gevokizumab was associated with a significant decrease in high-sensitivity C-reactive protein (hs-CRP) in all groups versus placebo (all p<0.02). The proportion of patients with more than 60% reduction in hs-CRP increased in a dose-dependent manner to 39% and 40% of patients treated with 0.1 and 0.3 mg/kg, respectively (both p<0.0001). Gevokizumab was well tolerated. There were no drug-related serious adverse events or injection site reactions. Incidences of infection in the gevokizumab and placebo groups were comparable (26% vs 23%); nasopharyngitis was the most frequent (5% vs 4%). Gevokizumab, a humanized monoclonal antibody that modulates IL-1, has been demonstrated to have a marked anti-inflammatory effect, reflected by a substantial reduction in hs-CRP in patients with T2DM. A dose-response effect was found in terms of proportion of patients with reduced hs-CRP. The decrease observed in the inflammatory status of such patients indicates potential cardiovascular beneficial effects, which merits further exploration.

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**ABSTRACT WITHDRAWN**

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The natural history of coronary atherosclerotic plaques assessed by serial virtual histology intravascular ultrasound

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**Purpose:** Histological plaque composition is a major determinant of the tendency of atherosclerotic lesions to provoke clinical events. Virtual histology intravascular ultrasound (VH-IVUS) offers an opportunity to assess the detailed quantitative information on plaque composition in vivo. The aim of this study was to assess the natural history of coronary atherosclerotic plaques to use serial VH-IVUS (base-line and 6-month follow-up) with proximal non-culprit, untreated lesions (plaque burden ≥40%) from patients with STEMI. Twenty-four patients (25 lesions) were prospectively enrolled. We classified and analyzed the target plaques into five types; pathological intimal thickening (PTI), VH-IVUS-derived thin-capped fibroatheroma (VH-TCFA), thick-capped fibroatheroma (ThCFA), fibrocalcic plaque, and fibrocalcific plaque.

**Results:** At baseline, 18 lesions were VH-TCFAs; during follow-up, 8 (45%) VH-TCFAs ‘healed’, 5 became PTIs, 2 became ThCFA s, 1 became fibrocalcic plaque, and 10 (55%) VH-TCFAs remained unchanged. 2 new VH-TCFAs developed; 1 late-developing VH-TCFA was PTI, and 1 was ThCFA at baseline. Patients with VH-TCFAs that remained VH-TCFAs were younger (59±7.4 vs. 61.38±11.5 years, p=0.036) and had lower baseline LDL-cholesterol (107.1±25.3 vs. 122.1±67 mg/dL, p=0.026). But, baseline VH-IVUS plaque composition did not differ between VH-TCFAs that healed and VH-TCFAs that remained VH-TCFAs.

**Conclusions:** About half of VH-TCFAs healed during 6-month follow-up, whereas new VH-TCFAs also developed.