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IMPAIRED PRODUCTION OF ANTI-ATHEROSCLEROTIC INTERLEUKIN-10 BY MACROPHAGE WITHIN CULPRIT PLAQUE IN DIABETIC PATIENTS WITH RESTENOSIS AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Background: Coronary intraplaque hemorrhage (IPH) accelerates atherosclerosis through the dual metabolic stresses of cholesterol-enriched erythrocyte membranes and prooxidant hemoglobin (Hb). IPH is frequently observed in vulnerable plaque, especially in diabetic patients with acute coronary syndrome (ACS). Extracellular Hb are cleared exclusively by macrophages with scavenger receptor CD163. These macrophages can counteract atherogenicity of IPH by secreting anti-atherosclerotic cytokine interleukin (IL)-10. We investigated IPH, macrophage phenotype, and IL-10 production in coronary plaques from ACS patients with diabetes, in association with bare metal stent (BMS) restenosis after primary percutaneous coronary intervention (PCI).

Methods: In 29 ACS patients (60±14 years, 19 male) with diabetes (HbA1c(NGSP)>6.5%), atherothrombotic debris was retrieved using filter-based distal protection device (Filtrap), during primary PCI with BMS implantation. The debris was stained with antibodies to glycophorin A (GPA, intraplaque hemorrhage), CD14 (proinflammatory macrophage), CD163 (Hb scavenging macrophage) and IL-10. These debris parameters were compared between patient with angiographic restenosis (R+, n=6) and those without restenosis(R-, n=23), after 9-month optimal medical treatment.

Results: Restenosis rate were 20.1%. Conventional risk factors, such as diabetes, dyslipidemia and hypertension were not different between the two groups. Stent diameter and length were not different (R+: 3.4±0.5 x 16.0±5.5, R-: 3.1±0.5 x 13.7±3.3). GPA (13.0±7.8 vs 21.9±14.6%), CD14 (19.6±9.8 vs 25.1±19.0%), CD163 (39.6±13.2 vs 28.3±19.8%), and IL10 (33.3±17.8 vs 47.9±28.3%) were not different between the two groups. However, IL10/CD163 ratio, an anti-atherosclerotic cytokine production capacity of Hb scavenging macrophages, were decreased in R+ compared to R- (0.92±0.54 vs 2.11±1.24, p<0.01).

Conclusions: Anti-atherosclerotic IL-10 production by Hb scavenging macrophages are impaired in diabetic patients with restenosis after primary PCI.