Methods: Five groups of rabbits were employed and fed normal chow-fed diet (Gp 1), high fat diet (Gp 2), normal chow-fed diet plus TAE (Gp 3), high fat diet plus TAE (Gp 4) and high fat diet plus atorvastatin (Gp 5) respectively for 6 months. Aortic lesions were excised and protein lysate was separated by Two-dimensional gel electrophoresis. Differentially expressed proteins were identified by MALDI-TOF in Linear Reflectron Mass Spectrometer.
Results: 850 spots could be detected among which 79 spots ($p<0.05$) matched among all 5 groups and 58 individual proteins were identified from 79 spots. Proteins like Interstitial collagenase, GRB2-related adapter protein 2, Interleukin 2, Myocyte enhancer-factor 2A, Protein S100-A9 and HSP60 with >10 fold expression were found to be differentially and significantly upregulated in Gp 2. TAE and atorvastatin treatment reduced the expression of these proteins to almost basal level (<1 fold change). TAE also significantly ($p<0.05$) downregulated expression of 5-lipoxygenase-activating protein, 72 kDa type IV collagenase, HSP90-alpha, and Vimentin proteins. Compared to atorvastatin, TAE was significantly more effective in downregulating all these proteins implicated in atherosclerotic disease.
Conclusions: This study reveals that Terminalia arjuna is a potent down-regulator of various atherosclerosis-related proteins, hence should be explored in future clinical trials.

W7:4.
MASSCYTOMETRY IDENTIFIES CD8 T-CELL DIVERSITY IN HUMAN ATHEROSCLEROTIC LESIONS

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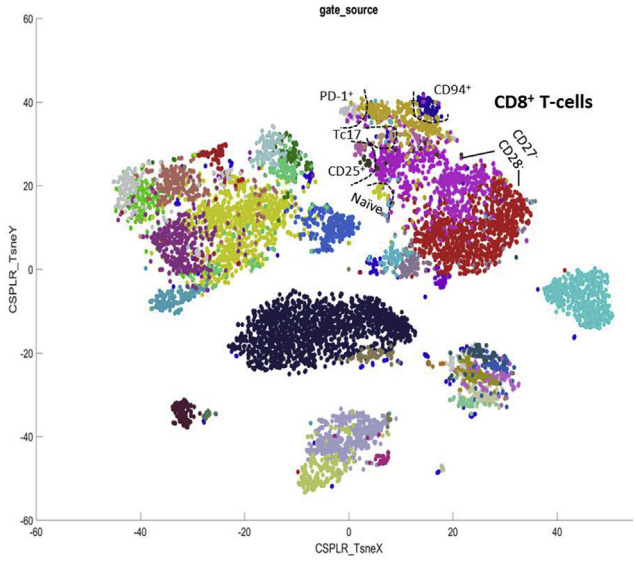
Aim: CD8+ T-cells are numerous in early and advanced atherosclerotic lesion, but their role in atherogenesis and plaque stability is still under debate. Recent work in murine models suggests the existence multiple CD8+ T-cell subsets that may differently impact the progression of disease. Here we aim to characterize the CD8+ T-cell population in human atherosclerotic lesions using a combination of histology, flow cytometry and mass cytometry (Cytof).
Methods: Fresh carotid or femoral endarterectomy and matching blood samples were collect from a local hospital. Part of the sample was fixed for histology and the remainder was digested to obtain single cell suspensions. Cells were labelled with fluorescently labelled antibodies for flow-cytometry and isotope labelled antibody for mass cytometry. Results were analyzed with Flowjo (flowcytometry and mass cytometry) and Cytosplore (mass cytometry) software.
Results: CD8+ T-cells were detected in every lesion (n=42) analyzed and on average constituted 23% of the total leukocyte. The percentage of CD8+ T-cells inversely correlated with the percentage of macrophages in the lesion, suggesting a role for CD8+ T-cells in preventing macrophage accumulation in the lesion. Mass cytometry revealed at least 13 phenotypically distinct CD8+ T-cells in the lesions, terminally differentiated CD27-/CD28- representing the largest CD8+ section.
Conclusions: Human atherosclerotic lesions contain various CD8+ T-cell populations that may differentially affect disease progression and lesion stability. Although the overall effect of CD8+ T-cell presence in the lesion appear to be beneficial, identifying the protective subsets and expanding them may open new avenues for treatment.



W7:4.

W7:5.
HIGH LDL CHOLESTEROL LEVELS AND RISK OF PERIPHERAL VASCULAR DISEASES - A MENDELIAN RANDOMIZATION STUDY INCLUDING 106,548 INDIVIDUALS FROM THE GENERAL POPULATION

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Aim: High LDL cholesterol is causally involved in the pathogenesis of atherosclerosis and is causally related to an increased risk of cardiovascular disease. It is unknown whether high LDL cholesterol levels are causally related to an increased risk of peripheral vascular diseases, such as retinopathy, neuropathy, chronic kidney disease(CKD), and peripheral arterial disease(PAD). We hypothesized that high LDL cholesterol is causally related to the risk of retinopathy, neuropathy, CKD and PAD in the general population.
Methods: We included 106,548 individuals from the Copenhagen General Population Study and used Mendelian randomization to examine causality between high LDL cholesterol levels and peripheral vascular endpoints. As genetic instrument we selected and genotyped nine variants in the LDLR, APOB, APOE and PCSK9 genes.
Results: Observationally we found no association between high LDL cholesterol levels and risk of retinopathy (P trend=0.78) or neuropathy (P trend=0.01). We found a stepwise increase in risk of CKD and PAD with higher LDL cholesterol levels, with a hazard ratio (HR; 95% confidence interval) of 2.56(2.40-2.74) for CKD and 1.25(1.06-1.47) for PAD in individuals with LDL cholesterol levels above the 95th percentile versus below the 50th percentile. In the genetic, causal analyses the risk ratio of disease for a 1 mmol/L higher LDL cholesterol was 1.11 (0.77-1.60) for retinopathy, 0.79 (0.62-1.01) for neuropathy, 1.10(1.01-1.18) for CKD and 1.17(1.01-1.36) for PAD.
Conclusions: Our study suggests that LDL cholesterol has no causal effect on peripheral microvascular diseases such as retinopathy and neuropathy; but has a causal effect on CKD and PAD.

Clinical studies

LB2:1.
LIPID MANAGEMENT OF PATIENTS WITH CORONARY HEART DISEASE IN 27 COUNTRIES IN EUROPE: RESULTS OF EUROASPIRE V SURVEY OF THE EUROPEAN SOCIETY OF CARDIOLOGY

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Aim: Background Five EUROASPIRE survey have been conducted under the auspices of the European Society of Cardiology, Euro Heart Survey/ EURObservational Research Programme spanning more than two decades: the first in 1995-1996 in 9 countries, the second in 1999-2000 in 15, the third in 2006-2008 in 22, the fourth in 2012-2015 in 26 and in 2017-2018 in 27.