SPRING 2020

Spring Meeting Giovani Ricercatori 2.0 Itinerante

SIIA   **SIMI**   **SISA**

Novità sulla prevenzione e cura della malattia cardiovascolare

Meeting online:

18 Giugno - 25 Giugno - 2 Luglio

Young investigators meeting

17.00-17.10   Introduzione •*Elena Buzzetti, Costantino Mancusi, Mario Luca Morieri*

Innovazione tecnologica e scientifica: approcci un-biased nella ricerca cardiovascolare

Moderatori: Elena Buzzetti, Costantino Mancusi, Mario Luca Morieri

17.10-17.40   **Artificial Intelligence and Machine Learning in cardiovascular medicine**
• *Martino Pengo e Sara Montagna*

17.40-18.10   Comunicazioni orali
A new genetic risk score for blood pressure strongly associates with the incidence of hypertension and cardiovascular endpoints in two Swedish cohorts
• *Alice Giontella*
The 1q25 T2D-specific cardiovascular locus is associated with Y-glutamyl cycle and glyoxalase system alterations in endothelial cells: a metabolomics study
• *Caterina Pipino*

Nutrizione e metabolismo: quale link con lo scompenso cardiaco?

Moderatrici: Antonella Giammanco, Rosanna Villani

18.10-18.40   **Scompenso cardiaco ed alterazioni metabolico-nutrizionali**
• *Alessio Molfino*

18.40-19.10   Comunicazione orale
Circulating cell-free DNA levels are associated with adverse outcomes in heart failure
• *Valeria Valente*

Comitato organizzatore
Elena Buzzetti (SIMI), Mario Luca Morieri e Chiara Pavanello (SISA), Costantino Mancusi (SIIA)
Dei gruppi giovani ricercatori SIIA, Società Italiana Ipertensione Arteriosa, SIMI, Società Italiana di Medicina Interna e SISA Società Italiana per lo Studio dell'Aterosclerosi.

Comitato scientifico
Revisione Abstract: Francesca Saladini e Giacomo Pucci (SIIA), Antonio Cimellaro e Rosanna Villani(SIMI), Vanessa Bianconi e Antonella Giammanco (SISA)
Workshop: Laura D'Erasmo (SISA)

Moderatori e relatori

Valeria Bisogni	Antonella Giammanco	Chiara Pavanello
Elena Buzzetti	Costantino Mancusi	Martino Pengo
Antonio Cimellaro	Giovanni Meli	Emanuele Rinninella
Andrea Dalbeni	Alessio Molfino	Raffaella Scardigli
Laura D'Erasmo	Sara Montagna	Rossella Spina
Alessia Di Costanzo	Mario Luca Morieri	Rosanna Villani

Programma Giovedì 25 Giugno

Microbiota intestinale, NAFLD e sindrome metabolica
Moderatori: Andrea Dalbeni, Chiara Pavanello

17.00-17.30 **Stile alimentare, infiammazione e malattie metaboliche: il ruolo del Gut microbiota**
• *Emanuele Rinninella*

17.30-18.00 Comunicazioni orali
Genetic background in diabetics: polymorphisms are novel markers for the prediction of NAFLD
• *Francesco Cavallone*
Impaired HDL cholesterol efflux capacity in subjects with metabolically-but not genetically- driven non-alcoholic fatty liver disease (NAFLD)
• *Annalisa Ronca*

Aging, neurodegnerazione e immunità: nuove prospettive in ambito cardiovascolare
Moderatori: Valeria Bisogni, Antonio Cimellaro

18.00-18.30 **Nuove evidenze sulla patogenesi del morbo di Alzheimer: Abeta oligomeri e neurogenesi adulta** • *Giovanni Meli e Raffaella Scardigli*

Comunicazioni orali

18.30-19.00 **Relationship between cognitive impairment and hypertensionmediated organ damage: the VOBARNO study**
• *Chiara Arnoldi*
Interaction between PCSK9 and indoleamine 2,3-dioxygenase in the regulation of the immune response during sepsis
• *Vanesssa Bianconi*

Programma Giovedì 2 Luglio

Workshop - Traslazione Base-Clinica:
Moderatrice: Laura D'Erasmo

17.00-18.30 **Leggere e interpretare le varianti genetiche, dal laboratorio alla clinica attraverso i papers**
• *Alessia Di Costanzo e Rossella Spina*

Informazioni generali

Spring Meeting dei gruppi Giovani Ricercatori di SIIA (Società Italiana Ipertensione Arteriosa), SIMI (Società Italiana di Medicina Interna) e SISA (Società Italiana per lo Studio dell'Aterosclerosi)

Obiettivi

Il meeting vuole favorire l'interazione tra i giovani soci delle società scientifiche coinvolte attraverso il confronto e la discussione di lavori con l'intento di creare nuove collaborazioni inter societarie.

Novità: partecipazione al congresso on-line

Il congresso si svolgerà solo in modalità on-line e potranno parteciparvi solamente coloro che avevano inviato un contributo ed erano già iscritti al meeting residenziale.

I partecipanti riceveranno via email i dettagli per la connessione. Gli incontri si terranno tramite Zoom; verrà inviato un link ad una pagina di registrazione al meeting su piattaforma zoom e in seguito tramite email verranno forniti i dettagli per il collegamento.

Per chi non l'avesse già fatto o non utilizzasse questa piattaforma, consigliamo di scaricare e installare il client zoom in anticipo

Segreteria organizzativa

Fondazione SISA per la promozione della ricerca sulle malattie da arteriosclerosi
Via Balzaretti, 7 - 20133 Milano

Referente

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Sessioni orali

Giovedì 18 Giugno

Giovedì 25 Giugno

Sessioni orali

Abstract selezionati

A new genetic risk score for blood pressure strongly associates with the incidence of hypertension and cardiovascular endpoints in two Swedish cohorts

A. Giontella[1,2], M. Sjögren[2], Luca Lotta[3], John Overton[3], Aris Baras[3], C. Fava[1,2], O. Melander[2]

[1.]Department of Medicine, University of Verona, Verona, Italy
[2.]Department of Clinical Sciences, Clinical Research Center, Lund University, Malmö, Sweden
[3.]Regeneron Genetics Center, Tarrytown, NY, USA.

Aim: The clinical value of the polygenetic component of blood pressure is commonly questioned. We constructed a new BP-GRS, including the most recently published variants genome wide significantly associated with either systolic or diastolic blood pressure (SBP, DBP), to investigate its association to the incidence of hypertension and cardiovascular endpoints in two urban-based cohorts: the Malmö Diet and Cancer (MDC, n=29295) and Malmö Preventive Project (MPP, n=9367).
Methods: The genotyping was performed with the Illumina GWAS chip (*GSA array v1*) and a weighted BP-GRS$_{858}$ based on 858 SNPs was calculated, normalized, and divided into deciles. Logistic and survival Cox regression models were used to test the associations of the new BP-GRS$_{858}$ with outcomes.
Results: At baseline, we found a difference of 11.2 mmHg (SBP) and 6 mmHg (DBP) between top and bottom deciles of BP-GRS$_{858}$. In MPP, the top vs bottom decile of BP-GRS$_{858}$ was associated with doubled risk of incident hypertension (OR, 95%CI:2.2, 1.7-2.8, p-value:$2.0E^{-10}$). In MDC, when comparing top and bottom deciles of BP-GRS$_{858}$, significant association was found between the age and sex adjusted BP-GRS$_{858}$ and the incidence of total cardiovascular events (HR, 95%CI:1.5; 1.3-1.7; p-value:$1.5E^{-12}$), stroke (HR, 95%CI:1.6, 1.4-1.8; p-value:$2.1E^{-9}$), coronary artery disease (HR, 95%CI:1.5, 1.4-1.8; p-value:$1.3E^{-11}$), heart failure (HR, 95%CI:1.5, 1.3-1.8, p-value:$2.5E^{-5}$), atrial fibrillation (HR, 95%CI:1.2-1.1,1.4; p-value:0.001) and total mortality (HR, 95%CI:1.1, 1.0-1.2; p-value:0.009).
Conclusions: Our findings confirm that adding novel genetic variants into a polygenic BP-GRS, despite very low effect sizes of individual variants, increases its predictive performance. BP-GRS$_{858}$ contributes with clinically meaningful predictive information regarding future hypertension and CVD risk. Given that the exposure to high polygenetic risk starts at birth, we suggest that the BP-GRS$_{858}$ might be useful to identify children or adolescents who would benefit from early hypertension screening and treatment.

The 1q25 T2D-specific cardiovascular locus is associated with Y-glutamyl cycle and glyoxalase system alterations in endothelial cells: A metabolomics study

Caterina Pipino[1], Hetal Shah[2], Pamela Di Tomo[1], Gloria Formoso[1], Natalia Di Pietro[1], Assunta Pandolfi[1], Alessandro Doria[2]

[1.]Department of Medical, Oral and Biotechnological Sciences, Università G. d'Annunzio Chieti-Pescara; Italy
[2.]Department of Genetics and Epidemiology, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA

Aim: A variant on chromosome 1q25 (rs10911021) has been previously associated with coronary artery disease (CAD) in individuals with T2D. In human umbilical vein endothelial cells (HUVECs), the 1q25 risk allele ('C') was found to be associated with decreased expression of the adjacent gene *GLUL* encoding the enzyme glutamine synthase catalyzing the conversion of glutamate to glutamine. To further investigate the mechanisms through which the 1q25 locus modulates CAD risk in T2D, the association between rs10911021 genotype and intracellular levels of metabolites involved in glutamate metabolism and gamma-glutamyl cycle was evaluated.
Methods: We performed targeted metabolomics study (LC-MS, Metabolon) in 62 HUVECs. Thirty of these HUVECs were homozygous for the rs10911021 C allele (C/C), 21 were heterozygous (C/T), and 11 were homozygous for the T allele (T/T). Cells were cultured in low (5.5 mM) or stimulated with high (25 mM) glucose.
Results: A total of 35 metabolites were included in this targeted metabolomics analysis and some gamma-glutamyl amino acids had increased levels in HUVEC carrying the 1q25 risk allele. Consistent with the higher gamma-glutamyl amino acids, the risk allele was associated with increased ophthalmate (p=0.04), a marker of gamma-glutamyl cycle malfunction, and decreased S-lactoylglutathione (p=0.016), a possible sign of defective detoxification of the AGE-precursor methylglyoxal.
Conclusions: In summary, we have identified several metabolites potentially mediating the 1q25 locus effect on CAD risk in T2D. These include impairment of the gamma-glutamyl cycle, possibly increasing susceptibility to oxidative stress, and downregulation of MG detoxification. Further studies of these pathways may lead to the identification of novel therapeutic targets to reduce CAD risk in T2D.

Comunicazione Orale - 18 Giugno - Presenting author: **Valeria Valente**

Circulating cell-free DNA levels are associated with adverse outcomes in heart failure

Valeria Valente[1], Muhammad Zubair Israr[2], Daniel Fernandez Garcia[3], Laura Middleton[3], Roberta D'Assante[1], Alberto M Marra[1], Michele Arcopinto[1], Yoshiyuki Yazaki[2], Dennis Bernieh[2], Shabana Cassambai[2], Karen Page[3], Giuseppe Rengo[4], Eduardo Bossone[4], Antonio Cittadini[4], Jacqueline A Shaw[3], Toru Suzuki[2] and Andrea Salzano[2]

[1.]Department of Translational Medical Sciences, Federico II University, Napoli, Italy
[2.]Department of Cardiovascular Sciences, University of Leicester, Leicester, NIHR Leicester Biomedical Research Centre, Leicester, United Kingdom
[3.]Leicester Cancer Research Centre, College of Life Sciences, University of Leicester, Leicester, United Kingdom
[4.]Division of Cardiology, AORN Cardarelli, Napoli, Italy.

Aims: Aims of the present study were to investigate cell free DNA (cfDNA) levels in stable chronic heart failure (HF) patients and their associations with HF clinical status, morbidity, and mortality.
Method : Serum levels of cfDNA were measured in Seventy-one patients with chronic stable HF with ejection fraction (EF) lower than 50% and compared to those of 64 healthy controls.
Results: Compared with cardiovascular disease-free participants, approximately 4-fold higher cfDNA levels were observed in HF patients (p<0.001). Considering only the HF population, when dichotomised at the median value, cfDNA was significantly associated with the composite of all-cause mortality or HF-hospitalisation (death/HF) at 30 months [hazard ratio (95% confidence interval) p value; 2.57 (1.36-4.87) p=0.004]. When adjusted for main clinical parameters (age, NYHA class, sex, aetiology, BNP, and eGFR) cfDNA was able to retain prediction abilities (2.12 (1.04-4.30) p=0.038). Kaplan-Meier survival analyses showed that cfDNA levels were associated with adverse outcomes when stratified by the median (chi-square: 9.32; log rank test p=0.002). In addition, when median BNP levels were considered, elevations in both BNP and cfDNA showed the worst prognosis, significantly different to elevations in only BNP and elevations neither in BNP nor cfDNA (chi-square 4.52, log rang test p<0.03 and 17.83, p<0.001 and respectively). Net reclassification index confirmed a significant gain in risk assessment for the death/HF when cfDNA was added to BNP [0.559 (0.103-1.0136), p= 0.016].
Conclusion: Cell free DNA levels are associated with morbidity and mortality in HF and may offer alternative non-invasive approaches to disease monitoring and risk stratification.

Genetic background in diabetics: polymorphisms are novel markers for the prediction of NAFLD

Cavallone Francesco[1], Villani Rosanna[1], Romano Antonino Davide[1], Serviddio Gaetano[1]

[1.]C.U.R.E. (Centro per la Ricerca e la Cura delle Epatopatie), Institute of Internal Medicine, Department of Medical and Surgical Sciences, University of Foggia, Italy.

Aim: The prevalence of NAFLD in T2DM patients ranges from 30 to 87% with a pooled prevalence of 60%. Several genetic modifiers of NAFLD have been identified, whereas the role of genetic factors on the development of steatosis or NASH in diabetic patients was not investigated to date. The aim of the present study was to assess whether the polymorphisms could improve the risk prediction of NAFLD in diabetic patients.

Materials and methods: We enrolled patients grouped in four study populations according to the presence or absence of T2DM and NAFLD (T2DM+/NAFLD+; T2DM+/NAFLD-; T2DM-/NAFLD+; T2DM-/NAFLD-). Ultrasound examination for detection and assessment of severity of hepatic steatosis, liver function tests, transient elastography and genotyping PNPLA3, SOD2, KLF6 and LPIN1 Single-Nucleotide Polymorphisms (SNPs) were performed.

The PNPLA3 rs738409 C>G, SOD2 rs4880 C>T, KLF6 rs3750861 T>C, and LPIN1 rs123445678 T>C SNPs were detected by Taqman assays. Frequencies of genotypes and alleles were recorded.

Results: One hundred and sixty-five patients were included in the final analysis. Prevalence of NASH in T2DM+/NAFLD+ group was 10% whereas 4% of patients had cirrhosis.

No differences were observed in genotype and allele frequencies of PNPLA3 rs738409, SOD2 rs4880 and KLF6 rs3750861.

Genotype frequencies of LPIN1 rs123445678 were statistically different between T2DM-/NAFLD- vs T2DM-/NAFLD+ patients (p=0.0084) and between T2DM-/NAFLD- vs T2DM+/NAFLD+ patients (p=0.0084). Most of T2DM patients with NAFLD were carriers of the LPIN1 rs123445678 C/C genotype. Eighty percent of patients with T2DM and liver steatosis carried allele C of LPIN1 rs123445678 and all patients with LPIN1 C/C genotype had liver steatosis (vs 70 % of patients with T/T genotype). All patients with T2DM and severe liver steatosis or NASH had LPIN1 C allele and concomitant KLF6 allele C.

Conclusion: Single-nucleotide polymorphisms of genes involved in lipid metabolism contributes to prediction of NAFLD in diabetic patients.

Impaired HDL cholesterol efflux capacity in subjects with metabolically- but not genetically-driven non-alcoholic fatty liver disease (NAFLD)

A. Ronca[1], A. Di Costanzo[2], L. D'Erasmo[2], M. Manfredini[3], F. Baratta[4], D. Pastori[5], L. Polito[2], M. Di Martino[6], F. Angelico[7], M. Del Ben[5], E. Favari[1], M. Arca[2]

[1.]University of Parma, Department of Food and Drug, Parma, Italy, [2.]Sapienza University or Rome, Translational and Precision Medicine, Rome, Italy, [3.]University of Parma, Parco Area delle Scienze, Department of Chemistry, Life Sciences and Environmental Sustainability, Parma, Italy, [4.]Sapienza - University of Rome, Department of Clinical, Internal, Anesthetic and Cardiovascular Sciences., Rome, Italy, [5.]Sapienza - University of Rome, Department of Clinical, Internal, Anesthetic and Cardiovascular Sciences., Rome, Italy, [6.]Sapienza University of Rome, Department of Radiological Sciences, Rome, Italy, [7.]Sapienza - University of Rome, Department of Public Health and Infectious Diseases, Rome, Italy

Aims: NAFLD is a common multi-factorial disease characterized by increased hepatic fat. Although NAFLD associates with increased risk of ASCVD, we speculate that this risk could differ in the different NAFLD subtypes, e.g. metabolically or genetically-*PNPLA3* I148M driven. Cholesterol efflux capacity (CEC) represents a key metric of HDL function able to predict ASCVD. This project was designed to test whether CEC is altered in metabolically- but not in genetically- determined NAFLD.
Methods: CEC was measured in 19 individuals with NAFLD due to metabolic disturbances and wild-type *PNPLA3* genotype (group M), 10 patients with NAFLD associated with the rs738409 *PNPLA3* GG genotype (group G) and 10 blood donors,*PNPLA3* wild-type and without NAFLD (Controls). Hepatic fat fraction (HFF) was measured using magnetic resonance (MRS/MRI). HDL CEC was evaluated by radio isotopic techniques.
Results: Compared with group G, CEC of group M was impaired both as a whole (-19%; $P<0.001$) and with respect to specific cholesterol transporters (-25% ABCA1; -16.3% ABCG1; -15.4% SRBI; -14.2% aqueous diffusion; all$P<0.04$). No difference in total CEC was found between group G and controls. As total CEC values positively correlated with HDL-C levels, we further distributed HDL-C values according to quartiles, showing that plasma isolated from group M individuals promoted significantly lower total CEC compared to group G cases with similar HDL-C levels ($P<0.025$).
Conclusions: Metabolically, but not genetically driven NAFLD may be associated with dysfunctional HDLs. These data led us to concentrate our attention on the functionality of HDL as a potential link between metabolic driven NAFLD and subclinical atherosclerosis.

Relationship between cognitive impairment and hypertensionmediated organ damage: the VOBARNO Study

C Arnoldi, S Capellini, L Zuccotti, A Paini, M Salvetti, L Rozzini, C Aggiusti, F Bertacchini, D Stassaldi, G Saccà, L Verzeri, A Padovani, ML Muiesan

Clinica Medica - 2 Medicina & Clinica Neurologica, Università di Brescia & ASST Spedali Civili di Brescia

Several studies have suggested the presence of a relationship between hypertension in mid-life and the subsequent development of mild cognitive impairment (MCI) and dementia.
Aim: to analyze the relationship between baseline blood pressure (BP), cardiovascular risk factors and presence of Hypertension Mediated Organ Damage (HMOD) and cognitive performances analyzed after a follow-up period of 12 years in 149 subjects participating into the Vobarno Study.
Methods: 149 subjects (52% female, mean age 54.9 ±8, 9±3.25 school years, 59% hypertensives) underwent blood chemistry, arterial pressure measurement, echocardiography, carotid doppler ultrasound and measurement of central arterial pressure (PWA) and carotid-femoral pulse wave velocity (PWV). All subjects underwent a neuropsychological evaluation with standardized tests performed at a follow-up visit 12 years later.
Results: 57 subjects with MCI at follow-up had baseline higher arterial pressure values (PAS and PP clinical and 24h $p<0.05$), IMT (1.23 ± 0.34 vs 1.12 ± 0.25 $p<0.05$), and PWV (11.45 ± 3.37 m/sec vs 10.49 ± 1.74 $p<0.05$) than those observed in the 92 subjects without MCI. Subjects with MCI were divided in two groups according to presence of amnesia (18 and 21% of total, respectively). Baseline IMT was significantly higher in subjects who developed non-amnesic MCI when compared with patients without MCI (Meanmax 1.30 ± 0.36 mm vs 1.12 ± 0.25 mm $p<0.05$; CBmax 1.30 ± 0.29 mm vs 1.16 ± 0.24 mm $p<0.05$); no differences were found between amnesic and non-amnesic subjects.
Conclusion: our results show that baseline presence of hypertension and HMOD may be associated with cognitive performance detected after a mean period of 10 years. Aortic stiffness (measured as PWV) appears to be a less sensitive predictor of cognitive decline than increased IMT.

Interaction between PCSK9 and indoleamine 2,3-dioxygenase in the regulation of the immune response during sepsis

Vanessa Bianconi[1], Massimo R. Mannarino[1], Marco Gargaro[2], Francesca Fallarino[2], Matteo Pirro[1]

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Aim: Exact mechanisms explaining immune regulation during sepsis stay unclear. Proprotein convertase subtilisin/kexin type 9 (PCSK9)-mediated degradation of low-density lipoprotein (LDL) receptor (LDLR) has been recently implicated in the persistence of circulating lipopolysaccharides (LPS) and activation of immune response during sepsis. The enzyme indoleamine 2,3-dioxygenase (IDO1) is currently considered to be crucial in counteracting Th1 immune activity during sepsis. We aimed to explore the existence of a possible crosstalk between IDO1 and PCSK9 in the regulation of the immune response during sepsis.
Methods: This is a case-control study enrolling 50 patients admitted to the Unit of Internal Medicine with diagnosis of sepsis (Sepsis-3 criteria) and 50 age-, sex-, and LDL-cholesterol-matched non-septic controls. Plasma PCSK9 concentration and kynurenine/tryptophan ratio (IDO activity) were measured, as well as plasma neopterin levels, reflecting macrophage activation in Th1 immune response.
Results: Patients with sepsis had significantly higher plasma PCSK9 levels [672 (336-859) vs 221 (120-334) ng/mL], IDO activity [93 (49-210) vs 41 (35-50) μmol/mmol] and neopterin levels [51,3 (23,3-80,9) vs 7,3 (5,2-9,9) nmol/L] as compared to controls. Among patients with sepsis no significant correlation between PCSK9 levels and IDO activity (rho=0,25, p=0,09) was found, whereas a positive correlation between PCSK9 and neopterin levels (rho=0,44, p=0,003) was observed. In the multivariate analysis a positive association between LG-IDO activity (dependent variable) and LG-PCSK9 levels (independent variable) (β=0,32, p=0,008) was found after adjustment for covariates of IDO1 activity, including age (β=0,43, p=0,001), gender (p=NS) and creatinine levels (β=0,38, p=0,002); however, this association (LG-IDO / LG-PCSK9) was abolished (β=0,15, p=0,21) by including in the same model LG-neopterin levels as an independent variable.
Conclusions:
This study suggests a crosstalk between macrophage activation and PCSK9 metabolism as well as IDO1 activity during sepsis. However, it does not support the existence of an independent interaction between IDO1 and PCSK9 in the regulation of the immune response.

Abstract selezionato - Presenting author: **Lorenzo Airale**

Prognostic role of the ascending aorta dilatation in patients with arterial hypertension

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Aim: the aim of the study was to evaluate the possible prognostic value of ascending aorta dilatation (AAD) as predictor of cardiovascular (CV) events in an essential hypertensive population.
Methods: patients were recruited prospectively and underwent 2D transthoracic echocardiography from 2007 to 2013. Follow-up has been established on November 2018 by phone call and by hospital information system. AAD has been defined using absolute parameters: 36 mm in female, 41 mm in male.
Results: 423 hypertensive patients were included in our study. Most of patients were male (79%) and overweight (66%). Means ascending aorta diameter was 35.1±5.3 and AAD prevalence was 16%, without sex difference. During a median follow-up of 7.4 years (interquartile range 5.6-9.1 years), a total of 60 events were observed. Within general hypertensive population, AAD showed to be able to stratify 7 years CV risk at Kaplan-Meyer analysis (HR=3.20, p<0.001). This result was confirmed at multivariable Cox regression including age, pulse wave velocity (PWV) >10m/s and left ventricular hypertrophy (LVH): AAD was the only independent predictor of CV events together with age. We simultaneously take into account the presence of AAD and LVH: among patients without LVH, AAD was associated with a higher 7-years-risk for CV event (HR=3.41, p<0.001). Moreover, we observed that in absence of AAD, isolated sinus of Valsalva dilatation (SVD) lost any prognostic value (HR= 1.50, p=0.525).
Conclusions: AAD is associated with an increased risk of CV events, regardless of the main confounders. Among patients without LVH, AAD is able to ristratify CV risk, whereas SVD seems to lose his prognostic power in patients without AAD. In perspective, ascending aortic evaluation could optimize CV risk stratification of patients with arterial hypertension.

Abstract selezionato - Presenting author: **Anna Astarita**

Central pulse pressure is inversely associated with proximal aortic remodeling

Anna Astarita[a], Francesco Tosello[a], Andrea Guala[b], Fabrizio D'Ascenzo[c], Martina Bollati[a], Dario Leone[a], Luca Sabia[a], Giulia Bruno[a], Giulia Mingrone[a], Fabrizio Vallelonga[a], Eleonora Avenatti[a], Claudio Moretti[c], Franco Veglio[a], Luca Ridolfi[d], Alberto Milan[a]

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Aim: Hypertension leads to aortic stiffening and dilatation but unexpected data from the Framingham Heart Study showed an inverse relationship between brachial pulse pressure and aortic diameter. Proximal aortic dilatation would be associated with lower pulse pressure, but would also predispose to a worse prognosis (cardiac events, heart failure).
The purpose of this study was to evaluate the relationship between invasively-measured central blood pressure and proximal aortic diameter adjusted for age, gender and body height (Z score).
Methods: In 71 consecutive patients referred to invasive hemodynamic study, proximal aortic remodeling was evaluated in terms of Z-score, comparing diameters measured at the Sinus of Valsalva to the diameter expected according to patients' age, gender and body height. Pressures were recorded directly in the proximal aorta by means of a catheter before coronary assessment.
Results: In this cohort, aged 67 ± 10 years (77.5% men) mean invasive aortic systolic and diastolic blood pressures were 146 ± 23 and 78 ± 13 mmHg, respectively, giving a central pulse pressure (cPP) of 68 ± 21 mmHg. Proximal aortic diameter was 34.9 ± 19.4 mm, while Z-score was -0.3 ± 1.7. In bivariate analysis, invasive cPP was inversely related to Z-score ($R = -0.271$, $p = 0.022$) and positively related to age and mean blood pressure. Subjects with higher cPP showed a significantly lower Z-score (-0.789 vs. 0.155, $p=0.001$).
In a stepwise multiple regression analysis Z-score at the sinuses of Valsalva was independently and inversely related to invasive aortic pulse pressure ($\beta = -0.241$, $p = 0.011$).
Conclusions: Aortic root Z-score is inversely associated with invasively-measured central pulse pressure in a cohort of subjects undergoing invasive coronary assessment. Remodeling at the sinuses of Valsalva may be a compensatory mechanism to limit pulse pressure.

Abstract selezionato - Presenting author: **Andrea Baragetti**

Early cellular senescence with elevated ldl cholesterol burden

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Background: Telomere length shortening (TLS) is believed a marker of cellular senescence and associates with chronic diseases, including cardiovascular disease (CVD). The impact of a number of CV risk factors on TL shortening was demonstrated, but that of elevated LDL cholesterol (LDL-C) has been investigated only in a small number of populations of clinically diagnosed FH subjects.
Objectives: We aimed at assessing the relationship between LDL-C levels and TLS in subjects with genetically determined familial hypercholesterolemia (FH), in those with clinically diagnosed, but not genetically confirmed FH (CD-FH) or normocholesterolemic subjects (as controls). Findings were then recapitulated in rodent models of hypercholesterolemia (LDLR-KO) to dissect whether premature ageing relates to hematopoietic concerns.
Methods: We measured leukocytes telomere length (LTL) on mononuclear cells-derived genomic DNA from 206 hypercholesterolemic subjects. Genome sequencing identified 135 heterozygous hypercholesterolemic subjects (HeFH) (mutations on *LDLR*) and 71 CD-FH. Clinical parameters and LTL were compared to those of 272 normocholesterolemic, age-matched subjects.
Results: LTL of HeFH was shorter (1.275±0.069 *vs* 1.592±0.042, p= 0.045) compared to controls; this was confirmed in young subjects (<35y) (1.339±0.081 *vs* 1.639±0.081, p=0.019) and in statin-naïve subjects (1.229±0.083 vs 1.583±0.040, p= 0.001). LTL was shorter in HeFH vs CD-FH (1.334±0.047 vs 1.547±0.082, p=0.029), matched for LDL-C levels. In LDLR-KO mice shorter TL in blood was found, which associated with higher long-term hematopoietic stem and progenitor cells (LT-HSPCs) but lower Multi-Potent Progenitor cells (MPPs) in bone marrow. These reductions paralleled altered proliferative capacity of yet at LT-HSPCs level. Also reduced CD34+CD45dim circulating cells, an indicator of human circulating hematopoietic precursors, were found in aged-matched HeFH subjects (n=25) compared to CD-FH (n=14) and controls (n=30), independently from statin treatment.
Conclusions: FH associates with TLS and reduced hematopoietic precursors counts, suggesting that genetically elevated LDL-C results in early cellular senescence. This alteration mirrors hematopoietic alterations both in replication and in egress from bone marrow niches. Whether these aspects contribute to premature CV morbidity in FH remains unexplored.

Serum bacterial lipopolysaccharides and platelet activation in NAFLD: the missing link between liver and cardiovascular disease?

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Aim: recent experimental and observational studies suggest a possible role of platelets in in non-alcoholic steatohepatitis (NASH) and a favourable effect of aspirin in for its prevention. However, the actual role of platelets in the pathogenesis of fatty liver and on the increased cardiovascular risk associated with it is still unclear. Aim of our studies was to investigate platelet activity in the liver and peripheral circulation and to evaluate the potential effect of LPS on its modulation.
Methods: first study was carried out in 44 patients with NASH, 50 with simple steatosis (NAFL) and 50 metabolic patients without NAFLD where we measured serum Thromboxane(Tx)B2, a marker of cyclooxygenase-1 activation, plasma soluble P-selectin (sP-selectin), an in vivo marker of platelet activation and serum lipopolysaccharide (LPS). Second study was conducted in 25 patients with NAFL, 25 patients with NASH and 10 liver donors where immunohistochemistry was performed in liver specimen to identify TLR4+ platelets and CD61+ platelets and LPS+ hepatocytes. In addition, serum LPS was measured.
Results: in the first study, serum TxB2 ($p<0.001$) as well as sP-selectin ($p<0.001$) were higher in patients with NASH/NAFL compared to controls; serum LPS correlated with serum TxB2 (rS=0.30;$p<0.001$) and with sP-Selectin (rS=0.32;$p<0.001$). The independent association between serum LPS above median and sP-selectin above median was confirmed at multivariate analysis (O% [???]=3.15,p=0.015). In the second study, NASH patients had higher serum LPS ($p<0.001$) and hepatocytes LPS localization than controls ($p<0.05$); NASH biopsies showed more CD61+ platelets, and most of them were TLR4+ ($p<0.05$). TLR4+ platelets correlated with serum LPS (p=0.001).
Conclusions: patients with NAFLD display enhanced systemic platelet activation, which is associated to cyclooxygenase-1 up-regulation, and higher number of activated platelets in liver biopsies. Both phenomena correlate with LPS which can favor systemic and local platelet activation.

Abstract selezionato - Presenting author: **Francesca Battista**

Functional capacity and comorbidities in patients with moderate and severe obesity.

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Aim: Cardiorespiratory fitness is a strong predictor of morbidity and mortality also in people with obesity. However, no reference values of aerobic capacity are currently available for subjects with severe obesity and comorbidities. This study describe the distribution of aerobic capacity in a group of patients with severe obesity and its relationship with comorbidities.
Methods: observational study on 542 patients (69% Females) with BMI ≥30 Kg/m^2 that consecutively performed a Cardiopulmonary Exercise Test (CPET) by using incremental ramp treadmill test (modified Bruce protocol) or bicycle ergometer test (+15W/minute). Anthropometric and clinical data were recorded simultaneously.
Results: The median (IQR) age is 47.0(62) years, mean BMI is 41.7±6.7 Kg/m2. Normal values curves have been developed for relative VO2peak (VO2peak/Kg) that shows mean value of 20.9±4.8 ml/min/Kg (median/IQR=20.3/37.6 ml/min/Kg). Upper limit of the lower quartile of VO2peak/kg is 17.87 ml/min/Kg. Mean absolute VO2peak is 2.410±6.7 L/min. Analysis of covariance (ANCOVA) displays that VO2peak/kg inversely correlates with age (p.0001) and BMI (p.0001) and also a significant effect of the interaction term age*BMI (p.0001). ANCOVA of absolute VO2peak shows direct correlation with BMI (p.0001), inverse correlation with age (p.0001) and significant effect of the interaction term age*gender (p.0006). Both relative and absolute VO2peak are lower in females than in males (p.0001). A multivariate logistic regression model points out that the odds of belonging to the lower quartile of VO2peak/kg is independently determined by age (age 47-54 years OR 2.549 IC 95% 1.205-5.392 p<.0001) and BMI (BMI >45 Kg/m2 OR 5.864 IC 95% 2.920-11.778 p<.0001), but not by number of comorbidities.
Conclusions: VO2peak/Kg decreases with increasing age and BMI both in males and females, but at highest BMI (>45 Kg/m2) the age effect is lower. Age and very high BMI, but not comorbidities, are independent determinants of low VO2peak/kg

Abstract selezionato - Presenting author: **Rossella Bellini**

Glycans profile in monocytes and lymphocytes under hypercholesterolemic conditions

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Aim Increased amount of glycosylation on T cells surface results in the augmented immune response. Our aim was to profile immune cells glycans signature during atherosclerosis.
Methods Sialic acid (SIA) and mannose expression on the surface of T cells and monocytes from blood of LDL-R KO mice fed with chow or WTD for 8 weeks and FH patients was analysed by flow cytometry via WGA (Sialic acid and N-acetyl-D-glucosamine) and ConA (mannose) lectin binding to immune cells.
Results In parallel with increase cholesterolaemia in WTD fed LDL-R KO mice compared to chow (635.7±36.77mg/dL;199.9±13.73mg/dL), circulating lymphocytes and monocytes from LDL-R KO mice fed with WTD presented increased expression of SIA compared to chow fed mice (1.88±0.14-fold for CD4^{+}, 1.78±0.51-fold for CD8^{+}, 2.03±0.1-fold* for Ly6c[Low] and 1.78±0.4-fold for Ly6c[High] cells). Viceversa, changes in mannose expression are not significant (0.83±0.04-fold for CD4^{+}, 0.79±0.04-fold for CD8^{+}, 0.87±0.05-fold for Ly6c[Low] and 0.76±0.05-fold for Ly6c[High] cells. (*$p<0.05$)
In line with these findings, circulating cells from FH patients presented increased SIA levels (5.44±0.83-fold** for CD4^{+}, 4±0.32-fold** for CD8^{+}, 2.95±0.13-fold** for CD14^{+} and 2.76±0.1-fold** for CD16^{+}) compared to controls, while no differences were observed in the amount of mannose (1.15±0.05-fold for CD4^{+}, 1.21±0.14-fold for CD8^{+}, 1.28±0.06-fold for CD14^{+}, 0.21±0.22-fold for CD16^{+}). (**$p<0.01$)
Conclusions Our data indicate that hypercholesterolaemia impacts glycans signature on circulating immune cells in humans and in experimental models. Whether the increased SIA/mannose ratio observed in hypercholesterolaemic conditions could mark a setting associated with augmented immune cells activation during atherosclerosis is under investigation.

Abstract selezionato - Presenting author: **Fabio Bertacchini**

Left atrial enlargement in patients undergoing an echocardiogram for cardiovascular risk stratification at an ESH excellence centre in Italy

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Background Left atrial (LA) enlargement (LAE) is associated to an increased risk of cardiovascular complications, and in particular of atrial fibrillation. The 2018 ESH/ESC Hypertension guidelines suggested the use of LA volume instead of linear dimensions, and for the first time proposed the indexation to height^2(h^2)

The aim of our study was to assess the prevalence of left atrial dilatation in a large sample of patients undergoing an echocardiogram for cardiovascular risk stratification at an ESH excellence centre in Italy.

Design and methods 3872 subjects undergoing a diagnostic work-up for arterial hypertension (known or suspect) were analysed. The mean age was 56±15 years, BMI 26±5, 44% normal weight, 39% overweight, 17% obese, 53% males. Left atrial volume was measured by the area-length method using the apical 4-chamber and 2-chamber views.

Results The prevalence of left ventricular hypertrophy (LVH) was 11% when indexing for BSA and 12% when indexing for height$^{2.7}$. LAE was observed in 30% of subjects when indexing for h^2 and in 9% when indexing for BSA. In obese or overweight subjects the prevalence of LAE was 38% of subjects when indexing for h^2 and in 11% when indexing for BSA. The different prevalence of LAE was particularly evident in extremely obese patients.

LAE was very common in patients with LVH: 62% and 26% when indexing for h^2 and for BSA, respectively. Interestingly, it was frequent also in patients without LVH, in particular when the indexation for h^2 was used (25% as compared to 7% when indexing for BSA).

Conclusions In a large sample of subjects undergoing a diagnostic work-up for arterial hypertension LAE was frequently observed, particularly when the new indexation proposed by the 2018 ESH/ESC hypertension guidelines was used. Even in the absence of clear-cut LVH, LAE was observed in one quarter of subjects. The indexation to BSA leads to an under-recognition of LAE, in particular in patients with overweight and/or obesity.

Development of systolic dysfunction in hypertension

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Aim While it is commonly thought that left ventricular (LV) systolic function may insidiously deteriorate in hypertensive patients, few prospective data are available to support this notion.
Methods We evaluated 680 hypertensive patients (66±7 years; 45% women) with ECG-LV hypertrophy enrolled in the LIFE echo-substudy. Only patients free of prevalent cardiovascular disease and with baseline ejection fraction (EF)≥55% were included. Echocardiographic exams were performed annually for 5 years during anti-hypertensive treatment. Development of reduced systolic function was defined as incident EF<50%.
Results During a mean follow up of 4.8±1 years, 37 patients developed reduced EF without an intercurrent myocardial infarction (5.4%). Patients who developed reduced EF were more often men (p<0.05). In analysis of covariance, patients who developed reduced EF had greater baseline LV diameter and LV mass, lower mean EF (all p<0.05), and similar diastolic function indices. At last available exam before EF reduction, independently of covariates, patients with reduced EF showed a significant increase in LA size, LV diameter, end-systolic stress and mitral E/A ratio, as compared to those who did not develop reduced EF (all p<0.05). In time-varying Cox regression analysis, also controlling for baseline EF, predictors of developing reduced EF were higher in-treatment LV diameter (HR=5.19 per cm; 95%CI:2.58-10.41) and higher in-treatment mitral E/A ratio (HR=2.37; 95%CI:1.58-3.56; both p<0.0001).
Conclusions In treated hypertensive patients, incident reduced EF is associated with the development of dilated LV chamber and signs of increased LV filling pressure. Higher in-treatment LV diameter and mitral E/A ratio are the strongest echocardiographic predictors of reduced EF.

Abstract selezionato - Presenting author: **Michele Bevilacqua**

Effects of Direct Acting Antiviral Agents on lipid and glucose profile in Hepatitis C virus patients with type 2 diabetes: A cohort study based on fibrosis grade

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Background and aims: Hepatitis C virus (HCV) infection is associated with an increased risk of type II Diabetes Mellitus (T2DM) and cardiovascular (CV) disease. To date, evidences regarding the effects of HCV eradication by direct acting antiviral agents (DAAs) on metabolic profile are scarce, especially in high CV risk patients. The aim of this study is to evaluate the effects of DAAs on plasma lipid and glucose in a cohort of HCV patients stratified according baseline fibrosis grade and diabetes.

Method: 413 consecutive patients were enrolled and followed for 8.7 (5.6-26.7) months after achieving sustained virologic response (SVR) after 12 weeks of DAAs. Fibroscan-Transient Elastography was performed to assess liver fibrosis. T2DM was diagnosed according WHO criteria.

Results: At baseline, 52 patients (12.6%) had T2DM (18 of them were F1-F3 and 34 of them were F4, according to METAVIR with FibroScan. At baseline, a better lipid profile was shown in F1-F3 diabetic patients compared with non-diabetic ones, which could mainly be due to a more frequent use of statins; no differences were found between diabetic and non-diabetic F4 participants. At follow-up visit, a significant improvement of transaminases, albumin and liver stiffness was found in both F1-F3 and F4 diabetic subgroups. As regards diabetics, F4 but not F1-3 patients showed a significant increase of total cholesterol (T0: 140 (101-249) mg/dL to T1: 153 (111-203) mg/dL; p= 0.018) and LDL cholesterol (T0: 60.3 mg/dL (32-120) to T1: 87.6 mg/dL (41.8-162); p=0.017) without changes in the glucose profile.

Conclusion: DAAs treatment was associated with worsening of lipid profile (in particular LDL), especially in F4. Our results suggest to carefully monitor CV risk factors and dyslipidaemia in all diabetic patients after HCV eradication with DAAs.

Abstract selezionato - Presenting author: **Paola Bigolin**

A strange case of acute ischemic lower limb

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Aim: Acute limb ischemia (ALI) is a rapid decrease in lower limb blood flow due to acute occlusion of peripheral artery and in ALI not only limbs but also life prognosis will be poor unless quick and appropriate treatment is given. The aetiology is broadly divided into embolism and thrombosis with various comorbidities. An atipical case of ALI is presented to illustrate the diagnostic and therapeutic approach.

Methods: A 87-year-old woman had history of hypertension, hypercholesterolaemia, permanent atrial fibrillation in dabigatran 110 mg twice a day interrupted by herself from about one month (CHA$_2$DS$_2$-VASc 4, HAS-BLED 1). In the last 15 days she presented asthenia in the legs, for which "she struggled to stand up" and tight calf claudicatio intermittens (at 50 meters) bilateral with paraesthesias of the feet at rest. Physical examination revealed pulsseless of dorsal pedis arteries, pallor, hypothermia, paralysis, tropic skin lesion. Electrocardiography showed atrial fibrillation. EchocolorDoppler (ECD) of legs described a bilateral peripheral artery disease of the lower limbs, more severe on the left, with prevalent localization of femoral popliteal and superficial and popliteal left femoral with acute thrombosis with total occlusion of both the popliteal artery. Ankle-brachial index (ABI) was abnormal (0,62 and 0,31 respectively on the right and on the left side). Computed tomography confirmed. The patient underwent endovascular therapy with thrombus fragmentation and the flow was restored.

Results: Her lower limbs became warm during therapy and symptoms improved (ABI 1,09 bilateral, normal result). Finally, the patient was discharged with non-vitamin K anti-coagulant.

Conclusion: ALI is a critical condition with high mortality and morbidity rate. Early recognition and early revascularization are essential. Endovascular treatment is one minimally invasive procedure with effect and quick response. History and objective examination are important for the classification of the problem (symptoms and signs, atrial fibrillation. known peripheral arterial disease, Previous revascularization intervention, date of onset of the problem). ECD is important to see the level of occlusion and useful for confirming the cause (however not always permanent). ALI is a serious disease requiring urgent treatment, and it is essential to promptly perform the best initial treatment that can be performed at each facility.

Abstract selezionato - Presenting author: **Simone Bini**

Evolving trends in the management of Heterozygous Familial hypercholesterolemia in Italy

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Background and Aims: The effective reduction of LDL-C in patients with heterozygous familial hypercholesterolemia (HeFH) is crucial to reduce their increased cardiovascular risk. Diagnostic and therapeutic (PCSK9 inhibitors) tools to manage HeFH improved in recent years. However, the impact of these progresses in ameliorating the contemporary real-world care of these patients remains to be determined. Aim of this study was to assess the evolution of treatments and LDL-C control in a cohort of HeFH patients in Italy.
Methods and Results: Four hundred six clinically diagnosed HeFH followed in a single, tertiary lipid centre were included in this survey. Data on lipid levels and medications were collected at baseline and during a median 3-year follow-up. At baseline, 38% of patients were receiving conventional high-potency lipid lowering therapies (LLT) and this percentage increased up to 68% at last visit. Females were less treated than males and the knowledge of results of molecular diagnosis was associated with a significant increase in treatment intensity and LDL-C lowering. Nevertheless, the new LDL-C target (<70 mg/dl) was achieved only in 3.6% of HeFH patients under conventional LLTs and this proportion remained low (4.7%) also in those exposed to maximal conventional LLT. In 51 patients prescribed with PCSK9 inhibitors, 64.6% and 62.1% reached LDL-C<70 mg/dl at 3- and 12-month follow-up, respectively.
Conclusions: Although treatments of HeFH improved over time, LDL-C target achievement with conventional LLT remains poor, mainly among women. The use of molecular diagnosis and even more the prescription of PCSK9i may improve LDL-C control in these patients.

Abstract selezionato - Presenting author: **Marco Biolcati**

Clinical and echocardiographic features of patients affected by heart failure with mid-range ejection fraction compared to reduced and preserved

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Aim: The 2016 ESC guidelines classify Heart Failure (HF) according to levels of Ejection Fraction (EF) in HF with reduced EF (HFrEF, EF<40%), preserved (HFpEF, EF≥50%) and the newborn mid-range (HFmrEF, EF 40-49%). The aim of our work is to analyse clinical and echocardiographic features of patients hospitalized for HF when divided accordingly to their admission EF, focusing on HFmrEF.

Methods: We enrolled 192 patients hospitalized in the Internal Medicine of our hospital between January and September 2017. We collected data on clinical history, P.E., laboratory tests, pharmacological treatment and echocardiography; follow-up for subsequent fatal and non-fatal events ended in May 2018.

Results: Prevalence of HFpEF (55.21%) is higher than HFrEF (23,60%) and HFmrEF (17,19%). Mean age is 80.9±8.3 years, and does not differ among groups. HFpEF are more commonly female, show higher SBP at the presentation (p<0,001) and have more non-cardiac comorbidities, such as renal dysfunction (p<0,001), anemia (p=0,05), COPD (p=0,036) and also AF (p=0,04); in this group hypertensive aetiology is significantly prevailing (p=0,002). On the contrary previous myocardial ischaemia and higher NT-proBNP levels on the admission (p=0,038) are typical in HFrEF. Diastolic and systolic dysfunctions co-exist in patients and many candidates show marks of inverse remodelling. HFmrEF carry intermediate attributes (prevalence of CAD and systemic multimorbidities) and exhibit a 'hybrid' US hypertrophy pattern (high RWT, medium LVMi); compared to the other groups, they include the lowest trend on NYHA classification (I-II, p=0,027), a less aggressive treatment with the shortest number of drugs and dosages (p=0,04) and show decreased mortality and rehospitalization rates. During the follow-up, patients with HFmrEF experience more longitudinal transition among groups (33% becomes HFpEF and 23% HFrEF).

Conclusions: HFmrEF share features of both HFrEF and HFpEF, with a high prevalence of CAD and non-cardiac comorbidities, and a large longitudinal transition to the other two classes.

Abstract selezionato - Presenting author: **Andrea Boccatonda**

Ultrasound evaluation of abdominal fat: correlation with anthropometric and bioimpedenziometric data in obese patients

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Aim: the aim of our study was to correlate the values obtained through the ultrasound evaluation of subcutaneous fat (SAT), previsceral and visceral (VAT) with anthropometric and bioimpedenziometric data.

Methods: a clinical evaluation was performed with measurement of anthropometric parameters and bioimpedenziometry. A 3.5 MHz convex probe was placed 2 cm above the navel along the xipho-umbilical line to determine the VAT, by measuring the distance between the internal surface of the abdominal rectum and the anterior wall of aorta. The thickness of the SAT was measured as the distance between the external surface of the rectus abdomen and the skin. The thickness of the pre-peritoneal fat was measured on the xipho-umbilical line as the distance between the internal surface of the alba line and the liver surface [1].

Results: we recruited 14 subjects (4 males and 10 females), with an average age of 49 years. The SAT value showed a median value of 3.34 cm; the preperitoneal 0.7 cm; and VAT 6.43 cm. SAT correlated with weight ($p = 0.02$; Rho = 0.613), with BMI ($p = 0.014$; Rho = 0.640), with waist circumference ($p < 0.001$; Rho = 0.850), WHR ($p = 0.023$; Rho = 0.601), with MG kg bas ($p = 0.033$; Rho = 0.673), basal visceral fat ($p = 0.034$; Rho = 0.706), MB bas ($p = 0.015$; Rho = 0.810). Preperitoneal fat correlates with BMI ($p = 0.027$; Rho = 0.587), with hip circumference ($p = 0.03$; Rho = 0.579), with VAT ($p = 0.002$; Rho = 0.726). VAT correlated with BMI ($p = 0.025$; Rho = 0.596), with waist circumference ($p = 0.019$; Rho = 0.616).

Conclusions: ultrasound measurement of abdominal fat seems to be a method of simple application, at low cost, without contraindications. It shows a good correlation with the bioimpedance measurement.

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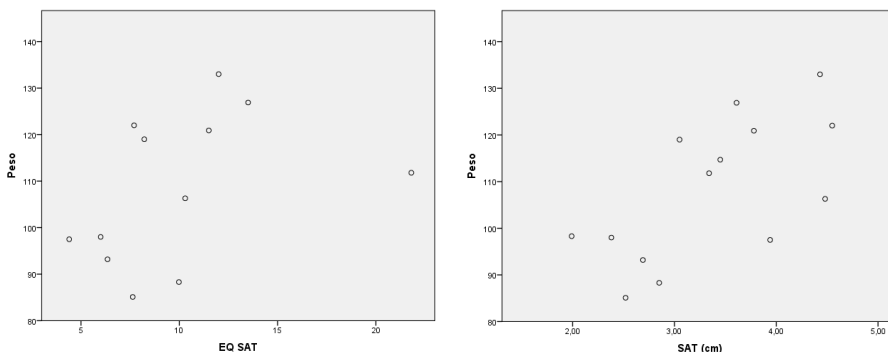
Low density lipoprotein receptor (LDLR) deficiency perturbs CD8+ T cell metabolism and activation

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Aim: Cholesterol is essential for immune cell homeostasis. We evaluated the role cellular cholesterol acquired via the LDLR pathway on Tcell biology.
Methods: Immunophenotypic characterization of T cells from WT and LDLR KO mice was performed in vitro (anti-CD3/CD28) and in vivo (vaccination, homeostatic proliferation in Rag2 KO mice adoptively transferred with Tcells from LDL-R KO and WT mice). In parallel, T cells from FH patients with LDLR mutations were tested.
Results: LDLR expression increased after in vitro activation of CD8+ Tcells and its deficiency mainly affected CD8+ proliferation (-35%, $p<0.01$) paralleled by a reduction in INFγ production (-39.6%,$p<0.01$). In vivo antigen-specific activation (vaccination with ovalbumin), but not homeostatic proliferation, resulted in a decreased proliferation and cytokines production (↓IFNγ $p<0.001$, ↓IL13 $p<0.01$, ↓perforin $p<0.05$) in CD8+ of KO mice together with reduced expression of CD69 (-32%,$p<0.01$) and decreased AKT phosphorylation, a downstream molecule of the TCR. These defects were associated to significant reduction of neutral lipids and lipid rafts staining suggesting an altered lipid rafts distribution in KO CD8+ Tcells. Of note, memory CD8 Tcells from FH patients presented a decreased granzyme production when tested in vitro.
Conclusions: LDLR plays a critical role in regulating the immunometabolic responses in CD8+ Tcells, and thus might represent a checkpoint linking cellular cholesterol metabolism to adaptive immune response.

Homozygous, double and compound heterozygous familial hypercholesterolemia in Italy: genotype and phenotype characterization

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Aim Homozygous Familial Hypercholesterolemia (HoFH) is a rare inherited disorder, with a prevalence estimated to be 1/160.000 – 1/320.000. True HoFH is caused by the same mutation in both alleles of LDLR, PCSK9 or APOB genes, however compound heterozygotes (HeFH) with different mutations in one gene and, in some cases, also double heterozygotes with mutations in two causative genes, show a similar severe phenotype. We aimed at evaluating the biochemical parameters and the clinical signs of patients with genetic diagnosis of HoFH, double HeFH, and compound HeFH enrolled in the LIPIGEN-FH study.
Methods The LIPIGEN study is an observational, multicenter, retrospective, prospective study aimed at improving the identification of FH patients in Italy. The presence of clinical signs of FH or history of coronary heart disease (CHD), mean levels of LDL-cholesterol (LDL-C), and any genetic variants in the common genes causing FH were collected.
Results This analysis was carried out on 146 adult patients (mean age at diagnosis 28.6±16.3 years; 51.7% men; 74.0% index cases). Of this sample, 63 were HoFH, 67 compound HeFH, and 16 double HeFH. At clinical evaluation, 83.6%, 71.0% and 35.0% had tendon xanthoma, and 33.3%, 30.8% and 25.0% had arcus cornealis before 45 years old, respectively. Among the three groups, 61.7%, 48.4%, and 14.3% had clinical history of premature CHD. Mean pre-treatment LDL-C levels were 586.6 mg/dL in HoFH, 500.0 mg/dL in compound HeFH and 348.8 mg/dL in double HeFH. The majority of the cohort (65.2%, 61.4%, and 46.2%, respectively) was on lipid-lowering treatment, mainly statins.
Conclusions This preliminary analysis offers an overview on HoFH, compound and double HeFH patients enrolled in the LIPIGEN-FH study. HoFH is a heterogeneous disease that sometimes overlaps with the clinical phenotype of some severe cases of HeFH. This heterogeneity seems to depend in part on the causative genetic defect.

Abstract selezionato - Presenting author: **Elena Bortone**

Parathyroid hormone levels predict carotid plaque echogenicity in postmenopausal women

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Aim: Increased ultrasound echogenicity of carotid atherosclerotic plaques may reflect the amount of intralesional calcium deposition. Parathyroid hormon (PTH), which has a crucial role in calcium homeostasis, has been shown to promote both bone resorption and vascular calcification (the so-called "calcification paradox"). We investigated the association between serum PTH levels, femoral bone mineral density (BMD) and echogenicity of carotid atherosclerotic plaques in postmenopausal women.

Methods: We enrolled 63 postmenopausal women with asymptomatic carotid atherosclerotic plaques. Traditional cardiovascular risk factors were evaluated. Serum PTH levels were measured. The ultrasound grey-scale median (GSM) analysis was performed to estimate carotid plaque echogenicity. Femoral BMD was assessed through dual-energy X-ray absorptiometry (DXA).

Results: Max and mean GSM values of carotid atherosclerotic plaques were significantly higher in osteoporotic women (45,6 ± 13.4 and 53,6 ± 19,9) compared to those with osteopenia (30,7 ± 11.6 and 31,6 ± 12,6) or normal femoral BMD (36,8 ± 11.7 and 39,1 ± 12,1). An inverse association was observed between femoral neck BMD and mean GSM values (rho=-0.26, p=0.039), whereas a positive association was observed between serum PTH levels and max and mean GSM values (rho=0.57, p<0.001 and rho=0.59, p<0.001, respectively). Femoral neck BMD and serum PTH levels predicted mean GSM values independently from body mass index and age (β=-0.24, p=0.05 and β=0.39, p=0.002, respectively).

Conclusion: Serum PTH levels and femoral neck BMD predict the echogenicity of atherosclerotic plaques in postmenopausal women. Increased serum PTH levels may represent the pathophysiological link between postmenopausal osteoporosis and carotid atherosclerotic plaque calcification.

Primary aldosteronism and obstructive sleep apnea: a multicenter multi-ethnic cross-sectional study

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Aim: despite current evidences are limited, 2016 Endocrine Society guideline recommends screening for primary aldosteronism (PA) in all individuals with arterial hypertension and obstructive sleep apnea (OSA). We performed a multicentre, multi-ethnic, cross-sectional study, designed to investigate the prevalence of PA in patients with OSA and the prevalence of OSA in patients with PA.
Methods: we screened 203 patients with OSA (102 of Caucasian and 101 of Chinese ethnicity) for PA. In case of positive screening, patients underwent confirmatory test for PA and subtyping diagnosis. 207 patients with PA (104 Caucasians, 100 Chinese and 3 of African descent) were screened for OSA by cardio-respiratory polygraphy.
Results: 8.9% of patients with OSA had confirmed PA diagnosis (11.8% in Caucasian and 5.9% in Chinese patients). The prevalence of PA in patients without other indications for PA screening, other than OSA diagnosis, was very low (1.5%).
The prevalence of OSA was 67.6% (64.4% in Caucasian and 70.0% in Chinese patients). OSA was more prevalent in PA patients with idiopathic hyperaldosteronism than aldosterone-producing adenoma (75.8% vs 59.2%, p=0.031). We observed a significant correlation between aldosterone levels and apnea/hypopnea index in Caucasian group with PA (R^2 = 0.360, p = 0.013), but not in the Chinese group with PA. Similarly, multinomial logistic regression confirmed a significant association between plasma aldosterone and moderate to severe OSA in Caucasian patients (OR 1.002, p=0.002), independently of the main confounding factors. No association was present in Chinese patients with PA.
Conclusion: patients with OSA do not have an increased risk of PA, challenging the current recommendation of the Endocrine Society guideline for screening all patients with OSA for PA, independently of hypertension severity. However, OSA is frequent in patients with PA and aldosterone level can worsen OSA severity in Caucasian patients.

Abstract selezionato - Presenting author: **Raffaele Buganza**

Five cases of Lysosomal Acid Lipase deficiency, a rare and often misdiagnosed disease

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Aim: Lysosomal Acid Lipase deficiency (LAL-D) is a rare metabolic storage disease with accumulation of cholesteryl esters and triglycerides in lysosomes. The later onset variant of LAL-D, known as cholesterol ester storage disorder (CESD), usually presents with dyslipidemia and liver involvement and, due to its nonspecific clinical features, is often misdiagnosed as hereditary dyslipidemia, NAFLD or cryptogenic cirrhosis. We report our experience with five cases.
Subjects and methods: five patients (age 6-8-8-30-52 years) were diagnosed by genetic analysis of LIPA gene and evaluation of LAL activity. We evaluated lipid profile, transaminases and abdominal RM at diagnosis and after treatment with low-fat diet, ezetimibe, statins.
Results: mean values of TC, LDL-C, HDL-C and triglycerides at diagnosis, before any treatment, were respectively 266, 203, 34, 140 mg/dl, AST and ALT were 62 and 105 U/l. The three younger patients did not have steatosis at diagnosis, one of them developed steatosis during the 7 years of follow up, whereas in the two older patients it was present at diagnosis and remained stable without cirrhosis. Three patients (age 8-8-30) were treated with low-fat diet and ezetimibe with the following results: TC -21%/-5%/+11%, LDL-C -30%/-3%/+7%, TG -13%/-6%/+3% and ALT -59%/+32%/-46%, respectively. One patient (age 52) was treated with low-fat diet, statins and ezetimibe with a decrease of TC, LDL-C, TG and ALT of 53, 65, 41, 64%, respectively. One patient (age 6) was treated only with low-fat diet with the following results: TC -1%, LDL-C -22%, TG +1% and ALT -30 %, respectively.
Conclusions: the diagnosis of LAL-D is essential for correct follow-up and treatment, considering in particular cardiovascular risk and liver damage. Low-fat diets, statins, ezetimibe should be used to treat dyslipidemia and, to a lesser extent, hepatic impairment; replacement therapy with sebelipase alfa has been recently introduced.

Screening of primary aldosteronism with a novel renin-angiotensin-aldosterone system triple-a analysis

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Aim: Primary aldosteronism (PA) is a frequent cause of secondary hypertension and its screening is expected to become a routine evaluation in patients with hypertension. The interference of antihypertensive medications with the Aldosterone-to-Renin-Ratio (ARR) is a major confounder during screening testing. Renin-angiotensin-aldosterone-system (RAAS) triple-A analysis is a novel liquid chromatography/tandem mass spectrometry diagnostic assay that allows simultaneous quantification of aldosterone, equilibrium angiotensin I (eqAngI) and angiotensin II (eqAngII). The aim of the present study was to assess the reliability of RAAS triple-A analysis for PA screening.
Methods: We evaluated the diagnostic performance of the Aldosterone-to-AngII-Ratio (AA2R) and five renin based diagnostic ratios, differing in methods to determine aldosterone levels and renin activity, either based on chemiluminescence or radioimmunoassay.
Results: We enrolled a cohort of 110 patients with hypertension and suspected PA referred to a single hypertension unit (33 patients with confirmed PA and 77 with essential hypertension). All ratios showed comparable areas under the curves ranging between 0.924 and 0.970 without significant differences between each other. The evaluation of the AngII-to-AngI ratio revealed persistent ACE inhibitor intake in some patients as cause for suppressed renin-based diagnostic ratios, while AA2R remained unaffected, allowing a AA2-R-based PA screening in presence of ACE inhibitor. The optimal cut-off value for the AA2R was 6.6 [(pmol/L)/(pmol/L)] with a sensitivity and specificity of 90% and 93%, respectively, non-inferior to the ARR while pointing to the potential for an interference free application in patients under ACE-inhibitor therapy.
Conclusions: This study shows for the first time the accuracy and reliability of RAAS triple-A analysis for the screening of PA, even in the presence of therapy with ACE inhibitors. Combining information on drug efficacy and compliance monitoring with PA screening, this method might have a significant impact on the overall performance of PA screening.

Impact of dietary choline on atherosclerosis development in conventionally raised ApoE-KO mice expressing different levels of ApoA-I

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Aim. Gut microbiota can influence atherosclerosis development by metabolizing dietary choline: experimental and observational studies have highlighted a positive correlation between increased plasma choline-derived TMAO concentrations and adverse cardiovascular events. This study was aimed at investigating, for the first time, how apoA-I/HDL levels can influence atherosclerosis development by modulating gut microbiota composition.
Methods. Chow diets with different choline contents (0.09% or 1.2%) were administered for 20 weeks to conventionally-raised, atherosclerosis-prone mice expressing different levels of apoA-I: extremely low-HDL mice (A-IKO/EKO) or high-HDL mice, deficient for both murine apoA-I and apoE, but overexpressing human apoA-I (hA-I/A-IKO/EKO).
Results. Choline supplementation did not influence plasma cholesterol and triglyceride concentrations that were dramatically reduced in A-IKO/EKO vs hA-I/A-IKO/EKO mice. Atherosclerosis, evaluated at the aortic sinus and in the entire aorta, was unsurprisingly increased in A-IKO/EKO vs hA-I/A-IKO/EKO mice. Less predictably, choline supplementation significantly worsened plaque development only in hA-I/A-IKO/EKO mice (aortic sinus: 66,870 ± 46,870 vs 147,360 ± 42,750 mm2 in females; 63,691 ± 37,432 vs 110,030 ± 42,937 mm2 in males; aortic arch: 0.34 ± 0.65 vs 3.29 ± 3.65 % in females; 0.87 ± 1.03 vs 2.45 ± 2.59 % in males). To characterize plaque composition, O.R.O. staining for neutral lipids and Mac-2 specific IHC for macrophages were performed. An increased dietary choline content did not result in an increased deposition of neutral lipids nor of the amount of infiltrating macrophage in atherosclerotic plaques of both genotypes.
Conclusions. Our results indicate that dietary choline supplementation worsens atherosclerosis development only when apoA-I is expressed. Further studies are ongoing to better clarify: i) how apoA-I can modulate gut microbiota composition (i.e. the presence of choline-degrading bacteria); ii) the pathophysiological mechanisms influenced by the choline- TMA-TMAO metabolic pathway.

Abstract selezionato - Presenting author: **Ilenia Calcaterra**

Changes in carotid stiffness in patients with familial hypercholesterolemia treated with Evolocumab: A prospective cohort study

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Aim: Protein convertase subtilisin kexin type 9 (PCSK-9) inhibitors demonstrated efficacy in cholesterol reduction and in the prevention of cardiovascular events. We evaluated changes in lipid profile and carotid stiffness in patients with familial hypercholesterolemia during 12 weeks of treatment with a PCSK-9 inhibitor, Evolocumab.

Methods: Patients with familial hypercholesterolemia starting a treatment with Evolocumab were included. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), small dense LDL (assessed by LDL score) and carotid stiffness were evaluated before starting treatment with Evolocumab and during 12 weeks of treatment.

Results: Twenty-five subjects were enrolled (52% males, mean age 51.5 years). TC and LDL-C were reduced of 38% and 52%, respectively during treatment, with LDL score reduced of 46.1%. In parallel, carotid stiffness changed from 8.8 (IQR: 7.0-10.4) m/sec to 6.6 (IQR: 5.4-7.5) m/sec, corresponding to a change of 21.4% ($p < 0.001$), with a significant increase in carotid distensibility (from 12.1, IQR: 8.73-19.3 $kPA^{-1} \times 10^{-3}$ at T_0 to 21.8, IQR: 16.6-31.8 $kPA^{-1} \times 10^{-3}$ at $T12_w$) corresponding to a median change of 62.8% ($p < 0.001$). A multivariate analysis showed that changes in LDL score were independently associated with changes in carotid stiffness ($\beta = 0.429$, $p = 0.041$).

Conclusions: Small dense LDL reduction, as assessed by LDL score, is associated with changes in carotid stiffness in patients with familial hypercholesterolemia treated with Evolocumab

Abstract selezionato - Presenting author: **Canclini Laura**

Differential association of proprotein convertase subtilisin/kexin 9 (PCSK9) to lipoproteins in patients treated with Monoclonal Antibodies

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Aim: Monoclonal antibodies (mAbs) blocking PCSK9 reduce LDL-cholesterol (LDL-C) levels possibly throughout the prevention of PCSK9 binding to the LDL receptor. PCSK9 is assumed to interact with lipoproteins. This project aims at studying the association of PCSK9 with lipoproteins. To reach this goal, we isolated different lipoproteins from patients treated with Evolocumab and Alirocumab to see if there is a differential association of PCSK9 to lipoproteins in comparison with non-treated individuals.
Methods: Fresh sera were collected from more than 60 subjects, including patients treated with Evolocumab and Alirocumab. Lipoprotein fractions were obtained using iodixanol gradient (IGr) ultracentrifugation. Their PCSK9 content was detected with ELISA while Lp(a), ApoB, ApoA1 and Cholesterol were quantified using clinical-grade turbidimetry assays.
Results: 22.55± 8.54% of PCSK9 was found in LDL fraction in non-treated subjects. 14.7 ± 4.9% was the percentage observed in patients treated with mAbs, which in turn had LDL levels much lower in comparison with the healthy individuals. The PCSK9/LDL-C ratio in treated patients was more than three times higher than in non-treated once.
Conclusions: Based on our observations, it appears that the association of PCSK9 and LDL particles remains, even if the LDL level reduces dramatically. mAbs-treated patients showed an higher association of PCSK9 to LDL, in comparison with non-treated subjects.

Thoracic radiotherapy as a risk factor for heart ischemia in subjects with chest irradiation and without classic cardiovascular risk factors

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Objective: Radiation induced heart disease represents a late effect of chest irradiation and it contributes to increase mortality in oncology patients due to the damage produced to the pericardium, myocardium, valves and coronary arteries. Current guidelines suggest to perform a cardiac screening using exercise stress electrocardiography 5 to 10 years after radiotherapy. Objective of this study is to determine the incidence of myocardial ischemia in a population of patients without any cardiovascular risk factor who underwent thoracic radiotherapy.

Methods: We enrolled a total of 250 patients and we divided them into two groups. The first group included 115 patients without any cardiovascular risk factor with a history of thoracic radiotherapy who were screened using exercise stress electrocardiography to detect myocardial ischemia. The control group included 135 patients who presented a high-risk cardiovascular profile without any oncologic medical history who underwent stress testing for primary prevention or because of atypical thoracic pain.

Results: Irradiated patients without cardiac risk factors had a lower average age compared to the control group (48.7±10.1 vs 60.5±10.8 years, p<0.001) and there was a lower percentage of males. Concerning cardiovascular risk factors, in the control group 25.9% of patients had diabetes, 62.9% dyslipidemia, 67.4% hypertension and 19.2% were active smokers. Despite these important disparities regarding the cardiovascular risk profile, no significant differences were found in the number of positive exercise stress electrocardiography tests in the two groups (10.4% vs 5.9%, p=ns).

Conclusions: Chest irradiation represents a strong cardiovascular risk factor and it was found to be able to equalize the incidence of positive exercise stress tests among two cohort of patients with significant differences in their cardiovascular risk profile.

Abstract selezionato - Presenting author: **Filippo Cattazzo**

Effect of continuous positive airway pressure treatment on glycemic and lipid profiles in patients with obstructive sleep apnoea: a systematic review and meta-analysis of randomized controlled trials

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Aim. Continuous Positive Airway Pressure (CPAP) is the main therapy for obstructive sleep apnoea (OSA); nevertheless, uncertainty remains about the effectiveness of CPAP not only in controlling OSA-related hypertension, but also in improving the metabolic dysregulation that characterizes OSA patients. This meta-analysis of randomized controlled trials (RCTs) aimed to investigate whether CPAP, compared to other treatments, could improve glucose and/or lipid metabolism in OSA patients.
Methods. Relevant papers were searched in three different databases (MEDLINE, EMBASE, Web of Science) from inception to 31st Dec 2018 through specific search terms and selection criteria.
Results. From 2,289 articles, 26 RCTs were included. Regarding glycemic metabolism, neither fasting plasma glucose nor HbA1c were reduced by CPAP. However, patients on CPAP therapy showed an improvement in insulin sensitivity, as witnessed by a significant reduction of fasting plasma insulin (Standardized difference in means [SDM]=0.205[95%CI,0.07-0.339],p=0.003) and HOMA-IR (SDM=0.176[95%CI,0.056-0.296],p=0.004). Sensitivity analysis revealed that the favourable effects of CPAP were maintained in prediabetic/type 2 diabetic patients and in those that presented an apnoea-hypopnea index≥30 events/h at baseline. Regarding lipid metabolism, OSA patients in CPAP intervention groups showed a significant reduction of total cholesterol (TC; SDM=0.138[95%CI,0.034-0.242],p=0.009). In subgroups analysis, greater adherence to CPAP along with severe nocturnal oxygen desaturations at baseline (SpO2-nadir<77%) was associated with a significant decrease of TC. Furthermore, dividing the primary studies according to the median TC at baseline, the positive effects of CPAP were maintained only in those that presented a TC above the median. Conversely, CPAP did not modify triglycerides, HDL, and LDL-cholesterol.
Conclusions. CPAP treatment significantly improves insulin sensitivity and reduces TC in OSA patients. The effectiveness of CPAP is higher in patients with greater CPAP usage, and with a greater number of apnoeic events and oxygen desaturations at baseline. Concerning TC, patients presenting higher levels at baseline benefit the most from CPAP.

Abstract selezionato - Presenting author: **Alessia Cavicchioli**

Lipoprotein(a) is significantly higher and associated with increased prevalence of atherosclerotic cardiovascular disease in mutation-negative familial hypercholesterolemia patients

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Introduction and aim: High lipoprotein(a) (Lp(a)) concentrations may be a cause of clinical familial hypercholesterolemia (FH) and are associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD) [Langsted, Lancet Diabetes Endocrinol 2016]. We evaluated if Lp(a) concentrations and their association with ASCVD may differ between mutation-negative and mutation-positive FH patients.

Methods: 177 consecutive patients with clinical suspicion of FH from the Lipid Clinic in Modena underwent comprehensive evaluation, including Lp(a) measurement and genetic analysis, within the LIPIGEN Project. We considered high Lp(a) concentrations (hyper-Lp(a)) when more than 50 mg/dl. Patients were defined as mutation-positive if "pathogenic" or "likely pathogenic" mutations were detected in FH-causing genes; mutation-negative patients were defined by the presence of "variants of uncertain significance" or absence of genetic variants.

Results: 135 FH patients (76.3%) were mutation-positive. Mutation-positive patients showed significantly higher LDL-cholesterol (LDL-c) levels (p<0.001) and Dutch Lipid Clinic Network (DLCN) score (p<0.001) than mutation-negative patients, whereas the prevalence of ASCVD was not significantly different between the two groups (15.6% vs. 19.0%; p=0.593). Conversely, Lp(a) concentrations were significantly higher (34.7 [10.7-88.9] vs. 22.8 [8.0-49.6] mg/dl; p=0.043) and hyper-Lp(a) was significantly more frequent (40.5% vs. 23.7%; p=0.034) in mutation-negative than mutation-positive patients. When adjusting LDL-c for Lp(a) cholesterol content (by subtracting 30% of the individuals' Lp(a) total mass from LDL-c), the Lp(a)-adjusted DLCN score tended to be more frequently lowered in mutation-negative than mutation-positive patients (28.6% vs. 15.6%; p=0.059). Hyper-Lp(a) was significantly associated with an increased prevalence of ASCVD in mutation-negative patients (p=0.003), but not in mutation-positive patients (p=0.269). Of note, 7 out of 8 (87.5%) mutation-negative patients with a personal history of ASCVD had hyper-Lp(a).

Conclusions: Our study confirms that high Lp(a) concentrations may represent a significant risk factor for clinical FH. In mutation-negative FH patients hyper-Lp(a) may be a major contributing cause of clinical FH and increased ASCVD risk.

Abstract selezionato - Presenting author: **Alberto Cerasari**

Relationship between echocardiographic and functional parameters in patients with heart failure undergoing cardiopulmonary exercise test

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Aim: HF patients typically show effort intolerance due to a reduction in peak exercise oxygen (peak VO_2) consumption, which is related to inability to adapt systolic function to increased demand. Left ventricular ejection fraction (EF) is a surrogate marker of cardiac contractility and a powerful predictor of adverse prognosis in chronic heart failure (HF). The aim of the study was to explore the relationship between EF and other echocardiographic findings with peak VO_2 in a population of HF individuals HF undergoing cardiopulmonary exercise testing (CPX).
Methods: We evaluated 101 HF patients (61% hypertensives, 74% with documented coronary artery disease) undergoing both resting echocardiography and symptom-limited CPX in a secondary Sport Clinic.
Results: Mean age was 58±13 years, men 83%. Mean EF was 55±12%; 20% of the patients showed EF<40%. Mean test duration was 9.4±2.2 min. Average peak VO_2 was 21±6 mL/Kg/min. Peak VO_2 showed a robust positive correlation with EF (R=0.42, p<0.001). Other independent predictors of peak VO_2 were age, male sex, height and tricuspidal anular plane systolic excursion (TAPSE), this latter reflecting right ventricular (RV) dysfunction. When subjects were dichotomized according to predicted peak VO_2 values, those with higher-than-predicted peak VO_2 showed significantly lower VE/VCO_2 slope, and higher values of oxygen pulse and VO_2/WR slope.
Conclusions: EF and TAPSE are two independent predictors of peak VO_2. For each individual, a predicted threshold of peak VO_2 could be estimated from anthropometric and echocardiographic parameters. The evaluation of observed-to-predicted peak VO_2 may help in unraveling potentially relevant mechanisms affecting exercise capacity in HF patients.

Aortic strain impairment in ascending aorta dilatation

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Background: Ascending aorta (aA) dilatation is a condition observed in 13% of hypertensive patients. Little is known about elastic features of aA in hypertensive patients affected by aA dilatation. Aortic strain analysis can describe mechanical properties of aA. The functional evaluation of aA may help in risk assessment and stratification of patients with known aortopathy.

Aim: To assess mechanical properties of aA by aortic strain in terms of β_2-*Stiffness index* (Beta-SI) analysis in hypertensive patients with different severity of aA dilatation and to evaluate the association between mechanical properties of aA and cardiovascular damage.

Methods: 100 hypertensive outpatients underwent clinical evaluation, transthoracic echocardiography (TTE) and assessment of pulse wave velocity (PWV). Strain analysis of aA was performed with speckle-tracking TTE software. Beta-SI was defined as:
100*Ln(systolic blood pressure/diastolic blood pressure)/maximal transversal deformation of aA.
Hypertensive patients were divided in three groups based on aA diameter: < 40 mm, 40-45 mm and ≥45 mm.

Results: Beta-SI resulted to rise exponentially with aA dimensions ($p<0.001$) with especially in patients having aA >45 mm. A progressively greater proportion of patient with impaired (i.e. elevated) Beta-SI was present in groups identified by progressively dilated aA (18.2% vs 48.4% vs 80% respectively, $p<0.05$). On multivariate logistic regression only an impaired Beta-SI predicted aA dilatation ($p<0.001$). Beta-SI was also related to cardiovascular organ damage in terms of left ventricular mass (LVMi, $p=0.030$) and PWV ($p=0.028$). Patients with high Beta-SI had grater LVMi (94±24 vs. 117±47 g/m^2; $p=0.010$) and PWV (8.63±1.88 vs. 10.20±2.99 m/s; $p=0.013$).

Conclusions: aA dilatation in hypertensive subjects is associated with increased local aortic stiffness. Strain analysis adds functional information to the mere morphological evaluation of aortic dimension and it could be an useful tool to better stratify cardiovascular risk in this specific population.

Abstract selezionato - Presenting author: **Arturo Cesaro**

PCSK9 inhibitors: adherence and perceived health

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Aim: Lowering LDL-C is a critical intervention to contrast cardiovascular risk. The association of PCSK9 inhibitors (PCSK9i) with available therapies represents a successful therapeutic strategy in patients with high and very high cardiovascular risk who do not reach the target values despite standard therapy with statins and ezetimibe. Over the last years, data regarding health-related quality of life (HRQOL) and quality-adjusted life years (QALYs) has been increasingly taken into consideration to support medical decisions. The aim of our study is to assess the impact of treatment with PCSK9i on quality of life in high and very-high cardiovascular risk patients.
Methods: In this prospective study, we evaluated patients at high or very-high cardiovascular risk admitted to our Cardiology Center. Patients who didn't reach recommended LDL-C goals despite maximal tolerated lipid-lowering therapy with statins and ezetimibe were treated additionally with evolocumab 140 mg or alirocumab 75/150 mg bi-weekly, according to National regulations. We measured the health status perceived by patients through the self-administered EuroQoL (or EQ-5D-3L) in Italian language at enrollment, and at 1-year follow-up.
Results: 51 patients were enrolled. The study population included 15 patients (29%) with a genetically-confirmed diagnosis heterozygous familial hypercholesterolemia. 34 patients (66%) received evolocumab and 17 patients (33%) alirocumab. The mean EQ-5D score improved from 0.49 (95% confidence interval (CI) 0.40 to 0.58) at enrollment to 0.85 (95%, CI 0.79 to 0.90) at 1-year follow-up (p<0.001). The mean EQ by visual analogue scale (VAS) improved from 63.5 at baseline (95% CI 60.5 to 66.5) to 80.2 at 1-year follow-up (95% CI 77.6 to 82.9) (p<0.001).
Conclusion: Our study showed that most patients treated with PCSK9i experienced an improvement in health related QoL. Most patients reported an improvement in all five dimensions of the EQ-5D with greatest improvement in patients' anxiety/depression dimension.

Abstract selezionato - Presenting author: **Stefania Cicolari**

Circulating oxysterol levels are modulated by a cholesterol-lowering nutraceutical combination (Bifidobacterium longum BB536, red yeast rice extract) in subjects with moderate hypercholesterolaemia: results from a randomized, double-blind, placebo-controlled study

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Aim: Nutraceuticals are effective tools to manage moderate hypercholesterolemia in patients with low CVD risk, although their impact on cholesterol metabolism has not been assessed yet. The main cholesterol metabolites, the oxysterols 24-, 25- and 27-hydroxycholesterol (24-OHC, 25-OHC and 27-OHC), are key substrates of bile acid synthesis and, having a greater water solubility than cholesterol, are also able to modulate nuclear and membrane receptors, thereby modulating cholesterol synthesis, immune system function and cerebral compartment homeostasis. A nutraceutical combination with Bifidobacterium longum BB536, red yeast rice extract (10 mg/day monacolin K), niacin, coenzyme Q10 (Lactoflorene Colesterolo®) has been shown to reduce LDL-C levels by 25.7% in subjects with moderate hypercholesterolaemia. In the present study, we investigated the effect of this nutraceutical mix on cholesterol metabolism by evaluating 24-OHC, 25-OHC and 27-OHC plasma levels.

Methods: Thirty-three subjects (18–70 y) with low CV risk and in primary CV prevention (SCORE: 0–1% (n=24), 2–4% (n=9); LDL-C: 130–200 mg/dL) were recruited in a randomized double-blind, parallel, placebo-controlled study and treated with the above-reported nutraceutical combination or placebo for 12 weeks. Baseline/post-intervention plasmatic 24-OHC, 25-OHC and 27-OHC were evaluated by gas chromatography-mass spectrometry analysis.

Results: At the end of the intervention, 24-OHC and 24-OHC/TC (total cholesterol) ratio were unaltered. 25-OHC levels were unchanged in both groups, while 25-OHC/TC ratio significantly raised over baseline just in the treated group (P=0.047; +21.9%). In the nutraceutical group, 27-OHC concentration was significantly reduced (p=0.005; -10.6%), whereas the 27-OHC/TC ratio was the same between the two groups.

Conclusions: Treatment with this nutraceutical mix resulted in a peculiar oxysterol profile, that further supports the safety of this product. Moreover, the observed reduction of 27-OHC level represents a favourable effect on different targets, in addition to LDL-C lowering.

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Abstract selezionato - Presenting author: **Maria Cinquegrani**

Prevalence of vascular involvement and liver fibrosis in a cohort insulin sensitive mixed hiperlypemic patients

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Aim: Familial combined hyperlipidemia *(FCHL)* is the most prevalent primary dyslipidemia. Frequently it remains undiagnosed. It is characterized by fluctuations in serum lipid concentrations and may present as mixed hyperlipidemia, isolated hypercholesterolemia, hypertriglyceridemia, or as a normal serum lipid profile in combination with abnormally elevated levels of apolipoprotein B. An increased risk of hepatic steatosis has been observed in FCHL, with consistent associations for both NAFLD and non-alcoholic steatohepatitis (NASH) and up to 20-37% of the variability in intrahepatic fat content attributable to genetic factors in FCHL. The aim of our study was to evaluate the prevalence and incidence of NAFLD and/or NASH in FCHL' patients.
Methods: in collaboration with general practitioners, we enrolled 69 patients (mean age 53 years; 35 male, 34 female) whose satisfied inclusion and exclusion criteria (HOMA-IR <2.4; ApoB >124 mg/dl and LDL-C >160 mg/dl, or HDL-C <50M and <60F mg/dl or Tg >180 mg/dl). Clinical and instrumental examination consisted of carotid ecocolorDoppler with PWV estimation, liver ultrasonography with Fibroscan.
Results: at baseline we found a mean CT level of 247.94±30.24, HDL-C level 56.26±16.29 in men and ± in women, Tg 124.14±65.91 mg/dl. ApoB was 131.38±29.53 on the average. HOMA-IR was 1.53±0.49. We found a carotid artery involvement, as cIMT >0.9 mm, in 28 pts (38%), and pts 24 (33%) had already carotid plaque. Any grade of liver steatosis was found in pts 35 (50%). Mean liver stiffness value was 5.38±1.76.
We found a significant correlation between PWV and LS: r=0.83, p<0.001.
Conclusions: we found that about one third of included patients presented with carotid atherosclerosis already at diagnosis; moreover, mean LS was; PWV was also higher than age-related expected values. Moreover, we found a strong correlation between PWV and LS as measured by Fibroscan, also in our cohort of insulin-sensitive subjects.

Abstract selezionato - Presenting author: **Nicholas Cocomello**

Nonalcoholic Fatty Liver Disease and Fibrosis Associated With Increased Risk of Cardiovascular Events in a Prospective Study

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Background & Aims: Patients with non-alcoholic fatty liver disease (NAFLD) are at increased chance for cardiovascular events (CVEs). Severity of liver fibrosis is used to determine prognosis for patients with NAFLD, but little is known about the relationship between liver fibrosis and CVEs in the real world.
Methods: We analyzed data from the prospective observational progression of liver damage and cardiometabolic disorders in non-alcoholic fatty liver disease study, comprising 898 consecutive outpatients screened for liver steatosis by ultrasound. Liver fibrosis was defined as FIB-4 score greater than 2.67 and NAFLD fibrosis score greater than 0.676. Patients were followed by phone every 6 months and examined every 12 months in the outpatient clinic. CVEs were recorded (fatal or nonfatal ischemic stroke and myocardial infarction, cardiac or peripheral revascularization, new-onset arterial fibrillation and cardiovascular death). The primary outcomes were incidence rate of CVEs in patients with vs without NAFLD and factors associated with CVEs in patients with NAFLD.
Results: Over a median follow-up time of 41.4 months (3044.4 patient-years), 58 CVEs (1.9%/year) were registered. The rate of CVEs was higher in patients with (n=643, 2.1%/year) vs without NAFLD (n=255, 1.0%/year) (P=.066). In multivariable Cox proportional regression analysis, NAFLD increased risk for CVEs (hazard ratio [HR], 2.41; 95% CI, 1.06-5.47; P=.036), after adjustment for metabolic syndrome. Among patients with NAFLD, male sex, previous CVEs, metabolic syndrome and FIB-4 scores greater than 2.67 (HR, 4.02; 95% CI, 1.21-13.38; P=.023) were independently associated with risk of incident CVEs. NFS scores greater than 0.676 were also independently associated with risk of incident CVEs (HR, 2.35; 95% CI, 1.05-5.27; P=.038).
Conclusions: NAFLD patients had more than a 2-fold increase in risk of CVEs. In patients with NAFLD, liver fibrosis indexes were independently associated with a 4-fold increased risk for incident CVEs.

Abstract selezionato - Presenting author: **Alice Colombo**

Chronic rupatadine treatment worsens atherosclerosis progression in apolipoprotein E knockout mice fed Western-type diet

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Aim. Rupatadine is an N-alkyl pyridine derivative exerting anti-inflammatory properties through the inhibition of a range of mediators. Its primary mechanism of action is through the histamine H1 receptor, with an additional antagonist activity towards PAF. The potent anti-inflammatory effects displayed by rupatadine could be exploited against atherosclerosis development.
Methods. Apolipoprotein E-deficient (EKO) mice (n=15 per group) were fed Western-type diet, with (Rupa) or without (Ctrl) 0.17 g/kg rupatadine for 12 weeks (~16 mg/kg/die).
Results. Weight gain, food/water intake, organ weights were similar in both groups. Plasma total cholesterol and triglyceride levels were also comparable. No difference in inflammatory infiltrates was detected in liver, kidney and lungs. Atherosclerotic plaque extent in arch, thoracic and abdominal segments of aorta (en-face) was comparable between groups. Ctrl and Rupa plaques were remarkably similar in the macrophage content (anti-Galectin3), necrotic core and plaque matrix content (Masson's trichrome). However, plaque area at the aortic sinus (H&E) was higher in Rupa (+14.8%, p=0.02).
Conclusions. Rupatadine treatment in apoE-KO mice fed Western diet resulted in a moderate worsening of atherosclerosis development. Shedding light on controversial in vitro results, our findings are in line with evidences from other related molecules (cetirizine, fexofenadine). While the molecular mechanism is still under investigation, it would be worthwhile to assess the impact of rupatadine treatment on human health, especially in chronically treated patients.

Abstract selezionato - Presenting author: **Ornella Colpani**

Nutrition and body composition parameters in adult men and women in primary cv prevention: an analysis of plic study

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Aim: Nutritional habits and body composition are important factors affecting cardiovascular risk. Obesity, as well as alterations in lipids and inflammatory state, negatively affect cardiovascular homeostasis. The aim of our work is to describe cardiovascular and metabolic risk factors, nutrition and body composition parameters in adult men and women in primary CV prevention.
Methods: The sample included 164 subjects who completed the fifth visit of PLIC study. Besides a comprehensive medical examination, participants were asked to keep food diaries and underwent dual energy x-ray absorptiometry (DEXA). A B-mode ultrasound examination for measurement of the common carotid intima-media thickness (c-IMT) was performed.
Results: We evaluated 67 men (M) and 97 women (W), mean age±SD 65±12 in both groups. There were no significant differences in systolic blood pressure, LDL-cholesterol, triglycerides. Total cholesterol was 187±30 M and 206±32mg/dL W, HDL-cholesterol was 53±11 M and 65±13mg/dL W (both $p<0.001$). High-sensitivity C-reactive protein (hs-CRP) was higher, although not significantly different, in men (0.29±0.63 vs 0.22±0.37 mg/dL). Obesity affected 19.6% W and 14.9% M; proportion of total fat was 40.2% and 30.9%, respectively. Metabolic syndrome was present in 26.9% M and 30.9% F. c-IMT was indicative of plaque in 42.4% M and 32.0% W. The percentage distribution of macronutrients was similar between sexes; however, saturated fat and simple sugar consumptions were higher in men (19.3 vs 17.1g, p 0.020 and 67.3 vs 59.9g, p 0.044, respectively), as well as the dietary inflammatory index (1.34±1.60 vs -0.06±1.69, $p<0.001$). In both sexes, bone mineral content (BMC) was significantly lower in subjects with plaque (2691 vs 2833g M, 1872 vs 2023g W).
Conclusions: Although metabolic imbalances were more prevalent in women, the c-IMT suggested a worse atherosclerotic profile in men, along with higher inflammation, both measured by hs-CRP and derived from diet. Coherently with literature data, we confirmed the inverse association between BMC and c-IMT.

Abstract selezionato - Presenting author: **William Cordeddu**

Echocardiographic detection of subclinical right ventricular disfunction in patients with Systemic Lupus Erithematosus

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Aim: evaluation of the correlations between subclinical echocardiographic alterations of the right ventricle detected using 3D speckle-tracking echocardiography (3DSTE) and clinical variables in SLE patients.

Methods: data from 29 SLE patients (age 45.55 ± 12.19, F / M 26/3) with no history of cardiovascular disease were collected. Patients' data included positivity for anti-SSA antibodies (n = 11), SLICC / ACR Damage Index score (n = 24 SDI = 0, n = 4 SDI ≥ 2), SELENA-SLEDAI-2k score, state of LLDAS (n = 7) and Clinical Remission (n = 6), mean daily prednisone dose (n = 17 ≤ 7.5 mg / day, n = 12 > 7.5 mg/day). Echocardiographic parameters of the right ventricle acquired included: EDV (end-diastolic volume), ESV (end-systolic volume), SV (stroke volume), EF (ejection fraction), LS (longitudinal strain) of the septum and the free wall, FAC (fractional shortening of the area).

Results: Significant differences of EF (p = 0.01), septum (p = 0.004) and free wall (p = 0.002) LS and FAC (p = 0.01) emerged between the two subgroups with SDI = 0 and SDI ≥ 2. No significant correlations were found between echocardiographic data and disease duration, SELENA-SLEDAI-2k, LLDAS or Clinical remission. A positive linear correlation was found between EDV (r = 0.43, p = 0.02), ESV (r = 0.42, p = 0.02), SV (r = 0.42, p = 0.02) and average daily dose of prednisone. The latter result was confirmed in a comparison of two subgroups (prednisone ≤ or > 7.5 mg / day) respect to values of EDV (p = 0.02), ESV (p = 0.02) and SV (p = 0.03). Values of TAPSE (p = 0.03) and FAC (p = 0.02) were significantly different in patients with and without positivity for anti SSA /Ro.

Conclusions: This work confirms the power of 3DSTE in identifying subclinical abnormalities in structure and function of the right ventricle in asymptomatic SLE patients, in particular the extent of reduction of septum and free wall LS, SV and EF correlates with high SDI values.

Abstract selezionato - Presenting author: **Bernadette Corica**

Adherence and Persistence in Real-World Patients treated with Non-vitamin K Oral Anticoagulants: Protocol for a Systematic Review and Meta-Analysis

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Aim: Non-vitamin K Oral Anticoagulants (NOAC) emerged as alternatives to Vitamin-K antagonist (VKA) in several medical conditions which require long-term anticoagulation, such as atrial fibrillation. Evidences from both randozimed controlled trials and real-world observational studies demonstrated that NOACs are at least as effective as VKA, while showing consistently better safety profiles. However, several alarming reports have underlined that adherence and persistence with NOACs are broadly and consistently poorer than previously expected, with non-persistence reported in half patients at 1 year. Aims of this study is to explore and quantifying the adherence and persistence in real-world patients treated with NOACs through a comprehensive sytematic review and meta-analysis of current literature.

Methods: We performed an extensive database search on PUBMED and EMBASE, using structured combination of keywords encompassing all the relevant terms related to adherence, persistence and NOACs. As with the PRISMA statement, two reviewers will independently screen all the retrieved records, according to pre-specified inclusion and exclusion criteria. Risk of bias will be assessed according to the recommendations of the Agency for Healthcare Research and Quality. A meta-analysis will be performed according to data extracted from the included studies, with the main pre-specified outcome consisting of rates of adherence and persistence with NOAC therapy.

Results and Conclusions: Data from this systematic review and meta-analysis will help to clarify the actual burden of unsatisfactory adherence and persistence in patients treated with NOACs, as well as potential determinants of poor medication adherence. Data from this meta-analysis will deepen our knowledge of the problem, allowing the identification of potentially modifiable detrimental factors that may impair compliance in these patients. Identification of the modifiable determinants is pivotal to design and implement effective strategies to improve patient compliance, which results in better outcomes and allocation of resources.

Abstract selezionato - Presenting author: **Elena Cosentini**

Uric acid elevation and atrial fibrillation: where does the link lie?

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Aim: Uric acid (UA) is an end product of purine metabolism produced by xanthine oxidoreductase. A number of epidemiological studies suggest the existence of a direct association between elevated serum UA level and the new onset of atrial fibrillation (AF). However, since serum UA concentration is influenced by many modifiable/non-modifiable factors, it remains uncertain as to whether such an association is independent or not. We aimed to analyze the relationship between UA levels and the presence of AF among acutely hospitalized patients.
Methods: In this case-control study, 131 inpatients from an Internal Medicine ward with history of AF (either paroxysmal, permanent, persistent, or longstanding) and 131 age- and sex-matched controls without history of AF were retrospectively recruited. Data regarding medical history, concomitant medications, physical examination, echocardiographic parameters and biochemical analyses were collected.
Results: Serum UA levels were significantly higher in cases than in controls ($p=0.027$), whereas systolic blood pressure (SBP) and ejection fraction (EF) were significantly lower in cases than in controls ($p=0,005$ and $p=0,003$, respectively). In the overall study population, serum UA significantly correlated with body mass index (BMI) ($rho=0,140$; $p=0,033$), SBP ($rho=-0,210$; $p<0,001$), triglycerides ($rho=0,142$; $p=0,043$), HDL cholesterol ($rho=-0,164$; $p=0,020$), estimated glomerular filtration rate (eGFR) ($rho=-0,501$; $p<0,001$) and EF ($rho=-0,162$; $p=0,049$). However, only SBP, EF and eGFR were significant covariates of serum UA levels among patients with AF ($p=0,037$, $p=0,028$ and $p<0,001$, respectively). In a binary logistic regression model including AF as dependent variable and logarithmic (LG)-BMI, LG-SPB, HDL cholesterol, LG-triglycerides, LG-UA, LG-EF, LG-eGFR as independent variables, LG-UA was the only independent predictor of AF (B:3,040, SE:1,514, $p=0,045$). However, when adding either age or sex as independent variables, the significant association between UA and the presence of AF was abolished (B:0,178, SE:0,101, $p=0,078$ and B:0,198, SE:0,102, $p=0,052$, respectively)
Conclusions: Our data indicate that there is a possible age- and gender-specific mechanism underlying the relationship between UA and AF.

Atherosclerosis in paleopathology: updates and news

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NOTA: *l'intervento proposto è sicuramente "non convenzionale". L'intento è quello di raccontare la storia dell'aterosclerosi puntando a far conoscere aspetti non immediatamente noti dell'epidemiologia e della diffusione nella storia di questa patologia.*
Rimango a disposizione per eventuali delucidazioni.

Paleopathology, a discipline that allows to connect the diseases of the past with the current Medicine through the analysis of the signs left by various pathologies in the bioarchaeological human remains, has indelibly demonstrated how atherosclerosis affected various populations throughout history.
The lecture aims to illustrate an overview of paleopathological research on atherosclerosis starting from the anatomo-pathological findings detected by Sir Marc Armand Ruffer in the first studies of Egyptian mummies, to the contemporary HORUS study that uses CT to identify arterial calcifications (2011-2013), to the very recent techniques of identifying an early stage atherosclerotic lesions in mummified bodies through the use of near-infrared spectroscopy (2019).
Paleopathological studies on atherosclerosis contribute to the re-evaluation of epidemiological data, which wanted the atherosclerotic lesion mainly related to contemporary lifestyles typical of well-being and advanced age. The studies led to understand how atherosclerosis is a ubiquitous pathology in space and time in populations of nowadays as much as in the past.

Abstract selezionato - Presenting author: **Rosa Curcio**

Effects of n-3 polyunsaturated fatty acids supplementation on circulating apolipoprotein B: a systematic review and meta-analysis

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Aim: Current guidelines recommend to reduce circulating apolipoprotein B (apoB)-containing lipoproteins, for both the primary and the secondary prevention of CV events. Results of previous clinical trials evaluating the effect of supplementation with n-3 polyunsaturated fatty acid (PUFAs) on circulating apoB are controversial. Therefore, we aimed to assess the impact of n-3 PUFAs on circulating apoB through a systematic review of literature and meta-analysis of available randomized, placebo-controlled clinical studies.
Methods: Literature search included SCOPUS, PubMed-Medline and ISI Web of Science up to the 10th December 2019, to identify randomized, placebo-controlled clinical studies investigating the impact of n-3 PUFAs, supplemented in capsule formulation, on circulating apoB. Two investigators independently extracted data on study characteristics, methods, and outcomes.
Results: The impact of n-3 PUFAs in capsule formulation on apoB was reported in 23 randomized, placebo-controlled clinical studies (2076 in the n-3 PUFA arm and 2055 in the placebo arm). Meta-analysis showed a significant reduction of total cholesterol (percentage mean difference [%MD]: -4.470; 95% CI:-7.162 to -1.779; P=0.001), non-HDL cholesterol (%MD: -7.034; 95% CI:-8.492 to -5.575; P<0.001), and triglycerides (%MD: -18.803; 95% CI:-29.426 to -8.180; P=0.001), whereas did not show a significant reduction of LDL cholesterol (%MD: -0.350; 95% CI:-2.070 to 1.369; P=0.690), HDL cholesterol (%MD: -0.636; 95% CI:-0.411 to 1.683; P=0.234) and apoB (%MD: -2.099%; 95% CI:-4.808 to 0.610; P=0.129), regardless of the type of PUFA. A significant reduction of apoB was observed after eicosapentaenoic acid (EPA) supplementation (%MD: -6.003%; 95% CI:-7.803 to -4.169; P<0.001), whereas a non significant reduction was observed after either docosahexaenoic acid (DHA) or EPA + DHA supplementation (%MD: 7.321%; 95% CI:-2.640 to 17.283; P=0.150 and %MD: -1.201%; 95% CI:-2.877 to 0.474; P=0.160, respectively).
Conclusions: EPA supplementation is associated with a significant reduction of circulating apoB levels.

Abstract selezionato - Presenting author: **Marco D'Abbondanza**

Gender related differences in two types of weight loss intervention

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Background and aims: historically, women have been underrepresented in clinical trials: particularly, only a few studies described gender effect on surgical and non-surgical interventions, with discordant results.
The aim of our study was to investigate whether and how gender influences weight loss (WL) in two different populations, after sleeve gastrectomy and Ketogenic diet.
Methods: 125 patients with morbid obesity (BMI 40 kg/m^2 or 35 kg/m^2 + comorbidity) eligible to sleeve gastrectomy (group1) and a group of 40 patients following a ketogenic diet (group2). We evaluated anthropometric parameters, peripheral BP, biochemical and serum analysis at the enrollment and at twelve months after interventions.
Results: in the whole population there was a female prevalence (70% in group1 and 60% in group2). Males presented increased adiposity (measured as VFA and fat mass) in both groups and a worse glyco-metabolic profile in group1.
Only after ketogenic diet we observed a significant difference between sexes in total body WL (7.4% in males vs 5.9% in females, $p < 0.05$) and excess of body WL (15.7% in males vs 12.1% in females, $p < 0.05$) in favour of male population. However, only in group1, we observed a larger and significant improvement in adiposity (VFA, fat mass) and glyco-metabolic (HOMA-IR, HbA1c) parameters in males rather than in females.
Conclusion: male subjects, beyond a higher weight and BMI, had a worse glyco-metabolic pattern. No significant difference between sexes was found in WL in group 1 patients; on the contrary, male patients seemed to have a major benefit in WL from ketogenic diet in comparison to female population. In both groups, male sex was an independent predictor of EBWL.
Gender differences in WL intervention could be determined by several factors: hormonal profiles, different body composition or higher initial weight in males. Further studies are necessary to investigate the determinants of these differences.

Effects of next generation tobacco and nicotine products on smooth muscle cell phenotypic modulation

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Background and aims: Hypercholesterolemia and cigarette smoke (CS) are main risk factors for cardiovascular disease. Cholesterol-loading of smooth muscle cells (SMCs) causes a phenotypic switch resulting in less-differentiated cells that lack SMC markers but have an increased inflammatory profile, consequent to a downregulation of the myocardin axis in a Kruppel-like factor 4 (Klf4)-dependent manner. Whole cigarette smoke is made up of over 7000 chemical components distributed between the condensate (CSC) and gas phases. Cigarette smoke aqueous extract (AE) contains water soluble components present in both the condensate and gas phases. Alternative next generation tobacco products (such as E-cigarettes (e-cig) and tobacco heating products (THP)) are being developed as less toxic cigarettes. To characterize the role of CS on SMC behavior, we studied the effects of CSC and AEs (from conventional cigarette, E-cig and THP) on SMC phenotypic modulation.
Methods*:* human aortic SMCs (HSMCs) were incubated for 48 hours with both CSC and AEs and gene/protein expression analyzed by real-time PCR, western blot analysis and confocal microscopy.
Results*:* CSC incubation promoted SMC phenotypic switch (reduced α-actin and
both contractile (α-actin, calponin and SM22) and extracellular matrix genes (collagen, type 1, alpha1, decorin and lumican). Myocardin and Klf4 expression is upregulated (2-fold) and downregulated (-30%) by AE treatment. Interestingly, the expression of pro inflammatory markers such as IL-1β and NLRP3 are increased by the conventional cigarette (2-fold) and halved by the E-cig and THP AEs.
Conclusions: Our data suggest that differently from CSC and cholesterol, AEs promote the contractility state of HSMC and the expression of extracellular matrix components**.** Interestingly, the expression of pro inflammatory cytokines (IL-1β) and NLRP3 are upregulated by the AE of a conventional cigarette and reduced by the E-cigarette and THP AEs.

Abstract selezionato - Presenting author: **Damiano D'Ardes**

Ultrasonographic and elastographic evaluation of lifestyle treatment on patients with Metabolic Syndrome and Non-Alcoholic Hepatic Steatosis

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Aim: Metabolic syndrome (MS) is triggered by expansion of adipose tissue and involved in developing of diabetes, dyslipidemia and CV disease. There is a strong relation between MS and NALFD.
The aim of the study was to investigate the effects of lifestyle treatment on patients with metabolic syndrome and NALFD.
Methods: Between 123 patients screened with elastographic US, 18 patients with MS and NAFLD were studied, analyzing anthropometric, clinical and laboratoristic parameters, including neck circumference, body bioimpedance analysis, HOMA index and upper abdomen US associated to liver elastography. All patients observed lifestyle changes.
Results: After 4 months of lifestyle treatment, a marked decrease in weight, BMI, waist and hip circumferences, fat mass and visceral fat ($p<0.0001$), neck circumference ($p<0.0005$) and blood pressure ($p<0.05$) was observed.
The values of total cholesterol and LDL ($p<0.0005$), basal glycaemia and HOMA index ($p<0.05$), TSH ($p<0.05$), γ-GT and vitamin D ($p<0.005$) had a consistent improvement. The US examination showed improvement in the degree of steatosis ($p<0.05$) and kPa values ($p<0.02$). From the analysis of linear regression in basal conditions, it has been documented that liver dimensions correlated with insulin ($p=0.02$) and HOMA index ($p=0.03$). Moreover, hepatic stiffness correlated with glycaemia ($p=0.005$), insulin ($p=0.04$) and HOMA index ($p=0.006$): all these correlations markedly improved after 4 month of intervention.
Conclusions: Our data demonstrated that not only metabolic profile but also US and elastographic parameters improved in patients with MS and NAFLD, as a confirmation of the fact that a radical change in the lifestyle play an important role in terms of clinical benefit and outcomes. This study showed that the modern elastographic methods, as the shearwave, give us the possibility to assess hepatic stiffness and represent a concrete and non invasive possibility to strictly follow up and manage patients with MS and NAFLD, monitoring their metabolic improvement.

GRK2 expression in immune cells predicts cardiac systolic function after STEMI

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Aim: Cardiac remodeling after an acute myocardial infarct is characterized by molecular, cellular, and interstitial changes leading to changes in size, shape, and function of the heart. Inflammation and immune responses play a crucial role in infarct healing and subsequent LV remodeling. In the setting of heart failure (HF) the observed increased level and activity of GRK2 is correlated to harmful effects on cardiac function and a worse prognosis. GRK2 levels and activity in peripheral blood mononuclear cells (PBMC) are increased in patients with acute myocardial ischemia and associated with a poor prognosis. The possible role of GRK2 in the regulation of the immune system during AMI and involvement in the following cardiac remodeling is not known.
Methods: We enrolled 49 patients with the diagnosis of STEMI. Levels of GRK2 were evaluated in peripheral blood mononuclear cells (lymphocytes, monocytes, and granulocytes), by FACS analysis at hospital admission (time 0) and 24 and 96 hours post-admission.
Results: At the admission, all patients showed a depressed cardiac systolic function as estimated by an EF<40%. After five days post-admission 53.85 (n=31) displayed a recovering of cardiac systolic function (EF>45%) while 46,15% (n=18) did not show a significant recover of systolic function (EF<45%). At time 0, white blood cells (monocytes, lymphocytes, and granulocytes) from patients with EF<45% (fig1), showed an increased level of GRK2 expression compared to the EF>45% group (lymphocytes: 73.4% vs 11.3%, monocytes: 73.5% vs 3%, granulocytes 9.4% vs 2.3%) (fig2). The levels of GRK2 in EF<45% group were persistently higher also at 48 and 96 h post-admission. Interestingly, in the group with EF>45%, the level of GRK2 in lymphocytes and monocytes increased at 96 h post-admission respect to 0 and 48h post-admission.
Conclusions. Our data demonstrate that the different patterns of expression of GRK2 in white blood cells can predict the outcome of the systolic cardiac function in a short time.

Abstract selezionato - Presenting author: **Cristina De Colle**

Awareness of modifiable cardiovascular risks factors

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Aim Cardiovascular risks factors are specific conditions that are associated with increased risk of cardiovascular disease. Awareness of modifiable cardiovascular risks factors is of paramount importance in secondary CV prevention. We aim to assess awareness of modifiable cardiovascular risks factors among patients with recent acute myocardial infarction (AMI).

Methods We interviewed fifty patients (38 men; 12 women) with AMI (50% STEMI; 50% NSTEMI), admitted to Cardiology Rehabilitation Unit of the Federico II university hospital, Naples, from June 2019 to December 2019. We submitted them a questionnaire concerning awareness of life style cardiovascular risks factors.

Results In our study's population the whole sample (100% of patients) identified like CV risk factors hypertension, hypercholesterolemia and obesity; 20% of patients do not recognize conditions like diabetes mellitus and smoke as CV risk factors; moreover, most patients did not recognize daily physical activity and in Mediterranean diet protective factors for cardiovascular disease (respectively 37% and 44% of patients). Patients with AMI-NSTEMI had more awareness of modified cardiovascular risks factors compared to patients with AMI-STEMI.

Conclusions Among patients admitted to Cardiac Rehabilitation Unit for acute AMI awareness of modifiable CV risk factors is suboptimal. In particular physical activities and Mediterranean diet are not recognize as important life style modification for secondary CV prevention. Therefore the important aim for patient care purposes is information and education about life style advices.

Abstract selezionato - Presenting author: **Irene Dominioni**

Effects of anti-hypertensive drug classes on 24-hour pulse pressure amplification

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Introduction: Anti-hypertensive drugs may have differential effects on central (cBP) and peripheral (pBP) office BP, and consequently on their relationship, namely pressure amplification (PPA). We aimed at assessing the effect of anti-hypertensive treatment on PPA evaluated over the 24-hour period.

Methods: 281 treated hypertensives patients (59 ± 14 years, 58% men) underwent ambulatory 24-hour cBP and pBP monitoring (ABPM) using the Mobil-o-Graph. This system determines cBP from brachial oscillometric pressure waveforms by applying a proprietary generalized transfer function. PPA was calculated as pPP/cPP. We excluded severe valvulopathy, LV dysfunction, arrhythmias and peripheral atherosclerotic disease. Daytime and night-time intervals were calculated after removing intermediate shift hours (daytime 09.00-21.00, night-time 01.00-06.00).

Results: 31% patients were treated with monotherapy, 36% with ≥3 drugs. 84% were treated with ACE/ARBs. Mean 24-h PPA was 1.26 ± 0.07, mean daytime PPA (dPPA) was 1.31 ± 0.09, mean night-time PPA (nPPA) was 1.22 ± 0.07. Mean 24-h pBP was 128/78$\pm$14/9 mmHg. In pairwise comparisons, subjects treated vs untreated with ACE/ARBs (60 ± 14 years vs 54 ± 15 years, p=0.01), and with diuretics (63 ± 13 years vs 58 ± 14 years, p<0.01) were older. Treated with calcium-channel blockers (CCBs) were more frequently males (67% vs 50%, p<0.01), whereas treated with beta-blockers (BB) were more females (46% vs 66%, p<0.01). BB were associated with lower 24-h PPA (1.24 vs 1.26, p=0.04) and dPPA (1.29 vs 1.32, p<0.01), whereas CCBs were associated with higher 24-h PPA (1.27 vs 1.25, p<0.01). After adjustment for age, sex and height, only BB were associated with lower dPPA (p=0.02); such association, however, disappeared after further adjustment for HR (p=0.49).

Conclusions: With the exception of BB, all the anti-hypertensive drugs have similar impact on 24-h PPA. BB are associated with reduced dPPA, which is mainly explained by the associated HR-lowering effect, but not with reduced nPPA. BB may be responsible for an increased central hemodynamic load during daytime.

Control of cardiovascular risk factors according to SCORE system in hypertensive patients: ESC/EAS 2016 and 2019 dyslipidemia guidelines comparison

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Aim: Prevalence and control of dyslipidemia, hypertension and diabetes mellitus in patients referred to our ESH ''Hypertension Excellence Centre'' for high blood pressure (BP) and evaluated by ambulatory blood pressure monitoring (ABPM).

Methods: Observational study on 1219 consecutive outpatients referred for high BP with valid ABPM. Low-density lipoprotein cholesterol (LDLc) targets and the cardiovascular risk stratification (SCORE) were defined according to 2016 and 2019 ESC/EAS Dyslipidemia Guidelines. Diabetics with glycated hemoglobin (HbA1c) <7% were considered controlled.

Results: Mean age: 56.5 ± 13.7 years. Male prevalence: 55.6%. Diabetics: 10.8%. Lipid lowering drugs were taken by 23.1% of patients. LDLc control according to 2019 ESC/EAS dyslipidemia guidelines are lower then observed with 2016 ESC/EAS Guidelines (19.2% vs 28.5%, p<0.001). The higher the cardiovascular (CV) risk, the lower was the prevalence of LDLc control (p<0.001). Only 19.2% of treated patients took high-intensity statins and only 25.9% within patients in secondary prevention. BP was controlled in 41.5% and only in 22.3% of high risk patients (p<0.001). Median Hb1Ac: 6.0% (5.6-7.0%) with 27.1% of uncontrolled patients. The prevalence of diabetics increased with CV risk, while their HbA1c control worsened (40.7% of uncontrolled in very high risk).

Conclusion: Cardiovascular risk factors, especially dyslipidemia and diabetes mellitus, are still often neglected in hypertensives, in particular in patients at higher CV risk. After the new lower LDLc targets proposed by the 2019 guidelines, physicians should pay further attention–recommending statins at the right dosages and/or high-intensity statins, in order to control this important CV risk factor.

Lipoprotein(a) levels in patients with premature coronary artery disease: impact on the prognosis and clinical management

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Aim. The association between elevated lipoprotein(a) [Lp(a)] levels and the incidence of the atherosclerotic cardiovascular disease is well established. To date, evidence supporting the role of Lp(a) in predicting recurrent cardiovascular events and influencing the decision-making in young patients with coronary artery disease (CAD) remains limited. We sought to investigate the impact of Lp(a) levels on the recurrence of cardiovascular events and clinical management in patients with premature CAD undergoing percutaneous coronary intervention (PCI).
Methods. From 2013 to 2017, we prospectively screened for Lp(a) consecutive patients undergoing PCI for premature CAD (less than 50 years-old), with both stable and acute presentation. The primary outcome was the occurrence of new major adverse cardiovascular events (composite of cardiovascular death, myocardial infarction, stroke, coronary revascularization, and hospitalization for cardiovascular cause) comparing groups with different Lp(a) concentrations. We also investigated the impact of Lp(a) levels in the clinical decision-making, considering the indication for lipoprotein apheresis in patients with very high Lp(a) levels (≥ 60 mg/dL).
Results. In our population of 63 patients presenting with premature CAD undergoing PCI, Lp(a) resulted elevated (≥ 30 mg/dL) in the 38.03% (n=27) of subjects. Also, 16.90% (n=12) of patients showed severe Lp(a) elevation (≥ 60 mg/dL). In patients with Lp(a) ≥ 60 mg/dL, indications for lipoprotein apheresis was discussed, and apheretic sessions were started in 2 cases. The Kaplan–Meier estimates indicated that the 2-years event-free survival rate for primary endpoint was 91.1% in the group with Lp(a) <30 mg/dL, 79.4% with Lp(a) ≥ 30 mg/dL and <60 mg/dL, and 45.7% with Lp(a) ≥ 60 mg/dL (p-value <0.001).
Conclusion. Elevated levels of Lp(a) are highly prevalent in young patients with CAD undergoing PCI and resulted associated with a higher rate of recurrent cardiovascular events. Systematic screening for Lp(a) might improve their clinical management in terms of prognostic assessment and treatment intensification, including lipoprotein apheresis.

Abstract selezionato - Presenting author: **Ilaria Fucile**

The role of Inferior Vena Cava evaluation in the diagnosis of Acute Heart Failure among dyspnoic patients

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Background: Acute dyspnea is one of the main reason for admission to the Emergency Department (ED). A rapid and accurate diagnosis can be lifesaving for this patients. Particularly, it is important to differentiate between dyspnea of cardiac origin and dyspnea of pulmonary origin. The aim of this study is to evaluate the real accuracy of the evaluation of diameter and collapsibility of IVC for the diagnosis of AHF among dyspnoic patients.
Methods: We analyzed 155 patients admitted for acute dyspnea to the ED of "Maurizio Bufalini" hospital in Cesena (Italy) and "Antonio Cardarelli" hospital in Naples (Italy) from November 2014 to April 2017. All patients underwent ultrasound (lung-cardiac-inferior vena cava) examination with a hand-held device in addition to the traditional pathway. Patients were classified into AHF group or non-AHF group according to the current guidelines.
Results: The final diagnosis was acute dyspnea of cardiac origin in 64 patients and dyspnea of non cardiac origin in 91 patients . The diameter of IVC and the collapsibility of IVC showed low sensitivity (70.3% and 76.6% respectively) and low specificity (75.8% and 69.2% respectively) for the diagnosis of HF. AUC was 0.729 (0.647-0.811) for IVC collapse and 0.731(0.648-0.813) for IVC dilatation.
Conclusion: Our study demonstrated that the sonographic assessment of IVC diameter and / or collapsibility is not really accurate for differentiating acute dyspnea due to AHF or other causes in the emergency setting.

Abstract selezionato - Presenting author: **Jessica Fusaro**

Alterations of the acid-base balance predict circulating levels of HDL cholesterol during sepsis

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Aim: Sepsis, a dysregulated immune response to infections leading to organe damage, is one of the most frequent causes of hospitalization and death in Internal Medicine wards. A large body of evidence shows that circulating HDL cholesterol levels decrease during sepsis and that low levels of HDL cholesterol are associated with increased mortality and adverse clinical outcomes during sepsis. Similarly, disturbances of the acid-base balance are very common in patients with sepsis and contribute significantly to sepsis outcomes. We aimed to assess the relationship between the quantitative changes in HDL cholesterol during sepsis and the concomitant alterations of the acid-base balance.
Methods: In this cross-sectional study, 120 patients admitted to the Unit of Internal Medicine with diagnosis of sepsis, as defined according to the Sepsis-3 criteria, were enrolled. Data regarding medical history, concomitant medications, as well as physical examination, biochemical and blood gas analyses at the admission were collected.
Results: Plasma HDL cholesterol levels significantly correlated with arterial blood pH (rho=-0.251; p=0.006) and pCO2 (rho=0.283; p=0.002), but not with arterial blood HCO3 (rho=0.068; p=0.458). In addition, plasma HDL cholesterol levels were significantly higher among patients with respiratory acidosis as compared to patients with respiratory alcalosis (p=0.024), whereas they were not significantly different between patients with metabolic alcalosis and acidosis (p=0.305). In the subgroup of patients treated with oxygen therapy at the admission, both the correlation between plasma HDL cholesterol and arterial blood pH and that between plasma HDL cholesterol and arterial blood pCO2 were significant (p=0.005 and p=0.020, respectively). Instead, no significant correlation was found between HDL cholesterol and either pH or pCO2 among patients who were not treated with oxygen therapy at the admission.
Conclusions: Plasma HDL cholesterol levels correlate with respiratory disturbances of acid-base balance during sepsis. Oxygen therapy influences the strenght of this correlation.

Abstract selezionato - Presenting author: **Danila Galluccio**

Awareness of cardiovascular risk among hypertensive patients

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Aim: To assess the level of awareness of cardiovascular risk factors among patients from our hypertension clinic and to evaluate the effect of an education-based intervention on healthy lifestyle behaviours on blood pressure and body weight values.

Methods: At the end of the visit, patients were asked to fill out a interviewer-assisted questionnaire focused on their everyday life habits. After they completed it, they received a basic educational intervention from a trained nurse on cardiovascular risk factors. On the same day, they were asked to send a SMS with home blood pressure values and to send two more SMSs with home blood pressure and body weight values one month after the visit.

Results: 64 patients were included in this survey. 56 patients stated they knew that salt plays a role in the development of CVD, but only 28 followed a low-sodium diet. 61 patients were aware that alcohol consumption in small doses could reduce cardiovascular risk and 53 drank it in adequate amount. 59 patients knew that daily aerobic exercise could protect from CVD but only 36 practiced it regularly. All 64 patients were aware of the harmful effects of cigarette smoking. Nonetheless 11 of them smoked and among the latter, 3 smoked more than 20 cigarettes a day. 42 patients had heard about Mediterranean diet and the average score calculated by the MEDI LITE score was 11.38. Only 24 patients knew the correct BMI target and of the 40 patients with BMI> 25 only 13 followed a weight loss diet. Regarding body weight and pressure values, no significant differences were found between the measurements made before and after the educational intervention.

Conclusions: Our survey suggest that although most patients believe themselves to be aware of the main cardiovascular risk factors, this is not always sufficient to stimulate behavioural changes. An insufficient awareness was found about diet and overweight.

Abstract selezionato - Presenting author: **Marta Gazzotti**

Characterization of Familial Hypercholesterolemia in italian children and adolescents enrolled in the LIPIGEN Paediatric group

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Background and Aim: Familial hypercholesterolemia (FH) is a common genetic disorder characterized by elevated LDL cholesterol (LDL-c) concentrations from birth, predisposing to early atherosclerotic lesions and premature coronary heart disease (CHD). Early detection and treatment in childhood or adolescence are crucial to achieve a normal life expectancy. In 2018, the LIPIGEN paediatric group was constituted within the Italian LIPIGEN Network to improve detection, diagnosis, and management of paediatric FH patients.
Methods: In this preliminary analysis, we selected LIPIGEN patients <18 years to evaluate clinical characteristics, biochemical parameters, and genetic profile.
Results: The analyses were carried out on 1562 LIPIGEN patients (48.0% males) with valid data. At diagnostic visit, the study population was composed by 16.8% of subjects with age 0-5 years, 39.9% with 6-10 years, 24.3% with 11-13 years, and 18.9% with 14-17 years. The mean age at diagnosis was 9.1±3.9 years. Excluding subjects with missing data, the family history of early CHD was positive in 12.1% of cases, while the prevalence of LDL-cholesterol (LDL-c)>190 mg/dL among first-degree family members was 57.7%. The mean LDL-c levels among untreated subjects (N=1405), stratified by the four age classes, were 210.2±68.4, 181.5±69.5, 176.9±63.2, and 196.3±61.8 mg/dL, respectively. Among the subjects with genetic testing (N=1148), 60.6% had a positive genetic diagnosis of FH: 96.5% heterozygous for mutations on LDL receptor gene (LDL-R) and two homozygous subjects (2 and 6 years old with LDL-c 877 and 849 mg/dL, respectively).
Conclusion: This preliminary analysis offers a general view of all paediatric data collected until now in the LIPIGEN study, providing a characterization of the clinical and genetic features of paediatric FH. This evidence sets the stage to plan an in depth data collection to better understand the specific diagnostic approach required for paediatric patients.

Abstract selezionato - Presenting author: **Ameneh Ghadiri**

ANGPTL3 facilitates beta-adrenergic dependent lipolysis through increasing insulin resistance in 3T3-L1 cells

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Detection of loss-of-function (LOF) mutations in ANGPTL3 gene in humans revealed the existence of a new lipid phenotype, called familial combined hypolipidemia (FHBL2) and characterized by markedly reduced levels of all lipoproteins. ANGPLT3 protein is known to be involved in the inhibitory regulation of extracellular lipases (LPL and HL), so that its absence increases the lipolytic degradation of TG-rich lipoproteins (in particular VLDL) and HDL. Accordingly, the FHBL2 status is also characterized by reduced levels of circulating free fatty acids (FFA), revealing that ANGPTL3 also plays a role in regulating the metabolism of FFA. Our previous data indicate ANGPTL3 facilitates β-adrenergic-dependent lipolysis in adipocytes and ANGPTL3 treated 3T3-L1 cells showed high levels of ERK1/2 as well as pPKA/PKA and pHSL/HSL, downstream the cAMP-dependent signaling pathway. In order to understand mechanisms through which ANGPTL3 regulates lipolysis in adipose tissue, our purpose is to demonstrate ANGPTL3 can be involved in insulin-resistance development.
Aim: The main aim of present study is to investigate changes in cAMP-dependent pathways induced by the addition of ANGPTL3 to 3T3-L1 cell line
Methods: Changes in release of FFA and in expression of genes (AMPK, P38, AKT and HSL) involved in the canonical and non-canonical activation of lipolytic pathways will be investigated by a combination of biochemical measures, Western blot and RT-qPCR analyses.
Results: Compared to β-agonist (isoproterenol) stimulated cells, adipocytes treated with isoproterenol (Iso), in presence of ANGPTL3, showed highest levels of intracellular cAMP (Iso 4,25 nM; ANGPTL3 pre-treatment 7,89 nM; *p<0,001)* and increased activation of kinases.
Conclusion: Recently, it was shown that AMPK-P38-AKT pathway activation increases insulin-resistance in adipocytes, which leads to a greater availability of cAMP within the cell. According to literature, our findings indicate ANGPTL3 facilitates FFA release in adipose tissue counteracting the insulin inhibitory action against β-adrenergic-dependent lipolysis.

Abstract selezionato - Presenting author: **Valentina Giani**

Neurological hypertensive emergencies: correlation of blood pressure values with in-hospital mortality and discharge disability

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Aim: definitive data on acute management of Blood Pressure (BP) in neurological Hypertensive Emergencies (HE) are still lacking. Aim of our study was to evaluate BP values and management as a determinant of in-hospital mortality and early complications in stroke patients.

Methods: we collected data of 267 patients, who presented with ischemic stroke and BP≥180/120 mmHg at the Emergency Department of Niguarda Hospital from 2015 to 2017. In-hospital mortality, hospitalization length and discharge disability (evaluated with modified Rankin score – mRs) were considered as outcomes.

Results: Mean age was 75.7 ± 11.7 years with SBP values of 194.9 ± 14.9 mmHg at admission. 34.8% of the patients received anti-hypertensive treatment with those achieving a higher SBP reduction in comparison with the untreated one (∆SBP 37.8 ± 26.8 mmHg vs 30.7 ± 20.8 mmHg p=0.034). At the multivariate analysis in the overall population, no SBP values are related to all causes in-hospital mortality. Instead, higher admission SBP relates to high discharge disability and hospitalization length. Furthermore, BP values at admission in Emergency Department appear as disability determinants in patients who did not receive systemic thrombolysis and in patients who did not receive antihypertensive drugs. In these two subgroups, higher SBP values at department entrance determine a higher in-hospital mortality.

Conclusions*: In overall population, no BP values are related to all causes in-hospital mortality while higher admission BP relates to high disability and hospitalization length.

Abstract selezionato - Presenting author: **Mariagrazia Gueli Alletti**

Management of Homozygous Familial Hypercholesterolemia: genotyping as driver of appropriate Therapeutic Approach

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Aim: Homozygous Familial Hypercholesterolemia (HoFH) is a rare genetic disorder characterized by very high levels of LDL-C and premature atherosclerotic cardiovascular disease (ASCVD). HoFH due to LDLR gene mutations are classified into two groups based on the residual functional activity of LDL-R: patients < 2% of normal LDLR activity are classified as receptor negative and patients with 2 to 25% of normal LDLR activity as receptor-defective. We describe the clinical characterization of a subject with severe hypercholesterolemia.
Methods: The proband is a 52-year-old man. Severe hypercholesterolemia (about 400 mg/dL) was first noted when he was 23 and a treatment with simvastatin was prescribed. He suffered an episode of acute coronary syndrome at 38 years of age and he underwent a PTCA procedure. The coronary angiography revealed a diffuse non stenotic atherosclerosis of the coronary tree beside the treated culprit lesion. Treatment with high efficacy statin at the maximum tolerated dose (rosuvastatin 20 mg/d) in association to ezetimibe did not allow to reach the suggested LDL-C goal. Genetic analysis was performed by Next Generation Sequencing (NGS) using Ion Torrent PGM in order to analyze candidate genes involved in FH.
Results: We identified an homozygous LDLR gene mutation (c.2359G/A; p.Val797Met) previously classified as receptor-defective. On top treatment with evolocumab 420 mg very effectively reduced We decide to add PCSK9 monoclonal antibody therapy in order to improve clinical and biochemical conditions. After one month of treatment with REPATHA at 420 mg we observed a relevant decrease of LDL-c levels (from 150 mg/dL to 22 mg/dL).
Conclusions: Residual LDLR expression in HoFH is a major determinant of LDL-C levels and seems to drive their individual response to evolocumab.

Abstract selezionato - Presenting author: **Gianfranco Inglese**

Progression of heart damage in well-controlled hypertensives: a single center study

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Aim of this study was to investigate the changes in heart and vessel wall parameters during treatment in patients already treated

Materials and Methods. Out of 770 patients evaluated for secondary prevention, we studied 51 patients (27 women and 24 men, aged 59.2 ± 9.3 years) who have been revaluate after two years with the same tests (Time 0 vs Time 1). They were all well controlled hypertensives with a mean number of two drugs taken; moreover just 4 were smokers and 23 are also in statin's treatment. They resulted in overweight (BMI 27.39±3.69 kg/m^2)

Results. At Time 1 we found a slightly little but significant increase in SBP (Time 0 124.7 ± 7.78 vs Time 1 128.1 ± 6.28 mmHg, $p<0.05$) while no difference was found in DBP, HR and BMI. eGFR results significantly reduced despite it is still in normal range (Time 0 93.2±15.8 vs Time 1 82.7±14.7 ml/m^2, $p<0.05$). Left ventricle mass results increased both as absolute value (MLV; Time 0 215.7±53.1 vs Time 1 238.2±58.5 gr, $p<0.05$) and indexed for BSA (MLVi; Time 0 120.3±24.8 vs Time 1 130.6±28.1 gr/m^2, $p<0.05$). Similarly Left Atrium volume (LAV) results increased both as absolute value (Time 0 56.7±23.8 vs Time 1 66.7±20.8 ml, $p<0.05$) and indexed for BSA (LAVi; Time 0 31.6±13.5 vs Time 1 36.9±11.0 ml/m^2, $p<0.05$). On the contrary, no difference was find in interventricular septum and ejection fraction. Aortic Root diameter results decreased at Time 1 (Time 0 32.1±3.2 vs Time 1 30.8±4.4, $p<0.05$) as well as intima-media thickness (IMT; Time 0 1.3±0.7 vs Time 1 .1±0.2 , $p<0.05$).

Conclusion. These data show an increase of MLV, MLVi, LAV and LVAi after two years treatment continuation as well as Aortic diameter and IMT, despite SBP and eGFR worsening remains without a clinical significance. This could suggest an organ damage progression despite an optimized therapy.

Role of GLP1-RA in reducing epicardial fat thickness in type 2 diabetics with atrial fibrillation patients: a study protocol

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Background Visceral adipose tissue (VAD) is not only a way to storage lipids by organism. Furthermore, it acts also as an endocrine organ, having a key role in the development of some cardiovascular and metabolic diseases. Such tissue is strictly related to glucose metabolism: due to its vascular and nervous networks, VAD could drain into the portal system, exposing liver to adipocytes both endocrine and paracrine effects. These result in metabolic alterations such as reduced hepatic extraction of insulin and increased production of hepatic glucose (gluconeogenesis), which in turn, explains the link between visceral obesity and glucose dis-metabolism, included diabetes [1]. Furthermore, it has been demonstrated that cardiovascular risk is not simply dependent from overweight but more importantly, it depends from peri-visceral accumulation, particularly in the so-called epicardial fat (EAT)[2].
EAT is defined as the visceral intrapericardial fat contiguous with the myocardial surface. Several evidences suggest a key role of EAT in the onset of AF via structural and electrical remodeling of the atria by both direct (e.g. by the infiltration of adipose tissue leading to altered atrial electrophysiological properties) and indirect mechanisms (e.g. by acting as a source for paracrine modulators of myocardial inflammation and oxidative stress)[3].
On the other side diabetes increases the risk of developing AF through structural, electrical, electromechanical and autonomic remodeling [4]. It is well known that diabetic cardiomyopathy is associated with changes in sympathetic tone which, in turn, predispose to AF.
Of note, in type II diabetics patients, the amount of epicardial fat is significantly higher than non-diabetics [5].
GLP-1A (Glucagon-like peptide 1 agonists) are knew to have beneficial cardiovascular effects, reducing EAT, possibly through targeting GLP-1R (GLP-1 receptor) expressed on epicardial fat [6]. Current data on EAT remodeling by GLP1 RAs is derived by two studies, conducted with liraglutide and exenatide. On the other hand, how GLP1-RA exert their beneficial effects on cardio-metabolic disease are unknown yet.
Objectives We aim to demonstrate if GLP1-RA treatment in patients affected by type 2 diabetes mellitus is able to reduce the risk of atrial fibrillation Incidence Due To The Decrease Of Epicardial Fat.
Matherials and Methods This is an approximately 50-week, single-centre, prospective, non-interventional study assessing the effectiveness of once-weekly GLP1-RA in adult patients with type 2 diabetes in routine clinical practice. Data will be obtained through primary data collection. The study is non-interventional as the decision to initiate treatment with GLP1-RA is at the treating physician's discretion, and clearly separated from the decision to include the patient in the study. Patients with an history of paroxysmal AF and type 2 diabetes will divided into 2 groups, GLP1a and antidiabetic standard theraphy. Anthropometric measures (height, weight, body mass index (BMI), body circumferences), body composition (Bio-electrical impedance analysis-BIA), carotid intimal media thickness, artherial stiffness, pro-infiammatory cytokines, routine laboratory tests and epicardial fat thickness will be measured at enrollment and after six month.
Expected Results Basing on literature, we expect that GLP 1-RA playing a key role in reducing metabolically active fat, induce positive effects in reducing atrial fibrillation recurrence. To sum up, these observations could explain how GLP1-RA exert their cardio-protection effects.

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Abstract selezionato - Presenting author: **Simonetta Lugari**

The clinical relevance of genetic variants of uncertain significance in familial hypercolesterolemia

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Introduction and aim: Next-generation sequencing has resulted in rapid genetic diagnosis of patients with suspected familial hypercholesterolemia (FH); however, genetic variants of uncertain significance (VUS) with an unknown causal link to the disease are being increasingly identified. We aimed at evaluating the clinical significance of VUS in our FH cohort.

Methods: 191 consecutive patients with suspected FH from the Lipid Clinic in Modena underwent comprehensive evaluation, including genetic analysis, within the LIPIGEN Project. Patients were categorized in four groups according to the detection of "pathogenic"/"likely pathogenic" mutations (M) and/or VUS in autosomal dominant FH-causing genes (LDLR, APOB, PCSK9, STAP1, APOE) as follows: M-/VUS-, M-/VUS+, M+/VUS-, M+/VUS+.

Results: M and/or VUS were detected in 162 (84.8%) patients (147 M and 50 VUS). The vast majority of M affected LDLR (95.9%), whereas VUS were more heterogeneously distributed across FH-causing genes (LDLR 24%, APOB 60%, PCSK9 14%, APOE 2%).M-/VUS- (n=29) and M-/VUS+ (n=18) patients did not significantly differ for age, LDL cholesterol (LDL-c) and Lp(a) levels, Dutch Lipid Clinic Network (DLCN) score, duration of statin therapy, family and personal history of cardiovascular disease, presence of arcus cornealis or Achilles tendon xanthomas. M-/VUS+ patients showed significantly lower LDL-c levels (p<0.001), DLCN score (p<0.001) and duration of statin therapy (p=0.034) and were less likely to have Achilles tendon xanthomas (p=0.038) and a positive family history of cardiovascular disease (p=0.031) than M+/VUS- patients (n=116). Of note, polygenic LDL-c score was similar between M-/VUS- and M-/VUS+ (p=0.134), but significantly higher in M-/VUS+ than M+/VUS- patients (p=0.008). No significant differences were found between M+/VUS- and M+/VUS+ patients (n=28). Restricting the analyses to VUS in LDLR yielded to similar results.

Conclusions: In our FH cohort, VUS carriers had a biochemical and clinical profile similar to that of mutation-negative patients. Moreover, the coexistence of VUS did not increase the phenotype severity in mutation-positive patients.

Abstract selezionato - Presenting author: **Maria Giovanna Lupo**

MK7-based novel nutraceutical combination showed cholesterol-lowering activity in uremic rats: insights of its molecular mechanism in hepatoma cell line

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Aim: Appropriate nutraceutical combinations may represent a valid approach to prevent vascular calcification associated to chronic kidney disease (CKD). In the present study, we tested the effect of a new nutraceutical combination named RenaTris® containing MK-7, magnesium carbonate and Sucrosomial® Iron on vascular calcification in uremic rats.

Methods: Thirty-tree male rats were randomly subdivided into three groups of 11 rats each, with each group fed one of the specific diets for 6 weeks. The control group was fed the standard diet (1.2% phosphate, 19% protein); the uremic group was fed diets containing adenine (0.5%), high phosphates (1.2%) and low proteins (4.5% protein); the treated group was fed with the same diet that uremic group with MK-7 (3.5 µg/g of diet), MgCO3 (3,7 µg/g of diet) and Sucrosomial® Iron (1 mg/g of diet) (RenaTris®, PharmaNutra S.p.A.). At death, blood and aortas were collected. The examination of arterial medial calcification was performed both by von Kossa staining and by commercially available calcium kits. Serum total cholesterol were determined by colorimetric assay. Human hepatoma cells (Huh7) were incubated in MEM/10%FCS and treated with increasing concentrations of MK-7. LDLR, HMG-CoA reductase and PCSK9 mRNA and protein levels were assessed by RT-qPCR and western blot, respectively.

Results: Uremic diet increased creatinine and phosphate levels and extensive vascular calcification. The uremic condition also induced a mild hypercholesterolemia condition (+52% of total cholesterol; $p < 0.05$). Supplemented uremic diet did not reduce creatinine and phosphate levels as well as vascular calcification, however we observed a significant hypocholesterolemic effect (-18.9% in supplemental uremic vs uremic diet; $p<0.05$). Similarly to simvastatin, incubation of Huh7 with MK-7 significantly reduced cholesterol biosynthesis (-35÷40%) and induced HMG-CoA reductase and LDLR at both mRNA and protein levels. The effect of MK-7 on LDLR was counteracted by the co-incubation with squalene. Differently from simvastatin, MK-7 reduced PCSK9 in Huh7.

Conclusions: These results indicated that this new nutraceutical combination has a significant impact on cholesterol metabolism and its supplementation may help to control the mild hypercholesteremic conditions in CKD patients.

Abstract selezionato - Presenting author: **Francesco Maiellaro**

Blunted heart rate reserve during vasodilator stress echocardiography in diabetic and renal failure patients.

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Background A blunted heart rate reserve (HRR) during dipyridamole stress echo (SE) is a marker of cardiac autonomic dysfunction associated with poor outcome, independently of inducible ischemia, underlying coronary artery disease (CAD) and beta-blocker therapy. Patients with diabetes and/or renal failure have higher prevalence of underlying autonomic dysfunction.
Aim. To assess the value of HRR in patients undergoing dipyridamole SE.
Methods We prospectively recruited a sample of 61 patients with known or suspected CAD (mean age 75±10 years; 34 males, 55,7%; 50% on beta-blockers at the time of testing). Coexistent atrial fibrillation or previous pacemaker implantation were considered as exclusion criteria. Three groups were identified a priori: non-diabetic with normal renal function (n=43, Group 1); diabetics, with normal renal function (n=14, Group 2); severely impaired renal function on dialysis (n=4, Group 3). All patients underwent dipyridamole SE (0.84 mg/kg in 10').

Wall motion score Index (WMSI) was calculated with a 17-segment score of left ventricle, each segment scored from 1= normal to 4= dyskinetic. HRR was measured by ECG as the peak/rest HR ratio.
Results A positive SE (stress WMSI> rest WMSI) was present in 2 patients of Group 1 (4.7%), 4 of Group 2 (28.6%) and no patient in Group 3. Heart rate was different, although not significant, among the 3 groups both at rest (66.1±11.1 vs 64.6±8.5 vs 79.0±8.0, p=0.050) and at peak stress (83.8±12.6 vs 75.3±10.3 vs 86.5±11.1, p=0.059). Of note, HRR was statistically different among groups (1.29±0.20 vs 1.19±0.14 vs 1.09±0.06, p<0.047; see figure). There was no difference in HRR between patients off and on-beta-blockers (1.19±0.16 vs 1.24±0.24, p=0.421) and with or without positive SE (1.20±0.14 vs 1.25±0.20, p=0.530). Overall, HRR≤1.17 (median value) was reported in 39.5% of Group 1, 71.4% of Group 2, and 100% of Group 3 pts (p=0.024). No significant correlations between HRR and peak WMSI (p=0.183) or age (0.062) were reported.

Conclusion HRR is frequently abnormal in patients referred for SE testing, especially in presence of concomitant diabetes and advanced renal failure. The blunted chronotropic response is a simple, imaging independent marker of cardiac autonomic dysfunction and may usefully complement the conventional evaluation with regional wall motion abnormalities during vasodilator SE.   Figure title: HRR box plots
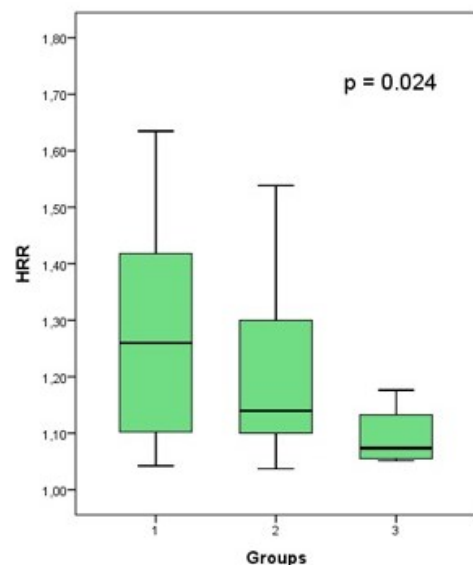
Genetic screening of patients suffering from Familial chylomicronaemia syndrome and multifactorial chylomicronaemia syndrome

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Aim. Severe hypertriglyceridemia consist in triglyceride (TG) levels above 10 mmol/L leading to increased risk of acute pancreatitis. This condition is due to impaired clearance of TG-rich lipoprotein from plasma associated with pathogenic variants in genes involved in metabolism of TG-rich lipoprotein (*LPL, APOA5, APOC2, GPIHBP1* and *LMF1).* The presence of two pathogenic variants leads to Familial chylomicronaemia syndrome (FCS), a very rare, inherited, autosomal recessive disorder. More often, high levels of TG are ascribable to multifactorial chylomicronaemia syndrome (MCS), due to the combination of predisposing variants in candidate genes with co-morbidities and environmental factors. We aimed to screen 28 unrelated patients with severe hypertriglyceridemia, recruited based on plasma TG>10 mmol/L.
Methods. The coding regions with the flanking intronic regions of candidate genes were analysed. Multiplex ligation-dependent probe amplification was used to search for large rearrangements in the *LPL* gene. Some patients were reanalysed by NGS with a custom panel of 28 genes involved in lipid metabolism.
Results. Nine patients resulted homozygotes or compound heterozygotes for 2 pathogenic variants. In 7 patients we found only 1 pathogenic/likely pathogenic variant. Rare variants in *APOB*, *ABCG5* and *ABCG8* genes were identified by NGS in 4/7 patients with only 1 pathogenic/likely pathogenic variants. One variant in *APOB* gene were classified as pathogenic while the rare variant found in the remaining gene were classified as variants of uncertain significance.
Conclusions. Our genetic screening revealed that 9 out of 28 patients presented 2 pathogenic variants, classified as FCS patients. The NGS method is useful for genetic diagnosis of FCS/MCS patients since it identifies potential modifying variants.

Abstract selezionato - Presenting author: **Anna Mantovani**

A multidisciplinary approach to Non-Alcoholic Fatty Liver Disease (NAFLD) improves cardiovascular risk factors

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Aim: Cardiovascular (CV) disease is the leading cause of death in unselected patients with non-alcoholic fatty liver disease (NAFLD). Although the need of a multidisciplinary approach is highlighted in guidelines, there is lack of data to demonstrate its effectiveness. We assessed the efficacy of a multidisciplinary clinic through control of metabolic comorbidities and surrogate markers of liver involvement.

Methods: Prospectively collected data of 273 patients referred to a multidisciplinary NAFLD clinic, comprehensive of a hepatological consultation, cardiovascular risk assessment and dietetic counseling were analyzed.

Results: Mean age was 56.4 ± 12.1 years, with 57% males. The median follow-up was 18 months. The prevalence of obesity, hypertension and diabetes was 60%, 67% and 50% respectively, while 13.2% had a positive history of CV events. At baseline, dyslipidaemia management was suboptimal in 64 patients (25.2%), while 57 (41.9%) patients with diabetes and 36 (19.6%) patients with hypertension needed modification of their treatment. During follow-up, there were statistically significant improvements in ALT (p=0.013), AST (p=0.013), systolic and diastolic blood pressure (p=0.002 and 0.014 respectively), total cholesterol (p<0.001) and glycated haemoglobin in diabetic patients (70.2 to 62.5 mmol/mol, p=0.04). 142 patients (52%) achieved weight loss during the follow-up ($\geq10\%$, $\geq7\%$ and $\geq5\%$ in 8.2%, 6% and 7.3% of the cohort respectively). The total number of patients with a QRISK3 score$\geq10\%$ decreased from 156 (62.7%) to 97 (48.5%).

Conclusions: A multidisciplinary NAFLD approach was effective in improving liver-related and CV risk factors. A strong collaboration between primary and secondary care is essential to implement and maintain these improvements in the long term.

Fat-Shaped Microbiota Affects Lipid Metabolism, Liver Steatosis And Intestinal Homeostasis In Mice Fed A Low-Protein Diet

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Aim. Protein malnutrition is characterized by stunted growth, hepatic steatosis and a damaged gut mucosal architecture. Since high-fat shaped gut microbiota (HFM) has an increased ability in providing nutrients and energy from food to the host, the aim of this study was to determine whether such a microbiota could beneficially impact on the consequences of malnutrition.

Methods. The cecal content of specific pathogen free C57Bl/6 mice fed a high-fat diet or a low-protein diet was transplanted in two groups of germ-free C57Bl/6 recipient mice, which were subsequently fed the same low-protein diet for 8 weeks.

Results. Body weight gain was comparable between the two groups of microbiota-recipient mice. The high-fat shaped microbiota (HFM) led to a worsening of microvesicular steatosis and a decrease of plasma lipids compared to the low-protein shaped microbiota (LPM). In the ileum of mice receiving HFM, villi length, crypt depth and presence of neutral and acid mucins were not different. On the contrary, the expression of antimicrobial genes promoting oxidative stress and immune response at the gut epithelium (Duox2, Duoxa2, Saa1, Defa5, Ang4) was increased. In the colon, the same histological parameters were evaluated, and the crypt depth was reduced in HFM- compared to LPM-recipient mice.

Microbiota composition was evaluated shortly after the transplant and at the end of the study by next generation sequencing, and we found signatures specific to the two experimental groups.

Conclusion. The transplant of HFM in mice fed a low-protein diet represents a noxious stimulus for the ileal mucosa and impairs hepatic lipoprotein secretion, favoring the occurrence of hepatic microvesicular steatosis.

Abstract selezionato - Presenting author: **Denise Marcon**

Ethnic disparities in hypertension-mediated organ damage and its usefulness for the clinical management of subjects with grade I hypertension

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Background: Ethnic disparities in the prevalence of hypertension (HT) exist but data on hypertension-mediated organ damage (HMOD) are conflicting. Here we explored if ethnic differences in HMOD can be found in a dual ethnic cohort of subject with grade I HT and we tested if the evaluation of HMOD provides additional information for the clinical management of untreated patients compared to the estimation of 10-year cardiovascular risk (CVR).

Methods: In subjects with grade I HT and self-described ethnicity as "Black" or "White" HMOD was assess with albumin/creatinine ratio (ACR, urine spot), left ventricular mass index (LVMI, cardiac ultrasound) and carotid-femoral pulse wave velocity (cfPWV, Sphygmocor) alongside with brachial blood pressure (BP) measurements. In untreated subjects, 10-years CVR was estimated using QRISK3 calculator.

Results: 58 Black (26 female) and 61 White (17 female) subjects were recruited. White subjects were older compared to Black ones (49 years vs 43 years respectively) but there were no difference in their duration of hypertension (~ 4.5 years) and BP (mean ± standard error) 146.3 ± 0.8 vs 146.8 ± 0.9 mmHg for systolic BP and 89.2 ± 0.9 vs 89.2 ± 0.7 for diastolic BP respectively). LVMI (101.4 ± 3.6 vs 81.6 ± 3.2) g/m^2, ACR (7.5 ± 2.9 vs 1.9 ± 2.8)mmol/mol and cfPWV (10.6 ± 0.4 vs 9.2 ± 0.4)m/s were higher in Black subjects compared to White after adjustment for confounders (BP, age, gender, body mass index, creatinine, diabetes and dyslipidaemia); all $P<0.05$. In untreated subjects (n=59), 14 had evidence of HMOD including microalbuminuria, left ventricular hypertrophy and/or cfPWV>10 m/s. Of these, 4 had CVR > 10%.

Conclusions: For a similar level of BP, HMOD is more prevalent in Black compared to White subjects with grade I HT. Evaluation of HMOD is superior compared to CVR estimation in identifying subjects who may be started on medical treatment.

Abstract selezionato - Presenting author: **Giulia Massini**

The therapeutic approach of primary hyperlipidemia in children

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Aim: This study was addressed to hyperlipidemic children in order to evaluate the effect of three step options on LDL-cholesterol (LDL-C) target in children/adolescents affected by primary hyperlipidemia.

Methods: Children and adolescents (n.910; mean age 8.9±4.2yrs) with familial hypercholesterolemia (FH) and polygenic hypercholesterolemia (PH) were selected. Normocaloric CHILD I/CHILD II diets enriched of cereals, legumes, fish, plant foods, nuts, olive oil, daily moderate consumption of dairy products, eggs and small amount of meat were suggested and the compliance checked by week diaries. Phytosterols were added to improve LDL-C target while statins were administered to FH patients or other drug strategies were applied.

Results: The diet efficacy was considered in compliant patients (n.343) who achieved total cholesterol (CT) and LDL-C reduction (7.3%, 9.8% respectively). Significant positive correlations between total fat and TC, and LDL-C, SFAs and TC was demonstrated in FH patients. Phytosterols (n.130) led to a significant drop in TC and LDL-C (11.2%, 14.3% respectively). Pravastatin 20 mg/day reduced LDL-C by 25.4% but just 18% of patients achieved LDL-C ≤ 130 mg/dl while on Rosuvastatin 10/20 mg/day the target was reached by the majority.

Conclusions: Diet and food supplements represent the first efficacious step of an early treatment of hyperlipidemia in children. Limits are represented by the compliance then family education is of great value. Moreover, lipid improvement was correlated to total fatty acids change, particularly to the SFAs reduction. Statins are well tolerated and requested to achieve the therapeutic target in subjects with high cardiovascular risk.

Abstract selezionato - Presenting author: **Rosanna Matturro**

Effects of PCSK-9 inhibitors on carotid atherosclerosis

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Aim: Proprotein convertase subtilisin/Kexin type 9 (PCSK9) inhibitors reduce LDL-C in statin-ezetimibe treated patients and improve outcomes of myocardial infarction and stroke. The GLAGOV trial demonstrated that Evolocumab in patients treated with statin therapy had a favourable effect on the progression of coronary atherosclerosis as measured by IVUS. However, the effects of PCSK9 inhibitors on carotid plaques have not yet been evaluated.

Methods: We enrolled 46 patients aged more than 18 years, with CIMT>1.1 mm, affected by Heterozygous Familial Hypercholesterolemia (HeFH) with LDL-cholesterol values > 70 mg/dL in secondary prevention or > 130 mg/dL in primary prevention or affected by non-Familiar Dyslipidemia or Mixed Dyslipidemia in secondary prevention with LDL-cholesterol levels> 100 mg/dL. All patients were on maximum tolerated statin dosage and ezetimibe and treated by evolocumab or alirocumab. Supra-aortic trunks echo-color-Doppler was performed before starting the therapy (time 0), after 6 months and then after 12 months of therapy.

For each carotid CIMT, PSV (Peak Systolic Velocity), EDV (End Diastolic Velocity) and ICA / CCA PSV ratio were measured.

Results: We observed after 6 months a reduction of right mean CIMT of -0.09 ($p=0,000$ vs. baseline) and of -0,14 of left CIMT ($p=0,008$ vs. baseline); the reduction was for right CIMT after 12 months of - 0.16 ($p=0,006$ vs 6 months) and for left CIMT of -0.15 ($p= 0,005$ vs 6 months).

Between 0 time and 12 months of treatment we observed a reduction of -0,16 ($p=0,05$) for right CIMT and of -0,18 ($p=0,004$) for left CIMT. LDL-C levels were reduced from 134 ± 35,73 mg/dL at baseline to 65,61 ± 41,43 mg/dL after 6 months ($p=0,000$) and to 51,50 ± 18,67 mg/dL after 12 months ($p=0,000$).Moreover, we observed a progressive "remodeling" of the plaques, modifying from a soft/dense composition to a predominantly fibro-calcific composition ($p=0,000$ for 0 vs.12 months).

Conclusions: This is the first study showing that the inhibitors of PCSK9, can decrease or even reverse the progression of carotid atherosclerosis, reducing the intima-media thickness, the lipid content of atheromatous plaques leading to a reduction of clinical adverse events.

Abstract selezionato - Presenting author: **Serena Melandri**

Does POINT of CARE US (PoCUS) affect diagnostic management of acute respiratory failure?: The challenge of a non-invasive tool to help differential diagnosis

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Acute dyspnea is a common symptom in ED and Internal Medicine wards. Differential diagnosis includes acute decompensated heart failure (ADHF), pneumonia, COPD, pulmonary embolism (PE), sepsis, exc. An erroneous diagnosis increases the risk of prolonged hospital stay and mortality. Standard approach relies on chest x-Ray (CXR) and lab results (CRP, blood count, ABG, BNP) but supine CXR shows low sensibility and lab tests are time consuming. Our goal is to determine the accuracy of an integrated PoCUS approach for differential diagnosis of acute dyspnea.

40 consecutive adult patients presenting with dyspnea to ED were enrolled. After initial clinical evaluation, EKG and ABG, a PoCUS was performed and initial diagnostic hypothesis was formulated. We scanned the lungs for PNX, pleural effusion, interstitial syndrome (B-pattern in >2 lung scan per hemithorax), pneumonia; the heart for qualitative measure of EF, chambers' size and valve defects; the ICV for diameter and collapsibility index and deep leg veins in the suspicious of PE. After PoCUS, every patient underwent CXR and lab tests. Then we compared US diagnosis with the final one, independently determined by physicians blinded to PoCUS. Cohen's k is used as a measure of agreement between the two diagnosis.

Mean age of patients was 77.5 (SD +/-13.6). Final diagnosis was cardiologic in 14/40, pulmonar in 19/40, mixed in 7/40. Concordance between US and final diagnosis resulted optimal (0.84<k<1) for pneumonia, PE, ADHF and pleural effusion; good for COPD (0.63) and ARDS (0.655). Lung interstitial sindrome is associated with ADHF (81% ADHF pts vs 10% non-ADHF; $p<0.001$) such as its combination with dilated and fixed IVC (61.1% ADHF pts vs 0% of non-ADHF; $p<0.001$).

PoCUS represents a feasible and reliable diagnostic approach to the dyspnoic patients, allowing a reduction of the diagnostic time.

Abstract selezionato - Presenting author: **Martina Milani**

Uric acid in acute coronary syndromes: correlation with in-hospital mortality and complications

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Background: Uric acid (UA) has been related to in-hospital mortality in patients with acute coronary syndromes (ACS), to early relapse, after ACS, of non-fatal cardiovascular events and to negative intermediate outcomes such as use of intra-aortic balloon pump, non-invasive ventilation, longer inward stay, bleeding, clinical presentation with Atrial Fibrillation (AF) or Heart Failure (HF). Aim of this study was to evaluate the role of UA as a possible determinant of primary (in-hospital mortality) and secondary outcomes defined as variables of relapsing ischemia (myocardial re-infarction, in-stent thrombosis, bleeding, stroke), worse clinical presentation (with HF or AF, admission EF, trivasal coronary artery disease (CAD) at the coronary angiography), in-hospital complications (use of inotropes, intra-aortic balloon pump and non-invasive ventilation during hospital stay) and worse recovery (discharge EF).
Methods: 563 patients, admitted for ACS to Cardiological Intensive Care Unit of Niguarda Ca' Granda Hospital, were enrolled for this retrospective cohort study. Cox regression analysis was performed to evaluate the association between UA and primary and secondary outcomes, adjusting for the following covariates: age, gender, previous myocardial infarction, arterial hypertension, Charlson Comorbidity Index and creatinine.
Results: mean age was 66.5 ± 12.3 years, 79.2% of the patients were males and 49.9% were ACS-STEMI. Hyperuricemic subjects were older, with more prominent cardiovascular risk factors and history of previous myocardial infarction. They more frequently died during hospital stay, had HF and AF as clinical presentation, more commonly had trivasal CAD and needed intra-aortic balloon pump and non-invasive ventilation. Also EF at admission and discharge were lower in hyperuricemic patients. At multivariate analysis, UA was a significant determinant of primary and secondary outcomes (except for trivasal CAD, bleeding, stroke, re-infaction and in-stent thrombosis).
Conclusions: UA is an independent determinant of in-hospital mortality and a variable suggestive for worse clinical presentation, in-hospital complications and worse recovery.

Abstract selezionato - Presenting author: **Giulia Mingrone**

Global longitudinal strain changes during Carfilzomib therapy in patients with multiple myeloma

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Aim: Carfilzomib improves dramatically the prognosis of refractory multiple myeloma (MM) patients, but it seems to increase the heart failure incidence. Left ventricular ejection fraction (LVEF) is the most common echocardiographic parameter to evaluate cardiac toxicity related to oncological treatments, but the speckle tracking technology has been increasingly used to early identify alterations in cardiomyocytes contraction and subclinical myocardial damage. We sought to assess the left ventricular function variation, including global longitudinal strain (GLS), during Carfilzomib therapy.

Methods: 48 patients with MM and indication for Carfilzomib treatment were enrolled. They performed a baseline cardiovascular evaluation comprehensive of transthoracic echocardiogram; a second evaluation was performed at about 6 months (median 5.61; interquartile 4.9-6.7) from the beginning of Carfilzomib. To determine the incidence of cardiovascular events (CVAEs) all patients were followed-up during therapy.

Result: LVEF did not change after Carfilzomib therapy (62.4 ±6 vs 61.6±5.5; p=0.4), but GLS measurements had a significant impairment (-21.9± 2.5 vs -21.1±2.25; p=0.007). A proportion of 52% of patients had CVEAs after about 4 months of therapy (median 3.4; interquartile 0.8-6.2), 90% of them had uncontrolled hypertension. The subgroup of patients with CVEAs had not a statistically significant impairment in GLS values (-21.9 ± 2.8 vs –21.2 ±2.7; p= 0.057) and LVEF remained stable (62.1± 6 vs 61.2 ± 5.3; p=0.5).

Conclusions: Carfilzomib seems to lead to an impairment of left ventricular function early demonstrated only by GLS changes. However, in the subgroup with CVEAs, the LVEF and GLS are not statistically significant impaired. These preliminary findings, may suggest a pre-clinical ventricular damage related to Carfilzomib

Abstract selezionato - Presenting author: **Ilenia Minicocci**

Monogenic versus polygenic familial hypercholesterolemia: genetic risk score and response to treatment

Ilenia Minicocci[a,*], Laura D'Erasmo[a,*], Alessia Di Costanzo[a], Giovanni Pigna, Daniela Commodari[a], B Pharm, Fabrizio Ceci[b], Anna Montali[a], Marianna Maranghi[a], Marcello Arca[a]
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Background: A polygenic background can be recognized in part of patients with clinically diagnosed familial hypercholesterolemia (FH). The phenotypical distinction between monogenic (due to causative mutations in major LDLR, APOB or PCSK9 genes) and polygenic FH is not completely clarified.

Aims: We aimed to compare the clinical phenotype and response to treatment in monogenic *vs.* polygenic FH

Methods: Five hundred patients with clinical FH diagnosed based upon DLCNC> 3 were genotyped. Causative monogenic variants were identified by NGS and the polygenic score (GRS) was estimated by the 6-LDL-rising SNPs panel. Patients' clinical characteristic and LDL-C changes during cholesterol-lowering treatments were retrospectively obtained.

Results: 323 (64.6%) patients were FH-mutation positive (monogenic FH) and 177 (35.4%) patients were classified as FH-mutation negative (FH/M-)**.** In comparison with normocholesterolemic subjects, FH/M- patients had higher mean GRS (0.71± 0.19 and 0.61±0.20, p<0.001). Based on a GRS value above 0.69 (the best cut-off discriminating FH/M– and normocholesterolemic individuals), 21% of clinically diagnosed FH were classified as polygenic. Polygenic FH were older and showed lower untreated total and LDL-C as compared to monogenic FH. During about 33 months of follow-up, monogenic FH showed higher on-treatment, last visit and best LDL-C as compared with FH/M-patients (P<0.005). These differences persisted even after adjustment for intensity of cholesterol-lowering therapies.

Conclusions: Our results highlight that a polygenic GRS might explain the elevation of LDL-C observed in FH/M- patients. In these patients, the burden of LDL-C is lower than that in monogenic FH patients.

Prognostic role of pulse pressure in patients hospitalized for acute heart failure with reduced ejection fraction

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Aim: pulse pressure (PP) is an established risk factor for cardiovascular disease, since its elevation is associated with the stiffening of the arterial wall. More recently, PP has emerged as a favorable prognostic factor in patients with acute heart failure and reduced ejection fraction (HFrEF). The study aims to evaluate the relationship between PP and 30-days mortality in patients with HFrEF.
Methods: we enrolled 50 patients admitted to the Internal Medicine ward of the Perugia University Hospital for acute heart failure between June 2019 and December 2019. HFrEF was defined as an ejection fraction <50%.
Results: 30 subjects (64%) had HFrEF. 30-days mortality was 20% in the HFpEF group and 29% in the HFrEF group. During the hospital stay, HFrEF patients experienced a significant reduction of PP and survivors had significantly higher values of PP at the discharge. PP was also positively correlated to the days of survival, with a "j" shaped function. A PP <50 mmHg has been associated with a higher mortality.
Conclusions: PP is a simple, non-invasive and simple measurement, which is associate to survival in patients with HFrEF. It could be regarde as an estimate of balance between stroke volume and afterload, and it could be an adjunctive therapeutic goal to improve the survival of HFrEF patients after discharge.

Lp(a) predicts functional improvement in patients with intermittent claudication undergoing a home-based combined aerobic and resistance training

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Aim: Elevated levels of Lp(a) are associated with a higher severity and a worse prognosis of peripheral arterial disease (PAD). Exercise training is the first step treatment in patients with mild-to-moderate PAD because it improves walking capacity and regional perfusion.
Methods: We measured Lp(a) in a group of 35 patients with PAD stage II (Lériche-Fontaine) and in a control group of 10 healthy individuals. Ten IC patients were randomly assigned to perform a 12-week home-based exercise training program. Maximum walking time (MWT), pain-free walking time (PFWT) ankle-brachial pressure index (ABI) flow-mediated dilation (FMD) at brachial artery were measured at the baseline and after the exercise training program.
Results: compared with the healthy control group, patients with PAD had significantly higher levels of Lp(a), which was positively correlated with ABI. Among subjects assigned to the training program, we observed a significant correlation between Lp(a) and the improvement of MWT and PFWT. The improvement of MWT and PFWT can be predicted by Lp(a) in a regression analysis.
Conclusions: Lp(a) levels can predict the improvement of functional capacity in patients with mild-to-moderate PAD and it might help identifying patients who can benefit from more aggressive non-pharmacological treatments.

Abstract selezionato - Presenting author: **Silvia Monticone**

Prevalence of Hypokalemia and Primary Aldosteronism in 5,100 patients referred to a tertiary hypertension unit

Jacopo Burrello[1], Silvia Monticone[1], Isabel Losano[1], Giovanni Cavaglià[1], Fabrizio Buffolo[1], Martina Tetti[1], Michele Covella[1], Franco Rabbia[1], Franco Veglio[1], Barbara Pasini[2], Tracy Ann Williams[1], Paolo Mulatero[1]

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Aim. Historically, primary aldosteronism (PA) was considered a rare condition, always associated with hypokalemia. The widespread screening of patients with hypertension resulted into an increased prevalence of PA, with normokalemic hypertension being the most common phenotype. The Endocrine Society guideline recommend to screen for PA patients affected by hypertension and hypokalemia, but the prevalence of PA in patients with hypokalemia is unknown. The aim of the study was to define the prevalence of hypokalemia in referred patients with hypertension and the prevalence of PA in patients with hypokalemia and hypertension.

Methods. Design: retrospective observational study. Between 2007 and 2018, 7,110 patients were referred to our tertiary hypertension unit; 5,100 had at least two visits to our center, concluded the diagnostic work-up for secondary hypertension and were included. To define hypokalemia ($K^+ < 3.7$ mmol /L) we considered the lowest recorded serum potassium concentration and the highest to define hyperkalemia ($K^+ > 5.2$ mmol/L).

Results. The prevalence of hypokalemia was 15.8% (804/5,100), whereas 76.9% were normokalemic, and 7.3% hyperkalemic. The prevalence of PA in patients with hypokalemia was 28.1% and increased with decreasing potassium concentrations up to 88.5% of patients with spontaneous hypokalemia and potassium concentrations below 2.5 mmol/L.

A multivariate regression analysis demonstrated the association of hypokalemia with the occurrence of cardiovascular events independent of PA diagnosis. An association of PA with the occurrence of cardiovascular events and target organ damage independent of hypokalemia was also demonstrated.

Conclusions. Our results confirm that PA is a frequent cause of secondary hypertension in patients with hypokalemia and the presence of hypertension and spontaneous hypokalemia are strong indications for PA diagnosis. Finally, we show that PA and hypokalemia are associated with an increased risk of cardiovascular events.

Abstract selezionato - Presenting author: **Annalisa Moregola**

Role of MCT1 lactate transporter in T lymphocytes activation and function during obesity

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Introducion: T lymphocytes(T cells) accumulate in the adipose tissue during obesity. Their activation lead to a switch in their metabolism which involves the production of elevated amount of lactate that is toxic for the cell. Aim of this project is to investigate the relevance of T cells lactate transporter MCT1 in the context of adipose tissue inflammation during obesity.

Materials and Methods: MCT1[f/f]CD4-cre mice, with specific deletion of MCT1 in T lymphocytes, and MCT1[f/f] littermates were fed with an HFD for 20 weeks. Body weight was measured weekly; glucose tolerance and insulin resistance were checked at 10 and 20 weeks. Immunophenotyping of different tissues was performed at 20 weeks by flowcytometry.

Results: Following high fat diet feeding, MCT1[f/f] CD4-cre mice in spite of a similar weight gain and glucose response compared to MCT1[f/f], present a decreased visceral(VAT) and subcutaneous(SCAT) adipose tissues fat accumulation. Moreover, MCT1 deficiency in T cells results in a reduction of CD8+ T lymphocytes number in VAT and SCAT($p<0.05$); this profile was associated with a different T cells subsets distribution(T effector memory(Tem) CD8+ VAT: MCT1[f/f] 84.20%±5.72, MCT1[f/f]CD4-cre 57.29%±8, $p<0.001$; Tem CD8+ SCAT: MCT1[f/f] 72.2%±14.16, MCT1[f/f] CD4-cre 44.93%±14.25, $p<0.001$), but a similar number of innate immune cells infiltrating adipose depots. The difference in T cells was not the consequence of increased T cell death in MCT1[f/f]CD4-cre mice.

Conclusions: Our data suggest that MCT1 transporter impacts T lymphocytes activation, in particular CD8+ T lymphocytes, during obesity, independently from systemic metabolism. Whether this difference can affect adipose tissue inflammation during obesity is under investigation.

Abstract selezionato - Presenting author: **Franca Morselli**

Dietary nitrate influences vascular remodelling through BP-independent mechanisms in patients with or at risk of type 2 diabetes mellitus: results from the double-blind, randomized-controlled, factorial VaSera trial

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Background and Aim: Dietary nitrate has several beneficial actions on the cardiovascular system[1,2]; however, its effect on atherogenesis has not been studied. We tested if long-term intervention with dietary nitrate (NO3) and spironolactone could affect carotid structure and stiffness compared to placebo/doxazosin, used as control for blood pressure (BP)[3,4].

Methods: Participants in our double-blind, randomized-controlled, factorial VaSera trial, were randomized to spironolactone or doxazosin and NO_3^- as active nitrate-containing beetroot juice or placebo nitrate-depleted juice. Vascular ultrasound for carotid diameter (CD, mm) and intima-media thickness (IMT, mm) was performed at baseline and repeated at 3- and 6-months follow-up. Carotid local stiffness (CS, m/s) was estimated from aortic pulse pressure (Arteriograph) and carotid lumen area. Data was analysed by modified intention to treat and using mixed-model effect, adjusted for confounders.

Results: 93 subjects had a baseline evaluation and 86% had follow-up data. No statistical interactions occurred between the juice and drug arms. IMT was significantly lower on nitrate-containing compared with placebo juice [-0.06 (95% Confidence Interval -0.12, -0.01), p = 0.022], with no effect on CD. CS reduction was similar between juices [-0.38 (-0.67, -0.10) with placebo, -0.13 (-0.42, 0.16) with active juice] and the drugs [-0.30 (-0.58, -0.02) with doxazosin, -0.21 (-0.51, 0.09), with spironolactone]. No differences were detected between spironolactone or doxazosin on IMT and CD. BP did not differ between the juices or between the drugs.

Conclusion: Our exploratory results show that long-term intervention with dietary nitrate influences vascular remodelling, but not carotid stiffness or diameters. Neither spironolactone nor doxazosin had a BP-independent effect on carotid structure and function.

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Abstract selezionato - Presenting author: **Jasmine Nour**

Adoptive cell therapy with engineered T regulatory cells improves atherosclerotic plaque phenotype in experimental mouse model

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Aim: Immunosuppressive T regulatory cells exert a pivotal role in dampening the inflammation driving the aggravation of the atherosclerotic plaque. Our group has already established the use of engineered Treg to target the atherosclerotic lesion in mice models, here we investigated the impact of engineered Treg therapy in atherosclerosis progression, as a potential treatment for the immuno-inflammatory response associated to atherosclerosis.

Methods: LDLR-KO mice fed to high-cholesterol diet (WTD) for 8 weeks received engineered Treg retrovirally transfected with CX3CR1 or an empty vector. 4-week after mice were sacrificed for flow cytometry, histological stainings, immunofluorescence and proteomics analysis to evaluate atherosclerosis progression.

Results: Preliminary results showed that Treg engineered to overexpress CX3CR1 localized preferentially in the aorta of 8-week WTD LDLR KO mice. One month after the injection, treatment with CX3CR1+-Treg resulted in reduced atherosclerosis with a significantly decreased plaque area (99658 ± 11782 vs 65016 ± 9446 µm2). This was associated with increased fibrosis (+25%) and α-SMA+ area (+29%), and a lower lipid content (-12%) denoting a higher plaque stability. These results were confirmed by the activation of correlated pathways, as proteomics analyses indicate. In the CX group fibroblasts movement (z-score=2,727) and integrin signaling (z-score=1,732) pathways are activated. Apoptosis (z-score=-0,888) and necrosis (z-score=-1,498) were reduced, and so was cell infiltration (z-score=-2,206), while pathways involved in positive response to phagocytosis (as endocytosis, organization of actin cytoskeleton and LXR activation) were upregulated. In parallel, several modulators of efferocytosis resulted increased (such as MFGE8, LRP1 and calreticulin), while markers of decreased phagocytic ability -such as high mobility group box 1 (HMGB1)- were decreased.

Conclusions: Administration of aorta-targeting T regulatory cells to an atherosclerosis mouse model resulted in a stabilization of the plaque and a reduction of its inflammatory component, suggesting its potential as therapeutic tool for atherosclerosis.

Abstract selezionato - Presenting author: **Daniela Palma**

Phenotypic heterogeneity of Familial hypercholesterolemia in unrelated patients carrying the most frequent variants in Southern Italy

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Aim: Familial hypercholesterolemia (FH) is a genetic disease caused by impaired LDL uptake due to pathogenic variants in *LDLR*, *APOB* and *PCSK9* genes. The patients show high LDL-cholesterol (LDL-c) levels and premature coronary heart diseases. Based on the most frequent variants, we aim to analyze the phenotype heterogeneity of unrelated FH patients carrying the same pathogenic variant.

Methods: A population of 778 patients (557 unrelated) with a clinical suspect of FH was analyzed by direct sequencing of causative genes. We analyzed the lipid profile before the therapy and clinical signs in heterozygote patients carrying the most frequent pathogenic variants. LDL-c levels were reported as median and interquartile range.

Results: Causative variants were identified in 410/557 unrelated FH patients (detection rate 73.6%): 387 heterozygotes and 23 homozygotes carrying 95 different pathogenic variants, mainly (>99%). Based on variant frequency, 6 variants account for 210/387 heterozygotes (54.3%): 32 patients carried the c.1586+1G>A, 42 the c.2312-3C>A, 28 the p.Cys379Arg, 33 the p.Gly549Asp, 47 the p.Gly592Glu, 28 the p.Val523Met. A wide range of LDL-c levels were observed among the unrelated carriers of each variant. The worst phenotype was associated with the variant c.2312-3C>A, LDL-c 290 (244-348) mg/dL (range 196-568 mg/dL) and the variant p.Gly549Asp LDL-c 263 (240-299) mg/dL (range 184-413 mg/dL) and a large variability was also observed in the response to therapy.

Conclusions: We confirm the high genetic heterogeneity and the presence of variant clusters as key aspects of the FH genetics. Despite different pathogenic variants are associated with different phenotypes, a very variable phenotype was revealed among patients carrying each variant. The identification of additional common genetic variants modulating the patient phenotype will improve the prognostic values of genetic screening.

Abstract selezionato - Presenting author: **Marcella Palumbo**

Effects of gender affirming hormone therapy on cholesterol efflux capacity in transgender individuals

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Aim: The main proposed atheroprotective function of HDL lays on their role to promote macrophage cholesterol efflux. An insightful way to learn more about the effects of sex hormones on HDL function is to study changes during hormone therapy. The present study was aimed at evaluating the effects of gender affirming hormone therapy on HDL cholesterol efflux capacity (CEC) within transgender individuals.

Methods: Transmen were treated with testosterone gel, a mix of testosterone esters once every three weeks or testosterone undecanoate once every twelve weeks, whereas transwomen were treated with either oral estradiol valerate or a transdermal application of estradiol. Cyproterone acetate was prescribed as a testosterone-blocking agent to all transwomen. HDL function was evaluated by a radioisotopic technique. Hormone levels, lipids and HDL function were evaluated after one year of follow-up.

Results: In transmen (n=15), testosterone markedly increased (+97%;p<0.0001), whereas luteinizing hormone (LH) decreased significantly (-64%;p=0.049). Total cholesterol and LDL-C were not affected by testosterone treatment, whilst TG were raised (+11.76%;p=0.0078) and HDL-C reduced (-19.6%;p=0.0103). Concerning HDL CEC, only the aqueous diffusion (AD) process was lowered (-9.8%;p=0.0032), an effect directly correlated with HDL-C changes (r=0.6242;p=0.0002). Total-, ABCA1- and ABCG1-mediated CEC were not affected by testosterone treatment. In transwomen (n=15), estradiol levels were raised (+200%;p=0.013) whereas LH and testosterone significantly reduced. Estradiol supplementation reduced total cholesterol (-10.7%;p=0.0017), HDL-C (-14.3%;p=0.0024) and LDL-C (-10.9%;p=0.0058). Total HDL CEC decreased (-11%;p=0.0001) with a specific decrement in CEC mediated by the ABCA1 (-24%;p=0.0003) and AD (-4.7%;p=0.0014). This last was associated to a reduction in HDL-C (r=0.4084;p=0.0251). Conversely, the drop in ABCA1 and total CEC did not associate to reductions in HDL-C levels.

Conclusions: In transmen, testosterone supplementation was associated with a reduction in AD-mediated CEC, an effect potentially dependent to HDL-C changes. In transwomen, estrogen significantly decreased HDL function (CEC), independent of HDL-C levels changes.

Sphingosine 1-phosphate (S1P) receptor type 1 signaling induces an anti-atherogenic phenotype in macrophages and attenuates atherosclerosis in LDL-receptor-deficient mice

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Aim: Sphingosine 1-phosphate (S1P) accounts for antiatherogenic properties of high-density lipoproteins, but the S1P receptor subtype mediating the atheroprotective effects of S1P and the underlying molecular mechanisms remain enigmatic. Experimental models engineered to amplify the signaling of endogenous S1P over its specific receptors may help in clarifying this issue. To this purpose, we generated a peculiar mouse model basing on Cre-LoxP technology, able to overexpress S1P receptor type 1 (S1P1) specifically in myeloid compartment, and studied the effects on atherosclerosis development.

Methods: Mice overexpressing S1P1 in myeloid cells (monocytes and macrophages) were generated by crossing mice expressing the murine S1P1 gene under a promoter containing a floxed blocking element with mice expressing Cre recombinase under the control of lysozyme (LysMCre) promoter. Bone marrows from these or control mice were transplanted into low density lipoprotein receptor (LDL-R)-deficient mice and resulting chimeras were fed a Western diet for 14 weeks.

Results: S1P1 overexpressing macrophages showed increased expression and activity of transcription factors PU.1, IRF8 and LXR. This skewed macrophages towards an anti-inflammatory M2 phenotype with enhanced production of IL-10, IL-1RA and IL-5. In addition, S1P1 overexpressing macrophages showed increased ABCA1- and ABCG1-dependent cholesterol efflux, increased expression of MerTK and Axl1 and efferocytosis, and reduced endoplasmic stress-induced apoptosis. Atherosclerotic lesion formation in aortic roots and brachiocephalic arteries, as well as necrotic core formation, was reduced in mice overexpressing S1P1 in myeloid cells.

Conclusion: S1P1 signaling produces a unique anti-inflammatory and anti-atherogenic macrophage phenotype and countervails the development of atherosclerotic lesions in mice.

Abstract selezionato - Presenting author: **Giulia Quinto**

Autonomic nervous system balance in obese patients: heart rate recovery evaluation before and after sleeve gastrectomy

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Aim: In obese patients, Autonomic Nervous System (ANS) imbalance, evaluated with Heart Rate Recovery (HRR) after exercise, is an independent predictor of cardiovascular disease and mortality. Aim of this study was to evaluate HRR in severe obese patients before and after weight loss obtained by Sleeve Gastrectomy (SG).
Methods: 38 sedentary asymptomatic obese patients were evaluated with cardiopulmonary maximal exercise test, 1 month before and 6 months after SG, with the same incremental protocol on treadmill. Patients did not take any drugs acting on heart rate.
Results: Patients (age $39,42\pm10,62$ years old and BMI $43,39$ kg/m^2) were $84,2\%$ female and they have a mean weight loss of $32,36\pm9,60$ kg. Heart rate (HR) at rest before SG was $80,08\pm11,06$ bpm and after SG was $65,42\pm8,68$ bpm ($p<0,0001$). Heart rate recovery at first minute after exercise was $20,87\pm6,87$ bpm and $28,05\pm6,87$ bpm respectively before and after SG ($p<0,0001$). Heart rate recovery at fourth minute after exercise was $64,16\pm9,82$ bpm and $76,89\pm12,63$ bpm respectively before and after SG ($p<0,0001$). Differences of HRR at second, third and fourth minute of recovery phase increases with increasing weight loss before and after SG ($p=0,03$, $p=0,02$ and $p=0,04$ respectively).
Conclusion: After weigh loss obtained 6 months after SG, HRR improves during all recovery phases. His increase during early phase can show a greater gain in vagal tone, supported by a reduction of HR at rest. Better HRR during later phases of recovery can reflect an enhanced sympathetic tone withdrawal. Reduction of sympathetic tone in ANS balancing, that usually characterize obese patients, is correlated with weight loss after SG, suggesting a relationship between sympathetic tone and the weight of patients. Further evaluations are needed to better examine ANS and his link to rapid and important changes of weight in severe obese patients.

Abstract selezionato - Presenting author: **Ilaria Radano**

A case of Kounis Syndrome type II

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Introduction Kounis Syndrome (KS) is a peculiar entity defined as the concurrence of acute coronary syndrome in the setting of allergic or hypersensitivity and anaphylactic or anaphylactoid insults. Three variants of KS have been described: type I, characterized by coronary vasospasm without significant coronary disease; type II, including patients with pre-existing coronary disease in which the release of pro-inflammatory mediators can cause vasospasm or instability of atherosclerotic plaques; type III, including patients with coronary artery stent thrombosis associated with a hypersensitivity reaction. Several different triggers may be involved in KS onset such as drugs, food items or environmental factors. KS is not a rare disease, but maybe it's often underdiagnosed; moreover, differential diagnosis with Takotsubo Syndrome occurring during allergic reactions should be made.

Case presentation We report the case of a 69 years-old Caucasian man admitted to our emergency department because of an urticarial rush involving trunk and limbs associated to labial edema, occurred at seventh day of intramuscular therapy with ceftriaxone and prednisone. A therapy with corticosteroids was promptly instituted. The next day, soon after the allergic manifestation, the patient complained sudden epigastric and chest pain. An ECG was performed, showing a transient ST segment elevation from V1 to V6 leads *(Figure 1,2); l*aboratory analysis detected elevation of cardiac biomarkers with troponin I (cTnI) 0,48 ng/mL, creatine kinase-MB (CK-MB) 57 U/L and myoglobin 38 ng/ml. Transthoracic echocardiography revealed a mildly reduced left ventricular ejection fraction with akinesia of septal apex and mid-apical segments of lateral and posterior-lateral walls associated to hypokinesia of the apical segment of anterior wall. Patient promptly underwent a coronary angiography which revealed two critical stenosis of the left anterior descending coronary artery at medium segment (LAD), treated through implantation of two drug eluating stent. In-hospital course was uneventful and he was discharged on 9th day of recovery.

Conclusion In literature, there are three cases previously reported due to ceftriaxone assumption. Our case represents the first case of type II variant of KS due to vasospasm triggered by ceftriaxone therapy. The management of these patients is challenging, due to the needed to treat both cardiac and allergic symptoms simultaneously. Patients with systemic allergic reactions associated with clinical, electrocardiographic and laboratory findings of acute myocardial ischemia should be promptly suspected as having KS, in order to institute the correct management, even if their past medical history is not positive for any allergic reactions.

Figure 1. ECG at admission demonstrates ST segment elevation in V1-V6 leads.

Figure 2. Repeated ECG after 10 min demonstrates resolution of St segment elevation.
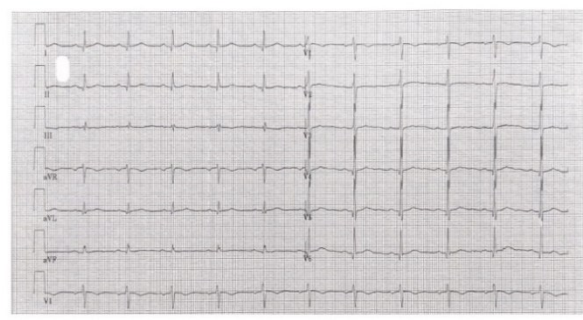
Abstract selezionato - Presenting author: **Antonella Rispoli**

Clinical and echocardiographic benefit of Sacubitril/Valsartan in a real-world population with HF with reduced ejection fraction

Maria Vincenza Polito[1], Angelo Silverio[1], Antonella Rispoli[1], Gennaro Vitulano[1], Federica D'Auria[1], Elena De Angelis[1], Francesco Loria[1], Alberto Gigantino[2], Domenico Bonadies[2], Rodolfo Citro[2], Albino Carrizzo[3], Gennaro Galasso[1], Guido Iaccarino[4], Carmine Vecchione[1], Michele Ciccarelli[1]

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Aims. To evaluate the effects of Sacubitril/Valsartan (S/V) on clinical, laboratory and echocardiographic parameters and outcomes in a real-world population with heart failure with reduced ejection fraction (HFrEF).
Methods and results. Prospective observational study enrolling patients with HFrEF undergoing treatment with S/V. The primary outcome was the composite of cardiac death and HF rehospitalization at 12 months follow-up; secondary outcomes were all-cause death, cardiac death and the occurrence of rehospitalization for worsening HF. The clinical outcome was compared with a retrospective cohort of 90 HFrEF patients treated with standard medical therapy by using the propensity score weighting technique. At 6 months follow-up, changes in symptoms, echocardiographic parameters, estimated glomerular filtration rate (eGFR) and furosemide dose were also evaluated. The study population consisted of 90 patients (66.1±11.7 years; 86.7% males). At 6 months follow-up, a significant improvement in NYHA class, left ventricular ejection fraction (LVEF, from 31.0% to 34.0%; p=0.001), left ventricular end systolic volume (LVESV, from 115.0 to 101.0 mL; p=0.033) and systolic pulmonary arterial pressure (sPAP, from 31.0 to 25.0 mmHg; p=0.024) was observed. Moreover, S/V did not affect negatively eGFR and was associated with a significantly lower dose of furosemide prescribed. The propensity score weighting adjusted regression analysis showed a significantly lower risk for the primary composite outcome (HR, 0.31; 95% CI, 0.11- 0.83; p = 0.019) and for HF rehospitalization (HR, 0.27; 95% CI, 0.08-0.94; p = 0.039) among patients treated with S/V as compared to the standard therapy group.
Conclusions. In this real-world HFrEF population, S/V reduced the risk of HF rehospitalization and cardiac death at 1 year. Moreover, S/V improved significantly NYHA class, LVEF, LVESV and sPAP at 6 months, preserving renal function and reducing the need of furosemide.

Gender-related Determinants of Adherence to the Mediterranean Diet in Adults with Ischemic Heart Disease

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Aim: The reasons behind low adherence to a Mediterranean diet (Med-diet) are still not entirely known. We aimed to evaluate the effect of biological (i.e. sex-related) and psycho-socio-cultural (i.e. gender-related) factors on Med-diet adherence.
Methods: Baseline Med-diet adherence was measured using a self-administered questionnaire among adults with ischemic heart disease (IHD) from EVA (Endocrine Vascular disease Approach) study, A multivariable analysis was performed to estimate the effect of sex- and gender-related factors (i.e. identity, roles, relations and institutionalized gender) on low adherence.
Results: Among the overall EVA cohort, 366 participants (66±11 years; 31% women) were included in present analysis. Adults with low adherence (22%) had more frequently diabetes, no-smoking habit, lower male BSRI (Bem Sex Role Inventory) (median [IQR]: 4.8 [4.1-5.5] vs 5.1 [4.5-5.6], p=0.048) and higher Perceived Stress Scale-10 (PSS-10) (median [IQR] 19 [11-23] vs 15 [11-20], P=0.07] scores than those with medium-high adherence. At multivariable analysis, active smoking [Odds Ratio, OR=2.10, 95% Confidence Interval, CI 1.14-3.85, p=0.017], PPS-10 [OR=1.04, 95%CI 1.00-1.08, p=0.038] and male BSRI [OR=0.70, 95%CI 0.52-0.95, p=0.021] were independently associated with low adherence.
Conclusions: Gender Identity, including male personality traits and perceived stress, were associated with low Med-diet adherence regardless of the sex, age and comorbidities. Gender-sensitive interventions should be explored to improve adherence in IHD.

Abstract selezionato - Presenting author: **Francesca Savarino**

Evaluation of Endocan levels in clinical subsets characterized by chronic inflammatory status: a possible link to high cardiovascular risk

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Background and Aim: Endocan is a proteoglycan secerned by several cell type, including endothelial cells, involved in the onset and progression of atherosclerosis. Recent researches suggest a role of Endocan in inflammation and neovascularization; thus, it has been proposed as a marker of vascular stress. It was found elevated in multiple conditions, including sepsis, oncology, autoimmune or infectious diseases. In the light of these findings, we aimed to assess Endocan levels in other clinical settings: Familial Hypercholesterolemia (FH), Systemic Sclerosis (SSc), IBD.

Materials and Methods: we tested adult patients affected by FH (10), IBD (10) or SSc (15). All patients and healthy controls (10) underwent blood sampling on which we tested an Elisa immunoassay to assess circulating Endocan levels. FH and IBD patients underwent bloody sampling and the Elisa assay both when on conventional treatment either after the therapy with biologics (i-PSCK9 or anti-TNFα Ab, respectively).

Results: highest levels of Endocan were detected in patients affected by SSc (2.1 fold, $p<0.001$ vs controls). IBD patients refractory to conventional therapy showed higher Endocan levels when compared with control group (1.66 fold, $p=0.02$ vs controls), however the same patients showed a reduction of Endocan levels after the induction treatment with Biologics (1.18 fold, $p=0.50$ vs controls). FH population on conventional therapy (statin plus Ezetimibe) showed Endocan levels lower than healthy controls (0.7 fold, $p<0.001$). i-PCSK9 therapy seemed to slightly but not significantly reduce Endocan plasma levels (0.55 fold, $p=0.32$).

Conclusions: high circulating levels of Endocan were detected in high cardiovascular risk conditions as FH, IBD, SSc. Our data on FH seem to show that statin treatment could improve endothelial function even better if taken in association with i-PCSK9. Poor controlled IBD correlates with higher Endocan levels, while optimizing therapy could reduce Endocan plasma levels.

Abstract selezionato - Presenting author: **Davide Sinicropi**

Familial Mediterranean Fever and early cardiovascular damage: a preliminary data

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Aims: Familial Mediterranean fever (FMF) is the most common monogenic periodic fever syndrome, characterized by recurrent episodes of fever, serositis, arthritis, dermal manifestations, and long-term renal complications. The MEFV gene responsible of FMF encodes for mutated protein pyrin, an important player in the innate immune system and the component of inflammasome which leads to exaggerated inflammatory response through uncontrolled production of interleukin-1. Inflammatory diseases are known to be associated with increased cardiovascular risk. Few studies have investigated the association between FMF and cardiovascular disease. To evaluate early cardiovascular damage in subjects suffering from FMF on the basis of the estimate of the Pulse Wave Velocity, the cIMT, liver stiffness, the biohumoral indices and the circulating hematopoietic cells.

Results: Preliminary data from patients with FMF were compared to normal values and divided according to age strata: ≤20 (PWV 5.94 vs 6.1 m/s, cIMT 0.47 vs 0.44 mm, liver stiffness 3.8 vs 4.7 kPa), 20-50 (PWV 7.5 vs 7 m/s; cIMT 0.62 vs 0.55 mm; liver stiffness 7.8 vs 3.9 kPa, $p < 0.001$), 50-70 (PWV 10.7 vs 8.8 m/s, cIMT 1.1 vs 0.85 mm, liver stiffness 7.8 vs 3.9 kPa, all $p < 0.001$).

Conclusions: in this explorative study, we found that FMF patients could present higher risk to develop cardiovascular/cardiometabolic disease; in fact, they presented with a time-dependent acceleration of vascular – and also liver - involvement, as suggested by the increased cIMT and PWV values in the highest age stratum (50-70) with respect to controls; moreover, we found a significant increase of liver stiffness values, likely as consequence of chronic inflammatory status (the link between serum amyloid A precursor levels in FMF subjects and liver fibrosis should be deepened). These data need to be replicated on larger scale.

Abstract selezionato - Presenting author: **Nicola Susca**

Echocardiographic alteration in patients with systemic lupus erythematosus affected by hepatic steatosis: a cross-sectional single center study

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Aim. We looked for a correlation between Systemic Lupus Erithematosus (SLE) disease activity, evaluated by SLEDAI and SLICC-DI score, and heart involvement comparing those who presented a hepatic steatosis to those who do not.

Materials and Methods. 19 SLE patients (Steat-SLE: 13 women, 51.89 ± 10.37 years) affected by hepatic steatosis were compared to 51 with no evidence of steatosis (No-Steat-SLE: 42 women, 46.24 ± 14.27 years). Patients came in follow-up for revaluation and therapy adjustment.

Results. Anti-dsDNA Ab, C3, C4, ESR and PCR were not different between the groups. Hepatic dysfunction was not detect in Steat-SLE. No difference were found in SLEDAI, while SLICC-DI results increased if steatosis was detected (Steat-SLE 3.57 ± 3.36 vs No-Steat-SLE 2.27 ± 2.15, $p<0.05$). Patients with Steatosis present a longer disease (Steat-SLE 232.0 ± 129.8 vs No-Steat-SLE 121.4 ± 110.6 months, $p<0.05$). We highlight that patients with steatosis had an increased left ventricular mass (MLV) both as absolute value (Steat-SLE 226.2 ± 57.53 vs No-Steat-SLE 194.4 ± 58.17 gr., $p<0.05$) and MLV indexed (MLVi) for body surface area (BSA) (Steat-SLE 135.0 ± 48.17 vs No-Steat-SLE 112.3 ± 27.47 gr/m^2, $p<0.05$) but no in interventricular septum thickness. At the same time no difference was found in left atrium (LA) as volume absolute value (LAV) while it was increased as LA volume indexed (LAVi) for body surface area (BSA) (LAVi Steat-SLE 41.67 ± 19.49 vs No-Steat-SLE 34.12 ± 9.74 ml/m^2, $p<0.05$). Moreover, a correlation was find in both Steat and No-Steat SLE between SLICC-DI, MLV and MLVi.

Conclusion. These data show an increase of LAVi, MLV and MLVi in patients with steatosis. At the same time, these patients present an increased disease damage and duration. This could suggest heart involvement as result of systemic inflammation similarly to that related to hepatic stetosis. At the same time, the detection of hepatic steatosis should suggest a worsening in heart damage in SLE patients.

Abstract selezionato - Presenting author: **Monika Svecla**

Shotgun proteomics-identified alternations in glycosylation patterns in LDL-R KO aorta

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Background: Vascular wall proteins undergo several post-translation modifications, including N glycosylation. Our aim was to investigate changes in N-glycosylation pathways during atherosclerotic plaque development in animal models.

Methods: Shotgun proteomics was performed in aorta from LDL-R KO mice, fed in chow or WTD diet using orbitrap Fusion™Tribrid™MassSpectrometerfollowed by protein inference, label free quantification and pathway enrichment analysis.

Results:Apoptosis, fibrosis, and ROS production were upregulated (z-score 2,9 to 2.2) while cholesterol efflux, phagocytosis and ATP production resulted decreased (z-score -1.6 to -2.7) in the aorta of WTD fed mice compared to chow. When the analysis was focused on enzymes for N-glycosylation cascade, OST1, which controls glycans transfer from Dolicol-P-P to asparagine in ER, was up-regulated (p=0.02) while glucosidases (Ganab, Prkcsh) which favor proper protein folding in concert with the lectin chaperon Calnexin/Calreticulin and ERp57 were downregulated. In parallel ERGIC-53 that operates the transport of glycoproteins from ER to Golgi was significantly down-regulated (p<0.01) while BiP which increases during unfolding proteins response was up-regulated. These data suggest that a reduced production of glycosylated proteins occurs during atherosclerosis coupled to an increased unfolded protein response in the plaque. Indeed, the abundance and side-specific N-glycosylation of integrin β-1, laminin subunit γ-1, integrin α-8 were reduced in the plaque of WTD fed mice.

Conclusion: Our data suggest that altered protein glycosylation takes place in the aorta of WTD fed LDL-R KO mice. This can further affect the synthesis of atheroprotective glycoproteins.

Abstract selezionato - Presenting author: **Chiara Tognola**

Effects of chronic heart failure unconventional therapies on endothelial function

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Aim: Endothelial Dysfunction (ED) of peripheral arteries in Chronic Heart Failure (CHF) subjects has been demonstrated. We assessed endothelial function in subjects undergoing unconventional treatments for CHF, namely Heart Transplantation (HTX), continuous-flow Left Ventricular Assist Device implantation (LVAD), and repeated Levosimendan infusions (r-LEVO).
Methods: Twenty HTX recipients (median time from HTX 21 months), 20 patients supported with LVAD (median time from implant 39 months), and 20 patients receiving monthly Levosimendan infusions (median time on treatment 28 months) were enrolled and compared to a group of 20 healthy subjects. ED was evaluated with ultrasound assessment of the diameter before and after ischemic stress at the brachial artery level. The difference between the two diameters normalized for the baseline value (Flow Mediated Dilation - FMD) has been used for the analysis. All the patients were stable at the time of FMD assessment, with those on r-LEVO being evaluated prior to infusion.
Results: FMD was significantly lower in HTX and LVAD groups with respect to controls (9.8±7.4, 9.3±5.7, and 15.6±6.4% respectively, p=0.01), but not in r-LEVO group (12.5±6.9%).
When patients were analyzed according to time from the operation or on treatment, (< *versus* $\geq$ of the median value), no differences were seen in HTX and r-LEVO group, while in LVAD group FMD was borderline significantly higher in patients with longer follow-up (8.4±6.4% *versus* 10.2±5.2%, p=0.05).
Conclusions: Based on this preliminary data we can inference the following:
1- FMD is abnormal in HTX recipients, despite their good functional status, probably due to factors unrelated to CHF (e.g. hypertension, renal insufficiency, denervation, and drug effects);
2- LVAD patients also show ED, with possible better adaptation in very long-term survivors;
3- Near-normal FMD values in CHF patients who remain stable with r-LEVO suggest that pulsed treatment may obtain favorable effects at peripheral level, persisting after clearance of the drug and its metabolites.

Abstract selezionato - Presenting author: **Marta Turri**

Molecular mechanisms of HDL-mediated cardioprotection in Acute Coronary Syndrome

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Background Low plasma HDL cholesterol levels are associated with unfavorable prognosis in patients with acute coronary syndrome (ACS). It has been shown that HDL are able to preserve cardiac function when given before ischemia or at reperfusion by acting on cardiomyocites. The multitude of mechanisms of HDL-mediated cardioprotection are still unclear.
Aim To investigate the cardioprotective capacity of HDL in an ischemia/reperfusion (I/R) injury model.
Methods HDL cardioprotective capacity has been evaluated by incubating healthy donors' HDL purified by ultracentrifugation at different concentrations with cultured rat cardiomyoblast cells (H9c2), followed by a hypoxia/re-oxygenation process. ROS production, apoptosis and cell viability have been evaluated by standardized methods.
Results ROS production after 5 hours of hypoxia and one night of re-oxygenation shows a significant reduction ($p < 0.05$) in cardiomyocites pre-treated with HDL compared to untreated cells, with a dose-dependent trend. The viability assay of cardiomyocites treated with HDL demonstrates an increase in ATP production, that reflects the metabolic activity of cardiomyocites ($p < 0.01$). Also in this case it has been shown a dose-dependent trend.
The evaluation of apoptosis, in the previously described conditions, displays a reduction in caspase activity, which reflects programmed cell death mechanisms, for all HDL concentrations ($p < 0.01$).
Conclusions All these data confirm that HDL at physiological concentrations have a cardioprotective activity in a dose-dependent way. The HDL exert their function through an anti-oxidant mechanism, with a reduction in enzymatic activity of caspases and a consequent reduction in cell death by apoptosis. Furthermore there is an increasing trend in cells survival and viability.

A novel clinical-based risk stratification score in acute hypertensive disorders

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Aim: Hypertensive emergencies are characterized by an acute and severe blood pressure (BP) rise with associated acute hypertension-mediated organ damage. Poor scientific evidence is currently available about the role of symptoms in acute hypertensive disorders; no specific risk stratification models have been specifically designed for medical decision-making in suspected hypertensive emergencies.
Therefore, the aims of the studies were:
- to assess the accuracy of symptoms in discerning hypertensive emergencies from uncontrolled hypertension without organ damage;
- to develop and validate a risk stratification model to improve medical decision making in the Emergency Department (ED).
Methods: Data from 718 patients presenting to the ED of the "Città della Salute e della Scienza" Hospital of Turin between January and June 2018 with systolic BP >180 and/or diastolic BP >110 mmHg were analysed. The accuracy of the typical symptoms (chest pain, dyspnoea, neurological signs, headache, visual impairment) for identification of hypertensive emergencies was assessed. A risk stratification model using symptoms and clinical data was developed and validated.
Results: Patients with hypertensive emergencies (n=79, 11% of the sample) were older and with higher prevalence of coronary artery disease and chronic heart failure than patients with uncontrolled hypertension. No differences in gender, cardiovascular risk factors and BP values on ED admission emerged. Typical symptoms could correctly discriminate true hypertensive emergency from uncontrolled hypertension with 94% sensitivity (99% negative predictive value). The developed risk model (called PrES-70) including symptoms, age, cardiovascular events and ongoing antihypertensive therapy (score 0-4), might stratify acute hypertensive patients from low (4%) to very high (40%) risk of having hypertensive emergency (AUC 0.784).
Conclusion: Typical symptoms might be used as screening test to select for further evaluations patients with suspected hypertensive emergencies. PrES-70 score might further improve medical decision in ED.

Abstract selezionato - Presenting author: **Valeria Visco**

When the acute event goes unnoticed: a surgical solution for a dyspnoic patient

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Background: Dyspnea affects up to 25% of the patients observed in a clinic and without an effective etiological treatment it is a short-term negative prognostic factor.
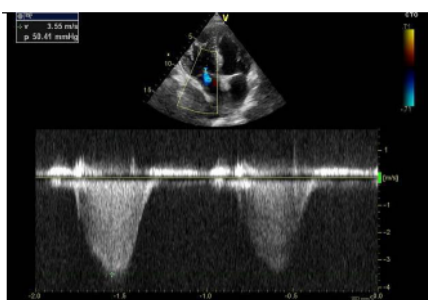

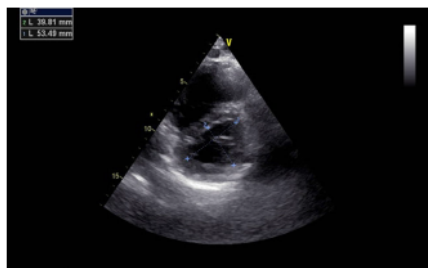Fig. 1 CW Doppler of tricuspid regurgitation.

Fig. 2 D-shaped left ventricle.

Clinical case: The patient S.G., 70 years, arrived at our cardiology clinic for worsening dyspnea, which had been present for 2 years. In patient history: previous removal of right pulmonary echinococcus cysts, deep vein thrombosis of the right popliteal vein and HBP. Echocardiography showed signs of pulmonary hypertension (PAPS 65 mmHg) (Fig. 1) without left ventricle disease. The patient performed chest CT angiography that documented bilateral pulmonary thromboembolism and started oral anticoagulants. Laboratory tests showed: hyperhomocysteinemia with heterozygous mutation of MTHFR and absence of autoimmune disease.

After 3 months of oral anticoagulant therapy, the TTE showed persistence of dilation of the right chambers with D-shape left ventricle (Fig. 2) and small circle pressures still severely increased, while the echocolordoppler of lower limbs was normal. Lung scintigraphy showed multiple defects; chest CT angiography showed marked indirect lung signs of chronic thromboembolism disease, with scars of previous pulmonary infarctions: chronic thromboembolic disease was confirmed. Consequently, the patient was referred to a center experienced in pulmonary endarterectomy (PEA), where he had right catheterization which concluded for severe pre-capillary pulmonary hypertension (pulmonary artery pressure 101/56/28 mmHg, wedge 5 mmHg, RVP 1028 dyne*sec*cm-5) and significant reduction of cardiac index (2 l/min/m2). Therefore, filter placement was made in inferior vena cava at the subrenal level; then, was performed bilateral PEA. At scintigraphic control was obtained perfusion improvement and right catheterization showed: 55% reduction in lung pressures (25 vs 56 mmHg), 85% of RVP (154 vs 1028 dyne*sec*cm-5) and an increased cardiac index (2.6 vs 2 l/min/m2).

Discussion and conclusion: CTEPH is a pathological condition linked to unabsorbed and fibrous organization of the thrombus within the pulmonary artery lumen following an acute pulmonary embolism and PEA is the gold standard. The challenge remains the clinical suspicion for an early diagnosis with multidisciplinary approach.

Abstract selezionato - Presenting author: **Veronica Zampoleri**

Prevalence Of familial hypercholeSTerolaemia (FH) in Italian Patients with coronary artERy disease: The POSTER Study

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Background and Aims: Familial hypercholesterolaemia (FH) is a risk factor for cardiovascular (CV) events. High levels of low density lipoprotein cholesterol (LDL-C) since birth are linked to the early onset of atherosclerotic disease. A genetic mutation determining FH is about in one subject out of 250; FH should be more represented among subjects with a documented diagnosis of coronary artery disease (CAD). The POSTER Study evaluated the prevalence of FH in Italian patients with recent cardiovascular event.
Methods: Eighty-two cardiology centers enrolled patients with a documented CAD event; CV risk profile, drug therapy and biochemical parameters were collected. Patients with a Dutch Lipid Clinic Network (DLCN) score $\geq$ 6 underwent to a whole blood sample withdrawal to perform a genetic test based on full gene sequencing of genes involved in FH.
Results: Overall, 5415 patients were enrolled and the main index event was an acute coronary syndrome, myocardial infarction with or without ST-elevation, or a recent coronary revascularization (34.8%, 37.2% and 28% respectively). Mean age was 66±11 years, men were 78%; about 40% were already treated with statins, proportion that increased after the acute event (96.5%). Based on the DLCN score, the prevalence of potential FH (score $\geq$6) was 5.1%, 0.9% had a diagnosis of definite FH (score >8). These patients were younger than patients with a score <6 (56±10 *vs* 66±11, *p*<0.001), and LDL-C levels were in most of them ($\sim$87%) >190 mg/dL. The genetic test has been performed in 259 patients: 37 patients (14,29%) were positive for the diagnosis of FH, in 63 (24.3%) patients there was a mutation, but the genetic diagnosis was defined as not-conclusive for FH.
Conclusions: Results underscore a prevalence of FH in patients with a recent CAD. Therefore, an early identification of these subjects may help to improve their high cardiovascular risk.

Abstract selezionato - Presenting author: **Mirko Zoncapè**

A new vision of Non-Alcoholic Fatty Liver Disease: a "cardiac" disease per se and a "vascular" disease only with hypertension

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Background and Aim: Non-alcoholic fatty liver disease (NAFLD) is associated with an increased cardiovascular (CV) risk. However, it is still not clear whether NAFLD contributes independently to the development and progression of CV disease. This study aimed to assess the differences between NAFLD patients with or without hypertension (HT) and patients with HT but no NAFLD through markers of subclinical and clinical atherosclerosis, cardiac function and morphology and liver fibrosis.
Method: Eighty-seven participants (51,9±9y; males=83,7%) were divided according to the presence of NAFLD and essential HT in three groups: only-NAFLD, only-HT and NAFLD+HT. Patients with BMI>35 and type II diabetes were excluded. Blood pressure (BP) measurement, carotid ultrasonography, echocardiography and transient elastography were performed. Carotid intima–media thickness (cIMT), Carotid Distensibility (CD) and Carotid-femoral pulse wave velocity (cf-PWV) were measured as markers of subclinical atherosclerosis and arterial stiffness.
Results: The prevalence of atherosclerotic plaques was significantly higher in NAFLD+HT group compared with only-NAFLD group (p<0,001). Belonging to NAFLD+HT group, rather than other clinical variables, was independently associated with atherosclerotic plaques in stepwise multiple logistic regression analysis (beta±SEM=2.083±0.958; p=0,01; exp(B)=15,88 [95%CI, 1,62-155,00]). No differences in cIMT, CD, cf-PWV, echocardiographic parameters and liver stiffness were found among the three groups; nevertheless, a significant prevalence of concentric cardiac remodeling (RWT>0,42) was detected in all groups (only-HT, NAFLD+HT and only-NAFLD group at 40,9%, 35,7% and 33,3%, respectively; p=not significant).
Conclusion: Overt atherosclerosis, rather than subclinical atherosclerosis and arterial stiffness, was more evident in NAFLD+HT patients. A surprising finding was the high prevalence of concentric cardiac remodelling in all groups, including in the only-NAFLD one, suggesting a possible direct involvement of NAFLD in cardiac structural changes. Therefore, the impact of NAFLD on vascular and cardiac structure could be different and partially dependent on the presence of HT.