Background and Aims: Statin associated muscle symptoms (SAMS) are one of the main reasons for poor treatment adherence and/or discontinuation, but a definitive diagnosis of SAMS is challenging. The PROSISA study is an observational retrospective study aimed at assessing the prevalence of SAMS in dyslipidaemic patients.

Methods: Demographic/anamnestic data, biochemical levels, and occurrence of SAMS were collected. Adjusted logistic regression was fitted to estimate OR and 95% confidence intervals for association between probability of reporting SAMS and several factors.
Results: This analysis was carried out on 16,717 statin-treated patients (mean±SD age 60.5±12.0 years; 52.1% men). During statin therapy, 9.6% of patients reported SAMS, mainly myalgia (71.9%). Women and physically active subjects were more likely to report SAMS (OR 1.23 [1.10-1.37] and OR 1.35 [1.14-1.60], respectively), while older patients (OR 0.79 [0.70-0.89]), presence of type II diabetes mellitus (OR 0.62 [0.51-0.74]), use of concomitant non-statin lipid-modifying drugs (OR 0.87 [0.76-0.99]), of high-potency statins (OR 0.79 [0.69-0.90]) and of potential interacting drugs (OR 0.63 [0.48-0.84]) were associated with a lower probability of reporting SAMS. Among patients reporting SAMS, 761 underwent dechallenge, with disappearance of muscular symptoms in 87.2% of cases, while overall 908 patients underwent rechallenge (468 with change of statin/dose reduction without interruption of therapy), with reappearance of muscular symptoms in only 248 patients.
Conclusions: The reported prevalence of SAMS was 9.6%, but the percentage of patients in whom intolerance has been confirmed by dechallenge/rechallenge was between 23-28%, emphasizing the need for a better management of SAMS to provide a definitive diagnosis and treatment re-evaluation.

036 / #251, TRACK 3 - PATHOGENESIS OF ATHEROSCLEROSIS, VASCULAR REMODELING, 10-06-2020 10:30 AM - 11:13 AM.
TRANSCRIPTOMIC PROFILING OF EXPERIMENTAL ARTERIAL INJURY REVEALS NEW MECHANISMS AND TEMPORAL DYNAMICS IN VASCULAR HEALING RESPONSE

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Background and Aims: Endovascular interventions cause arterial injury and induce a healing response to restore vessel wall homeostasis. Complications of defective or excessive healing are common, resulting in increased morbidity and repeated interventions. Experimental intimal hyperplasia models are vital for understanding vascular healing mechanisms and resolving clinical problems of restenosis, vein graft stenosis and dialysis access failure. Our aim was to systematically investigate the transcriptional, histological and systemic reaction to vascular injury over a prolonged period of time.

Methods: Balloon injury of the left common carotid artery was performed in male rats. Animals (n=69) were euthanized prior to or post-injury, either directly or after 2h, 20h, 2 days, 5 days and 2, 6, 12 weeks. Injured and contralateral arteries were microarray profiled, followed by bioinformatic exploration, histological biopsy characterization and plasma lipid analyses.
Results: Immune activation and coagulation were key mechanisms in the early response, followed by cytokine release, tissue remodeling and smooth muscle cell (SMC) modulation several days after injury, with re-acquisition of contractile features in later phases. Clonal expansion, inflammatory transformation and chondro-osteogenic differentiation were novel pathways identified and immunolocalized to neointimal SMCs. Analysis of uninjured arteries revealed a systemic component of the reaction following local injury, underlined by altered endothelial signaling, changes in tissue bioenergy metabolism and plasma HDL levels.
Conclusions: We demonstrate that vascular injury induces dynamic transcriptional landscape and metabolic changes identifiable as early, intermediate and late- response phases, reaching homeostasis after several weeks. This study provides a temporal 'roadmap' of vascular healing as a public resource for the research community.

037 / #78, TRACK 3 - PATHOGENESIS OF ATHEROSCLEROSIS, VASCULAR REMODELING, 10-06-2020 10:30 AM - 11:13 AM.
EFFECT OF SHEAR STRESS ON VASCULAR CELL TRANSCRIPTOMICS IN AN VITRO SETTING OF DRUG-ELUTING BIORESORBABLE VASCULAR SCAFFOLDS (BVS)

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Background and Aims: Aim of this sub-study of H2020 EU funded InSilc project is to evaluate vascular cell response to different shear stress levels in an in vitro setting of Drug-eluting Bioresorbable Vascular Scaffolds (BVS).

Methods: Human Coronary Artery Endothelial Cells (HCAECs) and Smooth Muscle Cells (HCASMCs) were cultured in dynamic conditions at flow rates corresponding to low and normal shear stress (1 and 20 dyne/cm^2 respectively), with and without BVS under Everolimus 600 nM for 6 hours. Cell RNA-Seq and bioinformatics analysis provided gene modulation by direct comparison of shear stress conditions and Gene Ontology of biological processes shared by the two cell types.
Results: A significant (> 3-fold) upregulation of MEOX2, related to proliferation and inflammation, in HCAECs, and of SEMA3E, with a role in migration and proliferation, in HCASMCs, is evidenced by low shear stress, with and without BVS. HCASMCs and HCAECs share four biological processes, two specifics for HCASMCs and two for HCAECs: three genes are constantly upregulated by low shear stress, BMP4 (neointima formation), HMOX1 (inflammation, proliferation, thrombosis) and SELE (lymphocytes homing in inflammation).
Conclusions: Transcriptomic analysis of dynamic cell culture in vitro identifies candidate genes of low shear stress-related pro-restenotic and pro-thrombotic processes in an in vitro BVS setting, thus contributing to unravel the mechanism of vascular cell response to BVS stenting in vivo.
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038 / #1196, TRACK 3 - PATHOGENESIS OF ATHEROSCLEROSIS, VASCULAR REMODELING, 10-06-2020 10:30 AM - 11:13 AM.
MICROCALCIFICATION: A PATHOLOGICAL CHARACTERISTIC AND MEDIATOR OF ABDOMINAL AORTIC ANEURYSM FORMATION

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Background and Aims: Abdominal aortic aneurysms (AAAs) are highly lethal diseases without effective clinical predictors and therapeutic targets. Vascular microcalcification as detected by fluorine-18-sodium fluoride (^{18}F-NaF) has recently been recognized as a valuable indicator in predicting of atherosclerotic plaque rupture and AAA expansion. However, whether vascular microcalcification is involved in the pathogenesis of AAA remains elusive.

Methods: Microcalcification was analyzed in human aneurysmal aortas histologically and in angiotensin II (AngII)-infused ApoE$^{-/-}$ mouse aortas by ^{18}F-NaF PET-CT scanning in chronological order in live animals.
Results: AAA patients' aortic tissue showed markedly enhanced microcalcification in the aortic media within the area proximal to elastic fiber degradation, compared to non-AAA patients. Enhanced ^{18}F-NaF uptake preceded significant aortic expansion in mice. Microcalcification-positive mice on day 7 of AngII infusion showed dramatic aortic expansion on subsequent days 14 to 28, whereas microcalcification-negative AngII-infused mice and saline-induced mice did not develop AAA. The application of hydroxyapatite, the main component of microcalcification, aggravated AngII-induced AAA formation in vivo.RNA-sequencing analysis of the suprarenal aortas of 4-day-AngII-infused ApoE$^{-/-}$ mice and bioinformatics analysis with ChIP-Atlas database identified the potential involvement of the osteogenic transcriptional factor Runx2 in AAA. Consistently,