atherosclerosis

Atherosclerosis newsletter

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The June issues contains several articles on the assessment of cardiovascular disease risk either by assessment of vascular physiology and structure or by lipoprotein related biomarkers.

Exploring the relationship between biomechanical stresses and coronary atherosclerosis

The pathophysiology of coronary atherosclerosis is multifaceted. Plaque initiation and progression are governed by a complex interplay between genetic and environmental factors acting through processes such as lipid accumulation, altered haemodynamics and inflammation. There is increasing recognition that biomechanical stresses play an important role in atherogenesis, and integration of these metrics with clinical imaging has potential to significantly improve cardiovascular risk prediction. In this review, Cameron et al. present the calculation of coronary biomechanical stresses from first principles and computational methods, including endothelial shear stress (ESS), plaque structural stress (PSS) and axial plaque stress (APS). They discuss the current experimental and human data linking these stresses to the natural history of coronary artery disease and explore the future potential for refining treatment options and predicting future ischaemic events.

Coronary perivascular epicardial adipose tissue and major adverse cardiovascular events after ST segment-elevation myocardial infarction

Perivascular epicardial adipose tissue (pEAT) plays a key role in the progression of atherosclerosis, plaque rupture, and thrombosis. However, the relationship between pEAT and prognosis after revascularization of ST-segment elevation myocardial infarction (STEMI) is unknown. Toya et al. investigated the relationship between pEAT thickness and prognosis after STEMI.

180 STEMI patients, who underwent cardiac magnetic resonance (CMR) imaging within 1 week of prompt infarct-related artery revascularization, and 52 age/sex/body mass index-matched controls were included in the study. pEAT thickness indexed to body surface area at five locations, infarct size, left ventricular ejection fraction (LVEF), and coronary microvascular obstruction (MVO) were evaluated by CMR. Associations between pEAT index and 1-year composite major adverse cardiovascular events (MACE), infarct size, LVEF, and MVO were analyzed.

Mean pEAT indices were significantly higher in STEMI patients than controls. In STEMI patients, higher pEAT indices at the superior and inferior interventricular groove (SIVG and IIVG, respectively) were significantly associated with larger infarct size, and higher prevalence of MVO, and inversely correlated with post-infarct LVEF. SIVG pEAT index was an independent predictor of composite MACE in post-STEMI patients, with an odds ratio of 2.26 after adjustment for age, sex, LVEF, and 2.71 after adjustment for age, sex, previous myocardial infarction, diabetes mellitus, and renal function.

STEMI patients have significantly higher pEAT indices than controls. SIVG pEAT index independently predicts composite MACE in revascularized STEMI patients, underscoring the potentially prognostic value of this variable.

Endothelial glycocalyx and severity and vulnerability of coronary plaque in patients with coronary artery disease

The endothelial glycocalyx is a polymeric sugar-rich network covering the endothelial surface of the vessels, and maintaining vascular integrity. Deterioration of the EG has been demonstrated in advanced age, diabetes, end-stage renal disease, and cerebrovascular disease. Thus, EG may be highly impaired in patients with advanced coronary atherosclerosis. However, its association with the severity and vulnerability of coronary artery disease (CAD) remains to be elucidated. Nemoto et al. aimed at investigating such association by assessing the levels of serum syndecan-1, a core component of EG, and correlating the findings with angiogram and intracoronary optical coherence tomography (OCT) results.

A total of 259 consecutive patients with stable CAD requiring percutaneous coronary intervention (PCI) were prospectively enrolled. Patients were classified into 2 groups according to the median value of serum syndecan-1 (lower syndecan-1 group [syndecan-1 <99.0 ng/mL], higher syndecan-1 group [syndecan-1 ≥99.0 ng/mL], n = 129). Severity of CAD and focal plaque vulnerability in culprit lesion were evaluated using angiography and optical coherence tomography.

There was no significant difference in clinical characteristics between the lower syndecan-1 group and the higher syndecan-1 group other than the prevalence of family history of CAD, prior PCI history and estimated glomerular filtration rate. Although disease severity on angiogram was comparable between the 2 groups, the prevalence of lipid-rich plaque and thin-cap fibroatheroma was significantly higher in the lower syndecan-1 group than the higher syndecan-1 group. Lower syndecan-1 level was independently associated with higher prevalence of lipid-rich plaque.

Lower syndecan-1 level was associated with higher prevalence of vulnerable plaque in patients with CAD. This finding suggests the association between impaired endothelial glycocalyx and the development of vulnerable plaque.

Relationship between elevated plasma ceramides and plaque rupture in patients with ST-segment elevation myocardial infarction

Ceramides (Cer), a key sphingolipid product of sphingomyelinase (SM), are an integral part of the cell membrane of eukaryotes. They contribute to the structural stability of the cell and act as bioactive lipids in various cell signalling pathways including apoptosis, inflammation, cell-cycle arrest. Ceramides play critical roles in the development and progression of atherosclerosis. However, the association between specific plasma Cer levels and culprit plaque morphology in ST-segment elevation myocardial infarction (STEMI) patients is unclear. Pan et al. aimed to explore the associations between plasma major adverse cardiovascular events (MACEs)-related ceramide concentrations and culprit plaque morphologies evaluated by optical coherence tomography (OCT) in patients with STEMI.

The study consisted of two parallel cohorts: 100 consecutive patients with STEMI were screened as discovery cohort while the validation cohort consisted of 30 normal donors, 30 stable angina pectoris (SAP) and 315 STEMI patients. All STEMI patients underwent emergency percutaneous intervention (PCI) and OCT examination for culprit plaque. Based on established diagnostic criteria, STEMI patients were classified into plaque rupture (PR) and plaque erosion (PE) group, respectively. Rapid resolution liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (RRLC-Q-TOF/MS) was used to evaluate plasma Cer levels of the screened patients.

STEMI patients had higher plasma Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/24:1) and Cer(d18:1/24:0) levels than normal donors and SAP patients. Plasma Cer levels were significantly higher in STEMI patients with PR than with PE. The frequency of PR increased with increasing tertiles of plasma Cer. The fully adjusted per SD odds ratios for PR were 9.375 for Cer(d18:1/16:0), 3.586 for Cer(d18:1/18:0), 8.171 for Cer(d18:1/24:1), and 3.831 for Cer(d18:1/24:10).

The study show novel, positive and independent associations between plasma Cer concentrations and the presence of PR, suggesting plasma Cer may act as a potential biomarker for PR to improve risk stratification.

High density lipoprotein functionality and cardiovascular events and mortality: A systematic review and meta-analysis

There are only a few articles evaluating the association between high-density lipoprotein (HDL) functionality and cardiovascular disease (CVD) outcomes, and the available evidence has never been systematically summarized. Soria-Florido et al. conducted a systematic review and meta-analysis to synthesize studies assessing the associations between high-density lipoprotein functionality and risk of cardiovascular disease and mortality.

Medline and Embase were searched for the identification of observational studies meeting the inclusion criteria. The meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and was registered in the PROSPERO International Prospective Register of Systematic Reviews. Risk estimates with a random-effect model were pooled separately for cardiovascular disease (fatal and non-fatal) and all-cause mortality.

Out of 29 manuscripts, 20 articles investigated cholesterol efflux capacity (13 prospective and 7 cross-sectional), 10 antioxidant capacity (7 prospective and 3 cross-sectional) and two anti-inflammatory capacity of high-density lipoprotein (1 prospective and 1 cross-sectional). A greater cholesterol efflux capacity was associated with lower risk of cardiovascular disease in 8 studies and of mortality in 5 studies. Better antioxidant capacity was non-significantly associated with lower cardiovascular disease risk in 2 studies, and significantly associated with mortality in 3 studies. HDL anti-inflammatory ability was associated with a lower cardiovascular disease risk in the only prospective study.

Greater high-density lipoprotein cholesterol efflux capacity and antioxidant/anti-inflammatory capacities are associated with lower risk of cardiovascular disease. However, the heterogeneity between studies and evidence of publication bias warrants caution and highlights the need for larger prospective studies with standardized assays and specific outcomes.