SPRING 2025

Spring Meeting Giovani Ricercatori

SID SIGG SIIA SIMI SIPREC SISA

Spring MeeTEeNg

tra PASSATO e FUTURO della ricerca, lo Spring sempre PRESENTE

Rimini, 6-8 Aprile 2025

Young investigators meeting

European Atherosclerosis Journal

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SPRING 2025

Carissime Colleghe e Colleghi,

con grandissimo piacere vi invitiamo a partecipare alla **X Edizione dello Spring Meeting Nazionale dei Giovani Ricercatori 2025**, che quest'anno celebra un importante traguardo. Per la decima edizione, il Meeting non sarà solo un'occasione per presentare e discutere i più recenti progressi scientifici, ma rappresenterà anche un momento speciale per ripercorrere i successi e i progressi della ricerca realizzati negli ultimi dieci anni in campo cardiometabolico e tracciare insieme la strada per il futuro.

Quest'anno, il Congresso si arricchisce della partecipazione di una nuova Società Scientifica, la **SIGG (Società Italiana di Geriatria e Gerontologia)**, che si unisce alle cinque già consolidate: **SID (Società Italiana di Diabetologia), SIIA (Società Italiana Ipertensione Arteriosa), SIMI (Società Italiana di Medicina Interna), SIPREC (Società Italiana per la Prevenzione Cardiovascolare) e SISA (Società Italiana per lo Studio dell'Aterosclerosi).**

Il Meeting si svolgerà **dal 6 all'8 aprile 2025 a Rimini**, confermandosi come un momento cruciale di incontro interdisciplinare. L'evento sarà dedicato non solo alla presentazione dei risultati della ricerca scientifica promossa dai giovani soci delle sei Società Scientifiche coinvolte, ma anche a una **riflessione sui progressi realizzati nel decennio passato**, evidenziando le scoperte più significative e i cambiamenti più rilevanti, per definire con slancio le prossime sfide scientifiche.

Anche questa edizione seguirà il format consolidato delle precedenti, con sessioni dedicate allo stato dell'arte della ricerca clinica e di base sui principali fattori di rischio e patologie cardiovascolari, metaboliche e dell'invecchiamento. Particolare attenzione sarà rivolta alle innovazioni emergenti e alle prospettive future in questi campi. Sarà inoltre garantito spazio per la partecipazione attiva con **comunicazioni orali** e **presentazioni poster**, insieme a workshop su aspetti critici e metodologici della ricerca biomedica.

Infine, come da tradizione, il Meeting offrirà numerose opportunità di networking e scambio di idee, creando un ambiente fertile per la nascita di nuove collaborazioni e la crescita professionale di giovani ricercatori.
Vi aspettiamo numerosi a Rimini per condividere questa straordinaria esperienza e opportunità di crescita!

Buon lavoro a tutti!

Il comitato organizzatore

Domenica, 6 Aprile 2025

13.00-13.45 *Light Lunch*

13.45-14.15 Registrazione dei partecipanti

14.15-14.30 **Apertura lavori**
Leonardo Bencivenga (SIGG), Vanessa Bianconi (SISA), Rosa Curcio (SIMI), Lorenzo Da Dalt (SISA), Mario Daidone (SIMI), Damiano D'Ardes (SIMI), Luca D'Onofrio (SID), Giovanna Gallo (SIPREC), Carla Greco (SID), Rosa Lombardi (SIMI), Alessandro Maloberti (SIIA), Chiara Pavanello (SISA), Federica Piani (SIIA), Giulia Rivasi (SIGG), Francesco Spannella (SIIA), Valeria Visco (SIIA).

14.30-14.45 **Saluto dei Presidenti:**
Raffaella Buzzetti (SID), Agostino Virdis (SIIA), Dario Leosco (SIGG), Nicola Montano (SIMI), Massimo Volpe (SIPREC), Alberico L. Catapano (SISA)

14.45-16.45 **Sessione 1 – Fattori di Rischio "Non Tradizionali": Da dove veniamo? Chi siamo? Dove andiamo?**
Moderatori: Ludovico Di Gioia (Bari), Matteo Landolfo (Ancona)

Basic Research – Impatto dell'inquinamento sulle malattie cardiovascolari: dall'epidemiologia alla fisiopatologia
● Manuela Montanaro *(Bologna)*

Clinical Research – Diabete autoimmune e rischio cardiovascolare
● *Luca D'Onofrio (Roma)*

Discussione congiunta
Comunicazioni Orali (n. 7)

16.45-17.15 *Coffee Break*

17.15-19.15 **Sessione 2 – Dal Dire al Fare: La Ricerca Traslazionale**
Moderatori: Giovanna Gallo (Roma), Rosa Curcio (Terni)

Basic Research - L'evoluzione delle vescicole extracellulari: da semplici scarti cellulari a importanti strumenti terapeutici
● *Chiara Macchi (Milano)*

Clinical Research - **Vascular aging: from bench to bedside**
● *Rosa Maria Bruno (Parigi)*
Discussione congiunta
Comunicazioni Orali (n. 7)

19.15-20.30 **AperiPoster - Sessioni Poster 1-5**

Sessione Poster 1: *Andrea Baragetti, Giada Di Betto*
Sessione Poster 2: *Alessandro Maloberti, Federica Galimberti*
Sessione Poster 3: *Federica Piani, Sebastiano Cicco*
Sessione Poster 4: *Francesco Baratta, Marialuisa Sveva Marozzi*
Sessione Poster 5: *Valeria Visco, Alfredo Caturano*

20.45 *Cena*

Lunedì, 7 Aprile 2025

08.15-08.30 Registrazione dei partecipanti

08.30-10.30 **Sessione 3 – PCSK9: Un Decennio da Mito a Leggenda**
Moderatori: Simone Bini (Roma), Mario Daidone (Palermo)

Clinical Research – PCSK9: A star is born
● *Damiano D'Ardes (Chieti)*

Basic Research – Nuove Frontiere nell'Ipercolesterolemia: Epigenome Editing di *PCSK9*
● *Martino Alfredo Cappelluti (Milano)*

Discussione congiunta
Comunicazioni Orali (n. 7)

10.30-11.00 *Coffee break*

11.00-13.00 **Sessione 4 – Oltre il Genere: Quando Maneggiare con Cura**
Moderatori: Leonardo Bencivenga (Napoli), Bianca Papotti (Parma)

Basic Research - Fattori di rischio CV nella diade materno-fetale
● *Federica Moscucci (Roma)*

Clinical Research - La fragilità: il genere dell'anziano
● *Ilaria Parrotta (Venezia)*

Discussione congiunta
Comunicazioni Orali (n. 7)

13.00-14.15 *Lunch*

14.15-15.30 **Sessioni Poster 6-10**

Sessione Poster 6: *Giulio Francesco Romiti (SIMI), Chiara Ceolin (SIGG)*
Sessione Poster 7: *Francesco Spannella (SIIA), Maria Luisa Poli (SIPREC)*
Sessione Poster 8: *Fabrizia Bonacina (SISA), Alessandro Mengozzi (SID)*
Sessione Poster 9: *Giovanna Gallo (SIPREC), Giulia Rivasi (SIGG)*
Sessione Poster 10: *Antonella Giammanco (SISA), Alessandro Croce (SIIA)*

15.30-18.30 **WORKSHOP – "*BeInnovative, BeSmart, BePrecise: From Ideas to Impact in Research*" – Parte 1**
Mario Luca Morieri (Padova), Davide Soranna (Milano), Martino Pengo (Milano)
Comitato workshop

18.30-19.30 **AperiCelebration**

20.30 *Cena*

Martedì, 8 Aprile 2025

08.15-08.30 Registrazione dei partecipanti

08.30-10.30 **Sessione 5 – Contrastare l'Obesità su Più Fronti: dal Tessuto Adiposo al Muscolo**
Moderatori: Lorenzo Da Dalt (Milano), Paola Di Pietro (Salerno)

Basic Research – Contrastare l'obesità sarcopenica nell'anziano: uno SPRINTT verso la longevità
● *Riccardo Calvani (Roma)*

Clinical Research – Obesità: nuove basi fisiopatologiche e rivoluzione farmacologica
● *Carla Greco (Modena - Reggio Emilia)*

Discussione congiunta
Comunicazioni Orali (n. 7)

10.30-11.00 *Coffee Break*

11.00-12.45 **WORKSHOP – "*BeInnovative, BeSmart, BePrecise: From Ideas to Impact in Research*" – Parte 2**
Mario Luca Morieri (Padova), Davide Soranna (Milano), Martino Pengo (Milano) Comitato workshop

12.45-13.30 **WORKSHOP: "Non ce n'è coviddi": Viaggio nel Mondo del Negazionismo**
Intervengono: Fabrizio Elia (Torino), Giovanni Talerico (Roma)

13.30 ***Chiusura Lavori, Premiazioni e Lunch***

Il comitato organizzatore

Leonardo Bencivenga, Vanessa Bianconi, Rosa Curcio, Lorenzo Da Dalt, Mario Daidone, Damiano D'Ardes, Luca D'Onofrio, Giovanna Gallo, Carla Greco, Rosa Lombardi, Alessandro Maloberti, Chiara Pavanello, Federica Piani, Giulia Rivasi, Francesco Spannella, Valeria Visco.

Abstract

Sessioni Orali

Sessione 1

Fattori di Rischio "Non Tradizionali": Da dove veniamo? Chi siamo? Dove andiamo?

Domenica 6 aprile 2025 - ore 14.45-16.45

Moderatori: Ludovico Di Gioia (Bari), Matteo Landolfo (Ancona)

Sessione 2 – Dal Dire al Fare: La Ricerca Traslazionale

Domenica 6 aprile 2025 - ore 17.15-19.15

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Sessione 3 – PCSK9: Un Decennio da Mito a Leggenda

Lunedì 7 aprile 2025 - ore 08.30-10.30

Moderatori: Simone Bini (Roma), Mario Daidone (Palermo)

Sessione 4 – Oltre il Genere: Quando Maneggiare con Cura

Lunedì 7 aprile 2025 - ore 11.00-13.00

Moderatori: Leonardo Bencivenga (Napoli), Bianca Papotti (Parma)

Sessione 5 – Contrastare l'Obesità su Più Fronti: dal Tessuto Adiposo al Muscolo

Martedì 8 aprile 2025 - ore 08.30-10.30

Moderatori: Lorenzo Da Dalt (Milano), Paola Di Pietro (Salerno)

Sessioni Poster

Domenica 6 aprile 2025

Sessione Poster 1

Moderatori: Andrea Baragetti (SISA), Giada Di Betto (SIMI)

Sessione Poster 2

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Sessione Poster 5

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Lunedì 7 aprile 2025

Sessione Poster 6

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Sessione Poster 9

Moderatori: Giovanna Gallo (SIPREC), Giulia Rivasi (SIGG)

Sessione Poster 10

Moderatori: Antonella Giammanco (SISA), Alessandro Croce (SIIA)

Abstract n SO1_1 - Presenting author**: Martina Bollati**

A retrospective longitudinal study on the association between urine metanephrines and cardiovascular risk in patients in primary prevention without chromaffin tumors

M. Parasiliti-Caprino, M. Bollati, E. Febbraro, D.G. Candela, M. Procopio, S. Arata, C. Lopez, F. Ponzetto, E. Ghigo, M. Maccario

Division of Endocrinology, Diabetes and Metabolism; Department of Medical Sciences; University of Turin, Italy

Background: Urine metanephrines, catecholamine metabolites used for diagnosis of pheochromocytoma or paraganglioma (PPGL), may represent markers of sympathetic hyperactivity and are associated to cardiometabolic complications. However, no longitudinal studies in the literature have investigated their role in predicting cardiovascular events (CVE).
Objective: This retrospective longitudinal study aims to establish the association between urine metanephrine (dU-MT) and normetanephrine (dU-NMT) levels and the development of CVE.
Methods: Adult subjects in primary prevention, who had undergone urine metanephrine measurement, excluding PPGL, at the A.O.U. Città della Salute e della Scienza di Torino between 2007 and 2015, were enrolled. The subsequent development of CVE was evaluated by searching for relevant discharge diagnoses (via ICD-9 codes) between the test date and 31/12/2023.
Results: The study included 1170 subjects (41.5% male, 58.5% female, mean age 54±14 years), 86% of whom had arterial hypertension. Over a mean follow-up period of 11.7±4.1 years, 14.7% of the patients developed a CVE. Patients were divided into tertiles based on dU-MT and dU-NMT values. Multivariate analysis using Cox regression showed that the risk rate of CVE in patients in the 3rd tertile of dU-NMT (367-2300 µg/day) was 1.76 times higher compared to patients in the 1st tertile (20-231.6 µg/day), with a p-value of 0.01, independent of other traditional cardiovascular risk factors (age, gender, smoking, family history of CVE, hypertension, diabetes mellitus, renal function, number of antihypertensive medications, and lipid-lowering therapy). No significant differences in CVE risk were observed between the dU-MT tertiles.
Conclusions: The study highlights a relationship between higher dU-NMT values and the development of CVE, regardless of traditional risk factors, in subjects undergoing primary prevention. These results therefore support the hypothesis that these metabolites may be useful in cardiovascular risk stratification, as they appear to have a predictive role for future CVE by serving as markers of sympathetic hyperactivation.

Abstract n SO1_2 - Presenting author**: Martina Ciarnelli**

Monocyte immunometabolism: A new therapeutic target in metabolic dysfunction-associated steatohepatitis progression

M. Ciarnelli[1], T. Colangelo[2,3], R. Villani[1], A.D. Romano[1], R. Bianco[1], G.G. Bufano[1], G. De Girolamo[1], G. Di Gioia[1], G. Savino[1], G. Serviddio[1], M. Sangineto[1]

[1] C.U.R.E. (University Center for Liver Disease Research and Treatment), Liver Unit, Department of Medical and Surgical Sciences, University of Foggia, Italy;
[2] Department of Medical and Surgical Sciences, University of Foggia, Italy;
[3] Cancer Cell Signalling Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Foggia, Italy

Aim: Monocytes (Mos) play a pivotal role in the progression from metabolic dysfunction-associated steatotic liver disease (MASLD) to metabolic dysfunction-associated steatohepatitis (MASH), as they infiltrate the liver in response to Kupffer cell (KCs) depletion and tissue injury. Here, we examined the possibilities of studying Mos immunometalic alterations in MASH.
Methods: Circulating CD14+ Mos from both MASH patients and healthy subjects were used for *ex vivo* bioenergetics studies with Seahorse Mini Analyzer (Agilent). Assessment of mitochondrial functionality, gene and protein expression, were also conducted. In a second step, the impact of succinate dehydrogenase (SDH) inhibition, using dimethyl malonate (DMM), *in vitro* on circulating Mos and *in vivo* on a MASH mouse model, was examined.
Results: Monocytes from MASH patients exhibited a hypermetabolic phenotype, characterized by increased glycolysis, mitochondrial respiration, and heightened pro-inflammatory activity, associated with mitochondrial dysfunction and oxidative stress. Moreover, elevated electron transport chain (ETC) complexes activity, particularly complex II (SDH), with significant ROS generation, were observed. This process was transcriptionally sustained through the involvement of the AMPK-mTOR-PGC-1α axis. However, treatment with DMM successfully modulated mitochondrial function, restoring a balance between glycolysis and mitochondrial respiration and reducing cytokine production in MASH Mos. Analysis of a public scRNA-seq dataset revealed that, in mice, Mos, transitioning Mos (t-Mos), and lipid-associated macrophages (LAMs) exhibited significant upregulation of mitochondrial energy metabolism (MEM) and glycolytic pathways (GLY), compared to KCs, with numerous differentially expressed genes (DEGs), suggesting a metabolic shift that likely fuels monocyte recruitment and differentiation. Furthermore, the intraperitoneal injection of DMM in preclinical MASH murine model reduced hepatic inflammation, cellular damage and restored the expression of Mo-MØ and LAMs markers to normal levels demonstrating its *in vivo* potential as an immunometabolic modulator.
Conclusion: Investigating monocyte immunometabolism represents a promising therapeutic approach for addressing MASH.

Abstract n SO1_3 - Presenting author**: Alberto Finazzi**

Neurological responses to cardiac stress: Prognostic role of delirium subtypes in Acute Heart Failure

A. Finazzi[1], C. Okoye[1], E. Esposito[1], L. Tinelli[1], E. Mangili[1], L. Vitali[1], M. Marelli[1], M. Manna[1], A.A. Bruni[2], G. Bellelli[1]

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[2] IRCCS San Gerardo of Tintori Foundation, Monza, Italy

Aim: Delirium, a critical but often unrecognized condition in cardiology, frequently arises in patients with acute heart failure (AHF) due to inflammatory and hypoxic stress. Despite its significance, the prevalence, motor subtypes, and prognostic impact of delirium remain underexplored in AHF. This study examines delirium prevalence, incidence, and motor subtypes in older adults with AHF admitted to an acute geriatric unit (AGU) and evaluates its effect on 90-day post-discharge survival.
Methods: A prospective observational study was conducted from April 2022 to November 2024. Delirium and its motor subtypes were identified using the 4AT tool and DSM-5 criteria. Sociodemographic, clinical, and follow-up data were collected. The OS function was estimated using the Kaplan-Meier method and compared via the log-rank test. Cox proportional-hazards regression models, both univariable and multivariable, were applied. Explanatory variables were selected clinically and considering previous reports.
Results: Among 399 AHF inpatients (median age 87.4, 52% female), 132 (33%) experienced delirium, with a prevalence of 13.8% and incidence of 19.2%. Of these, 48% were hyperactive, 31% hypoactive, and 21% mixed subtype. Delirium increased 90-day mortality risk (36% vs. 19%, $p<0.001$), with the mixed and hypoactive subtypes showing the highest mortality rates (41% and 44%) compared to the hyperactive form (28%) and those without delirium (19%; $p=0.004$). Kaplan-Meier curves support these findings ($p<0.001$). Multivariable analysis revealed a twofold increased risk of 90-day mortality for mixed (HR 2.33, 95% CI 1.21-4.48, $p=0.012$) and hypoactive (HR 2.03, 95% CI 1.15-3.59, $p=0.015$) delirium compared to those without delirium.
Conclusions: Delirium is common in older adults with AHF, significantly worsening 90-day survival, particularly in hypoactive and mixed subtypes. These findings underscore the urgent need for increased awareness and targeted interventions to manage delirium in this vulnerable population.

Abstract n SO1_4 - Presenting author**: Leonardo Antonio Natola**

Statins in advanced HCC patients treated with Atezolizumab/Bevacizumab: a propensity score-matched and an inverse probability of treatment weight analysis from prospective ARTE multicentric Italian dataset

A. Dalbeni, F. Cattazzo, M. Vicardi, L.A. Natola, E. Franceschini, C. Campani, G. Cabibbo, C. Vivaldi, A. Palloni, T. Pressiani, M. Iavarone, A. Auriemma, P. Federico, F.R. Ponziani, G. Svegliati-Baroni, B. Stefanini, C. Soldà, F.G. Foschi, S. De Lorenzo, I. Garajova, F. Marra, C. Celsa, G. Masi, G. Brandi, L. Rimassa, B. Daniele, A. Stella, D. Sacerdoti , F. Tovoli on behalf of the ARTE study group

University of Verona and Azienda Ospedaliera Universitaria Integrata di Verona, Italy

Background and Aims: Statins have been suggested to exert anticancer properties by modulating angiogenesis, fibrosis, inflammation, and tumour microenvironment, generating interest in their clinical use for chronic liver diseases (CLD) and hepatocellular carcinoma (HCC) chemoprevention. However, the effects of statin therapy in patients treated with immune checkpoint inhibitors for CLD-associated HCC remain unknown. This study primarily aimed to assess the potential effect of statins on overall survival (OS) and progression-free survival (PFS) in patients with advanced HCC treated with Atezolizumab and Bevacizumab (A+B).

Materials and Methods: The ARTE dataset, a prospectively maintained database, includes 305 consecutive patients with unresectable HCC treated with A+B, enrolled from 12 tertiary care centres in Italy. From the original cohort, a 1:1 propensity score matching was performed to balance potential confounding factors between the 63 patients on statin therapy and those who were not. To reduce the possibility of a type 1 error due to the loss of statistical power in the matched analysis, we also performed an inverse probability of treatment weighting (IPTW). The primary outcomes were OS and PFS, while secondary outcomes included liver-related death, treatment interruption, and incidence of liver decompensating events.

Results: Among the overall population of 305 patients, the prevalence of liver cirrhosis was 75%, the main aetiology was viral (59%, HCV 44% and HBV 15%), followed by metabolic disfunction-associated steatotic liver disease (MASLD) (28%), alcoholic liver disease (ALD) (23%) and metabolic and alcohol-associated liver disease (MetALD) (8%) (Table 1). No significant differences were found between statin users and non-users for OS (Figure 1), PFS (Figure 2), or liver-related death. Additionally, the log-rank test revealed no significant difference between the groups in terms of treatment interruption due to liver decompensation events (p=0.28). The IPTW analysis largely confirmed these results, there was no differences in OS [HR 0.701, 95% CI 0.423-1.131, p=0.127] after applying weights.

Conclusion: Statin use did not show any benefit in terms of OS, PFS, or reduction in mortality or treatment interruption due to liver-related decompensation events in patients with advanced HCC treated with A+B.

	WHOLE POPULATION	NO STATINS	STATIN	P VALUE
	(N=305)	(N=242)	(N=63)	
Age, years	69.1 ± 10.3	69.8 ± 10.7	72.9 ± 6.7	**P<0.01**
Gender (M) n, %	251, 82	191, 78.9	60, 95.2	**P<0.01**
BMI, cm²/kg	25.8 ± 4.6	25.5 ± 4.7	26.8 ± 4.1	**P=0.01**
Cirrhosis n, %	229, 75	185, 76.4	44, 69.8	P=0.28
HBV n, %	47, 15	39, 16.1	8, 12.7	P=0.50
HCV n, %	133, 44	119, 49.1	14, 22.2	**P<0.01**
ALD n, %	71, 23	57, 23.5	14, 22.2	P=0.92
MASLD n, %	86, 28	56, 23.1	30, 47.6	**P<0.01**
MetALD n, %	24, 8	18, 7.4	6, 7.9	P=0.90
Hypertension n, %	183, 60	135, 55.8	48, 76.2	**P<0.01**
T2dm n, %	97, 32	67, 27.7	3, 4.8	**P<0.01**
NBBS n, %	72, 24	60, 24.8	12, 10	P=0.34
Number of nodules n, %				P=0.49
1	52, 17	43, 17.8	9, 14	
2	35, 11.4	24, 9.9	11, 17.5	
3	32, 10.5	26, 11.6	4, 6.3	
> 3	186, 61	147, 60.7	39, 61.9	
MTD cm	19 (1-150)	21.5 (1-150)	15 (1-82)	P=0.21
PVT n, %	96, 31	76, 31.4	20, 31.7	P=0.96
Metastasis n, %	114, 37	89, 36.8	25, 39.7	P=0.67
Hb g/dl	13.0 (12.0-14.3)	13.0 (12.0-14.3)	13.1 (11.9-14.9)	P=0.88
PLT mmc³	145 (76.0-223)	141 (76-222)	151 (74-236)	P=0.71
Bilirubin mg/dl	0.8 (0.56-1.30)	0.84 (0.54-1.31)	0.79 (0.57-1.23)	P=0.71
Albumin g/l	3.90 (3.60-4.20)	3.90 (3.60-4.20)	4.10 (3.80-4.30)	**P=0.02**
Creatinine mg/dl	0.88 (0.74-1.12)	0.84 (0.73-1.00)	0.97 (0.76-1.30)	**P<0.01**
AFP ng/ml	16.5 (4.84-212)	16 (5-320)	20 (5-204)	P=0.61
Best response				P=0.47
SD n, %	149, 48.9	12, 16.1	29, 46	
PR n, %	69, 22.6	54, 22.3	15, 23.8	
CR n, %	10, 3.3	8, 2.5	4, 6.3	
PD n, %	77, 25.2	62, 25.6	15, 23.8	
Death	142, 46.6	121, 50	21, 33.3	**P=0.02**
Treatment time days	195 (0-1249)	192 (0-1249)	199 (33-1135)	P=0.62

Table 1. General characteristics of the whole population and between the group of no statin users and statin users

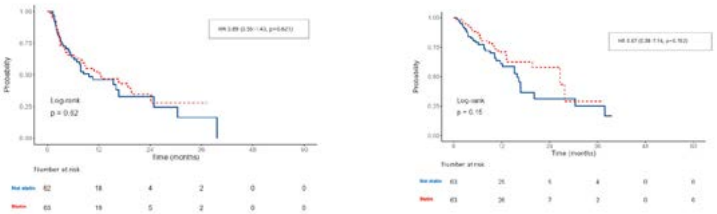

Figure 1 and 2. Overall survival (OS) and Progression Free Survival (PFS)

Abstract n SO1_5 - Presenting author**: Nicola Osti**

Very long-chain saturated fatty acids are inversely correlated with thrombin generation and linked to a reduced risk of coronary artery disease and myocardial infarction: preliminary findings from an angiographically-controlled study

M. Spizzo[1], G. Musuraca[2], N. Osti[3], P. Pattini[1], M. Donini[3], A. Castagna[1], C. Brocco[4], C. Angheben[2], S. Marconcini[4], C. Cemin[2], N. Cont[2], M. Baroni[5], M. Grusse[6], F. Presa[1], A. Anesi[4], M. Del Greco[2], P. Van Dreden[6], F. Bernardi[5], S. Friso[1], N. Martinelli[1]

[1] Department of Medicine, University of Verona, Italy;
[2] Division of Cardiology, "Santa Maria del Carmine" Hospital, Rovereto, Italy;
[3] Unit of Internal Medicine, "Valli del Noce" Hospital, Cles, Italy;
[4] Clinical Pathology Laboratory, Laboratories Department, APSS of Trento, Italy;
[5] Department of Life Sciences and Biotechnology, University of Ferrara, Italy;
[6] Clinical Research, Diagnostica Stago, Gennevilliers, France

Aim: The role of human plasma fatty acids (FAs) composition in coagulation cascade has received limited attention so far. We aimed to assess the relationships between plasma FAs and thrombin generation parameters in a single-center, angiographically-controlled, cohort of subjects with or without coronary artery disease (CAD).
Methods: Plasma FA concentrations were measured by gas-chromatography in clinically stable subjects undergoing an elective coronary angiography; the same subjects were also characterized for thrombin generation assay.
Results: The plasma FA profile was available for 245 subjects (males 73.9%; mean age 68.1±10.3 years): 54 with normal coronary arteries (CAD-free group) and 191 with coronary lesions with stenosis ≥50% (CAD group), of whom 51 with history of previous myocardial infarction (MI). In the 206 subjects not taking oral anticoagulants the saturated FAs 20:0, 22:0, and 24:0 were inversely correlated with peak of thrombin (R=-0.200 with P=0.004, R=-0.151 with P=0.031, and R=-0.182 with P=0.009, respectively) and endogenous thrombin potential (R=-0.217 with P=0.002, R=-0.170 with P=0.015, and R=-0.202 with P=0.004, respectively).
Defining very long-chain saturated FAs (VLSFAs) as those with 20 carbons or more, the sum of their levels remained inversely associated with both peak of thrombin and endogenous thrombin potential after adjustment for gender, age, CAD diagnosis and renal function in a linear regression model (standardized beta coefficient=-0.465 with P<0.001 and standardized beta coefficient=-0.400 with P=0.001, respectively).
In the whole study population subjects with CAD with or without MI had lower levels of VLSFAs than CAD-free subjects (1.43±0.34, 1.58±0.40, and 1.68±0.43 g/100g, respectively, P=0.005 by ANOVA).
Conclusions: Our data suggest an inverse correlation between VLSFA and thrombin generation, thereby indicating a potential antithrombotic effect of VLSFAs. Additionally, high VLSFA levels were linked to a lower prevalence of CAD and MI, consistently with the recent studies indicating that elevated VLSFA concentrations are associated with favourable cardiovascular outcomes.

Abstract n SO1_6 - Presenting author**: Moretti Arianna**

Engineered human CD34+ hematopoietic stem cells as an innovative approach to modulate the immunoinflammatory response during atherosclerosis

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Aim: Elevated plasma cholesterol levels contribute to atherosclerosis by promoting lipid accumulation in the arterial wall and the activation of an immune-inflammatory response. The growing recognition of the role of immune cells, coupled with the availability of biologics targeting specific pathways, highlight the need for experimental models for translating molecular mechanisms and therapeutic strategies for atherosclerosis. Here we will present the immune-metabolic characterization of an innovative immunodeficient mouse – on an atheroprone genetic background -, that is humanized with human hematopoietic cells.
Methods: Humanized TKO-LDLr KO mice (by crossing LDLr-KO with immunodeficient Rag2-KO/IL2rg-KO/CD47-KO mice, HuTKOL) were generated by hepatic injection of commercial or iPSCs-derived hCD34+ cells (250.000-300.000 cells/mouse), following low-dose irradiation (250 cGy) of 2-3 days old pups. Human cells engraftment was checked through tail blood and flow cytometry after 12 weeks. HuTKOL were then fed 12-week high-cholesterol diet to investigate immunometabolic phenotype and atherosclerosis.
Results: HuTKOL presented human leukocytes (%hCD45+ cells/total number of live leukocytes: 34,55%, SE±7,02%) in the circulation after engraftment with commercial hCD34+ cells, where CD19+ B lymphocytes were the most abundant population (%hCD19+/hCD45+: 79,15%, SE±1,76%), but they decreased over time (%hCD19+/hCD45+: 4,95%, SE±1,88%). Instead, CD4+ and CD8+ T lymphocytes increased (%hCD4+/hCD45+: 3,02%, SE±0,58%; %hCD8+/hCD45+: 5,51%, SE±1,26%), becoming the predominant population (%hCD4+/hCD45+: 37,44%, SE±6,79%; %hCD8+/hCD45+: 22,84%, SE±2,58%) at 24 weeks, similar to human lymphocyte profile. HuTKOL developed dyslipidemia (plasma cholesterol levels: 1211,96 mg/dl, SE± 63,72) and atherosclerosis (% aortic sinus plaque occlusion: 18,35%, SE±1,90%), when fed a high-cholesterol diet. Experiments are ongoing on iPSCs-derived CD34+, which showed a differentiation of 88.51% (SE±0,55%) in CD34+CD45- and 5.94% (SE±0.22%) in CD34-CD45- cells over all live cells by day 12 of the protocol.
Conclusions: hCD34+ humanized TKO-LDLR mice provide a valuable model for investigating the immune-metabolic response in atherosclerosis and could represent a valuable tool to test immunotherapies for CVD.

Abstract n SO1_7 - Presenting author**: Armando Ferrera**

Pre-participation Cardiovascular evaluation for Paris 2024 Olympic Games in Elite Athletes: The Italian Experience

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Aim: Olympic athletes represent a special subset of the athletic population and deserve a specialized medical approach. In view of the 2024 Paris Olympic Games, we developed and implemented a comprehensive medical protocol including (other than the standard screening with ECG, physical and history) cardiopulmonary exercise test, echocardiography and full blood and urine tests. Our aim was to assess the prevalence and type of cardiovascular abnormalities in athletes candidate to Paris 2024 Olympic Games, after implementation of this Olympic medical program.
Methods: We enrolled 772 elite athletes, who underwent a comprehensive, multidisciplinary evaluation, including full panel of blood and urine tests, electrocardiography, trans-thoracic echocardiography (TTE) and a cardiopulmonary exercise test (CPET).
Results: Of the 772 elite athletes, 363 (47%) were female. A substantial subset of 145 athletes (18.8%) showed one or more abnormalities. Specifically, either abnormal basal ECG findings (n=26, 17.9%), abnormal TTE results (n=45, 31%), high blood pressure (n=2, 1.4%) or exercise induced arrhythmias (n=49, 33.8%) were detected. 10 athletes (6.9%) showed both abnormal ECGs and exercise induced arrhythmias, and 13 athletes (9%) showed both ECG and echocardiographic abnormal findings. After further and more detailed investigations, of the 145 athletes showing cardiovascular abnormalities at the initial screening, in 4 of them were cardiac conditions implying potential risk of sudden cardiac death were identified and therefore they were withdrawn from competitive sport. Full blood test analysis identified metabolic abnormalities in 200 subjects. Of these, 165 (21%) showed hypercholesterolemia.
Conclusions: Olympic athletes, despite the highest level of physical performance, are not exempt from cardiovascular and metabolic diseases, including a small proportion of cardiac conditions at risk of SCD. More advanced diagnostic tools, including CPET, echocardiography and full blood tests, implemented in our protocol, were required to identify hidden cardiovascular abnormalities that could have jeopardized athlete's health and performance.

Abstract n SO2_1 - Presenting author**: Jacopo Burrello**

Circulating extracellular vesicles increase the expression of RhoA in normotensive subjects underwent dietary sodium modulation

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Aim: Sodium status affects osmoregulation and fluid balance, and recent evidence suggests a role in immune system modulation, endothelial cell function, and development of cardiovascular disease. Increase dietary sodium has been linked with hypertension. Circulating extracellular vesicles EVs) have been involved in vascular inflammation and endothelial dysfunction and may mirror physio-pathological processes occurring after manipulation of dietary sodium. The aim of the present study was to characterize circulating extracellular vesicles and assess their functional role in subjects underwent dietary sodium modulation.
Methods: Fifty normotensive subjects underwent 7 days of sodium restricted diet and then 7 days of sodium load. Circulating EVs were isolated after each diet phase and profiled by a flow cytometry multiplex bead-based platform, assessing the expression of their surface antigens. Bioinformatics was applied to identify intracellular targets of EV markers up regulated after high sodium diet (HSD) as compared to sodium restricted diet. Human microvascular endothelial cells (HMEC) were used as in vitro model to assess EV functional effects.
Results: EV-carried CD14, CD25 and CD40 (from immune system), CD29, CD42a and CD62P (involved in coagulation and platelets activation), and CD31 (endothelial marker) increased after HSD. Protein-protein interactor network analysis identify RhoA as target of circulating vesicles carrying the overexpressed antigens. After incubation of HMECs with patient derived EVs after HSD, we confirmed an increased expression of active RhoA.
Conclusions: The modulation of dietary sodium influences the expression of circulating EV surface antigens involved in vascular inflammation, platelet activation and endothelial dysfunction. EVs may be mediators of the effect of sodium load by interacting with endothelial cells, leading to the activation of RhoA, known as player in the development of salt-sensitive hypertension.

Abstract n SO2_2 - Presenting author**: Fabrizio Buffolo**

Small-RNAome of urinary extracellular vesicles reveals association of high sodium diet with renal pro-inflammatory pathways in individuals without hypertension

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Aim: Excessive sodium intake is associated with the development of arterial hypertension and cardiovascular diseases through mechanisms that extend beyond hemodynamic effects, including endothelial dysfunction, oxidative stress, and a pro-inflammatory environment. However, most studies have been conducted in preclinical models. This study aimed to explore the impact of dietary sodium modulation on human kidney pathophysiology by analyzing small RNA content in urinary extracellular vesicles (uEVs).
Methods: Fourteen individuals at high cardiovascular risk without hypertension were enrolled in a prospective study involving a 7-day low sodium diet (LSD) followed by 7-day high sodium diet (HSD). uEVs were isolated from 24-hour urine samples collected at the end of each dietary phase and subjected to small RNA sequencing and bioinformatic analysis. Differentially expressed microRNAs (miRNAs) were further investigated in human proximal tubular cells (HK-2 cells) to validate their mRNA target interactions.
Results: A total of 111 small RNAs were identified, with 30 showing significant expression changes between LSD and HSD (including 8 miRNAs differentially expressed). The correlation matrix revealed a positive correlation between 24h urinary sodium excretion and miRNAs upregulated in HSD (including miR-10b-5p) and a trend towards a negative correlation with miR-320b (downregulated in HSD). The bioinformatic-cluster-network analysis highlighted that HSD-enriched pathways were involved in the innate and adaptive immune response, interleukin, and interferon signaling, while LSD-enriched pathways were associated with peroxisome proliferator-activated receptor alpha (PPAR-alpha) regulation. Functional assays in HK-2 cells revealed that inhibiting miR-320b (down-regulated in HSD) increased intercellular adhesion molecule 1 (ICAM-1), potentially promoting pro-inflammatory effects. Conversely, inhibiting miR-10b-5p (down-regulated in LSD) elevated PPAR-alpha levels, known for its anti-inflammatory and anti-fibrotic roles in the kidney.
Conclusions: Small RNA profiling of uEVs suggests that a high sodium diet induces pro-inflammatory molecular changes, which may contribute to sodium-mediated low-grade renal inflammation and hypertension development.

Abstract n SO2_3 - Presenting author**: Alessandro Mengozzi**

Circulating mitochondrial DNA signature in cardiometabolic patients

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Aim: Circulating mitochondrial DNA (mtDNA) profiles could refine risk stratification, but current methods do not account for different fractions of circulating mtDNA. We aimed to explore whether patients with cardiometabolic disease have a specific signature of the total circulating mtDNA profile.
Methods: We performed a complete clinical assessment, including blood tests, 12-lead ECG and ultrasound at rest and during cardiopulmonary exercise. Ultrasound congestion was defined at rest as inferior vena cava of ≥21 mm, lung B-lines ≥4, or discontinuous renal venous flow. In fasting whole blood and plasma samples collected at rest, we simultaneously measured the copy number of the cellular and cell-free components of mtDNA by real-time quantitative polymerase chain reaction. We calculated the ratio of cell mtDNA to cell-free mtDNA as an index of mitochondrial efficiency.
Results: We enrolled 120 consecutive patients: 42% with HF and preserved ejection fraction (HFpEF), 33% with HF and reduced ejection fraction (HFrEF) and 25% at risk of developing HF; 35% had diabetes. Cell-free mtDNA was increased in patients with HF (and higher in HFrEF than HFpEF) and with diabetes. Cell-free mtDNA was higher in patients with systemic inflammation (high-sensitivity C-reactive protein [hs-CRP] ≥0.2 mg/dL with neutrophil-lymphocyte ratio [NLR] >3) and more ultrasound signs of congestion. The mtDNA ratio showed opposite trends (all $p<0.05$). Cell-free mtDNA and mtDNA ratio independently predicted the presence of ≥2 ultrasound signs of congestion and effort intolerance (peak oxygen consumption <16 mL/kg/min) at ROC analysis and using multivariable regressions after adjustment for age, sex, hs-CRP, NLR, high-sensitivity Troponin T and NT-proBNP.
Conclusions: Cardiometabolic patients have an altered circulating mtDNA signature characterised by higher cell-free mtDNA and lower mtDNA ratio. Both are associated with impaired response to exercise, higher systemic inflammation and increased congestion. Circulating mitochondrial profile could be a new biomarker of mitochondrial status in cardiometabolic diseases.

Abstract n SO2_4 - Presenting author**: Stella Covino**

Functional characterization of Variants of Uncertain Significance (VUS) in patients with Heterozygous Familial Hypercholesterolemia (HeFH) using a flow cytometry assay

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Background: Familial hypercholesterolemia (FH) is a genetic lipid disorder, primarily caused by pathogenic variants in the *LDLR* gene. Variants of uncertain significance (VUS) complicate diagnosis, making functional tests essential to confirm their pathogenicity.
Aim: To assess the functional impact of *LDLR* VUS found in patients with FH using flow-cytometry.
Methods: PBMCs were isolated from 33 FH patients and stimulated with CD3/CD28 beads in LPDS. The LDLR cycle (cell surface expression, LDL binding and uptake) was assessed using flow-cytometry. Results were expressed as the ratio of the mean fluorescence intensity (gMFI) of activated CD4 T-lymphocytes to gMFI of wild-type controls. Measurements were repeated three times and presented as median (IQR). LDL binding and uptake were validated via optical microscopy (Thunder Leica), using Oil Red O-labelled LDL and formaldehyde treatment to differentiate surface-bound from internalized LDL. Quantification of LDL particles was performed using ImageJ software. Variants were classified as defective if they showed less than 85% wild-type activity in LDLR expression, binding, or uptake, according to ClinGen FH Expert Panel Specifications (v 1.2).
Results: Out of 19 VUS tested, 14 (73.7%) showed deleterious effects on at least one of the LDLR functions. The c.1530_1532del, c.*34C>T and c.1007A>G variants disrupted the entire LDLR cycle, while others caused defects in expression (n=5-35.7%) or binding/expression or binding/uptake (n=6-42.8%). Thus, 28/33 FH-VUS patients (85%) showed at least one LDLR cycling defect. Interestingly, patients with defective VUS had slightly higher untreated LDL-C levels than those with non-defective variants (220±72.8 vs. 180.1±31.9 mg/dl; P=0.06) and were more prevalent among those with a DLCN score ≥6 (81.5%,P=0.05). All three VUS variants, which affected the entire LDLR cycle, were confirmed to be defective using the microscopy-based method.
Conclusions: This study illustrates the significance of functional testing for *LDLR* variants to clarify biological effects and include VUS in FH diagnosis.

Abstract n SO2_5 - Presenting author**: Isabella Fichtner**

Characterisation of extracellular vesicles in patients with heart failure

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Aim: Heart failure (HF) is a clinical syndrome involving structural and/or functional cardiac abnormalities, classified as reduced (HFrEF) or preserved (HFpEF) based on the ejection fraction percentage of the left ventricle. As extracellular vesicles (EVs) reflect onset and severity of cardiac diseases, they attract interest as potential liquid biopsies. Aim is to characterize EVs in HF and investigate their potential as biomarkers to assess HF progression and understand the underlying molecular mechanisms.
Methods: The study included 40 HF patients (13 HFpEF and 27 HFrEF) and 21 volunteers (CTR). EVs were isolated from plasma by size-exclusion chromatography and ultracentrifugation, then characterised using nanoparticles tracking analysis, transmission electron microscopy (TEM), Western blot (WB), flow cytometry (FACS) and targeted proteomic analysis.
Results: Diagnosis of HF relied on echocardiographic and biochemical parameters. Isolation of EV was confirmed by FACS and WB analyses (CD63, CD9, CD81, Alix and β1 integrin), while integrity by TEM. Median EV concentration was lower in HF *vs* CTR (EV/ml/cell count: $2.6*10^9$ *vs* $3.5*10^9$), while the size was larger (nm: 204 *vs* 182). Among tdifferent subpopulations analysed, EVs from cardiomyocyte ($CD172a^+$), endothelial cells ($CD62E^+$) and endothelial progenitor cells ($CD309^+$) were significantly reduced in HF. Conversely, EVs from T and B lymphocytes ($CD8^+$, $CD4^+$ and $CD19^+$), and lymphatic vessels ($CD310^+$) were significantly increased. Platelet and activated platelet-derived EVs ($CD154^+/CD41a^+$) were increased in HF patients. Proteomic analysis of EVs showed increased levels of surfactant proteins and markers of fibrosis (e.g. Galectin-3). When EV subtype analysis was stratified by clinical presentation (HFrEF *vs* HFpEF), the main differences between patients and CTR were driven by HFrEF.
Conclusions: EVs isolated from HF patients have a unique fingerprint which alignes with the hemodynamic characteristics of the condition. The characterization of EVs allows to distinguish HFpEF from HFrEF showing different activity of systemic mechanisms (e.g. endothelial and inflammation).

Abstract n SO2_6 - Presenting author**: Martina Rella**

Irisin restores the secretory function of pancreatic β-cells in experimental and human T2D

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Aim: In this study, the effects of irisin, a hormone secreted by skeletal muscle, able to improve metabolic homeostasis and promote energy expenditure, on the β-cell functional mass were evaluated both in diabetic mice in vivo and in human pancreatic islets isolated from subjects with type 2 diabetes (T2D) ex vivo. Moreover, the molecular mechanisms underlying irisin action were investigated.
Methods: C57Bl/6 mice (n=8) were made diabetic by a high-fat diet (HFD) and a single-dose of streptozotocin (STZ). 4 standard diet (SD)-fed mice were used as control. HFD/STZ mice were daily treated with 0.5 μg/g irisin (n=4) or vehicle (n=4) for 14 days. Fasting glycemia, insulinemia, body weight, glucose tolerance, and glucose-stimulated insulin secretion (GSIS) were assessed. Pancreatic islet architecture and β-cell apoptosis/proliferation were evaluated by immunofluorescence analyses. Pancreatic islets isolated from T2D patients (n=14) and non-diabetic subjects (ND) (n=10), as well as INS-1E cells, were exposed to 100 nM irisin for different times. GSIS and insulin content were measured by ELISA assays; intracellular signaling proteins and calcium levels were evaluated by immunoblotting and fluorimetric assay, respectively.
Results: Irisin administration improved glycemic homeostasis, reduced body weight, and increased β-cell functional mass by stimulating β-cell proliferation and enhancing GSIS in vivo. Moreover, in T2D islets irisin augmented insulin content and GSIS. Of note, irisin activated CREB and AKT in INS-1E cells under physiological conditions, but not under glucotoxic conditions. However, while chronic exposure to excess glucose blunted both GSIS and glucose-evoked increase in cytoplasmic calcium levels, irisin restored insulin secretion through the mobilization of calcium stores from the endoplasmic reticulum (ER).
Conclusions: These findings highlight the role of irisin as a hormone that counteracts β-cell failure under dysmetabolic conditions in both rodents and humans and could be used to delay T2D onset and/or progression.

Abstract n SO2_7 - Presenting author**: Federica Todaro**

Mediterranean diet effects on vascular health and serum levels of adipokines and ceramides

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Aims: The Mediterranean Diet is based on low saturated fat and high consumption of vegetable oils. Recent studies have highlighted its key role in reducing the risk of cardiovascular diseases.
In our randomized clinical trial we examinated the impact of a Mediterranean-style diet on various vascular health markers. The aims were to assess the impact of adhering to a Mediterranean-style diet on endothelial function and arterial stiffness; to evaluate the effects on the lipidic profile and on some serum ceramide levels; to investigate how a Mediterranean-style dietary plan influences the modulation of serum concentrations of specific adipokine levels.
Methods: The enrolled patients were subjects aged between 55 and 80, at high cardiovascular risk that were randomised to two different types of dietary schemes: Group A (experimental arm) - Mediterranean Diet and Group B (control arm) - Low-fat diet.
Results: A total of 101 patients were assigned to Group A, while 52 control subjects were randomized to follow a low-fat diet with dietary "counseling." At the six-month follow-up, participants in the Mediterranean Diet group had significantly lower average serum total cholesterol levels, lower serum levels of resistin and visfatin, higher levels of adiponectin, and a notably higher increase in reactive hyperemia index (RHI) values compared to those in the low-fat diet group. These results were confirmed at the twelve-month follow-up.
Conclusion: Our results reported a potential close connection between the lipid-related and vascular benefits of the Mediterranean diet, highlighting the pathogenetic role of certain adipokines like visfatin and resistin, along with some serum ceramide levels, as possible lipid-based cardiovascular markers. These findings offer another potential explanation for why a higher level of adherence to a Mediterranean-style diet can have favorable effects on a range of cardiovascular risk factors and the underlying mechanisms contributing to atherosclerosis.

Abstract n SO3_1 - Presenting author**: Sining Xie**

Network meta-analysis comparing the risk of specific adverse events between statins, ezetimibe, bempedoic acid, PCSK9 inhibitors, and their combinations in patients with dyslipidemia

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Aim: Statins, ezetimibe, bempedoic acid, and PCSK9 inhibitors (PCSK9i) are widely used treatments for hypercholesterolemia. Although their safety profile is known, there are no comprehensive comparative assessments. We aimed to compare the risk of muscle-related symptoms, diabetes, liver dysfunction, and neurocognitive disorders between these treatments.
Methods: We conducted a network meta-analysis according to PRISMA guidelines; databases were searched from inception to October 2024. Inclusion criteria were: (1) randomized controlled trials (RCTs) in adults (≥18 years), parallel design, phase II, III or IV; (2) English language; (3) using statins, ezetimibe, PCSK9i, bempedoic acid, or their combinations as intervention; (4) targeting patients with dyslipidemia; (5) reporting the information about any of the selected adverse events; (6) a total sample size of ≥200 subjects; (7) intervention duration of more than 3 weeks. Pooled estimates were assessed by both fixed-effect and random-effects models within a frequentist setting, assuming equal heterogeneity across all comparisons. Pooled risk ratios (RR) and their 95% confidence interval or p-score (possibility of being the lowest risk) were estimated.
Results: A total of 315,166 subjects from 149 RCTs were included. Bempedoic acid ranked the lowest risk of myalgia (p-score=0.94). Statins were associated with higher incidence of diabetes (RR 1.12 [1.03, 1.21]), but lower risk of neurocognitive disorders (RR 0.70 [0.60, 0.80]) comparing to PCSK9i. Statins (RR 1.33 [1.14, 1.59]), and bempedoic acid (RR 1.69 [1.20, 2.38]) had a higher risk of liver dysfunction than PCSK9i.
Conclusions: In conclusion, PCSK9i appear to have a more favorable safety profile regarding the risk of diabetes and liver dysfunction. Bempedoic acid or statins seem to be a better choice for subjects with high risk of myalgia or neurocognitive disorders, respectively. This information can be valuable when selecting therapy for specific patient subgroups at higher risk of certain adverse events.

Abstract n SO3_2 - Presenting author**: Riccardo Accioli**

Unravelling atrioventricular block risk in inflammatory diseases: Systemic inflammation acutely delays atrioventricular conduction via a cytokine- mediated inhibition of connexin43 expression

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Aim: Recent data suggest that systemic inflammation can negatively affect atrioventricular conduction, regardless of acute cardiac injury. Indeed, gap- junctions containing connexin43 coupling cardiomyocytes and inflammation- related cells (macrophages) are increasingly recognized as important factors regulating the conduction in the atrioventricular node. The aim of this study was to evaluate the acute impact of systemic inflammatory activation on atrioventricular conduction and elucidate underlying mechanisms.
Methods: We analyzed: (1) the heart rate corrected PR(PRc)-interval in patients with inflammatory diseases of different origins during active phase and recovery, and its association with inflammatory markers; (2) the existing correlation between connexin43 expression in the cardiac tissue and peripheral blood mononuclear cells (PBMC), and the changes occurring in patients with inflammatory diseases over time; (3) the acute effects of interleukin(IL)- 6 on atrioventricular conduction in an in vivo animal model, and on connexin43 expression in vitro.
Results: In patients with elevated C-reactive protein levels, atrioventricular conduction indices are increased, but promptly normalized (PRc-interval: 173.1 [39.4] vs. 162.5 [30.1] ms, $p=0.002$) in association with inflammatory markers reduction, particularly IL- 6 ($r=0.38$, $p<0.001$). In these subjects, connexin43 expression in PBMC, which is correlative of that measured in the cardiac tissue, inversely associated with IL- 6 changes ($r=-0.42$, $p=0.033$). Moreover, direct IL- 6 administration increased atrioventricular conduction indices (51.4 [2.4] vs. 58.2 [2.7], $p=0.007$) in vivo in a guinea pig model, and IL- 6 incubation in both cardiomyocytes and macrophages in culture, significantly reduced connexin43 proteins expression (mean percentage decrease=54%/43% respectively, $p<0.01$).
Conclusions: The data evidence that systemic inflammation can acutely worsen atrioventricular conduction, and that IL-6-induced down-regulation of cardiac connexin43 is a mechanistic pathway putatively involved in the process. Although reversible, these alterations could significantly increase the risk of severe atrioventricular blocks during active inflammatory processes.

Abstract n SO3_3 - Presenting author**: Martina Ugolotti**

Investigating PCSK9 inhibition as potential strategy in Alzheimer 's disease

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Aim: Alteration of cerebral cholesterol homeostasis and neuroinflammation are typical hallmarks of Alzheimer's disease (AD). The proprotein convertase subtilisin/kexin 9 (PCSK9), beyond regulating plasma cholesterol, is expressed in the central nervous system (CNS), where it may play a role in the pathogenesis of AD. We previously demonstrated *in vitro* that PCSK9 enhances the β-amyloid (Aβ)-induced neurotoxicity and neuroinflammation, while PCSK9 genetic deletion in an AD-mice model showed an improvement in cognitive performance. This research aims to investigate *in vitro* the potential protective effect of PCSK9 pharmacological inhibition with newly-synthesized small molecules (MR compounds).
Methods: After a preliminary screening on human hepatocarcinoma cells, three compounds were selected and compared to a known PCSK9 inhibitor (7030B-C5) in human neuroblastoma cells (IMR-32) to assess: cerebral PCSK9 inhibition activity (Western blot, ELISA assay), its target expression (LDLR by Western blot) and a potential neuroprotective effect against Aβ-induced neurotoxicity (MTT assay). The impact of the studying compounds on inflammation was evaluated by measuring IL-6 secretion (ELISA assay) on human microglial-like macrophages (THP-I) after stimulation with lipopolysaccharide (LPS). Statistical analyses were performed with T-test and one-way ANOVA.
Results: MR-3 and 7030B-C5 significantly reduced PCSK9 expression (-44%, $p<0.01$; -34%, $p<0.01$, respectively), as well as its secretion (-49%, $p<0.05$; -50%,$p<0.05$, respectively) at 10μM. Interestingly, all compounds were able to induce LDLR expression (20%;44%;26%;26% vs Basal). Moreover, all tested compounds significantly dampened Aβ-triggered cytotoxicity (-25%, $p<0.001$), with the most evident effect for MR-533 and 7030B-C5 that restored cell viability dose-dependently reaching a complete recovery at the highest concentration tested ($p>0.05$ vs Basal). In addition, LPS-induced IL-6 secretion was markedly decreased by all MR compounds (-75%; -96%; -96%, $p<0.001$).
Conclusions: Our *in vitro* results show the protective role of PCSK9 pharmacological inhibition with small molecules on Aβ-induced neurotoxicity and neuroinflammation on cerebral cell models. These data could potentially pave the way to propose a novel pharmacological strategy to counteract AD.

Abstract n SO3_4 - Presenting author**: Viola Salvini**

Anti-Ro/SSA antibodies blocking calcium channels as a potentially reversible cause of atrioventricular block in adults

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Aim: In ~ 50% of severe atrioventricular blocks (AVBs) occurring in adults <50 years, the underlying etiology remains unknown. Preliminary evidence from case reports suggests that autoimmunity, specifically the presence of circulating anti-Ro/SSA antibodies in the patient (*acquired form*), in the patient's mother (*late-progressive congenital form*), or in both (*mixed form*), could be involved in a fraction of idiopathic AVBs in adults by possibly targeting the L-type calcium channel (Cav1.2) and inhibiting the related current (ICaL). The aim of this study was to evaluate whether anti-Ro/SSA antibodies were causally implicated in the development of isolated AVBs in adults.
Methods: Thirty-four consecutive patients with isolated AVB of unknown origin and 17 available mothers were prospectively enrolled in a cross-sectional study. Anti-Ro/SSA antibodies were assessed by fluoroenzyme-immunoassay, immuno-Western blotting, and line-blot immunoassay. Purified immunoglobulin-G (IgG) from anti-Ro/SSA-positive and anti-Ro/SSA-negative subjects were tested on ICaL and Cav1.2 expression using tSA201 and HEK293 cells, respectively. Moreover, in 13 AVB patients, the impact of a short course of steroid therapy on AV conduction was evaluated.
Results: Anti-Ro/SSA antibodies, particularly anti-Ro/SSA-52kD, were found in 53% of AVB-patients and/or in their mothers, most commonly an acquired or mixed form (two-thirds of cases) without history of autoimmune diseases. Purified IgG from anti-Ro/SSA-positive but not anti-Ro/SSA-negative AVB patients acutely inhibited ICaL and chronically down-regulated Cav1.2 expression. Moreover, anti-Ro/SSA-positive sera showed high reactivity with peptides corresponding to the Cav1.2 channel pore-forming region. Finally, steroid therapy rapidly improved AV conduction in AVB- patients with circulating anti-Ro/SSA antibodies but not in those without.
Conclusions: Our study points to anti-Ro/SSA antibodies as a novel, epidemiologically relevant and potentially reversible cause of isolated AVB in adults, via an autoimmune-mediated functional interference with the L-type calcium channels. These findings have significant impact on antiarrhythmic therapies by avoiding or delaying pacemaker implantation.

Abstract n SO3_5 - Presenting author**: Carmine De Luca**

siRNA versus mAbs for proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition: real world evidence single-center study on lipid profile in familial hypercholesterolemia patients

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Background and aim: PCSK9 inhibitor (PCSK9i) mAbs showed a dramatic effect on low-density lipoprotein cholesterol (LDL-C) reduction. A double-stranded small-interfering RNA (siRNA) therapeutic agent that suppresses PCSK9 translation (inclisiran) has been recently licensed. RCTs showed that inclisiran administered every 6 months is associated to a similar LDL-C reduction compared to every 14 days PCSK9i mAb treatment. The aim of our study is to compare in real world evidence lipid lowering effect of siRNA versus mAbs.
Methods: We perfomed a prospective cohort study. Familial hypercholesterolemia (FH) patients with a stable treatment (>6 month) with PCSK9i mAbs were included. Group1 was switched to treatment with PCSK9i siRNA (inclisiran) and Group2 continued the treatment with PCSK9i mAbs (Alirocumab or Evolocumab). Lipid profile [total cholesterol (TC) and LDL-C] and % of LDL-C target achievement were evaluated at the baseline (T0) and at 6-months follow-up (T1).
Results: 52 FH patients were enrolled. Group1 (n=26) 56% males, average age of 56.1±14.8years; 50% in secondary prevention. At T0, TC was 179.6±67.5mg/dl, LDL-C was 105.7±62.2mg/dl. At T1, TC was 175.4±53.1 mg/dl and LDL-C value was 97.6±47.9 mg/dl. Group2 (n=26) 42% males, average age of 61.5±12.4years; 46% in secondary prevention. At T0, TC was 139.8±54.8 mg/dl, LDL-C was 65.8±51.0mg/dl. At T1, TC was 137.6±35.0mg/dl and LDL-C was 63.1±32.2mg/dl. No significant difference between T1-T0 LDL-C Δ mean % reduction was found comparing the 2 groups (10% for Group1 vs 35% for Group2 p=0,260). No significant difference in % of target achievement at T1 was found (31% for Group 1 and 50% for Group 2; OR: 95%CI:36.4-61.9, p=0.131).
Conclusions: Our preliminary results showed that no significant difference in efficacy were found between treatment with PCSK9i mAbs and siRNA, confirming siRNA a promising option mainly in low-adherent patients.

Abstract n SO3_6 - Presenting author**: Laura Gullà**

Hepatocyte- or Kupffer cell-derived ApoE differently affects lipoprotein metabolism in experimental models

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Background and Aim: Apolipoprotein E (ApoE) is a key protein involved in lipoprotein metabolism. While hepatocytes are the primary source of ApoE, myeloid cells – macrophages, as well as Kupffer cells (KCs, liver-resident macrophages) – have been shown to contribute to ApoE production. We previously showed that bone marrow transplantation from WT to ApoE KO animals results in normalization of KO plasma lipid levels with cholesterol profile resembling that of WT mice. This prompted us to further investigate the distinct contribution of Kupffer cell-derived ApoE versus hepatocyte-derived ApoE in modulating the immunometabolic response in experimental models.
Methods: Hepatocyte- and Kupffer cell-specific ApoE KO mice were generated by crossing ApoE flox/flox mice with Albumin-Cre (ApoE Hep-KO) and Clec4f-Cre (ApoE KC-KO) mice, respectively. Mice were fed a standard chow diet for 12 weeks, then poloxamer assay, FPLC, western blot (WB), 2D-electrophoresis and flow cytometry analyses were performed to characterize their metabolic and immune profiles.
Results: ApoE Hep-KO mice do not present ApoE in plasma, suggesting that these cells largely contribute to circulating ApoE. Analysis of cholesterol distribution by FPLC revealed an increase in the LDL fraction in ApoE Hep-KO mice compared to WT, with an impaired VLDL production (-46%, $p<0.0001$), as assessed by poloxamer assay.
In contrast, ApoE KC-KO mice showed reduced circulating ApoE levels (-45.2%, $p=0.0214$), suggesting that KCs also contribute to the ApoE plasma pool, but no difference in VLDL production. WB analysis showed reduced HDL-ApoE levels in ApoE KC-KO mice, confirmed also by 2D-electrophoresis, and was associated with a shift in the distribution of immature pre-beta HDL particles compared to WT (6.5% vs 2.1%, $p=0.0851$).
No significant changes in immune cell distribution were observed.
Conclusions: This study shows that beyond the role of hepatocytes in synthesizing ApoE containing lipoproteins, KCs contribute to systemic ApoE profile and more specifically to ApoE present in HDL. These findings provide insights into the cell-specific functions of ApoE in lipid metabolism, although the underlying molecular mechanisms remain to be elucidated.

Abstract n SO3_7 - Presenting author**: Heba Mansour**

The new HDAC3-selective inhibitor LA9498 improves the metabolic phenotype of adipocytes and induces the M2-like phenotype of macrophages

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Aim: Epigenetic regulation, mediated by histone deacetylase 3 (HDAC3), is recognized as a key mechanism underlying adipocyte and macrophage phenotypes in pathophysiology. We previously showed that genetic inactivation of HDAC3 induces metabolic reprogramming in white adipose tissue (WAT), promoting browning and enhancing the metabolic function of WAT. Furthermore, HDAC3 activity has been shown to drive macrophage polarization toward the pro-inflammatory M1-like phenotype, characterized by elevated secretion of inflammatory mediators, while its inhibition facilitates a shift toward the anti-inflammatory M2-like phenotype. This study evaluates the therapeutic potential of LA9498, a novel, highly potent, and selective HDAC3 inhibitor, in modulating adipocyte and macrophage phenotype.
Methods: C3H/10T1/2 adipocytes were differentiated in the presence of either LA9498, or the class I HDAC inhibitor MS-275, used as a reference compound. RAW264.7 macrophages were treated with LA9498 or MS-275, with or without stimulation with the proinflammatory cytokine interferon-gamma (IFNγ). Upon treatments, gene expression, protein levels, histone acetylation, lipid accumulation, mitochondrial mass, and mitochondrial functionality were evaluated.
Results: LA9498 demonstrated higher potency and efficacy vs. MS-275 in enhancing adipocyte differentiation and mitochondrial function. LA9498 upregulated genes involved in lipid mobilization, fatty acid β-oxidation, and mitochondrial activity, enhanced mitochondrial respiration (including ATP production, maximal respiration, and spare respiratory capacity), and elevated the expression of electron transport chain complexes II, III, and IV. In RAW264.7 macrophages LA9498 increased acetylation of histone H3, confirming HDAC inhibitory activity. In IFNγ-activated RAW264.7 macrophages, LA9498 reduced pro-inflammatory gene expression (*Il1b*, *Tnf*, *Nos2*) and upregulated the anti-inflammatory gene *Arg2*, an effect not observed with MS-275. LA9498 restored oxidative metabolism in IFN-γ-treated RAW 264.7 cells typical of M2-like macrophages.
Conclusions: LA9498 is a selective HDAC3 inhibitor that induces the browning of adipocytes and exerts anti-inflammatory effects in macrophages. This compound offers new perspectives for therapeutical applications in immuno-metabolic adipose tissue disorders associated with obesity.

Abstract n SO4_1 - Presenting author**: Nicolò De Biase**

Relation between exhaled breath acetone and disease severity across the spectrum of heart failure

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Aims: To investigate the utility of exhaled breath acetone (EBA) as a non-invasive marker of disease severity in ambulatory patients with HF, elucidating its relationship with cardiovascular structure, function, and exercise capacity.
Methods: We enrolled ambulatory patients with HF with reduced (<50%, HFrEF) or preserved (>50%, HFpEF) left ventricular ejection fraction (LVEF), together with subjects with cardiovascular risk factors and/or structural heart disease without established HF. All the participants underwent a comprehensive clinical and laboratory evaluation, resting transthoracic echocardiography, and a combined cardiopulmonary-echocardiographic stress test with EBA monitoring at rest (EBA_{rest}) and during exercise (EBA_{ex}).
Results: Patients with HFpEF (n=62) were older and more likely to be female than those at risk of HF (n=50) or with HFrEF (n=41). EBA_{rest} (1.5, interquartile range [IQR] 1.0-3.1 vs 0.9, IQR 0.7-1.2 mcg/L) and EBA_{ex} (2.4, IQR 1.5-4.4 vs 1.1, IQR 0.9-2.1 mcg/L; all p <0.0001) were significantly higher in patients with HF compared to others. Among patients with HF, those in the highest EBA_{rest} tertile had lower LVEF, greater left atrial size, more marked ultrasonographic congestion, higher NT-proBNP levels, and lower peak oxygen consumption denoting impaired exercise capacity. At multivariate regression analysis, NT-proBNP (p=0.0004) and the slope of minute ventilation to carbon dioxide production (p=0.0013) predicted EBA_{rest} concentrations independent of LVEF and other clinical confounders (adjusted R^2 0.458). In a different linear regression model, EBA_{rest} predicted NT-proBNP levels independent of age, body mass index, LVEF and other renowned predictors (adjusted R^2 0.715).
Conclusions: In outpatients with HF, increasing EBA is associated with more severe cardiac dysfunction, volume overload, and reduced functional capacity, irrespective of LVEF. Larger studies are needed to investigate whether EBA at rest, or its increment during exercise, can improve the identification, risk stratification, and management of patients with HF.

Abstract n SO4_2 - Presenting author**: Emma Esposito**

Prognostic impact of multimorbidity and frailty on 90-day survival in older patients hospitalised for acute heart failure: a prospective study

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Aim: Acute heart failure (AHF) is a leading cause of hospitalisation in older adults, where frailty and multimorbidity (MM) are highly prevalent and adverse prognostic factors. Limited evidence exists on their combined impact on short-term outcomes. This study aims to investigate the combined effect of MM and frailty on 90-day survival after discharge in older adults hospitalised for AHF.
Methods: This prospective observational study (April 2022–November 2024) define MM as ≥3 chronic diseases. Frailty was identified using a Clinical Frailty Scale ≥ 6, reflecting the high prevalence of moderate to severe frailty in the sample and aligning with recent cardiology guidelines. Patients were categorized into four groups based on MM and frailty: Group 1 (non-MM, non-frail), Group 2 (MM, non-frail), Group 3 (non-MM, frail), and Group 4 (MM, frail). Survival analysis was conducted using Kaplan-Meier estimates and the log-rank test, with Cox proportional hazards models used to adjust for potential confounders.
Results: Among 399 patients (median age 87.4, 52% female), 90-day mortality rates differed significantly: 8.3% in Group 1, 15% in Group 2, 30% in Group 3, and 29% in Group 4 (p=0.0051). Multivariable analysis showed frailty, regardless of MM, was associated with a three-fold mortality risk compared to Group 1 (Group 3: adj. HR 3.34, 95% CI 1.18–9.45; Group 4: adj. HR 3.11, 95% CI 1.11–8.75). In contrast, the presence of MM without frailty (Group 2) was not significantly associated with an increased 90-day mortality risk (adj. HR 1.94, 95% CI 0.58–6.46, p=0.28).
Conclusions: Frailty emerged as a more significant determinant of 90-day survival than MM in older adults hospitalized for AHF. These findings underscore the importance of frailty assessment in this population, suggesting that it may play a pivotal role in refining prognostic evaluations and guiding personalized care strategies.

Abstract n SO4_3 - Presenting author**: Elisa Acitelli**

Gender-specific risk of recurrent macrovascular events in type 2 diabetes mellitus: Analysis of a large Italian cohort

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Aim: Type 2 diabetes mellitus (T2DM) significantly contributes to the global burden of cardiovascular disease (CVD). Gender-specific differences in the risk of recurrent CVD complications among T2DM patients remain unclear, necessitating further investigation. Using conventional data mining techniques and real-world data from electronic health records (EMRs), we modeled patterns of recurrent macrovascular events in individuals with T2DM, analyzing their relative frequency and sequence in women and men. Additionally, we explored whether potential gender differences in the relative impact of diabetes vary with age or other cardiovascular risk factors.
Methods: We analyzed data from 320,267 individuals with T2DM collected between 2005 and 2018 through the Italian Association of Medical Diabetologists (AMD) outpatient clinics network. Patients with at least 5 years of follow-up and documented macrovascular complications were included. Using sequential rule mining, we modeled patterns of recurrent CVD events (coronary heart disease [CHD], peripheral artery disease [PAD], and cerebrovascular events [CVE]) and assessed gender-specific risks. Incremental risks were quantified using the Lift ratio, and statistical significance was estimated with permutation testing (n=10,000).
Results: Men showed higher absolute rates of first macrovascular complications (CHD: 21.8% vs. 11.1%, PAD: 15.9% vs. 10.2%, CVE: 2.4% vs. 1.7%; p<0.001). However, women exhibited a 20% higher relative risk of recurrent CVD across most combinations of events. For CHD→PAD, CHD→CVE, and PAD→CHD sequences, women consistently had higher incremental risks, independent of age and traditional risk factors, including diabetes duration, BMI, glycemic control, LDL-C, and renal impairment. Despite worse profiles, women received similar glucose-lowering and cardiovascular treatments than men during follow-up.
Conclusions: This study highlights gender-specific disparities in recurrent CVD risks among T2DM patients, with women experiencing higher relative risks despite lower absolute event rates. These findings underscore the need for tailored prevention and management strategies to mitigate gender disparities in diabetes-related CVD outcomes.

Abstract n SO4_4 - Presenting author**: Giuseppe De Girolamo**

Body composition, insulin sensitivity, and gender differences in sarcopenic obesity

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Aim: Sarcopenic obesity (OS) is a multifactorial condition characterized by the coexistence of excess fat mass and reduced muscle mass, associated with adverse outcomes and increased mortality. Despite its clinical significance, the lack of universally accepted diagnostic criteria for OS hinders the development of consistent clinical studies. This study adopted the 2022 ESPEN/EASO guidelines and evaluated body composition and glucose metabolism in individuals with normal weight, obesity, and sarcopenic obesity.
Methods: The study was conducted at Washington University (St. Louis, MO) and involved a retrospective analysis of 117 participants (Age=47.4±13.7), divided into non-obese (Non-Ob, n=35), obese (Ob, n=66), and sarcopenic obese (OS, n=16) groups. Body composition was assessed using DXA and MRI, while insulin sensitivity was measured using the hyperinsulinemic-euglycemic clamp, the gold standard for assessing insulin sensitivity. This technique involves a constant infusion of insulin to suppress hepatic gluconeogenesis, combined with a variable glucose infusion to maintain euglycemia: the glucose infusion rate (GIR) provides a direct and precise measure of insulin sensitivity. Key parameters included appendicular lean mass/weight (ALM/W), intra-muscular fat infiltration (IMAT), hepatic fat content, GIR/Free Fat Mass (GIR/FFM).
Results: The prevalence of OS was 13.7%. GIR/FFM was lower in the OS group than in the Ob group (6.4 mg/kg FFM/min vs 7.8 mg/kg FFM/min), though the difference was not statistically significant. ALM/W was also positively associated with GIR/FFM ($p<0.01$) and negatively with IMAT ($p<0.0001$). Gender-specific differences were observed: females had significantly higher IMAT than males (OS: 10.1%±1.9 vs. 7.3%±0.9, $p<0.01$), while males exhibited greater hepatic fat infiltration (OS: 16.6%±10.7 vs. 10.0%±8.3), though not statistically significant.
Conclusions: ALM/W was positively associated with insulin sensitivity and negatively with muscle quality but did not clearly differentiate OS from obesity alone. The data also revealed distinct lipid accumulation patterns between sexes, hepatic in males and muscular in females, highlighting potential differences in treatment approaches. In conclusion, these results emphasized the need for universal diagnostic criteria to better distinguish these populations.

Abstract n SO4_5 - Presenting author**: Giorgia Laureti**

Determination of NT-proBNP levels to define heart overload/failure and the effect of tripleinhaled therapy in older patients with chronic obstructive pulmonary disease: a multicenter longitudinal study

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Aim: Our study aimed at evaluating the prevalence of HF risk using N-terminal pro-B-type natriuretic peptide (NT-proBNP) assay, as endorsed by the 2023 Clinical Consensus Statement of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), in older COPD patients eligible for SITT. Moreover, we explored the impact of SITT on NT-proBNP levels after a 3-month follow-up.
Materials and methods: An observational multicenter longitudinal study was conducted on 165 consecutive older COPD outpatients, eligible for SITT. Patients with an overt or known HF history were excluded. Patients were classified according to age-comorbidity-adjusted NT-proBNP cut-points. Plasma for NT-proBNP assay was collected before the SITT initiation and after 3 months (n=116 patients).
Results: Mean age was 80.7±9.7 years with female prevalence (52.1%). Hypertension was the most prevalent comorbidity (83.3%). Age-comorbidity-adjusted NT-proBNP levels indicative of "HF likely" and "HF very high risk" were found in 43.0% and 24.2% of patients, respectively. The presence of HF risk was associated with AECOPD in the previous 30 days, lower hemoglobin levels and higher number of anti-hypertensive drugs taken. After 3 months of SITT, NT-proBNP levels were significantly reduced [from 1088.5 (338.5-2876.5) pg/mL at baseline to 624.0 (220.0-1716.3) pg/mL at 3-month follow-up, $p<0.001$], with a greater decrease in younger patients (p for interaction between ΔLn(NT-proBNP) and age tertiles=0.020).
Conclusions: We found a remarkable prevalence of heart overload and failure according to NT-proBNP levels in the initial clinical workup of older outpatients with recent AECOPD. The early detection of "HF likely" and "HF very-high risk" appears to be crucial in the management and prognosis of COPD patients, leading to echocardiographic evaluation and referral to a specialist for appropriate HF phenotyping and treatments. Moreover, SITT may help reducing cardiac overload, as highlighted by the significant reduction of NT-proBNP levels, and might be directly involved in reducing CV mortality.

Abstract n SO4_6 - Presenting author**: Maria Serena Iuorio**

Phenoage and phenoageaccel do not outperform chronological age in predicting physical function decline and mortality in community-dwelling older adults

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Aim: Chronological age is a strong predictor of physical decline and mortality but fails to capture inter-individual variability in health and aging. Biological age metrics, such as PhenoAge and PhenoAgeAccel, integrate clinical biomarkers (e.g., inflammatory markers) to better reflect physiological aging[1,2]. While these measures may predict well inflammation-driven outcomes, their utility for broader functional outcomes in general older populations remains unclear. This study compares their predictive power for physical function decline and all-cause mortality to chronological age in community-dwelling older adults.
Methods: Data from the InCHIANTI study were analyzed[3]. Participants aged ≥ 65 years with complete biomarker data for PhenoAge calculation (creatinine, albumin, glucose, C-reactive protein, red cell distribution width, mean corpuscular volume, lymphocyte percentage, white blood cell count, and alkaline phosphatase) and baseline Short Physical Performance Battery (SPPB) assessments were included (N=979; median age 73 years; 56% women). PhenoAgeAccel was calculated as the difference berween PhenoAge and chronological age. Physical function was assessed using the Short Physical Performance Battery (SPPB)[4]. Linear mixed models and Cox regression assessed associations with longitudinal changes in a continuous rescaled score of SPPB (rSPPB) and 10-year all-cause mortality. Logistic regression examined, in a subset of participants with normal physical function at baseline (N=504) the associations of these metrics with the onset of compromised physical function, defined as a drop in SPPB score from normal (≥10) at baseline to impaired (<10) at 6-year follow-up.
Results: Chronological age showed the strongest association with rSPPB decline (-0.50 points/10 years, p<0.001) and all-cause mortality (HR 1.15, p<0.001). PhenoAge and PhenoAgeAccel were associated with physical function decline (-0.32 and -0.15 points/10 years, respectively; p<0.001) and mortality (HR 1.10 and 1.09, respectively; p<0.001) but did not outperform chronological age. For the onset of compromised physical performance, chronological age demonstrated the strongest association and the highest predictive accuracy (OR 1.17, AUC=0.71) compared to PhenoAge (OR 1.10, AUC=0.69) and PhenoAgeAccel (OR 1.05, AUC=0.55).
Conclusions: While significantly associated with physical function decline and mortality, PhenoAge and PhenoAgeAccel do not surpass chronological age as predictive tools for these outcomes in general older populations. These outcomes are likely influenced by a complex interplay of factors – including musculoskeletal, psychosocial, and environmental determinants – that extend beyond those captured by these measures biomarker panels. These findings highlight the need for more comprehensive biological aging metrics to improve risk stratification and intervention planning in geriatric populations.

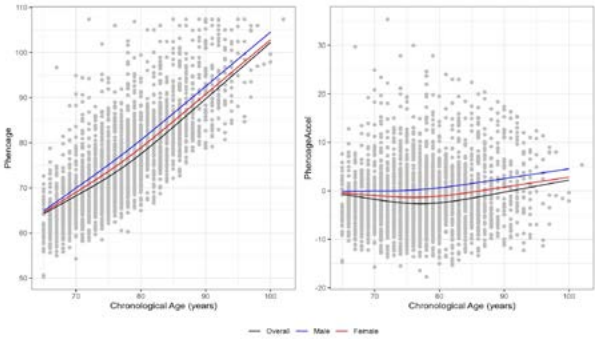

Figure. Relationship of Phenoage (left panel) and PhenoageAccel (right panel) with Chronological Age.

Abstract n SO4_7 - Presenting author**: Marialuisa Sveva Marozzi**

Women HEalth and PREgnancy complications (HER): a physician-based survey of the Young Investigator Group of the Italian Society of Hypertension (SIIA)

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Aim: Management of hypertensive disorders in pregnancy (HDP) remains challenging, with various healthcare providers involved and no uniform approach. This survey aim to investigate Italian physicians' foundational knowledge on HDP and examine their clinical practices.
Methods: We collected multi-regional data from Italian physicians through a survey consisting of 19 multiple-choice questions. Topics included patient access pathways for suspected HDP, choice of diagnostic assessments, first- and second-line therapies, follow-up modalities, and postpartum recommendations after blood pressure normalization. Statistical analyses, including chi-square tests and Cramér's V, were performed to evaluate correlations between demographic and professional factors and clinical practices.
Results: The survey was completed by 140 respondents, including 54 internists, 22 cardiologists and 31 gynecologists from 16 of 20 Italian regions. Among respondents, 73 were female, and 58% were under the age of 40. Only 16% of participants were aware of the actual risk of preeclampsia (PE) in women with chronic hypertension, and 50% recognized the long-term cardiovascular risks of HDP. Regional differences significantly influenced the number of pregnant patients managed annually ($p<0.001$, $V=0.332$). Awareness of specific long-term risks, such as heart failure and myocardial infarction, correlated with physician age ($V=0.3$). Specialization impacted knowledge of atrial fibrillation risk, use of diagnostic tools, and follow-up practices. Hypertension Centers were responsible for follow-up in 64% of cases, while the first antihypertensive prescription was issued by specialists in less than 10% of cases. The most common first-line agent was nifedipine, followed by alpha-methyldopa, with 72.6% of respondents selecting treatments based on maternal hemodynamic profiles.
Conclusions: This study highlighted significant gaps in awareness and variability in management practices for HDP among Italian physicians, influenced by age, specialization, and regional factors. Addressing these gaps can enhance patient outcomes and reduce the long-term cardiovascular burden associated with HDP.

Abstract n SO5_1 - Presenting author**: Alessandro Csermely**

Continuous glucose monitoring and assessment of long-term islet function in autologous islet transplantation after total pancreatectomy for pancreatic neoplasia: preliminary data from the Verona cohort

A. Csermely[1], G. Lionetto[2], M. Pilati[1], A. Turazzini[1], S.S. Sheiban[1], M. Colombini[1], F. Nocilla[1], M. Fontana[2], R. Melzi[3], R. Nano[3], A. Mantovani[1], R.C. Bonadonna[1,4], M. Trombetta[1], L. Piemonti[3,5], M. Tuveri[2,6], R. Salvia[2]

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Aim: Total pancreatectomy with autologous islet transplantation (TPAIT) has been proposed as an alternative to high-risk pancreatic anastomosis after pacreaticoduodenectomy for prevention of surgical complications, while maintaining low risks to develop brittle pancreatogenic diabetes. However, few studies have investigated the relationship between continuous glucose monitoring (CGM) profiles and TPAIT outcomes.
Methods: Between September 2023 and December 2024, 10 subjects with pancreatic neoplasia underwent TPAIT (males/females 5/5, age 60 [IQR 55-68] years, islet infusion 1912 [IQR 1724 – 3074] IEQ/kg) at the University Hospital of Verona. All of them underwent a glucometabolic monitoring program with visits at 1 (n=9), 3 (n=9), 6 (n=7) and 12 months (n=6) after TPAIT, including hematological exams and CGM-derived 3-month glucose profiles. Islet metabolic function at 12 months was assessed through the most recent modified Minnesota criteria, and optimal outcomes were compared to not-optimal ones.
Results: Six subjects reached 12 months of follow-up: according to Minnesota criteria, their islet function was classified as optimal (n=3), good (n=2) and failure (n=1). All subjects with not-optimal islet function developed diabetes. Patients with optimal versus not-optimal outcomes displayed lower coefficients of variation at 3, 6 and 12 months (17.7% vs 27.9%, 20.4% vs 30.3%, 24.6% vs 29.4% respectively, all $p<0.05$), higher time in range (TIR) and tight range (TITR) and lower glycemia risk index (GRI) at 3 and 12 months (TIR: 99% vs 86%, 96% vs 84% respectively; TITR: 95% vs 60%, 85% vs 56% respectively; GRI: 2.4 vs 15.2, 4.8 vs 15.2, respectively; all $p<0.05$), and lower time above range at 12 months (3 vs 15%, $p<0.05$).
Conclusions: According to our preliminary data, optimal islet function at 12 months after TPAIT was associated with lower glycemic variability and longer time spent in euglycemia, thereby suggesting that CGM metrics may be a good clinical indicator of long-term islet glucose competence.

Abstract n SO5_2 - Presenting author**: Federica Cappelli**

Perivascular adipose tissue dysfunction is driven by meta-inflammatory changes in a cardiometabolic model characterized by the coexistence of hypertension and obesity

F. Cappelli[1], S. Costantino[2], E. Duranti[1], S.A. Mohammed[2], E. Gorica[2], A. Mongelli[2], S. Masi[1], S. Taddei[1], F. Paneni[2], A. Mengozzi[1,2], A. Virdis[1]

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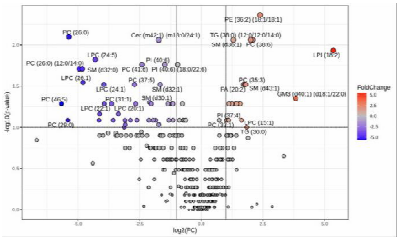
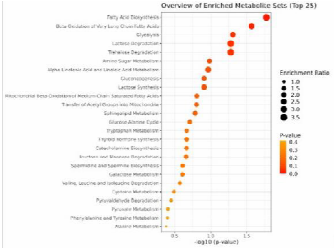
Aim: To investigate the role of perivascular adipose tissue (PVAT) in microvascular dysfunction linked to cardiometabolic disease by characterizing the PVAT phenotype and identifying mechanisms underlying its dysfunction.
Methods: Small vessels (100-300 μM), either in the presence or absence of PVAT, from healthy controls (n=13) and patients with hypertension and obesity were isolated and mounted for pressure myography. We adopted a mouse model characterized by exposure to high-fat diet and L-NAME supplementation. In vitro, we explored the cross-talk model between human PVAT-like adipocytes and human endothelial cells via direct (transwell) and indirect (conditioned media) co-culture. We investigated underpinning mechanisms via transcriptomic, metabolomic and lipidomic profiling and gain/loss-of-function assays.
Results: Ex vivo microvascular function is severely impaired in cardiometabolic patients ($p<0.0001$). ACh vasodilation and L-NAME vasoinhibition were reduced with a PVAT specific contribution of 14.31% ($p<0.001$) and 18.71% ($p<0.001$), respectively.
Transcriptomic, metabolomic and lipidomic analysis in diseased PVAT revealed an impaired TCA cycle with increased glycolysis and triglyceride storage. This was associated with an increased metabolic load and higher (2-to-5 fold, $p<0.01$) levels of inflammatory mediators (TNFa, IL1b, IL6) at the tissue level and in secretome. In vitro, overexpression of glycolytic genes in healthy adipocytes (gly-ACs) induces a pro-inflammatory phenotype. Human endothelial cells co-cultured directly and indirectly with pro-gly-ACs and PVAT- derived primary adipocytes from hypertensive and obese patients present similar molecular changes as well as a reduction in eNOS dimerization, a surrogate for endothelial dysfunction. Reduction of glycolytic enzyme activation by competitive pharmacological antagonism or gene silencing in PVAT- derived primary adipocytes from hypertensive and obese patients rescues the phenotype.
Conclusions: In the context of cardiometabolic disease, dysfunctional PVAT is characterized by stunned metabolic activity and increased inflammatory burden, disrupting endothelial cells' function. Targeting the metabolic shift in PVAT rescues the phenotype and prevents deleterious changes in the microvascular endothelium.





Abstract n SO5_3 - Presenting author**: Cassandra Morciano**

The significant reduction in epicardial adipose tissue thickness after dapagliflozin treatment is preserved, and even increased after 4 years: the DAPAHEART 4-year follow-up study

C. Morciano[1], S. Gugliandolo[1], G.P. Sorice[1,2], L. Leccisotti[3], U. Capece[1], L. Cappannoli[4], D. D'Amario[4,5], A. Guarneri[3], T. Mezza[1], G. Di Giuseppe[1], G. Ciccarelli[1], L. Soldovieri[1], M.a Brunetti[1], A. Avolio[1], A. Splendore[1], P. Iozzo[6], F. Crea[4], A. Giordano[3], A. Giaccari[1], F. Cinti[1]

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Introduction: Epicardial adipose tissue (EAT) is a key factor in coronary microvascular dysfunction in type 2 diabetes (T2D). We previously showed that 4-week treatment with sodium-glucose cotransporter 2 inhibitor (SGLT2i) dapagliflozin reduces EAT thickness by 19%, with 30% increase in coronary flow reserve (CFR), probably due to reduced EAT inflammation. We subsequently found that 30% increase in CRF was preserved over a 4-year treatment, but long- term effects on EAT remained unclear. We thus evaluated changes in EAT thickness after 4-yr dapagliflozin treatment in T2D patients with stable coronary artery disease (CAD).
Methods: Patients with T2D and stable CAD were enrolled in the DAPAHEART trial, a single-center, 4-week, randomized (1:1 dapagliflozin 10 mg/placebo), double-blind, controlled study. After 4 weeks, the placebo group also received dapagliflozin. All patients were followed-up over the 4-yr treatment. EAT thickness was measured via 13N-ammonia PET/CT at baseline and after 4 yrs. BMI was also monitored, and correlation with EAT thickness reduction analyzed.
Results: EAT thickness decreased significantly, (25.4%) in all patients over 4 yrs ($p = 0.03$). EAT reduction was statistically significant also in the placebo group ($p=0.04$), which started dapagliflozin after the 4-week trial. No significant correlation was found between BMI reduction and changes in EAT thickness ($R^2=0.0662$; $p=0.5038$).
Conclusions: EAT reduction after 4-week treatment with dapagliflozin is preserved and even increased after 4 yrs. The sustained improvement in CFR over 4 yrs may be attributed to reduced EAT thickness. Moreover, lack of correlation with BMI suggests a selective effect of dapagliflozin on EAT. These findings support the use of SGLT2i in mitigating CV risk in T2D.

Abstract n SO5_4 - Presenting author**: Carmen Tedesco**

The secretome of visceral adipose cells from obese subjects promotes epithelial-mesenchymal transition of human breast cancer cell line MCF7

C. Tedesco[1], G. Palma[1], C. Caccioppoli[1], R. D'oria[1], V.A. Genchi[1], I. Calderoni[1], A. Braun[2], A. Cignarelli[1], A. Natalicchio[1], L. Laviola[1], V. Zanghi Buffi[3], A. Pezzolla[1], F. Giorgino[1], S. Perrini[1,4]

Department of Precision and Regenerative Medicine and Ionian Area

Aim: The mechanisms linking obesity to heightened cancer risk and increased distal metastasis remain inadequately explored. This study investigates the potential harmful role of the secretome derived from abdominal visceral (AV) mature adipocytes (MA) of obese (Ob) subjects in promoting the epithelial-mesenchymal transition (EMT) in the non-advanced human breast cancer cell line MCF7.
Methods: AV mature adipocytes were isolated from 29 non-obese (n-Ob) and 30 obese (Ob) subjects. The secretome was collected after 96 hours of cell culture. MCF7 cells were exposed to the secretome from Ob and n-Ob subjects at different time points.
Results: The secretome of AV adipose cells from Ob subjects exhibited a distinct pattern of pro-inflammatory and anti-inflammatory cytokines. Levels of RANTES, MIP1B, and IFN-γ were significantly elevated in Ob compared to n-Ob subjects, with a direct correlation to BMI ($p<0.05$). Furthermore, pro-inflammatory cytokines RANTES and IFN-γ levels were significantly higher in both the secretome and serum of Ob subjects ($p<0.05$). Exposure of MCF7 cells to the secretome from Ob, but not from n-Ob subjects, resulted in increased phosphorylation of c-Jun and STAT3 ($p<0.05$), as well as impairment of actin filaments, evidenced by an increase in filopodia structures. The secretome from Ob subjects significantly upregulated protein expression of EMT markers such as Vimentin and COX2 ($p<0.05$), while reducing the epithelial marker E-Cadherin ($p<0.05$).
Conclusions: In human obesity, the secretome of AV mature adipocytes is enriched in pro-inflammatory cytokines that activate stress kinases, increase the expression of EMT markers, and induce cytoskeletal rearrangements, including the formation of filopodia structures. These changes are known to facilitate cell migration and tumor dissemination, highlighting a mechanistic link between obesity and cancer risk and progression.

Abstract n SO5_5 - Presenting author**: Pasquale Mone**

Effects of metformin treatment in patients with ischemia and no obstructive coronary artery

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Introduction: Ischemia with no obstructive coronary artery (INOCA) is an emerging determinant of adverse cardiovascular outcomes and re-hospitalizations. Vascular smooth muscle cells have been implied as fundamental actors in INOCA, although their actual contribution to the disease remains unclear.
Methods: We evaluated INOCA patients referred to the Casa di Cura "Montevergine", Mercogliano (Italy), from January 2016 to January 2021 for percutaneous coronary intervention. We examined patients at baseline and at 1-year follow-up for re-hospitalizations. We added an in vitro model assessing the effects of metformin on the mitochondrial generation of reactive oxygen species (ROS), by using MitoSOX-Red and MitoTracker-Green in human coronary artery smooth muscle cells (HCASMs).
Results: We observed 2874 patients (1918 normoglycemic and 956 hyperglycemic). We, then, propensity score-matched 220 hyperglycemic metformin-treated patients and 220 hyperglycemic untreated patients. We added 220 propensity score-matched normoglycemic patients. Metformin-treated patients exhibited a significantly lower re-hospitalization rate compared to untreated hyperglycemic patients and normoglycemic patients ($p<0.0001$). We then evidenced that metformin mitigated the increased oxidative stress induced by high-glucose in HCASMs, attenuating the augmented production of mitochondrial ROS evoked by high glucose concentration ($p<0.05$).
Conclusions: Metformin may reduce re-hospitalization risk and mitigate oxidative stress in INOCA patients with hyperglycemia.

Abstract n SO5_6 - Presenting author**: Parolini Anna**

The metabolic adaptations induced by short-term high fat diet feeding affect neutrophil metabolic reprogramming

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Aim: Neutrophils are short-living cells that play a role in the long-term metabolic effects of a High Fat Diet (HFD). Their egression from the bone marrow and movement are critically regulated by the CXCR4 receptor. We aimed to explore whether they promptly respond to metabolic adaptations induced by short term HFD feeding as a function of the CXCR4 signaling.
Methods: We studied the metabolic and the immunophenotypic profile of mice harboring a conditional deletion of CXCR4 (CXCR4fl/flMrp8Cre+) versus wild-type counterpart (CXCR4fl/flMrp8Cre-), when fed a HFD (60% Kcal from fat) for a short timeframe (seven days). The prandial profile of surrogate indicators of systemic metabolic adaptations to HFD feeding were measured, the expression of membrane immune markers was studied by flow-cytometry. To verify whether phenotypic changes on neutrophils indicate the movement towards peripheral sites, we initially explored the plasma quantity of proteins involved on neutrophils behavior by untargeted plasma proteomics.
Results: Short-term HFD feeding resulted into a dysmetabolic impact and together with increasing number of circulating neutrophils in CXCR4fl/flMrp8Cre-; By contrast, CXCR4fl/flMrp8Cre+ mice displayed persistent neutrophilia, which further increased, dependently on the metabolic adaptations, However, the reduced expression of CXCR4 and CD62L along with an increased expression of CD11b on the membrane that we observed in CXCR4fl/flMrp8Cre- neutrophils was also recapitulated in CXCR4fl/flMrp8Cre+ neutrophils. This suggests a phenotypic remodeling toward enhanced migratory and activated features, independent from the neutrophilia when the CXCR4 signaling is altered, but, rather, partially recapitulated by the quantity of proteins involved in cell structure, mobilization and chemotaxis. Metabolically, this derailment of neutrophil behavior impacted systemic metabolism, as CXCR4fl/flMrp8Cre+ displayed increased triglyceridemia upon HFD regimen.
Conclusions: Short-term HFD feeding alters the phenotype of peripheral neutrophils, in a CXCR4-dependent manner. Further evidence is needed to determine whether this phenomenon occurs independently from the canonical epigenetic reprogramming that happens in the bone marrow upon HFD feeding.

Abstract n SO5_7 - Presenting author**: Valeria Panella**

Hydroxytyrosol mitigates foam cell formation and endothelial inflammation via the PPARγ/LXRα/ABCA1 pathway: A promising strategy for managing hypercholesterolemia and obesity-related inflammation

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[2] Department of Innovative Technologies in Medicine & Dentistry, University "G. d'Annunzio" Chieti- Pescara, Chieti, Italy;
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Aim: Cholesterol buildup in macrophages generates foam cells, raising the risk of atherosclerosis. We studied whether hydroxytyrosol (HT), a phenolic compound with anti-inflammatory and antioxidant properties, can reduce this cholesterol accumulation in THP-1-derived foam cells and alleviate inflammation in obese patients.
Methods: The metabolic activity of THP-1 macrophage foam cells treated with varying concentrations of HT was assessed using the MTT assay, while the production of reactive oxygen species (ROS) was evaluated with an NBT assay. Oil Red O staining and high-performance liquid chromatography (HPLC) analyzed lipid accumulation and cholesterol content in these cells. The impact of HT on cholesterol metabolism-related molecules (SR-A1, CD36, LOX-1, ABCA1, ABCG1, PPARγ, and LXRα) was examined through RT-qPCR and Western blot analyses. Furthermore, hematoxylin-eosin staining, Western blot, and ELISA assays were conducted to assess HT's effect on THP-1 adhesion to HUVECs, focusing on PPARγ/LXRα signaling and inflammatory factors. In addition, in a clinical study with 50 obese patients divided into two groups, inflammation markers were measured over 30 days. One group received a placebo, while the other received 30 mg of HT extract daily. Measurements included oxidized low-density lipoprotein (ox-LDL), ICAM, IL-1β, TNF-α, and platelet factor 4.
Results: HT protects macrophages from oxidative damage caused by ox-LDL, inhibiting ROS production. Treatment with 50 μM HT downregulates CD36 expression without affecting LOX-1 and SRA-1 receptors. In foam cells, HT increases cholesterol efflux by upregulating LXRα and ABCA1 and enhances PPARγ expression, which is regulated through the PPARγ/LXRα signaling pathway. We also found that HT inhibits monocyte adhesion to inflamed HUVECs by decreasing adhesion molecules (ICAM-1 and VCAM-1) and inflammatory markers (IL-1β and TNF-α). In obese patients, HT extract decreased oxidative status by reducing oxLDL levels, and negatively affected inflammation by decreasing ICAM and TNF-α levels.
Conclusion: Our findings suggest that HT extract may effectively manage inflammation in obese patients by modulating inflammatory marker. However, additional studies are needed to evaluate the effect of HT on lipid profile using larger sample sizes or longer treatment durations.

Abstract n SP1_1 - Presenting author**: Elena Levati**

Impact of Lifestyle intervention on medications use in older adults: insights from The Sarcopenia and Physical fRailty iN older people (SPRINTT) and The Lifestyle Intervention and Independence for Elders (LIFE) Trials

E. Levati[1], M.B. Zazzara[1,2], A. Iurlaro[1], E. Marzetti[1,2], R. Calvani[2], F. Landi[1,2], R. Bernabei[1], A. Picca[1,2], G. Onder[1,2]

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Aim: Polypharmacy is a growing public health problem and implementing strategies to reduce its prevalence is considered a research and clinical priority. Healthy lifestyle impacts the onset and progression of chronic conditions. Yet, there is limited understanding of how this effect influences medication use. We aimed to assess the impact of lifestyle interventions on use of medications for chronic conditions.
Methods: Secondary analyses of two randomized clinical trials, LIFE and SPRINTT, were performed. LIFE study enrolled community-dwelling men and women aged 70 to 89 years had reduced physical function recruited in 8 centers in the United States. SPRINTT enrolled community-dwelling men and women aged 70 years or older with physical frailty and sarcopenia recruited in 16 clinical sites in Europe. Active intervention groups consisted of a physical activity program in LIFE and a multicomponent intervention based on physical activity and nutritional counselling/dietary intervention in SPRINTT. Change in cardiovascular, diabetes, mood and anxiety, and chronic pain medication use was measured by daily dose per day (DDD/day).
Results: A total of 1,519 LIFE participants (752 intervention vs 767 control group, mean age 78.9 y; 67.3% women) and 1,208 SPRINTT participants (602 intervention vs 606 control group, mean age 78.8 y; 72.8% women) were evaluated. For both studies, no significant difference was observed in the median number of DDDs at baseline and follow-up assessments for any of the medication classes considered. Longitudinal analysis performed using linear mixed models revealed no significant association between DDDs/day and lifestyle interventions, with the only exception of an increase in DDD/day of pain medications in the intervention group of SPRINTT (β=0.16; CI 0.06-0.26 at 6 months; β=0.12; CI 0.01-0.22 at 12 months; β=0.12; CI 0.01-0.22 at 18 months).
Conclusions: Lifestyle interventions did not significantly impact on burden of medications used to treat chronic conditions in frail older adults.

Abstract n SP1_2 - Presenting author**: Grazia Gabriella Bufano**

The influence of lifestyle on body composition alteration and masld progression: A multicentre cohort

R. Bianco[2], G. Di Gioia[2], M. Dallio[1], M. Sangineto[2], M. Romeo[1], M. Cipullo[1], A. Coppola[1], S. Mammone[1], M. Masarone[3], M. Persico[3], A. Federico[1], M. Ciarnelli[2], G. De Girolamo[2], G. Bufano[2], G. Savino[2], A.D. Romano[2], R. Villani[2], G. Serviddio[2]

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[2] University Center for Research and Treatment of Liver Diseases (C.U.R.E.), Liver Unit, University of Foggia, Italy;
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Aim: Lockdown restrictions during the COVID-19 pandemic led to acute lifestyle changes. This study investigates the effects of body composition modifications on Metabolic dysfunction-associated steatotic liver disease (MASLD) progression and hepatocellular carcinoma (HCC) occurence.
Methods: In this multicenter retrospective cohort study, 187 patients with MASLD were followed over four years, encompassing pre-pandemic, intermediate, and post-lockdown periods. Clinical, biochemical, and imaging assessments were performed to monitor patients. Body composition was evaluated using bioelectrical impedance analysis (BIA), while liver disease progression was assessed with non-invasive tools, including liver stiffness measurement (LSM) and controlled attenuation parameter (CAP). HCC occurrence was recorded via ultrasonography and staged according to the Milan criteria. Statistical analyses explored associations between body composition changes and MASLD progression or HCC development.
Results: Significant lifestyle changes during the follow-up period were observed, including increased dietary fat and carbohydrate intake, reduced physical activity, and corresponding rises in BMI and waist-hip ratio ($p<0.0001$ for all). Metabolic health markers, such as total cholesterol, LDL, HDL, triglycerides, glucose, insulin, HOMA-IR, and liver enzymes, significantly deteriorated (glucose: $p=0.0007$; $p<0.0001$ for the others). Liver fibrosis indices, liver stiffness, and CAP also worsened ($p<0.0001$ for all) during pandemic. BIA analysis revealed increased fat mass and reduced free fat mass and body cell mass ($p<0.0001$ for all). The incidence of HCC during the isolation period showed a marked increase, with hazard ratios (HR) for overall HCC and Milan-out HCC of: 2.398, 95%, confidence interval (CI): 1.16-5, $p=0.02$, and HR: 5.931, CI: 2-17.6, $p=0.008$ respectively. These outcomes were independently associated with body composition changes, irrespective of liver disease stage or comorbidities.
Conclusion: Acute lifestyle changes during the COVID-19 lockdown exacerbated MASLD progression by significantly altering body composition, thereby increasing the risk of HCC. These findings underscore the critical importance of maintaining healthy lifestyle habits in the management of MASLD and the prevention of its complications.

Abstract n SP1_3 - Presenting author**: Paola Bonicco**

Colonic polyphenol metabolites as promising tools to control inflammation and prevent cardiovascular disease

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Aim: Inflammation is a crucial biological process for the repair of injured tissues, but its persistence can lead to chronic conditions associated with numerous diseases, such as atherosclerosis. The development of anti-inflammatory agents, including those derived from natural resources, represents a strategic goal in pharmacological research aimed at creating functional products for use during the early stages of chronic inflammatory diseases. Based on these premises, this study focused on the *in vitro* analysis of the anti-inflammatory activity of γ-valerolactones, the colonic metabolites of flavan-3-ols, a widely consumed class of dietary flavonoids.
Methods: Human dermal fibroblasts were treated with 1µM of 10 compounds (corresponding to their plasmatic levels after ingestion and metabolism) for 48h, including 24h in the presence of LPS (1µg/ml) to induce an inflammatory response. The compounds belong to the hydroxyphenyl-γ-valerolactone family, in pure enantiomeric form, with some methylated, sulfated or hydroxylated variants. Evaluation of cytotoxicity was conducted by MTT assay. The anti-inflammatory effects were evaluated by measuring the secretion of IL-6 and IL-8 cytokines using ELISA. Data normalization was performed by relating the quantified levels of cytokines to the protein concentration in each well, determined using the BCA method.
Results: None of the compounds induced cytotoxic effects. R-C001 reduced IL-6 secretion by 76% (p=0.0001) and IL-8 secretion by 70% (p=0.0046). S-C001 inhibited IL-6 by 89% (p=0.0001) and IL-8 by 86% (p=0.0015). R-C002 showed an 83% reduction in both IL-6 (p=0.0001) and IL-8 (p=0.0019). S-C003 resulted in a 90% reduction in IL-6 (p=0.001) and 87% reduction in IL-8 (p=0.0014). R-C003 inhibited IL-6 by 78% (p=0.0001) and IL-8 by 71% (p=0.0032).
Conclusions: The mentioned compounds significantly reduced cytokine secretion, with inhibition rates ranging from 70% to 89%, comparable activity between enantiomers and independent of substituents. Future studies should investigate their pharmacokinetics and mechanisms of action in vivo to validate these findings and assess their potential preventive applications.

Abstract n SP1_4 - Presenting author**: Fabiola Castaldo**

HOMA-IR and TyG index differ for their relationship with dietary, anthropometric and cardiometabolic risk factors

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Insulin resistance is a pivotal discriminant of cardiometabolic health. The homeostasis model assessment for insulin resistance (HOMA-IR) and the triglyceride-glucose (TyG) index are widely used surrogate indexes of insulin resistance. However, it is unclear how they compare with regard to their relationship with dietary and cardiometabolic risk factors.
The aim of this study was to evaluate whether HOMA-IR and the TyG index differ for their relationship with dietary, anthropometric and cardiometabolic risk factors.
Four hundred and thirty-eight individuals, aged 66±5 years, were included in this study. Participants were characterized metabolically, with regard to their nutrient intake and cardiovascular risk. The relationship between HOMA-IR, TyG index, nutrient intake and cardiometabolic health parameters was assessed by Spearman correlation analysis. Stepwise multiple regression analysis was used to identify the predictors of HOMA-IR and TyG index.
Both surrogate indexes of insulin resistance, albeit to a different extent, positively correlated with anthropometric variables, circulating triglycerides, IL-18, hCRP and with the estimated 10-year risk of cardiovascular disease. While HOMA-IR correlated negatively with total cholesterol and did not correlate with LDL-cholesterol, the TyG index correlated positively with both total and LDL-cholesterol. HOMA-IR, but not the TyG index, correlated negatively with the intake of dietary fiber, the ratio between the intake of saturated and unsaturated fatty acids as well as the Mediterranean Diet adherence score. HOMA-IR was predicted by waist circumference, IL-18, fat mass and BMI. Instead, the only variables able to predict the TyG index were waist circumference and IL-18. Finally, only the TyG index was able to predict the estimated 10-year risk of cardiovascular disease.
HOMA-IR may be a better indicator to describe how anthropometric, inflammatory and nutritional variables modulate insulin sensitivity. On the contrary, the TyG index represents a better predictor of cardiovascular risk given its close relationship with the circulating lipid profile.

Abstract n SP1_5 - Presenting author**: Ioannis Lioudakis**

Cardiovascular risk factors and lifestyle habits in the general population: Results from a cardiovascular prevention day

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Aim: Health awareness is often limited, and many individuals fail to adopt preventive measures to reduce the risk of future cardiovascular diseases. During a day dedicated to cardiovascular prevention (August 29, 2024), an observational study was conducted on adult volunteers aged ≥18 years to assess the prevalence of key cardiometabolic risk factors and modifiable lifestyle habits in the general population.
Methods: Participants underwent standardized blood pressure measurements using automated devices and completed a questionnaire to collect demographic data, lifestyle information (diet, alcohol consumption, physical activity, smoking habits), and self-reported clinical data. The study aimed to determine the prevalence of high-risk conditions (hypertension, obesity, diabetes mellitus, hypercholesterolemia), identify health areas requiring preventive, diagnostic, therapeutic or care interventions, and examine temporal trends in risk factors and non-communicable diseases in representative population samples.
Results. A total of 106 subjects participated in the study (mean age 59.2±15.7 years; 54.7% women). The average blood pressure in this group was 126±18.8 / 79.2±10.3 mmHg. Among participants, 7.6% had type 2 diabetes mellitus, 31% reported arterial hypertension, with 88% receiving antihypertensive treatment. Additionally, 46.7% had hypercholesterolemia, with only 51% receiving treatment for this condition. Current or former smokers constituted 35.2% of the sample. Physical activity of at least 150 minutes per week was reported by 48.1% of participants.
A total of 89% of participants reported one or more risk factors, such as hypertension, diabetes, hypercholesterolemia, or a diet low in fruits and vegetables. Furthermore, 60.4% reported leading a sedentary/predominantly sedentary lifestyle, and approximately 4 out of 10 had measured their blood pressure at least once in the previous month.
Conclusions. In the relatively young sample of the general population examined, a high prevalence of cardiometabolic risk factors was observed. These findings highlight the need for targeted interventions aimed at improving lifestyle habits.

Abstract n SP1_6 - Presenting author**: Caterina Cangiano**

Role of multidisciplinary approach with nutritional counseling in MASLD patients on fibrosis and metabolic parameters

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Background and aims: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a
chronic liver condition affecting approximately 30% of the global population. The burden of MASLD is significantly impacted by the rising prevalence of obesity and type 2 diabetes (T2DM). There is no specific medical therapy approved and last guidelines (2024) primarily focus on lifestyle modifications and nutritional interventions. Aims of our study are to assess the effectiveness of a multidisciplinary hepatological and nutritional approach in adult patients with MASLD, focusing on changes in key anthropometric parameters such as weight, BMI, waist circumference and fibroscan value.
Patients and Methods: We enrolled 52 consecutive patients, affiliated to MASLD multidisciplinary Clinic, Liver Unit Verona. Patients were enrolled between January 2022 and September 2024. All patients underwent a hepatological and internistic visit followed by a nutritional evaluation at baseline. Patients were evaluated based on recent laboratory tests and an initial non-invasive assessment of liver fibrosis using TE with FibroScan (Echosens). The follow-up process included one or more reassessments, both hepatological and nutritional. In particular, the hepatological follow up consists in a 6-month follow up visit for a reassessment of blood tests and TE, the dietician follow-up usually consists on a 3-month evaluation in order to obtain a better compliance to the dietetic plan.
Results: All 52 patients, median age of 53 years (IQR 13.3), male 69%, underwent after hepatological visit to nutritional approach. At the baseline visit, pharmacological treatment for arterial hypertension was optimized in 26% of patients with hypertension. Lipid lowering therapy was introduced or optimized in 60% of dyslipidemic patients. Antidiabetic therapy was adjusted in 43% of patients with T2DM. TE showed a median liver stiffness of 6.10 KPa (IQR 2,75 KPa) and a median controlled attenuation parameter (CAP) value of 282 dB/m (IQR 71 dB/m).
After 6 months of follow up, we observed a median reduction of 2 Kg of body wight with a significant improvement ($p<0.05$) in the lipid profile with reduction in total cholesterol levels (median values: 194 to 172 mg/dL), in LDL levels (122 to 102 mg/dL), in triglyceride levels (143 to 120 mg/dL), and an increase in HDL levels (46 to 47 mg/dL at follow-up). We observed a slight decrease in HbA1c (41 to 40 mmol/mol at follow-up, $p=0.07$). No significant changes were found in the hepatic profile, TE at follow u 5.10 KPa (IQR 2,55 KPa) and CAP 280 dB/m (IQR 64 dB/m). Only in subgroup with higher TE value at baseline (upper third quartile) we observed a significant reduction ($p<0.05$)
Conclusion: The results of our study highlight that multidisciplinary approach with nutritional intervention, among patients with MASLD, reached a better biochemical profile and for those with a significant levels of liver stiffness at also an improvement in FibroScan value.

Abstract n SP1_7 - Presenting author**: Alessandra Corrado**

Blood glucose control and insulin requirement in the 48 hours following a prolonged aerobic exercise in people with Type 1 Diabetes on automatic insulin delivery systems

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Aim: Fear of exercise-related blood glucose disruption may limit physical activity in type 1 diabetes (T1D). Post-exercise hypoglycemia, due to increased insulin sensitivity, requires dose adjustments. This study compared hybrid closed-loop systems (HCLS) performance in managing glucose levels and insulin doses two days after prolonged aerobic exercise (After-EX) versus rest (After-REST) in individuals with type 1 diabetes.
Methods: Twenty-two moderately active individuals (34.9±20.6 Mets hour/week by IPAQ-SF) with T1D (17 men/5 women) on HCLS, aged 49.2±13.4 years, BMI 25.7±3.7 kg/m^2), underwent a 10 km, 4-hour hiking session, on several occasions one month apart, on Saturdays starting at 09:30 am. An authorized hiking guide and the multidisciplinary diabetes care team supervised the exercise sessions. CGM metrics and insulin doses automatically delivered by HCLS in the 48h following the exercise session (After-EX, n=129) were collected and compared to a similar time-frame period not preceded by exercise one week apart (After-REST, n=129) by paired t-test.
Results: No significant differences in blood glucose control evaluated by CGM metrics were detected between After-EX and After-REST. Over the 48h following exercise, total basal insulin was lower (60.4±23.3 vs. 64.9±26.2 IU/die, $p<0.001$), and insulin doses automatically delivered by HCLS was lower (17.3±12.3 vs. 19.3±14.7 IU/die, $p=0.035$) than After-REST. Total insulin boluses administered for meals did not differ (64.4±38.6 vs. 66.0±40.6 IU/die, $p=0.252$) between After-EX and After-REST.
Conclusions: In the 48 hours following a prolonged aerobic exercise, people with T1D on HCLS had comparable glycemic control with lower insulin doses compared to a similar period following rest, indicating good performance of the automatic systems in managing the improved insulin sensitivity after exercise. These findings highlight the potential of automated insulin delivery to enhance safety and support active lifestyles, paving the way for personalized, technology-driven diabetes care.

Abstract n SP1_8 - Presenting author**: Simona Persia**

Body Mass Index and QTc Interval: Electrocardiographic Insights into Obesity-Related Risks

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Aim: Obesity is associated with various cardiovascular alterations, including changes in electrocardiographic (ECG) parameters. This study aimed to evaluate the relationship between obesity levels and electrocardiographic QTc interval differences in a cohort of patients stratified by body mass index (BMI).
Methods: A total of 481 patients (264 males, mean age 63.2±10.94 years) were evaluated. All patients underwent physical examination, anthropometric measurements (weight, height, neck, and abdominal circumferences), blood pressure (BP) assessment, and heart rate monitoring. ECG, echocardiography, arterial tonometry, blood tests, and carotid Doppler ultrasound were performed. Patients were categorized into four groups based on BMI: normal weight, overweight, grade 1 obesity, and grade 2 obesity. Statistical analyses included descriptive statistics and ANOVA to compare parameters among the groups. Only significant differences were indicated in this abstract.
Results: A statistically significant difference in ECG was observed across the four BMI groups ($p<0.05$). In particular, higher BMI was associated with a prolonged QTc interval, reflecting a potential risk for arrhythmias, with no variations in heart rate, PR and QRS. In addition, significant differences were found in several cardiovascular and metabolic parameters across the groups as known in literature. Moreover, a significant correlation between QTc interval and diastolic dysfunction (E/e') was observed.
Conclusions: The study highlights a significant association between BMI and QTc interval prolongation, suggesting that increased adiposity may contribute to electrocardiographic changes indicative of cardiovascular risk. These findings emphasize the importance of early cardiovascular assessment in overweight and obese patients to mitigate arrhythmia risk.

Abstract n SP2_1 - Presenting author**: Michela Algeri**

Low density lipoprotein target achievement in very high and extreme cardiovascular risk patients during a cardiac rehabilitation program

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Background: Low Density Lipoprotein (LDL)-cholesterol is one of the most relevant CardioVascular (CV) risk factors. In fact, very low therapeutical targets have been set by guidelines in the secondary prevention setting in order to reduce the risk of ischemic events recurrence. However, many studies demonstrate that these targets are largely unreached in the real-life setting, particularly in the higher cardiovascular risk classes. Our aim was to evaluate LDL target achievement in very high and extreme CV risk patients during a cardiac rehabilitation program.
Methods: A total of 940 patients with recent acute coronary syndrome or a diagnosis of chronic coronary syndrome who participated in a Cardiac Rehabilitation (CR) program were enrolled between January 2012 and December 2023 at the Niguarda Hospital (Milan). For each patient, LDL and Lipid Lowering Therapies (LLT) were evaluated at the beginning and at the end of the CR program together with anthropometric, clinical, biochemical, and instrumental parameters. LDL targets were considered <70 mg/dL for patients before August 2019, <55 mg/dL after 2019 and <40 mg/dL for extreme CV risk subjects.
Results: Mean age was 66.9±0.6 years, 82.9% of the subjects were males and LDL cholesterol changes from 107.3±39.3 to 64.5±24.6 from the beginning to the end of CR. At CR discharge, 88% of the subjects were on high intensity statin (atorvastatin or rosuvastatin) therapies and 38.1% were on ezetimibe while only 4.6% of the subjects were treated with PCSK9-inhibitors and 0.9% with bempedoic acid. 53.1% of the patients reached the LDL therapeutic target with particularly positive peaks in 2018 (72.8%, the year before the release of the latest dyslipidaemia guidelines that reduced the target) and 2022 and 2023 (78.8% and 75.7% respectively). 29.8% of the patients had extreme CV risk, they achieved the target of LDL <40 mg/dL only in 16.4% with higher prevalence in the latest years (32% in 2022 and 22.7% in 2023).
Conclusions: Our results demonstrated higher achievement of LDL cholesterol target in secondary prevention program when compared to previous observational studies. The longer distance from guidelines publication together with the new pharmacological treatment could be the reason for these positive results. However, more attention should be paid to extreme CV risk both in terms of identification and treatment.

Abstract n SP2_2 - Presenting author**: Elena Olmastroni**

Lipid-lowering therapy initiation after an atherosclerotic cardiovascular event: a retrospective cohort study

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Aim: Guidelines on cardiovascular prevention recommend lipid-lowering therapies (LLT) after an atherosclerotic cardiovascular disease (ASCVD) event. This study investigated real-world LLT initiation rate and its effect on total mortality in the Lombardy region.
Methods: Individuals aged ≥40 with an ASCVD event between January and September 2022 were identified from administrative databases. Prevalence of patients prescribed with an LLT prescription within 3 months after the index event was estimated, and a multivariate logistic regression model was applied to assess the impact of covariates on the likelihood of initiating treatment (odds ratios [OR] and 95% confidence intervals [95%CI]). The mortality rate, occurring within one year of the first, was also examined.
Results: Among 16,025 patients with an ASCVD event, 41.14% did not receive a LLT. Treatment initiation was more likely in subjects hospitalized for a cardiovascular event (OR 2.22, 95%CI 2.07-2.38, vs cerebrovascular event), in patients aged 51-60 years (OR 1.30, 95%CI 1.16-1.46), and in patients previously treated with antidiabetic (OR 1.42, 95%CI 1.25-1.62), antihypertensive (OR 1.96, 95%CI 1.80-2.13), and thyroid hormone replacement medications (OR 1.34, 95%CI 1.10-1.63). Conversely, older age (71-80 years: OR 0.79, 95%CI 0.71-0.87; >80 years: OR 0.47, 95%CI 0.42-0.52), female sex (OR 0.73, 95%CI 0.68–0.79), previous exposure to antithrombotic medications (OR 0.65, 95%CI 0.59-0.72), and polypharmacy (OR 0.90, 95%CI 0.81-0.99 for 5-9 medications, OR 0.61, 95%CI 0.52-0.72 for ≥10 medications) reduced the likelihood of treatment. Within 1-year from the first ASCVD event, the mortality rate for those who had initiated treatment was 3.07%, compared to 11.66% in untreated subjects (p<0.001).
Conclusions: The study highlights suboptimal initiation of LLT in patients discharged after an ASCVD event. However, those who initiate therapy demonstrate a lower mortality rate within 1-year from the first event, emphasizing the importance of improving the management of patients in secondary prevention.

Abstract n SP2_3 - Presenting author**: Annalisa Giosuè**

Postprandial glucose dynamics reveal distinct subtypes of type 2 diabetes possibly pursuing personalized therapeutic strategies

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Aim: This study aims to evaluate the heterogeneity of the postprandial glucose response (PPGR) of individuals with type 2 diabetes (T2D) in relation to their clinical and metabolic features, in the perspective of a personalized therapeutic approach.
Methods: Continuous glucose monitoring was performed in 50 T2D patients. To characterize the PPGR to a standardized breakfast of each individual, 3 parameters of the 4-hr PPGR were estimated according to a previously developed mechanistic model: amplitude – the magnitude of the post-meal glucose levels; frequency – the velocity of the post-meal glucose response; damping – the rate of glucose decay after the meal. One-way ANOVA and post-hoc comparisons were performed to assess differences in clinical/metabolic parameters between individuals clustered according to PPGR patterns.
Results: Three patterns of PPGR were identified. Pattern 1 (n=18) was characterized by a high amplitude, pattern 2 (n=11) by a high frequency, and pattern 3 (n=21) by low damping and frequency. No differences emerged between the three groups for age, BMI, waist circumference, HbA1c and diabetes duration. However, pattern 2 – characterized by an earlier glucose peak – showed lower levels of C-peptide than pattern 3 (2.04±0.63 vs 2.61±0.82 ng/mL, $p<0.05$) suggesting a reduced insulin secretion. Individuals with pattern 3 (i.e., the most delayed and prolonged PPGR), instead, in comparison with the rest of the population, had higher levels of fasting insulin (16.67±9.23 µU/mL), HOMA-IR (2.07±0.65), GGT (37.95±28.45 U/L) and triglycerides (127.1±54.36 mg/dL) ($p<0.05$ for all comparisons), indicating an impaired insulin sensitivity.
Conclusions: Dynamic features of the glucose response to the same meal identified distinct clusters of PPGR in T2D patients. These patterns associated differently with metabolic features and markers of pathophysiological mechanisms of T2DM, despite similar anthropometric parameters and glucose control. If confirmed, these findings could allow personalized therapeutic strategies for PPGR optimization in T2D patients.

Abstract n SP2_4 - Presenting author**: Andrea Rossi**

Prioritizing medication review for older individuals: A real-world data study using administrative databases

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Aim: Optimizing drug treatments in older individuals is essential for improving health outcomes and reducing drug-related issues. However, targeting older adults for interventions is challenging and tools to identify and prioritize individuals with potentially inappropriate medications (PIMs) are lacking. This study aims to develop a prioritization algorithm for medication review, with a proof-of-concept established using Italian administrative data, and to assess the association between PIMs and all-cause hospitalization.
Methods: Eight indicators were selected:
1) medications that should be avoid in elderly,
2) drugs linked to fall risk or orthostatic hypotension,
3) drug-drug interactions,
4) Anticholinergic Cognitive Burden,
5) Sedative Load,
6) therapeutic duplicates,
7) polytherapy,
8) drugs with higher risk of adverse drug reactions.
This study focused on the first indicator. Administrative healthcare data from Local Health Units (LHUs) in Lombardy were used to identify over 65 individuals who redeemed a PIM between 2015 and 2018, with index date defined as the first PIM redemption. Risk-set matching was used to select controls, adjusted for high-dimensional propensity scores (HDPS) logistic regression models were used to assess the odds of all-cause hospitalization within 90 days.
Results: A total of 499,511 over 65 adults across the LHUs were evaluated. Between 27.4% and 37.7% individuals were exposed to at least one PIM with higher prevalence in adults aged 65-74 years and women. After matching, 128,063 pairs were analyzed. Hospitalization rates were higher among exposed individuals (8.3-10.2%) compared to controls (5.1-6.0%). Multivariate regression showed a 55% increased risk of hospitalization for those exposed to PIMs (OR 1.55, 95% CI 1.48-1.62).
Conclusions: This proof-of-concept study made it possible to develop an analytical model, which will be implemented for the other indicators. The strength of the association between each indicator and the risk of hospitalisation will be used as a weight in the construction of the prioritisation algorithm.

Abstract n SP2_5 - Presenting author**: Alessandro Croce**

Tailored interventions to improve adherence to antihypertensive treatment and reduce blood pressure: findings from a systematic review and meta-analysis

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Introduction: Adherence is defined by the World Health Organization (WHO) as "the extent to which an individual's behaviour – taking medication, following a diet, and/or making lifestyle changes - is consistent with agreed recommendations from a health care provider" Despite the availability of several effective blood pressure (BP) lowering drugs and behavioural recommendations the inadequate BP control due to non-adherence remains one of major causes of the increased risk of cardiovascular events worldwide. Among the possible solutions to non-adherence, tailored interventions (TIs) have been identified as the most appropriate. TIs to improve adherence are defined as personalized interventions designed to help individuals to follow prescriptions and/or take medications as prescribed, according to their specific clinical characteristics, personality factors, goals, needs, preferences, and circumstances.

Purpose: This study systematically reviews and analyzes the effectiveness of digital and non-digital TIs in improving adherence to lifestyle and medication and so in lowering BP hypertension.

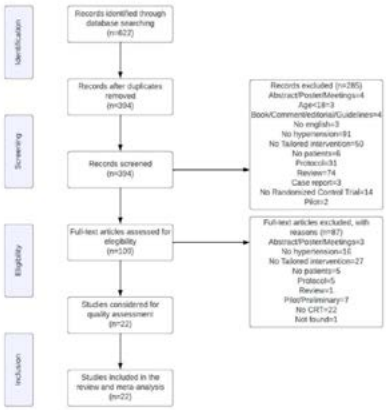
Method: A systematic search on PubMed, Medline, Scopus, EMBASE, Web of Science, and EBSCO included English RCTs on TIs for hypertension up to May 2024. Different combinations of keywords, including hypertension, tailored intervention, personalization, adherence and rehabilitation, were used in the search; after 2 reviewers independently screened the retrieved records and identified the eligible papers. The between-group mean difference at the end of follow-up was the measure of interest.

Results: Of the 622 papers identified in the databases, 228 duplicates were removed. After the title/abstract screening and reading the full text, 22 were considered for the quality assessment. Of these 6 were excluded because of missing data on BP or adherence. Of the remaining: 11 had BP as an outcome measure (Picture 1).

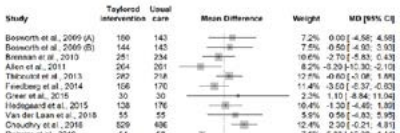
Forest plot for the Systolic blood pressure (SBP) shows a lower mean at follow-up of approximately 1.62 mmHg, in the TI group compared to control. Pooled estimates by follow-up duration were statistically different (p = 0.050), with the greatest reduction in studies with less than 6 months of follow-up (-3.37, 95% CI -5.18 to -1.56). (Picture 2)

Regarding sex: women showed a numerically greater BP effect than men, but the result is not statistically significant (p-value = 0.200). Investigating an ethnicity stratification, study with exclusive Afro-American population reported larger SBP differences but, again, the difference did not reach statistical significance (p=0.140). (Picture 3)

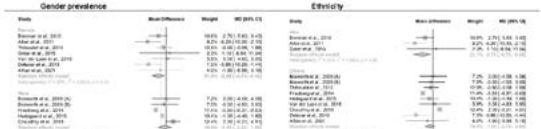
Conclusion: Our meta-analysis suggests that although TI may have a positive effect on short-term reductions in SBP and on self-reported adherence, the beneficial effect is modest and long-term sustainability of these effects is limited.



Picture 1. Flow diagram of the study selection, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.



Picture 2. Forest plot showing differences between the TI group and the control group for the SBP.



Picture 3. Forest plot showing differences between the TI group and the control stratifies for Gender and Ethnicity.

Abstract n SP2_6 - Presenting author**: Stefano Scotti**

Strategies for enhancing medication adherence in older adults with cardiovascular conditions: A systematic review

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Aim: Non-adherence to prescribed therapies is a significant public health issue, especially among older adults, where the presence of cardiovascular (CV) conditions requires the chronic use of multiple medications. Identifying effective strategies to improve medication adherence is crucial. As part of the Eldercare project, a systematic literature review was conducted to map strategies aimed at improving adherence in older adults (≥60 years) with CV conditions.
Methods: A systematic search of MEDLINE, Embase, and Web of Science was performed up until December 31, 2024. Any study reporting outcomes of interventions to improve medication adherence in this population was included.
Results: A total of 39 studies were included, of which 29 were randomized controlled trials and 10 were observational studies. Common conditions were hypertension or type 2 diabetes mellitus (n=30), hypercholesterolemia (n=6), heart failure (n=4), atrial fibrillation (n=3), and coronary heart disease (n=3). Interventions were delivered in primary care (n=10), hospital or specialized care settings (n=8), community services (n=8), or were integrated into healthcare systems (n=3). Fourteen studies employed multicomponent approaches, while 13 focused on health education, reminders, or cognitive-behavioral support. Eight studies utilized mHealth tools, including smartphone apps and electronic pill dispensers. Pharmacists led the interventions in 9 studies, multidisciplinary teams and researchers in 8 each, and nurses in 6. Thirteen studies monitored intervention outcomes for at least 12 months. Thirty-five studies demonstrated improved adherence post-intervention, with 4 reporting fewer CV-related hospitalizations.
Conclusions: Interventions to improve medication adherence in older adults with CV conditions show benefits, albeit often modest and short-term. Tailored approaches are most effective, with educational and behavioral strategies being optimal in simpler settings, and multicomponent interventions in more complex and advanced frameworks. The heterogeneity of strategies highlights the importance of stakeholder collaboration and policy changes. Standardized methodologies are essential for generating sustainable evidence to improve CV medication adherence.

Abstract n SP2_7 - Presenting author**: Artenca Shehu**

Constructive dialogue with the patient as a strategy to overcome statin intolerance

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Aim: Statin intolerance is a very big common problem in clinical practice for doctors that reduce the possibilities of the patients to reach LDL-C target. Even if now it is possible to use other drug strategies such as bempedoic acid and iPCSK9-is, statin still remains an important step of hypercholesterolemia treatment, in particular in high risk-patients. Our study has the aim to review the management of hypercholesterolemic patients with statin intolerance referring to our Clinic to investigate if specialistic counseling and therapeutic approach by expert lipidologists could have an impact on LDL-C target goal.
Methods: We retrospectively reviewed data from 1794 hypercholesterolemic patients referring to our Lipid Clinic. 1167 were treated with statins, 120 of them presented muscle-related symptoms (21 with clinically significant CPK elevation (i.e. >3 x UNL); 99 without CPK elevation).
Results: In the cohort of 120 patients with suspected statin-intolerance 48 patients were diagnosed of a rheumatic, neuromuscular or orthopedic disease; the remaining 72 patients underwent drug wash-out, therapeutic re-challenge and a specialistic counseling with an expert in Lipidology. Of these 72 patients, 51 became asymptomatic after re-challenge and only 21 patients continued to have muscle-related symptoms. They underwent a new re-challenge: 3/21 patients became asymptomatic.
Therefore only 18 (1% of all patients referring to our clinic in the analyzed study period) ultimately presented a significant increase in CPK and myalgia likely related to statin use; 2 out of 3 patients, after the re-challenge, no longer presented symptoms and the CPK values were reduced.
Conclusions: To date, although new and innovative drugs are available and help physicians to reach LDL-Cholesterol target, statins remain the core of therapy. This study highlights how the doctor's ability to patiently direct and follow the patient with suspected intolerance to statins, adopting not only the best therapeutic strategies in line with the current guidelines but also "*patient tailored*" communication strategies ("DOCebo" effect), in most cases help to resolve the suspected intolerance and make it possible to continue a therapeutic scheme comprehending statins.

Abstract n SP2_8 - Presenting author**: Jessica Goi**

Screening of primary aldosteronism and pheochromocytoma among patients with hypertension: an Italian nationwide survey

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Aim: A missed or delayed identification of secondary hypertension contributes to poor blood pressure control and an increase rate of cardiovascular events worldwide. The aim of the present study was to assess the diagnostic approach to primary aldosteronism (PA) and pheochromocytoma (PHEO) among Italian centers associated to European and Italian Societies of Hypertension.
Methods: A 10-items questionnaire was administered between July and December 2023 to experts from 82 centers of 14 Italian regions and to specialist in cardiology from the ARCA association (Associazioni Regionali Cardiologi Ambulatoriali). Data analysis was stratified according to geographical area, specialty, and center category (excellence vs. non-excellence centers).
Results: An average of 2 cases of PA and 0.2 cases of PHEO was diagnosed annually by single centers, with an higher rate in excellence centers. PA screening was performed mainly in patients with resistant hypertension (73.2%) or hypertension associated with spontaneous hypokalemia (84.1%), whereas only 17.1% and 35.4% of centers screened patients with grade 2-3 hypertension, respectively. Screening rate was lower for cardiologists compared to other specialists. Challenges in interpreting aldosterone-to-renin ratio under interfering medications and switching to non-interfering drugs were identified as main barriers to wider testing. Clinical scores to predict the likelihood of PA and the definition of Standard Operating Procedures were identified as potential tools to boost screening rates. Testing for PHEO was mostly conducted in patients with typical symptoms (75.6%) and/or hypertensive crisis (74.4%), while only 37.8% of centers screened all patients with an adrenal incidentaloma.
Conclusions: The present study highlights significant gaps in the screening and diagnosis of PA and PHEO across Italian centers and underscores the need for widespread and standardized diagnostic protocols.

Abstract n SP2_9 - Presenting author: **Simona Votta**

Screening of obstructive sleep apnea in patients with hypertension: results of an Italian survey

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Aim: Obstructive sleep apnea (OSA) is a common sleep disorder among patients with arterial hypertension, with a very high prevalence in resistant or refractory hypertension. In patients with hypertension, the presence of OSA is associated with a higher risk of cardiovascular events. At the same time, treatment of OSA with continuous positive airway pressure (CPAP) improves blood pressure control and reduces the cardiovascular risk.
The Survey aimed to evaluate the rate of OSA diagnosis in Italian hypertension centres, and the criteria adopted by the hypertension specialists for screening of OSA.
Methods: A questionnaire was administered to 82 medical specialists who work in Società Italiana dell'Ipertensione Arteriosa (SIIA) hypertension centres, including 25 excellence centres.
Results: The median rate of reported OSA diagnosis was 10 patients [5;20] for each centre, in the last 5 years, with similar figures in different medical specialities and geographical regions. The rate was higher in Excellence centres compared to other centres (20 [10; 45] versus 10 [3; 20] patients/5 years).
The presence of hypertension, snoring, and daytime somnolence was considered an indication for OSA screening for 90.2% of the specialists. The other main indications for OSA screening were the presence of hypertension and non-dipping profile during 24h ambulatory blood pressure monitoring (ABPM) (54.9%) and Epworth Sleepiness Scale (ESS) >10 (37.8%). A diagnosis of resistant hypertension was considered a criterion for OSA screening in only 23.2% of the centres.
Conclusions: In conclusion, clinical suspicion and screening for OSA in patients with hypertension are often overlooked by hypertension specialists. Implementing comprehensive management that integrates OSA identification and treatment is crucial for the optimization of hypertension control and cardiovascular risk reduction.

Abstract n SP3_1 - Presenting author**: Giuseppe Di Gioia**

The role of multiple chronic metabolic disorders on cognitive decline

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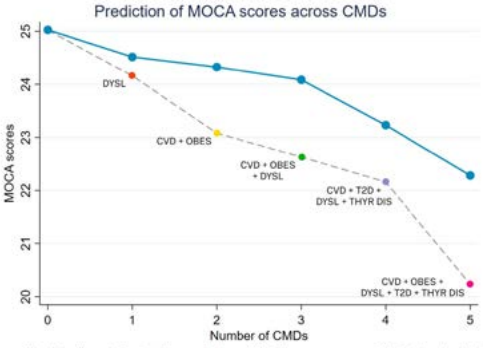
Aim: Chronic metabolic disorders (CMDs) are major contributors to cognitive decline, often sharing interconnected mechanisms and coexisting in older individuals. This study explores the cumulative impact of multiple CMDs on cognitive function.
Methods: A total of 202 outpatients aged≥60 years attending the Geriatric Clinic at the University of Foggia underwent cognitive assessment using the Montreal Cognitive Assessment (MOCA) test. Clinical and sociodemographic data were collected. The daily living abilities were evaluated using ADL and IADL assessments. Seven CMDs were examined: cardiovascular disease, type 2 diabetes, obesity, dyslipidaemia, kidney disease, liver steatosis, and thyroid disorders. Associations between CMDs, cumulative CMD burden, and cognitive outcomes including cognitive decline (MOCA<26) and moderate cognitive decline (MOCA<22) were evaluated through linear and logistic regression analyses, controlling for age, sex, education, physical activity, smoking, alcohol use, and depression. Additionally, the predictive capability of CMDs for moderate cognitive decline was compared with that of ADL-IADL.
Results: Participants had a mean age of 74.37±5.92 years (range 61–94). Most had two CMDs (n=68,33.66%), with CVD and dyslipidaemia as the most common combination (n=28,13.86%). A higher number of CMDs was linked to progressively poorer cognitive performance (β=-0.47,95%CI -0.78 to -0.16), with individuals having five CMDs showing the steepest decline (β=-2.72,95%CI -5.06 to -0.39). The odds of cognitive decline increased with the number of CMDs (OR=1.34,95%CI 1.04–1.72), with three or more CMDs associated with a markedly higher risk (OR=3.39,95%CI 1.03–11.37). Similarly, an increasing number of CMDs was associated with a moderate cognitive decline (OR=1.40,95%CI 1.04–1.88). CMDs demonstrated predictive ability for moderate cognitive decline comparable to ADL and IADL combined (AUROC 0.77, 95% CI 0.70–0.84 vs. 0.75, 95% CI 0.68–0.83).
Conclusions: This study highlights a cumulative detrimental effect of multiple CMDs on cognitive health. Older adults with multiple CMDs are at significantly increased risk for cognitive decline, underscoring the importance of comprehensive management of CMDs to preserve brain health.



The blue lines indicates the prediction of MOCA scores across CMDs. The dashed line indicates the combinations of CMDs associated with the most significant declines in MOCA scores.

Abstract n SP3_2 - Presenting author**: Chiara Ceolin**

The impact of atrial fibrillation on physical performance in older adults: a longitudinal study in relation to cognitive function

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Aim: Atrial fibrillation (AF), the most common arrhythmia in the older adults, is associated with an increased risk of dementia and a negative impact on quality of life. Given the links between cognitive decline and physical abilities, i.e. walking speed and muscle strength, it is hypothesized that AF may influence the deterioration of motor performance in patients with cognitive decline. This study aims to analyze the long-term impact of AF on physical abilities in the older adults, considering cognitive decline and how these effects evolve over time.
Methods: The Progetto Veneto Anziani (Pro.V.A.) is an observational cohort study involving individuals aged≥65. Data collected included sociodemographic and clinical history, functional autonomy, frailty status, and cognitive assessment. Patients were classified at baseline by cognitive function: preserved (MMSE ≥24) and impaired (MMSE <24). Physical performance (muscle strength, walking speed, sit-and-stand test), presence of AF, and AF onset during follow-up (FU) were assessed at enrollment and after 4 years. Regression analysis evaluated the relationship between physical performance and AF at baseline, stratified by cognitive function and sex. Changes in physical performance outcomes during FU were analyzed using mixed linear models.
Results: Among 2104 patients, 149 had AF at baseline. AF was not associated with significant changes in physical performance tests at baseline, regardless of cognitive status. However, over time, the interaction between AF and time was significantly associated with both grip strength and walking speed [-0.05 (-0.09; -0.003), p=0.03 and -0.14 (-0.23; -0.06), p=0.001], regardless of cognitive domain. In patients with MMSE ≥24, walking speed worsened over time in those with AF [-0.07 (-0.12; -0.01), p=0.02].
Conclusions: AF negatively affects the physical performance of old patients, particularly over time. Even in cognitively intact patients, AF compromises walking speed, highlighting the need for a functional-focused approach to clinical management to preserve autonomy and prevent disability.

Abstract n SP3_3 - Presenting author**: Silvia Santini**

Impact of cerebral hemodynamic impairment on cognitive performances in a cohort of patients with carotid occlusion

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Aims: This study aimed to investigate whether carotid artery occlusion (CO) may be associated with different cognitive performances in relation to the side of the occlusion and its hemodynamic consequences.
Methods: During 12 months, 61 asymptomatic patients, 32 with right and 29 with left CO, were enrolled. Each patient underwent an assessment of cerebrovascular reactivity (CVR) to hypercapnia with transcranial Doppler (TCD) ultrasonography using the breath-holding index (BHI). A complete neuropsychological assessment evaluating performances of the hemisphere ipsilateral to CO was administered at entry (T0) and then repeated after 2 years (T1).
Results: Scores obtained at Colored Progressive Matrices (CPM) and Rey Complex Figure Copy Test were significantly lower at T0 in patients with reduced BHI values ipsilateral to CO. Multivariate models showed that reduced BHI values were also associated to a significant decrease from T0 to T1 in scores obtained for CPM and Categorical Verbal Fluency tests, respectively, in patients with right ($P = 0.002$) or left CO ($P = 0.004$).
Conclusions: These findings suggest that hemodynamic alterations could be involved in reducing cognitive function regulated by the hemisphere ipsilateral to CO. The assessment of CVR with TCD ultrasonography may be a reliable approach for the individuation of asymptomatic patients with CO at increased risk of cognitive deterioration.

Abstract n SP3_4 - Presenting author**: Eleonora Cucini**

Short-term cognitive and functional decline in older patients undergoing elective cardiac surgery: preliminary results of a longitudinal study

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Aim: The implementation of new techniques has significantly reduced mortality and morbidity in older cardiovascular patients undergoing cardiac surgery. However, few studies have assessed post-surgery functional and cognitive outcomes in this demographic. This study aims to characterize baseline cognitive and functional status of patients undergoing elective cardiothoracic surgery (CS) and to evaluate their modifications over a 3-month follow-up.
Methods: Data were extracted from a prospective study starting May 2023. Patients aged 65+ undergoing elective CS received pre-operative geriatric assessments. Postoperative complications and delirium were monitored, with a 3-month follow-up assessing functional and cognitive status. Kruskal-Wallis and Fisher's tests analyzed clinical and demographic features, and linear regression examined the relationship between follow-up functional autonomy and preoperative cognitive status.
Results: Seventy-seven patients (median age: 72 [IQR, 68.00-75.25], 53% males) were included in the study, showing a median Instrumental Activities of Daily Living (IADL) of 8 [5.00-8.00]. The median pre-operative Montreal Cognitive Assessment (MoCA) was 22.88 [19.96-24.80]. 21.4% of patients with impaired cognitive performance at baseline experienced delirium, compared to 2.3% of those without impairment (p=0.052). At follow-up, 58 patients were re-assessed, showing a median IADL of 7.5 [5.00, 8.00] and an almost 64.3% prevalence of impaired cognitive performance on Telephone MoCA testing. At the linear regression analysis, pre-operative MoCA was correlated with three-month IADL decline [β = 0.144; 95% CI 0.044-0.243; p=0.005].
Conclusions: Routine cognitive assessments reveal significant cognitive deficits in older CS patients. Preliminary findings suggest a link between preoperative cognitive impairment and functional decline.

Abstract n SP3_5 - Presenting author**: Marcella Palumbo**

Cerebrospinal fluid and plasma HDL (dys)function in Multiple Sclerosis

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Aim: Multiple sclerosis (MS) is a multifactorial neurodegenerative disease in which cholesterol plays a key role. Neuronal cholesterol transport is essential to provide neurons with cholesterol, maintaining their physiological functions. It is mediated by lipoproteins similar to plasma HDL identified in human cerebrospinal fluid (CSF); the first step is the efflux of cholesterol from astrocytes, occurring through the major efflux transporters ABCA1 and ABCG1. Dysregulation of cholesterol homeostasis in the central nervous system has been associated with neurodegenerative disorders. However, the precise involvement of HDL-mediated cholesterol transport in the pathogenesis of MS is still not clear.
This study aimed to investigate the relationship between cholesterol metabolism and MS, focusing on cerebral HDL function to promote astrocyte cholesterol efflux. In parallel, circulating HDL cholesterol efflux-related function has also been evaluated.
Methods: We conducted an observational study including CSF and serum from MS patients (n=25) and age- and sex-matched controls (n=12). Cerebral and serum HDL cholesterol transport capacity was evaluated with a standardised radioisotopic technique using central and peripheral cell models.
Results: We observed that the CSF HDL-cholesterol efflux capacity (CEC) from astrocytes was significantly lower in MS subjects compared to controls (p=0.002631), and specifically CSF HDL-CEC ABCG1-mediated (p=0.02192). No significant differences were observed between the groups for serum HDL-CEC ABCA1- and ABCG1-mediated. The stratification of subjects by severity of pathology, based on the prognostic parameter Oligoclonal bands (OCB), CSF HDL-CEC from astrocytes (p=0.009179) and serum HDL-CEC ABCA1-mediated (p=0.02467) were significantly lower in subjects OCB+.
Conclusions: MS is associated with a defect in CSF HDL capacity to promote the first step of cerebral cholesterol transport, suggesting cerebral HDL as a potential pharmacological target. In addition, the observation that CSF and serum HDL-CEC are lower in MS subjects OCB+ suggests that HDL (dys)function may be correlated with the presence of OCB.

Abstract n SP3_6 - Presenting author**: Maria Cola**

Role of hyperhomocysteinemia in the exacerbation of ischemic brain injury through neurotransmitter mechanism: NMDA GluN2A

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Aim: To verify the possible contribution of homocysteine in exacerbating post-ictal ischemic brain damage through neurotransmitter mechanism (NMDA Glu N2A receptors). Plasma homocysteine is able to cross the blood-brain barrier and to determine synaptic dysgenesis through receptor mechanism by up-regulation of NMDA receptors and consequent accumulation of glutamate, responsible for cellular changes underlying phenomena such as learning, memory and attention. The increase in plasma amino acid levels hinders the methylation of neuronal cellular DNA through the increase of AdoHcy. DNA hypomethylation, activates the γ- and β-secretases of the amyloidogenic pathway, promoting the production and deposition of Aβ-amyloid and the formation of neurofibrillary tangles with increased risk of cerebral microinfarctions. Finally, homocysteine is able to activate metalloproteinases, causing a progressive worsening alteration of the permeability of the blood-brain barrier.
Methods: Given that it is necessary to have markers that indicate a dysfunction of NMDA receptors after the acute ischemic event, the study aims to evaluate biohumoral indices that make diagnoses of oxidative stress such as: uric acid, albumin, vit A, vit E, vit C, GSH, total cholesterol, LDL cholesterol, HDL cholesterol, 4HNE, 3NT, 8OHdG, Plasma homocysteine at T0 and after treatment. The extent of ischemic injury is assessed by MRI. Treatment involves vitamin support to reduce homocysteine levels and NMDA receptor antagonists such as memantine and amantadine.
Results: Patients undergoing vitamin replenishment and treatment with NMDA antagonists had a progressive decrease in homocysteine and oxidative stress markers and a progressive reduction in the infarcted area on MRI.
Conclusions: Reduction of homocysteine levels after the acute ischemic event is critical to halt the progression of damage.

Abstract n SP3_7 - Presenting author**: Gaetano Pacinella**

Single nucleotide polymorphisms (SNPs) in patients with acute ischemic stroke: A prospective study of the relationship between genetic, acute phase cytokine levels and stroke prognosis

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The genetic basis of complex diseases like ischemic stroke probably consists of several predisposing risk factors, such as genes involved in inflammation and thrombotic pathways. Some genetic polymorphisms have been associated with the risk of stroke.
Aim: On this basis the aim of this study was to evaluate:
- the frequency of some single nucleotide polymorphisms (SNPs) of genes of pro-inflammatory cytokines and coagulation factors in stroke patients;
- the relationship between each identified SNP and TOAST stroke subtype;
- the relationship between the serum levels of the cytokines analyzed and the diagnostic subtype of ischemic stroke;
- the relationship between the serum levels of the analyzed cytokines and stroke prognosis regarding event recurrence, AMI recurrence, and mortality.
Materials and methods: All patients aged > 18 years admitted for acute ischemic stroke in the period between 2011 and 2021 were prospectively enrolled. Each patient was subjected to genetic analysis to evaluate various genetic polymorphisms and to the analysis of the levels of cytokines circulating in the different collection times (T0, T1, and T2). Three different biallelic polymorphisms, of the IL-10 gene were identified.
Results: 624 subjects were enrolled, including 429 patients with ischemic stroke and 195 controls. Stroke subtype: 47% LAAS, 27% LAC, and 26% CEI. Regarding the immunoinflammatory variables, patients with CEI showed significantly higher levels of serum glucose and all the cytokines analyzed, compared to patients with both LAC and LAAS.
Logistic regression analysis revealed that elevated IL-10, TNF-alpha, IL-6, and IL-1beta values are predictive of LAAS and CEI subtypes, respectively. IL-10 levels were lower in patients who developed stroke during follow-up, whereas TNF-alpha, IL-1, and IL-6 levels were significantly higher in patients with recurrent stroke at follow-up, who developed a new vascular event or who experienced death during follow-up. From the analysis of the distribution of the genotypic frequencies of the polymorphisms analyzed, a statistically significant difference emerged between the cases and the controls for all the polymorphisms in the genes of pro-inflammatory cytokines, TPA and PAI-1.
These results demonstrated an association between some pro-inflammatory and prothrombotic polymorphisms and the risk of ischemic stroke.

Abstract n SP3_8 - Presenting author**: Emanuele Guerrieri**

Different clinical outcome of ischemic stroke related to onset-to-groin time: a real-life study

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Background and aims: International trial results suggest the efficacy of the enlargement of the therapeutic window for acute ischemic stroke (AIS). However, robust data regarding efficacy and safety are still lacking in real-life settings. This study aimed to compare patients submitted to mechanical thrombectomy (MT) with or without intravenous thrombolysis (IT) within 6 hours from symptoms' onset with patients treated at >6 and >12 hours.
Methods: All the AIS patients attending the Emergency Department of our hospital and submitted to MT were enrolled. Epidemiological, clinical, and radiological variables were collected. We adopted the National Insti-tutes of Health Stroke Scale (NIHSS) to evaluate our patients and calculated the delta(NIHSS) as the difference between NIHSS at admission and NIHSS at discharge.
Results: Delta(NIHSS) re-sulted statistically different between patients submitted to MT before or after 6 hours from the symptoms' onset, with a significant improvement in the first group. A significantly better delta(NIHSS) was obtained also for patients treated <12 hours, when compared to >12 hours. The overall prevalence of post-procedural intracranial bleeding was not significantly different both between patients with a time-to-groin ≤6 hours (32.3%) and >6 hours (38.2%; p=0.266) and between patients with a time-to-groin ≤12 hours (34.7%) and >12 hours (37.9%). In-hospital deaths significantly increased both for patients treated >6 hours and >12 hours.
Conclusions: Our results confirm favourable outcomes for AIS even when treated several hours after symptoms onset. However, better results were reached when IT and MT were performed early, confirming the "golden hour" concept.

Abstract n SP3_9 - Presenting author**: Giulia Savino**

Immunomodulatory properties of Krebs cycle intermediates in metabolic reprogramming of activated human microglia

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Aim: The pro-inflammatory activation of macrophages, including microglia, is linked to a metabolic shift from oxidative phosphorylation to glycolysis, with Krebs cycle (KC) intermediates serving as key signaling molecules. Microglia, as brain-resident immune cells, play a central role in the progression of neurodegenerative diseases, including Alzheimer's disease (AD) which is a compliance of metabolic syndrome. This study examines the bioenergetic profile of lipopolysaccharide (LPS)-activated human microglia cells (HMC3) and the impact of KC-derived compounds dimethyl fumarate (DMF) and itaconate (ITA) on this activation. Notably, DMF is an approved drug for treating psoriasis and multiple sclerosis.
Methods: HMC3 cells were stimulated with LPS (1 µg/mL) and treated with DMF (50 µM) or ITA (5 mM) for 24 hours. Cellular metabolic activity was analyzed via oxygen consumption rate (OCR) and proton efflux rate (PER) using the Seahorse XF HS Mini Analyzer (Agilent Technologies). Additionally, the expression of cytokines, using qPCR, ELISA, and mitochondrial function were assessed.
Results: LPS stimulation enhanced glycolytic and mitochondrial activities, indicating a hypermetabolic state in microglia. DMF and ITA treatments restored glycolysis and oxidative phosphorylation to baseline, but via distinct mechanisms. DMF normalized complex I activity, whereas ITA inhibited complexes I and II, offering stronger oxidative stress protection. Both compounds significantly counteracted LPS-induced oxidative stress, by reducing HNE- and MDA-protein adduct levels, with ITA being more protective. Additionally, both compounds lowered pro-inflammatory cytokines, including TNF-α and IL-1β, underscoring their anti-inflammatory properties.
Conclusion: DMF and ITA exhibit immunomodulatory effects through unique metabolic and mitochondrial reprogramming mechanisms. Their dual roles in modulating inflammation and metabolism underline their potential as therapeutic agents for conditions involving neuroinflammation and metabolic dysregulation.

Abstract n SP4_1 - Presenting author**: Adriano Massacesi**

Long-term follow-up of carotid atherosclerotic damage in non-diabetic patients with metabolic syndrome

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Aim: The study aims to evaluate atherosclerotic vascular damage in the carotid district by ultrasound in patients with a previous diagnosis of MetS that we recalled and re-evaluated after at least 15 years.
Methods: We performed a long-term follow-up study on 32 non-diabetic outpatients with a previous diagnosis of MetS and who received the indication to cardiovascular risk primary prevention treatments evaluated at the Clinical Medicine and Geriatrics Unit, IRCCS-INRCA Ancona, "Politecnica delle Marche" University. Participants were re-evaluated in a later outpatient visit after at least 15 years and underwent carotid bilateral ultrasonography. Based on the available demographic, anthropometric, metabolic, and therapeutic parameters, insulin resistance (IR) was calculated (triglyceride-glucose index or TyGi as a surrogate biomarker), and cardiovascular risk was assessed using the SCORE2-SCORE2OP score. A comparison within the study population was performed based on the presence of atherosclerotic plaque at the ultrasound assessment.
Results: The median follow-up was 18 years. 71% (n=23) of participants had carotid lesions compatible with atherosclerotic plaque. Patients with carotid plaque had a mean age of 72±8 years; 36% were male, with a mean body mass index (BMI) of 27±3 Kg/m², mean waist circumference of 101±12 cm, mean waist-to-height ratio of 0.60±0.06 cm, with a frequency of overweight and/or visceral obesity of 73%, mean systolic blood pressure (SBP) of 129±11 mmHg, mean diastolic blood pressure (DBP) of 81±7 mmHg, mean serum glucose of 103±14 mg/dL, mean total cholesterol (TC) of 163±23 mg/dL, mean HDL cholesterol (HDL-C) of 52±13 mg/dL, median triglycerides (TG) of 73 mg/dL (IQR 68-89), mean LDL cholesterol (LDL-C) of 90±17 mg/dL, and mean non-HDL cholesterol (non-HDL-C) of 113 ± 22 mg/dL. The median TyGi was 8.6 (IQR 8.2-8.7). Seventy per cent of patients were on anti-hypertensive therapy, and 70% were on lipid-lowering therapy. Seventy per cent had office BP controlled. Almost all participants had a high or very high cardiovascular risk (29% and 67%, respectively), according to SCORE2/SCORE2-OP. According to the individual cardiovascular risk, LDL-C and non-HDL-C therapeutic goals were achieved in 22% and 12%, respectively. There were no clinically significant differences between groups except for the prevalence of patients with LDL-C at a therapeutic goal based on cardiovascular risk, which was significantly lower in patients with carotid plaque than those without plaque (8% vs 22%, p=0.013).
Conclusions: In non-diabetic patients with MetS at high and very high cardiovascular risk, failing to achieve the LDL-C therapeutic goal is associated with the presence of carotid atherosclerotic plaque in long-term follow-up.

Abstract n SP4_2 - Presenting author**: Beatrice Invernici**

Association between carotid intima-media thickness and novel lipid parameters in hypertensive patients

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Aim: Carotid Intima-Media Thickness (IMT) is a marker of subclinical atherosclerosis and cardiovascular risk. Similarly, dyslipidemia is one of the main risk factors for atherosclerosis with novel lipid parameters recently emerging. The aim of our study was to assess the association between IMT and novel lipid parameters in hypertensive patients.
Methods: We analyzed the IMT of 821 hypertensive patients followed by the Hypertension Unit of our hospital. Classic (total, HDL, LDL and non-HDL cholesterol and triglycerides) and novel (non-HDL/HDL, LDL/HDL, total cholesterol/HDL, Log triglycerides/HDL and triglycerides-glucose index) lipid parameters were measured and calculated.
Results: Univariable analyses found a significant correlation between IMT and almost all lipid parameters. Linear multivariable analysis (IMT as the continuous dependent variable) showed a significant association with total cholesterol (β=0.104, p=0.001), LDL cholesterol (β=0.109, p=0.001), non-HDL cholesterol (β=0.121, p<0.001), non-HDL/HDL (β=0.128, p<0.001), LDL/HDL (β=0.127, p<0.001) and total cholesterol/HDL (β=0.128, p<0.001). Logistic multivariable analysis with IMT as the categorical (≥ or <0.9 mm) dependent variable demonstrated a significant association with total cholesterol (OR=1.110 per 10 mg/dL increase, p=0.002), LDL cholesterol (OR=1.130 per 10 mg/dL increase, p=0.001), non-HDL cholesterol (OR=1.120 per each unit increase, p=0.001), non-HDL/HDL (OR=1.411 per each unit increase, p=0.002), LDL/HDL (OR=1.623 per each unit increase, p=0.001) and total cholesterol/HDL (OR=1.411 per each unit increase, p=0.002).
Conclusions: Carotid IMT showed a significant association with several lipid parameters, most notably non-HDL/HDL, LDL/HDL and total cholesterol/HDL.

Abstract n SP4_3 - Presenting author**: Atea Shkodra**

Pulse wave velocity progression determinants: no significant association with novel lipid parameters

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Aims: Lipid profiles, both traditional and novel, have been associated with arterial stiffness (PWV) over time. This study examined the relationship between lipid parameters (e.g., non-HDL/HDL, LDL/HDL, total cholesterol/HDL, Log TG/HDL, and the triglyceride-glucose index [TyG]) and changes in PWV (ΔPWV) over 3.8 years in hypertensive patients.
Methods: We included 469 hypertensive outpatients (18-80 years) from our hospital's Hypertension Unit, recruited between September 2006 and October 2010. PWV was measured at baseline and after a mean follow-up of 3.8 years (I-III quartiles: 3.5-4.2 years). ΔPWV was calculated, and the population was stratified based on the best predictive values for CV outcomes (0.5 m/s).
Results: The cohort was 58.4% male, with a mean age of 53.6±12.9 years. Baseline fasting glucose, total cholesterol, HDL, LDL, and triglycerides were 89.1±21.4, 198.0±34.7, 53.0±13.5, 120.2±31.5, and 123.4±72.6 mg/dL. PWV increased significantly from baseline to follow-up (8.6±2.1 vs. 9.2±2.3 m/s; p=0.0001), with 51.6% showing ΔPWV≥0.5 m/s. These patients had lower baseline PWV (8.0±1.5 vs. 9.2±2.3 m/s) and HDL (51.5±13.5 vs. 54.7±13.3 mg/dL) but higher LDL/HDL (2.46±0.89 vs. 2.30±0.86), non-HDL/HDL (3.0±1.1 vs. 2.8±1.1), total cholesterol/HDL (4.0±1.1 vs. 3.8±1.1), and logTG/HDL (0.043±0.015 vs. 0.040±0.014, p<0.05 for all). No significant univariate link was found between lipid parameters and baseline PWV (continuous or PWV>10 m/s). Univariate analysis showed modest correlations between ΔPWV or ΔPWV≥0.5 and logTG/HDL (r=0.121, p=0.009; r=0.094, p=0.042), which did not persist in multivariate analysis adjusted for age, sex, ΔSBP, ACE inhibitors or ARBs, lipid-lowering therapy, diabetes, and GFR.
Conclusions: This study found no significant associations between emerging lipid parameters and PWV, assessed either as a continuous or dichotomous variable. Age and blood pressure values remain the main determinants of PWV and its changes over time.

Abstract n SP4_4 - Presenting author**: Maria Luisa Poli**

Unveiling the heart-liver connection: Global longitudinal strain as an early predictor of subclinical cardiac dysfunction

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Aim: Heart failure (HF) remains a significant health concern despite advances in the management of cardiovascular risk factors. Emerging evidence suggests an independent association between metabolic liver diseases and HF, underscoring the importance of identifying mechanisms linking the two conditions. Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD) is the most common liver disease associated with metabolic disorders, affecting approximately 25% of the global population. Left ventricular global longitudinal strain (LVGLS), assessed by 2D speckle-tracking echocardiography, serves as a sensitive marker of early myocardial dysfunction and a predictor of HF. This study aims to investigate the relationship between MASLD and subclinical cardiac dysfunction in patients with preserved ejection fraction (EF).
Methods: This observational study included 30 MASLD patients without overt cardiovascular disease. All patients underwent comprehensive 2D transthoracic echocardiography with speckle-tracking analysis to evaluate LVGLS and cardiac chamber deformation. Diastolic dysfunction is defined as mitral E/E' >9, and systolic dysfunction as LVGLS >-18%. Liver fibrosis is evaluated using standard indices and imaging techniques, while steatosis severity is assessed through specific imaging parameters. Exclusion criteria include significant valvular disease, reduced EF, prevalent liver diseases, atrial fibrillation, or substantial alcohol consumption.
Results: Preliminary echocardiographic analysis revealed that patients with significant liver fibrosis (SLF) had a significantly reduced LVGLS compared to those without SLF. Additionally, a potential negative correlation between the fatty liver index (FLI) and LVGLS is suggested, indicating that higher FLI scores may be linked to impaired LVGLS.
Conclusions: This study deepens the understanding of the interplay between MASLD and subclinical cardiac dysfunction. Liver disease severity seems to correlate with LVGLS abnormalities, independent of age, sex, and conventional cardiovascular risk factors. LVGLS emerges as a valuable marker for identifying HF risk, guiding preventive strategies, and improving care for MASLD patients.

Abstract n SP4_5 - Presenting author**: Francesco Corvasce**

Real world echocardiograpy evaluation in hypertensive according to international guidelines recommendation: preliminary results from a survey among heart specialists

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Aim: Hypertension induced heart changes evaluation is necessary to establish organ damage (OD). Both ESH and ESC international guidelines pointed out what is necessary to define OD. Moreover, international guidelines established all the needed measures. This survey aimed to evaluate if all these recommendations are fully evaluated by hypertension and heart specialists.
Methods: We provided an on-line survey to physicians signed to the Italian Society on Cardiovascular Imaging. Apart from a little information to establish sex, Italian region and hospital where the work is, and specialization, the survey focuses on the methods used to evaluate OD. These questions included the method to evaluate left ventricular hypertrophy, global longitudinal strain, ejection fraction, tissue doppler imaging, aorta, diastolic function, left atrium, and global imaging evaluation.
Results: 40 physicians (22 males, aged 47.43±13.09) participated in this survey. Most (70%) were cardiologists, 20% internists or emergency physicians, and they were most (65%) hospital physicians. About 10% did the echocardiography to hypertensives according to ECG abnormalities. The main part evaluates septa diameter (82.5%) and the majority the left ventricle mass (LVM) indexed for BSA (52.5%), while quite a fifth evaluate LVM indexed on height. Moreover, not all participants (60%) evaluate also the relative wall thickness and still a 12,5% evaluate only the interventricular septum diameter to evaluate the heart hypertrophy. Quite half evaluate GLS if a wall kinesis change was observed, while 17.5% do it to evaluate OD. Despite the large part of them measuring ejection fraction, a quarter do it based on self-experience estimation. Diastolic dysfunction was estimated combining data from E/A and E/e' ratio. However, tissue doppler was performed in all patients by 62,5% of participants. Less than half (47,5%) evaluate the left atrial volume indexed for BSA. Sovra-aortic ultrasound is performed by 60% according to the risk of atherosclerosis.
Conclusion: The main part of the heart specialist evaluates correctly the parameters to establish the hypertension mediated OD. However, a significant percentage of physicians did not follow the recommendation in guidelines. Therefore, scientific societies on the field must increase the efforts to have the best definition in OD for a better treatment.

Abstract n SP4_6 - Presenting author**: Sara d'Alesio**

Cardiovascular structural and functional parameters in idiopathic pulmonary fibrosis at disease diagnosis

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Aim: The prevalence of cardiac and vascular fibrosis in patients with Idiopathic Pulmonary Fibrosis (IPF) has not been extensively evaluated. In this study, we aimed to evaluate the heart and vessels functional and structural properties in patients with IPF compared to healthy controls. An exploratory analysis regarding disease severity in IPF patients has been done.
Methods: We enrolled 50 patients with IPF (at disease diagnosis before antifibrotic therapy initiation) and 50 controls matched for age and gender. Heart was evaluated through echocardiography and plasmatic NT-pro-brain natriuretic peptide that, together with patients' symptoms, allow to define the presence of Heart Failure (HF) and diastolic dysfunction. Vessels were evaluated through Flow Mediated Dilation (FMD – endothelial function) and Pulse Wave Velocity (PWV – arterial stiffness).
Results: Patients with IPF had a prevalence of diastolic dysfunction of 83.8%, HF of 37.8% and vascular fibrosis of 76.6%. No statistically significant difference was observed in comparison to the control group who showed prevalence of diastolic dysfunction, HF and vascular fibrosis of 67.3%, 24.5% and 84.8%, respectively. Disease severity seems not to affect PWV, FMD, diastolic dysfunction and HF.
Conclusions: Patients with IPF early in the disease course do not present a significant CV fibrotic involvement when compared with age- and sex-matched controls. Bigger and adequately powered studies are needed to confirm our preliminary data and longitudinal studies are required in order to understand the time of appearance and progression rate of heart and vascular involvement in IPF subjects.

Abstract n SP4_7 - Presenting author**: Spaggiari Riccardo**

The added value of combined clinical and instrumental assessments in identifying medical inpatients at risk for sarcopenia and worse health outcomes

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Aim: Reduced skeletal muscle mass (SM) in hospitalized patients is associated with worse clinical outcomes. Although SM loss is included among the phenotypic GLIM criteria for defining malnutrition, various clinical and instrumental methods are available to estimate SM, with no clear superiority among them. This study aimed to compare the different methods for identifying sarcopenia in hospitalized patients and to explore their association with mortality.
Methods: An observational study was conducted among medical inpatients admitted at the University Hospital in Ferrara. SM was assessed using calf circumference (CALF), bioimpedance analysis (BIA) to assess fat-free mass (FFM) and CT scan. Patients were classified according to CALF (0-25° percentile) or using the FFM index (FFMi, i.e. FFM standardized by height). For a subgroup of patients (n=37), SM area (SMA) and index (SMI) were obtained from CT scan. In-hospital mortalities were collected and nutritional status was defined according to GLIM criteria.
Results: A total of 142 patients were included (age 75.9±11.4 years, males 50.7%, BMI 25.4±5.7 kg/m^2). Patients with reduced CALF and FFMi demonstrated lower SMA (97.9±22.7 vs 120.4±33.9 cm^2, p=0.039; 95.7±24.6 vs 116.3±34.3 cm^2, p=0.150) and SMI (35.7±6.7 vs 41.9±8.7 cm^2/m^2, p=0.032; 33.8±7.4 vs 41.2±8.5 cm^2/m^2, p=0.046). Despite not reaching statistical significance, SMA and SMI were even lower when both methods, CALF and FFMi, agreed in classifying the patient as at risk for sarcopenia (93.4±25.9 cm^2; p=0,077; 33.3±7.4 cm^2/m^2, p=0.057). When both CALF and FFMi were reduced, compared to a single altered parameter or none, patients were more malnourished (87.0% vs 41.2% vs 34.1%, p<0.001) and showed a trend towards higher in-hospital mortality (21.7% vs 8.8% vs 7.1%, p=0.108).
Conclusions: Our findings suggest that combining instrumental and clinical methods for evaluating SM in medical inpatients may better identify sarcopenic/malnourished patients, leading to the development of early interventions to improve clinical outcomes.

Abstract n SP4_8 - Presenting author**: Arianna Toscano**

Cardiovascular risk stratification in patients with inflammatory bowel disease: The role of non-invasive imaging techniques and traditional risk scores

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Background: Patients with chronic inflammatory diseases, including inflammatory bowel diseases (IBD), have a 20% increased risk for atherosclerotic cardiovascular disease (ASCVD) and death as compared to non-inflamed subjects. A more in-depth screening of patients has become important with the EMA warning for JAK-inhibitors. The current validated cardiovascular risk (CVR) stratification algorithms are based on traditional risk factors, not taking into account the contribution of chronic inflammation.
Aim of the study: Our study aimed to stratify the CV risk of IBD patients using validated scores (SCORE2/SCORE2-OP/SCORE- 2Diabetes) and performing carotid ultrasonography to identify subclinical atherosclerosis.
Materials and methods: Data from 120 consecutive IBD patients [Ulcerative Colitis(UC): 67; Crohn's disease(CD):53] aged ≥40 years under care in the IBD Unit of the University Hospital of Messina (April-to-July 2024) were collected. We recorded data on age, gender, region of origin, body mass index, smoking history, family, personal and pharmacological history, blood pressure values, biochemistry (creatinine, fasting glucose, glycated hemoglobin, total cholesterol, HDL-cholesterol, triglycerides). LDL-C/non-HDL-C were thus calculated. Additional IBD-related parameters potentially associated with an increased CVR were investigated (i.e., disease activity, current therapies, duration of disease, and extraintestinal manifestations).
Results: Based on their medical history, 48% of patients were classified as at intermediate CVR, 34% as high CVR, and 18% as very high CVR. Carotid ultrasound detected subclinical atherosclerosis in 48.3% of patients. CV risk reclassification occurred in 21%, increasing the proportion of patients with high/very-high risk from 50% to 71%. Active disease (p=0.047) and concomitant spondyloarthropathies (p=0.03) were identified as additional risk factors.
Conclusions: Our findings demonstrate that carotid ultrasonography significantly reclassifies CV risk, revealing that traditional risk scores underestimate CV risk in IBD patients. Tailored CV risk stratification, incorporating chronic inflammation, is crucial before initiating therapies like JAK-inhibitors to minimize side effects, including CV complications. Active intestinal disease and spondyloarthritis further exacerbate CV risk, underscoring the need for integrated screening and management strategies in this population.

Abstract n SP4_9 - Presenting author**: Hermann Dalpiaz**

The association between intraventricular haemodynamic forces, traditional echocardiographic parameters and ventricular-arterial coupling in patients at high risk for heart failure

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Aim: Softwares that enable assessment of hemodynamic forces (HDF) of the left ventricle on pre-acquired echocardiographic images offer a new opportunity for advanced cardiac imaging, identifying early markers associated with the progression of cardiac damage toward heart failure (HF) in patients at high risk for the disease. HDF analysis can quantify intraventricular pressure gradients, recovering information on early wall dyssynchrony and left ventricular energetic expenditure. Our objective was to assess the relationship between the apex-to-base intraventricular forces (ABF, a measure of left ventricular contractile efficiency obtained from HDF analysis) and other measures of left ventricular systolic function and ventricular-arterial coupling in patients at high risk of developing HF.
Methods: A cohort of 57 patients at high risk for HF (stages A and B according to the AHA/ACC HF classification) underwent standard trans-thoracic echocardiography at rest. The ABF was recovered from the intraventricular haemodynamic forces analysis performed using the QStrain Echo v.4.4.30 (Medis Medical Imaging, Leiden, NL) software. The left ventricular wasted pressure effort ratio (LV-WPE), a measure of ventricular-arterial uncoupling previously validated was estimated from central blood pressure values obtained with applanation tonometry, central pressure wave decomposition and doppler flow sampled at the left ventricular outflow tract level.
Results: The patient's average age was 67.3±1.9 years, 63% males, while the BMI was 27.13±0.52, and the systolic and diastolic blood pressure values were 146±21/86±11 mmHg. The LV-WPE was 0.78±0.49, the ABF 9.5±0.65%, the left ventricular ejection fraction (LVEF) 58.6±1.7%, the global longitudinal strain (GLS) 14.3±4.4%. ABF was associated with both LVEF ($R=0.67$, $p<0.001$) and GLS ($R=0.58$, $p=0.003$). Furthermore, a higher ABF was correlated with a lower LV-WPE ($R=-0.28$, $p=0.04$) and age ($R=-0.43$, $p<0.001$).
Conclusions: Results suggest that the analysis of intraventricular forces, mainly the ABF, might provide important information on the left ventricular systolic function and inform the left ventricular-arterial coupling. While requiring further validation, the current data support using advanced echocardiographic analyses for the early identification of patients at higher risk of HF.

Abstract n SP4_10 - Presenting author**: Antonio Cutruzzolà**

The diastolic stress test in type 2 diabetes

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Aim: Subjects with type 2 diabetes (T2D) develop a typical form of cardiomyopathy (DCM) characterized by diastolic dysfunction (DD), left ventricular hypertrophy, and, finally, systolic dysfunction. As compared with overt forms, latent forms of DCM are more challenging and often misdiagnosed. To detect them, it was proposed the use of a diastolic stress test (DST).
Our aim was to characterize the structure and function of the heart of T2D, focusing on diastolic function at rest and during exercise.
Methods: We enrolled T2D, dividing them in two groups (*T2D<65y* vs.*T2D≥65y*) and healthy controls (*C*) age-matched with the T2D<65group. Exclusion criteria were ischemic cardiomyopathy, HF, significant valvular diseases, cardiomyopathies, and chronic severe illnessess. All participants underwent complete echocardiography at rest and DST, performed by supine bicycle exercise (start at 25 W, with 25W increment every 3 min to maximum effort).
Results: 54 subjects with *T2D<65* (81% M, age 56±6y, disease duration 11±7y, HbA1c 7.7±1.3%), 32 with *T2D≥65y* (81% M, age 68±4y, disease duration 18±9y, HbA1c 7.7±1.3%), and 20 *C* (85% M, age 53±5y) were enrolled.
T2D had higher BMI, SBP, DBP, HR and waist circumference than controls. Both *T2D<65*and *T2D≥65y* had higher left ventricular mass, relative wall thickness, left atrium volume than controls (p<0.01). Diastolic function parameters were also significantly different in both T2D groups vs. controls at rest (lower septal and lateral e', higher E/e').
Under exercise stress, we observed a reduced the diastolic reserve in T2D (*T2D<65* 48±229% vs. *T2D≥65* 41±27% vs. *C* 66±44%, p<0.02) and higher filling pressures (E/e': *T2D<65* 9.5±2.0 vs. *T2D≥65* 11.1±2.5 vs. *C* 7.1±1.1, p<0.001) with DST.
Conclusions: Subjects with T2D have significant cardiac abnormalities compared to healthy controls. The DST can identify form of latent DCM that could move towards heart failure, if not timely recognized.

Abstract n SP5_1 - Presenting author**: Tessa Mazzarone**

Clinical outcomes of early post-discharge cardio-geriatric ambulatory care in frail patients after acute heart failure. A controlled before-and-after study

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Aim: To assess whether an early post-discharge Cardio-Geriatric (CG) outpatient service reduces 1-year mortality compared to usual care (UC), and to evaluate 1-year rehospitalization rates and days alive and out of hospital (DAOH).
Methods: In this single-center, controlled before-and-after study, patients aged ≥75 years hospitalized for acute HF were included. In the UC group, patients discharged between January 2018 and December 2019 received standard follow-up with referrals to a cardiologist and general practitioner. In the CG group, patients discharged between January 2020 and December 2022 attended a Cardio-Geriatric ambulatory care within three weeks of discharge. Primary outcomes were one-year all-cause mortality, heart failure readmissions, and days out of hospital (DOAH). The effectiveness of CG follow-up was assessed using a 1:1 propensity score matched (PSM) analysis.
Results: A total of 652 patients (mean age 86 years, 56% female) were included in the study, with 477 receiving UC and 175 referred to CG follow-up. After propensity score matching of 350 patients (50% CG), we observed a significant reduction in 1-year rehospitalizations (36.5% vs. 50.8%, $p<0.001$) and mortality (20.0% vs. 40.0%, $p<0.001$) in the CG group. CG patients also had nearly double the days alive and out of hospital (DAOH) compared to UC patients (300±100 vs. 162±145 days, $p<0.001$). Cox regression analysis confirmed that the CG integrated approach was a protective factor for mortality [HR 0.34, 95% CI: 0.24-0.47]. Respiratory diseases, neurological conditions, and infections were common causes of readmission.
Conclusion: Early referral to a CG outpatients service post-discharge for acute HF significantly improves outcomes, highlighting the value of integrated care for older adults with complex needs.

Abstract n SP5_2 - Presenting author**: Musmeci Marco**

Sleep quality in elderly patients with type 2 diabetes: from glycemic control to anxiety depressive disorders

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Aim: Type 2 Diabetes Mellitus (T2DM) is a complex condition associated with numerous comorbidities. Recently, factors previously ignored, such as sleep disturbances, have been shown to play a much more significant role. Indeed, growing evidence has demonstrated that both qualitative and quantitative sleep alterations are associated with an increased risk of cardiovascular events, obesity, anxiety-depressive disorders, and poorer glycemic control in diabetic patients. The aim of our study was to evaluate the relationship between sleep disturbances, anxiety-depressive disorders, and quality of life in elderly patients with T2DM.
Methods: Elderly patients with T2DM aged over 65 years attending the Internal Medicine division of ARNAS Garibaldi-Nesima Hospital in Catania were recruited. Patients with obstructive sleep apnea syndrome, those receiving treatment for anxiety-depressive disorders, or those with known sleep disorders were excluded. Each patient underwent collection of anthropometric, laboratory, medical history data and completion of three questionnaires: the Pittsburgh Sleep Quality Index (PSQI), the Geriatric Depression Scale (GDS), and the WHOQoL-BREF to investigate sleep quality, depression, and quality of life, respectively.
Results: A total of 67 patients were recruited and divided based on their PSQI score into a PSQI≥8 group (n=24) and Controls (PSQI<8, n=43). Patients in the PSQI≥8 group showed a higher prevalence of depressive disorders (4.71±3.8 vs. 2.65±2.10, p=0.021) and poorer quality of life in physical domain (64.6±15.8 vs. 72.8±13.8, p=0.032), psychological domain (58.5±14.4 vs. 71.4±14.6, p<0.001) and social domain (60.1±20.5 vs. 77.0±16.4, p<0.001). Patients in the PSQI≥8 group also had a longer duration of diabetes (15.5±10.7 vs. 12.6±9.44 years, p=0.277), were more frequently undergoing insulin therapy (33.3% vs. 21.4%, p=0.26), and had a higher prevalence of retinopathy compared to controls (26.7% vs. 6.9%, p=0.07).
Conclusion: Sleep disturbances, being associated with greater use of insulin therapy, diabetic retinopathy, anxiety-depressive disorders, and poorer quality of life, should be an important factor to consider in the management of diabetic patients.

	PSQI ≥ 8 (n=24)	PSQI < 8 (n=43)	p value
Diabetes duration (year)	15.5±10.7	12.6±9.44	0.277
Geriatric Depression Scale	4.71±3.8	2.65±2.10	0.021
WHO-QoL BREF – physical	64.6±15.8	72.8±13.8	0.032
WHO-QoL BREF – psychological	58.5±14.4	71.4±14.6	<0.001
WHO-QoL BREF – social	60.1±20.5	77.0±16.4	<0.001
Diabetic Retinopathy	26.7%	6,9%	0.07
Insuline Use	33.3%	21.4%	0.26

Abstract n SP5_3 - Presenting author**: Lorenzo Annesi**

Arterial thrombosis sine materia in pregnancy: a case report and review of the literature

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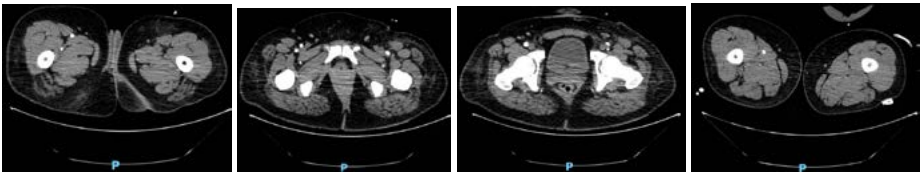
Aim: Pregnancy is a hypercoagulable state, with venous thromboembolism being the most common manifestation. Arterial thrombosis, however, is rare, and data on acute limb ischemia (ALI) during pregnancy are limited. After reviewing the existing literature on ALI during pregnancy, we present an unusual case of ALI occurring in the first trimester.

Methods: The patient has been followed at the Sant'Orsola University Hospital and gave informed consent for the sharing of clinical data. The CARE checklist guided the reporting of this case report. PubMed and Web of Science databases were used to review studies on ALI during pregnancy. Search terms used in the current search included: "Pregnancy" "Arterial thrombosis" and "Acute limb ischemia".

Results: A 43-year-old woman in the seventh week of her third pregnancy presented to the Emergency Department with acute left foot pain and sensory-motor deficit. Physical exam revealed a hypothermic foot and absence of the pedal pulse. Doppler ultrasound confirmed the clinical suspicion of acute limb ischemia (Rutherford IIB) with thrombotic occlusion of the superficial femoral extending to the popliteal arteries. Thromboembolectomy was urgently performed. Multiple investigations for underlying causes were negative. The pregnancy, complicated by preeclampsia, ended with an elective cesarean at 37 weeks, resulting in a healthy newborn (APGAR 9). ALI during pregnancy has been previously linked to triggering factors like arterial cannulation, popliteal entrapment syndrome, peripartum cardiomyopathy and thrombophilic conditions. To the best of our knowledge, this is the first reported case of ALI without an identifiable cause in the first trimester.

Laboratory analysis	Unit of measurement	Normal range of value	First measurement	Last measurement
Leukocytes	10^9/L	3,6-10,5	8,24	6,76
Erythrocytes	10^12/L	3,9-5,2	3,39	4,71
Hemoglobin	g/dL	12-15,6	8,7	11,6
Hematocrit	%	35,5-45,5	26,2	36,1
MCV	fL	80-99	77	77
MCH	pg	27-33,5	25,7	24,6
MCHC	g/dL	31,5-36	33,2	32,1
RDW	%	11,5-15	18,8	21,9
HDW	fL	39-51	52,6	60,5
Neutrophils	%	42-77	74	62,4
Lymphocytes	%	20-44	16,5	24,7
Monocytes	%	2-9,5	7,4	8,6
Eosinophils	%	0,5-5,5	1,6	3,4
Basophils	%	0-1,8	0,5	0,9
Neutrophils	10^9/L	1,5-7,7	6,1	4,22
Lymphocytes	10^9/L	1,1-4	1,36	1,67
Monocytes	10^9/L	0,1-0,9	0,61	0,58
Eosinophils	10^9/L	0,02-0,5	0,13	0,23
Basophils	10^9/L	0-0,2	0,04	0,06
Platelets	10^9/L	160-370	233	322
MPV	fL	8,5-11,5	9,3	9,7
INR		<1,2	1,05	1,11
aPTT		0,82-1,25	1,33	1,1
Fibrinogen	mg/dL	150-400	309	510
Glucose	mg/dL	60-110	109	116
Glycated hemoglobin	mmol/mol	20-42		50
Creatinine	mg/dL	0,5-1,2	0,4	0,49
Uric acid	mg/dL	2,4-5,7	4,6	
Sodium	mmol/L	136-145	134	
Potassium	mmol/L	3,5-5,3	4,5	
Proteins	g/L		49	70
Albumin	g/L	35-50	25,8	
Total bilirubin	mg/dL	<1,2	0,35	
AST	U/L	<35	12	12
ALT	U/L	<35	6	8
GGT	U/L	<38	18	
LDH	U/L	<248	159	

Conclusions: This case report supports the hypothesis that pregnancy acts as a stress test for the maternal organism, unmasking an underlying thrombophilic condition. Since not all such conditions are known, prophylaxis with low molecular weight heparin is essential to reduce the high morbidity and mortality associated with arterial and venous thromboses during pregnancy.



Abstract n SP5_4 - Presenting author**: Zixiong Tang**

In vitro characterization of extracellular vesicles' membrane lipid composition. New insights into their functional roles and for a possible use as new drug-delivery system

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Aim: Extracellular vesicles (EVs) are small particles released by cells mostly in pathological conditions (e.g. tumors) which transfer their cargo (lipids, proteins, genetics materials) from parental to target cells and may be utilized as pathology biomarkers or drug-delivery systems. Despite huge research, EVs role is not fully understood, due to intrinsic heterogeneity, biological contaminations and unproper separation methods. To overcome this problem, we proposed a flexible sequential ultracentrifugation method based on Livshits' algorithm (2015).
Methods: This method has been validated running on the five size-separated EVs subfractions secreted by the human lymph-node metastatic melanoma LM-16 line dimensional- (zetasizer, TEM, AFM), lipidomics and proteomics analysis (GLC, LC-MS, WB).
Results: Subfractions' dimensions range between >200 nm and <50 nm, with the smallest one ("non-vesicular extracellular particles", "exomeres") being the most obscure in origin and function. Lipidomics describes an increase of saturated fatty acid (SFA) concomitant with a decrease of monounsaturated ones (MUFA) ranging from parental cells to exomeres, together with a different distribution of free cholesterol/phospholipid. AFM data also suggest different membrane structure/fluidity among fractions. Intriguingly, exomeres are the smallest, most saturated and stiffest, thus conferring increased cargo protection and differential membrane exchanges compared with the other subfractions.
New experiments confirm that the smaller the particles are, the less prone are to chemical-physical opening and that EVs subfractions after opening display a SFA decrease together with a relative MUFA increase, suggesting losses of membranes rafts, potentially changing membrane properties and call for more *in vitro* proofs and analysis (RAMAN, proteomics, AFM) to validate quality and retainment of their characteristics (specific delivery, receptor and cargo).
Conclusions: These steps are fundamental before the use of EVs as drug-delivery systems *in vivo* models of different pathologies (tumor development, cardiovascular, neurological diseases) and the flexibility of this method allows to accomplish these aims.

Abstract n SP5_5 - Presenting author**: Marco Capacci**

Blood pressure effects of trazodone in hypertensive older adults

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Aim: Trazodone is commonly prescribed for anxiety and insomnia in older adults due to its perceived greater tolerability compared to benzodiazepines, though it may induce hypotension through α-adrenergic receptors blockade.
This study aimed to evaluate the effects of trazodone on orthostatic blood pressure (BP) response and risk of syncope and falls in hypertensive older adults**.**
Methods: This longitudinal observational study was conducted at two geriatric outpatient clinics in Careggi Hospital, Florence, and enrolled hypertensive adults aged ≥75 years. Baseline assessment consisted of a multidimensional geriatric assessment that included office BP measurement, 3-min active stand test, home and ambulatory BP monitoring. Syncope and falls were recorded at follow-up.
Results: Among 123 participants (mean age 81 years, 59% female), 12 (10%) reported regular trazodone use. Trazodone users showed lower office diastolic BP (71.8 vs. 80.1 mmHg, p=0.042) and also greater systolic and diastolic BP reduction immediately after standing (Δsystolic T0 23.8 vs. 14.3 mmHg, p=0.037; Δdiastolic T0 8.9 vs. 1.6 mmHg, p=0.004). A greater diastolic BP reduction after 1 minute of standing (Δdiastolic T1 6.5 vs 0 mmHg, p=0.029) was observed. No difference were found in home and ambulatory BP. During a median follow-up of 12 months, incidence of syncope and falls was 25%, with a significantly higher rate in patients receiving trazodone (58.3% vs. 21.2%, log-rank test p=0.001).
Trazodone use was associated with an increased risk of syncope or falls independently of age, poor physical performance, disability and previous fall history. This association was no longer significant when multivariate Cox analysis was adjusted for dementia diagnosis. BP values were not associated with the study outcome**.**
Conclusions: In older hypertensive adults, trazodone prescription is associated with a greater orthostatic BP drop and an increased risk of syncope and falls.

Abstract n SP5_6 - Presenting author**: Riccardo Rizzo**

Structure and trafficking of PCSK9 in LDL binding

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Introduction: Circulating PCSK9 is known to interact with the LDL-R thus promoting its degradation and blunting the uptake of LDL from the circulation. In this context, anti-PCSK9 mAbs and siRNAs are approved for the treatment of hypercholesterolemia. Previous studies have demonstrated that a significant proportion of circulating PCSK9 associates to LDL. The purpose of our research is to better understand the basis of the PCSK9-lipoprotein interaction and its synthesis.
Methods: A three-layered iodixanol gradient was used to isolate lipoproteins fractions from patients' plasma before and after treatments. Lipoproteins components were studied by spectrophotometric, lipidomic and proteomic approaches. PCSK9 structure and trafficking were studied using WB, FACS and cell colture techniques.
Results: The LDL-C levels decreased from 103±50 to 42±17 mg/dL after siRNA treatment and from 126±50 to 57±31 mg/dL after mAbs therapy. Circulating PCSK9 decreased 65% after siRNA, while plasma PCSK9 levels increased 10-fold after mAbs (n=20 and 30 respectively; $p<0.05$). Independent of the therapy, PCSK9-bound to LDL was on average 10% (n=30; $p<0.01$), and the same result was observed even when using recombinant PCSK9. Immunoblotting analysis demonstrated that PCSK9 binds to LDL with its active form. Lipidomic and LC-MS analyses revealed that PCSK9 associates with a subfraction of LDL that has a lower density and contains higher amounts of ApoE and ApoCs than average LDL. In post-prandial subjects, PCSK9 levels decreased from 468.6 to 407.2 ng/mL, by 10%.
Conclusions: Our study identified an LDL subfraction more buoyant than classical LDL (IDL-like lipoproteins) that is involved in PCSK9 binding. FACS experiments are currently underway to elucidate the binding site location. Although the therapies significantly modify the total circulating levels of LDL and PCSK9, the percentage of PCSK9-bound LDL remains constant. The active form of PCSK9 appears to be involved in binding both LDL and the LDL receptor. Further investigation of post-prandial samples could provide insights into the synthesis of the lipoprotein-PCSK9 complex.

Abstract n SP5_7 - Presenting author**: Carmela Colabufo**

Receptors for glucagon-like peptide-1, glucose-dependent insulinotropic polypeptide, and glucagon in human cardiac progenitor cells: potential pharmacological targets for protection against lipotoxicity-induced metabolic abnormalities

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Aim: Tissue turnover in the human heart requires the recruitment of multipotent cardiac progenitor cells (hCPC). Defective hCPC number and pro-angiogenic capacity contribute to diabetes- and obesity-related heart failure in humans. Evidence supports beneficial cardiovascular effects of GLP-1, GIP and glucagon receptor activation. The aim of this study was to evaluate whether hCPC express functional GLP-1R, GIPR, and GCGR, and to investigate the potential effects of their activation on palmitate-induced abnormalities.
Methods: hCPC were obtained from right auricle biopsies of non-obese, non-diabetic subjects undergoing elective cardiac surgery. GLP-1R, GIPR, and GCGR mRNA and protein expression were demonstrated by quantitative real-time PCR and immunoblotting, respectively. hCPC were exposed to 20 nM exendin-4, or to 10 nM GIP, or to 10 nM glucagon, or to 1 nM tirzepatide, for different times. hCPC, pretreated or not with exendin-4 or GIP for 1 h, were treated with 0.25 mM palmitate for 16 h. Apoptosis was evaluated by ELISA assay. LC3-II content and CREB, JNK 1/2, and p38 MAPK phosphorylation were evaluated by immunoblotting.
Results: hCPC express GLP-1R, GIPR, and GCGR. Exposure of hCPC to exendin-4 for 20 min, or to GIP for 20 min, or to glucagon for 60 min, or to tirzepatide for 5 min activeted CREB ($p<0.05$). Treatment of hCPC with palmitate activated stress kinases, apoptosis and autophagy ($p<0.05$). Pretreatment of hCPC with exendin-4 prevented palmitate-induced apoptosis and autophagy ($p<0.05$) by counteracting stress kinase activation ($p<0.05$), whereas GIP prevented apoptosis only ($p<0.05$), with no detectable effect on stress kinase activation.
Conclusions: hCPC express functional GLP-1R, GIPR, and GCGR. GLP-1R and GIPR signaling might protect hCPC from palmitate-induced damages. Hence, in humans pharmacological targeting through GLP-1R, GIPR, and GCGR might produce beneficial cardiovascular effects that go beyond glucose control and weight loss.

Abstract n SP5_8 - Presenting author**: Carla Ruscitti**

Aortic stenosis and intestinal angiodysplasia: co-protagonists in Heyde's syndrome

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Introdution: Heyde's syndrome is the association of gastrointestinal angiodysplasias and stenosis of the aortic valve secondary to acquired von Willebrand disease. It is characterized by the proteolysis of von Willebrand factor (vWF) with loss of platelet homeostasis by a proteinase that acts preferentially in situations of high mechanical stress (ADAMTS 13A). Platelets lose theirs adhesive capacity to the subendothelial components to stop bleeding, determining a predisposition to angiodysplasias, particularly in gastrointestinal tract.
Description: G.G. an 84-year-old woman with hypothyroidism due to Hashimoto's thyroiditis, stenotic aortic valve disease and scleroderma, was admitted in September 2023 to the Policlinico Tor Vergata for facial myxedema and asthenia. In the previous month she showed an episode of acute anemia treated with blood transfusions, search of occult blood on feces and esophagoduodenoscopy, which were both negative. Blood tests revealed hypochromic microcytic anemia, marked increase in TSH compatible with primary hypothyroidism. The hospitalization was characterized by a progressive improvement of the cognitive status and myxedema after endovenous infusion of Levothyroxine, although the anemia persisted. Colonscopy showed non-bleeding angiodysplasia of caecal fundus. Cardiac ultrasound confirmed the presence of moderate aortic stenosis. In consideration of the clinical scenario and comorbidities, it was decided to set up anti-aggregating therapy and advise the patient to perform an echocardiographic check-up 6 months later for indication of percutaneous treatment of aortic stenosis.
Conclusion: Acquired von Willebrand disease might also be associated with autoimmune disorders. Heyde's syndrome mainly affects patients with moderate-severe aortic stenosis. The treatment of aortic stenosis determines the disappearance of intestinal angiodysplasias and the resolution of the anemization. By considering high thrombotic and a haemorrhagic risks due to concomitant angiodysplasias, it must be paid great attention to antithrombotic/anticoagulant therapy in these patients, with in-depth risk-benefit assessment.

Abstract n SP5_9 - Presenting author**: Lara Ponsa**

Underlying arteriopathy in patients with spontaneous cervical artery dissection: Fibromuscular dysplasia and beyond

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Background and aim: Spontaneous cervical artery dissection (sCeAD) accounts for up to 25% of stroke in young and middle-aged adults. Although growing evidence showed a potential link between fibromuscular dysplasia (FMD) and sCeAD, the magnitude of this association remains uncertain due to incomplete vascular screening. This study aims to assess the frequency and types of cervical and extra-cervical arterial lesions, particularly of the FMD type, in a cohort of patients with a primary diagnosis of sCeAD.
Methods: We recruited all patients admitted with a diagnosis of sCeAD from January 2016 to December 2023. All patients underwent full-body vascular imaging screening to assess the presence of cervical and extra-cervical vascular abnormalities.
Results: Of the 94 patients included (65.7% male; 48.8±8.7 y.o.), carotid artery dissection was observed in 90.4% of patients while vertebral artery dissection in 14.9%, with 9.6% of patients experiencing recurrent sCeAD. 31.9% had imaging evidence of cerebrovascular FMD, with main involvement of the internal carotid artery (89.7%). In the 61 patients with a whole-body vascular screening, all-type of extra-cervical vascular abnormalities were identified in 47.5% of patients. 21.3% had evidence of extra-cervical FMD, affecting renal (11.5%), visceral (13.1%) and limb (6.7%) arteries. Prevalence of extra-cervical dissections and aneurysms was 14.8% and 9.8%, respectively. After a whole-body screening, overall prevalence of FMD raised from 32.8% to 39.3%.
Patients with FMD were mainly female ($p<0.0001$), had a history of migraine ($p=0.023$) and recurrent sCeADs ($p=0.025$). After a multivariate analysis, female sex ($P<0.0001$) and, almost, a positive history of recurrent sCeADs ($P=0.053$) were identified as significant predictors of FMD presence in patients with sCeADs.
Conclusions: The study reveals a high prevalence of FMD and other vascular abnormalities in patients with sCeAD, highlighting the importance of a comprehensive vascular screening, especially in women and in patients with a positive history of recurrent sCeAD.

Abstract n SP6_1 - Presenting author**: Albonetti Flavia**

Prevalence of low muscle mass and malnutrition in a cohort of hospitalized patients: Correlation with dietary habits and inflammatory markers

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Aim: Reduced skeletal muscle mass (SMM) is included among GLIM criteria for diagnosing malnutrition, an important prognostic factor in hospitalized patients. The aim of this study was to evaluate the prevalence of low SMM and malnutrition in hospitalized patients and to analyze its association with dietary habits or inflammatory status.
Methods: In this observational study, we evaluated the nutritional status according to GLIM criteria in 242 patients admitted to the Ferrara Hospital Medical Department. In particular, SMM was estimated using anthropometry (calf circumference, CC) and bioimpedance analysis (fat-free mass index, FFMI). Moreover, in a subgroup of patients (n=37) the L3 Skeletal muscle index (SMI) was obtained from CT-scan. The dietary habits were collected using a 24-hour recall upon admission and the Chrono Med Diet Score (CMDS) questionnaire. CRP levels were collected from clinical records.
Results: 242 patients were enrolled (age 76±11,6 years, females 47,9%, BMI 25,69±5,69 kg/m2); the prevalence of malnutrition was 40% while low SMM ranged from 13% to 53%, depending on the estimation method, with poor agreement between anthropometric and bioimpedance estimates ($p<0.001$). CC correlated to BMI ($\rho=0.501$, $p<0.001$), weight ($\rho=0.56$, $p<0.001$) and arm circumference ($\rho=0.72$, $p<0.001$), while there is an inverse correlation with age ($\rho=-0.234$, $p<0.001$). Regarding dietary patterns, CC inversely correlates with protein intake/kg/day ($\rho=-0.383$, $p<0.001$) and caloric intake/kg/day ($\rho=-0.397$, $p<0.001$). Lower CC correlated with higher CRP values ($\rho=-0.193$, $p<0.001$). Despite SMI was directly associated with CC ($\rho=0.52$, $p=0.001$) and weight ($\rho=0.475$, $p=0.003$) and inversely with age ($\rho=-0.410$, $p=0.012$), no correlations were observed with dietary intakes nor inflammatory status.
Conclusions: This study showed a high prevalence of malnutrition and low SMM among hospitalized patients, associated with an increased inflammatory status and suboptimal dietary patterns. Early identification of this clinical condition and validation of universally recognized cut-off would be beneficial for implementing targeted therapeutic strategies.

Abstract n SP6_2 - Presenting author**: Stefania Scaglione**

Novel biomarkers in acute kidney injury: the role of L-FABP, CYR61, TIMP-2, IGFBP-7, PENK e KIM-1 in the diagnosis of kidney dysfunction etiology and their predictive role of structural renal damage severity

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Background: Acute kidney injury (AKI) is a very common life-threatening disease. Early diagnosis is the cornerstone for limiting the progression and chronicity of renal damage and reducing mortality. Estimating the glomerular flow velocity is the most used method to evaluate renal function. However, detecting new circulating molecules has taken hold for the early identification of kidney damage. To investigate the correlation between the urinary and serum biomarker concentrations and renal dysfunction, we studied a cohort of patients with AKI, accounting for aetiology. **Aims**: Our study aimed to find an association between some new circulating markers of renal injury and the pathogenic mechanism of acute kidney failure. In particular, we have evaluated the possible association between the urinary and serum concentrations of LFABP, CYR61, TIMP2, IGFBP7, PENK, and KIM-1 and AKI's prerenal or intrinsic pathogenesis. The secondary aims of the study were (i) evaluating the possible association between the urinary or serum concentrations of the markers with the severity of the acute kidney injury by the estimation of the variation between the serum creatinine at the admission compared with the basal values reported on the previous documentation exhibited; (ii) identifying the prognostic role of these markers and evaluating their association with the range of variation of the creatinine at discharge versus the values at admission. **Method**s: In this cross-sectional, observational trial, 57 patients with acute kidney disease were consecutively enrolled and underwent a complete medical history to evaluate comorbidities, physical examination, and routine blood tests after eight hours of fasting; urinary and serum concentrations L-FABP, CYR61, TIMP-2, IGFBP-7, and PENK E KIM-1 were obtained in all patients. **Results**: Urinary TIMP2, NGAL, and IGFBP7 and serum PENK values were higher in patients with AKI compared with the control group, with statistical significance. Moreover, higher concentrations of FABP1, Cyr61, TIMP-2, NGAL, IGFB7, and TIMP-2 X IGFBP-7 were found in patients with renal AKI compared with prerenal aetiology. A significant association between the urinary values of FABP1 and TIMP-2 and the serum concentrations of KIM-1 (p= 0,0001) with the variation of the creatinine values from the baseline to the values at the enrollment was found. Furthermore, a statistically significant association was found between KIM-1 and the creatinine variation at the discharge compared with the admission values **Discussion**: In this trial, we evaluated the serum and urinary concentrations of some novel biomarkers of acute kidney injury in a cohort of 57 patients diagnosed with acute renal failure, divided on the aetiology. With the primary aim of finding an association between these markers and the aetiology of the kidney injury, we demonstrated a statistically significant association between the concentrations of FABP1, Cyr61, TIMP-2, NGAL, IGFB7, and TIMP-2 X IGFBP-7 and the intrinsic aetiology of the AKI. Evaluating these "early diagnostic" biomarkers could help identify the underlying physiopathologic mechanism of the renal injury: considering the role of IGFBP-7 and TIMP2 in the cellular cycle and, in particular, in the mechanisms of cellular death, it is clear how the expression of these biomarkers is increased after a direct injury to the renal cells rather than prerenal injury: the levels of IGFBP7 persisted statistically associated with the AKI's aetiology after the multinomial regression, as not affected by other variables. Furthermore, our study has found an association between some of these biomarkers and creatinine variations. In particular, urinary FABP1, TIMP2, and serum KIM-1 levels were associated with a higher variation between the creatinine values at admission compared with the basal values, supporting a possible role of these proteins in defining the severity of renal injury. Moreover, KIM-1 concentrations were proportionally associated with the change of the creatinine values during the hospitalization, with a higher KIM-1 value as much as a higher reduction of the creatinine at recovery compared with admission: we confirm the protective role of KIM-1 in the worsening of renal dysfunction, but the constitutive expression of this protein on the tubule results in gradual fibrosis and progression towards chronic nephropathy. Considering the protective role of KIM-1, the increased values of KIM-1 may be related to a higher probability of recovery from renal dysfunction. Finally, in our study, we confirm the diagnostic role of some of these molecules. In particular, we have found that urinary values of TIMP2, NGAL, and IGFB7 and serum concentrations of PENK were statistically higher in patients with AKI compared to controls. Our study provides further evidence concerning the possible use of these novel biomarkers of AKI in clinical practice. Given their diagnostic and predictive role, these molecules could be used to identify the population at risk for the development of AKI and to identify renal injury early, even before the increase in serum creatinine or cystatin C values.

Abstract n SP6_3 - Presenting author**: Shawn Gugliandolo**

A four-week treatment with dapagliflozin reduces insulin-stimulated renal glucose uptake

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Aims: Treatment with SGLT-2i reduces the risk of both cardiovascular and renal outcomes in type 2 diabetes (T2D). Recent findings indicate that in obese individuals, the kidney exhibits lower 18Fluorodeoxyglucose ([18F]-FDG) uptake rates compared to lean individuals, possibly due to insulin resistance. This study aims to evaluate changes in renal [18F]-FDG uptake in T2D patients following short-term treatment with dapagliflozin and to assess the long-term effects on kidney function after a four-year follow-up.
Methods: In our DAPAHeart Trial, a single-center, four-week, prospective, double-blind, controlled study, we enrolled T2D patients with stable coronary artery disease and preserved glomerular filtration rates (eGFR >60 ml/min/1.73m^2). Participants were randomly assigned in a 1:1 ratio to receive either dapagliflozin (10 mg daily) or a placebo. PET scans using [18F]-FDG were performed during a hyperinsulinemic-euglycemic clamp (HEC) to measure regional FDG uptake before and after the four-week treatment with SGLT-2i.
Results: After the four-week treatment, the SGLT-2i group showed a significant reduction in renal standardized uptake value (SUV) expressed as peak activity concentrations (SUVpeak; p=0.045) compared to the placebo group, with trends toward reductions in SUVmax and SUVmean. Additionally, long-term follow-up data revealed that four years of dapagliflozin treatment was associated with stable eGFR (pre-treatment: 81.4 ± 6.4 ml/min; post-treatment: 76.2 ± 6 ml/min; p=0.4).
Conclusions: Short-term treatment with dapagliflozin is associated with a reduction in renal SUVpeak, indicating decreased glucose uptake during an insulin-stimulated state (insulin clamp). While the causes of this reduction require further investigation, it is suggested that SGLT-2 inhibition decreases tubular energy requirements and glucose uptake, contributing to kidney function preservation, as confirmed by the four-year follow-up.

Abstract n SP6_4 - Presenting author**: Sebastiano Cicco**

Right ventricle to pulmonary artery coupling increases in obstructive sleep apnoea and relates to left ventricle hypertrophy

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Aim: Obstructive Sleep Apnea (OSA) is a known risk factor for myocardial profibrotic pathways in the left heart. This study aimed to evaluate whether changes in the right heart are related to OSA severity.
Methods: We analyzed 62 patients (45 males/17 females, aged 59±13 years) with confirmed OSA. Baseline chemistry was recorded. All patients underwent morning blood gas analysis, a full cardiorespiratory evaluation, including nocturnal polygraphy, and echocardiography. The left ventricle (LV) was evaluated for ejection fraction (EF%), LV diameters, mass, and diastolic dysfunction, as assessed by the trans-mitral E velocity to septal e' velocity (E/e' ratio). Right heart measurements included TAPSE, pulmonary arterial pressure (PAP), right atrium and ventricle area, and inferior vena cava diameter. The right ventricle to pulmonary artery coupling was assessed using the TAPSE/PAPs ratio. Patients were divided into two groups: Group 1 (non-severe OSA, AHI <30, 26 pts) and Group 2 (severe OSA, AHI >30, 36 pts). Statistical significance was set at $p \leq 0.05$.
Results: Group 2 had a higher BMI (32.58±6.16 vs 35.46±6.34 kg/m², p=0.041). No significant differences were found in other comorbidities. The interventricular septum was slightly thicker in Group 2 (12.89±1.39 vs 13.77±2.02 mm, p=0.04). Group 2 showed an increased E/e' ratio (7.28±2.06 vs 8.39±1.94, p=0.03). PAPs decreased in Group 2 (30.00±19.07 vs 23.94±6.66 mmHg, p=0.02), while TAPSE increased (26.81±4.26 vs 28.47±4.19 mm, p=0.03), resulting in a higher TAPSE/PAPs ratio (1.09±0.40 vs 1.26±0.34, p=0.02). TAPSE/PAPs correlated with interventricular septum diameter (r=0.37), posterior wall diameter (r=0.35), LV mass, and left atrial volume (r=0.32 and 0.36).
Conclusion: Severe OSA is associated with a hyperdynamic cardiovascular system. Increased right heart coupling with the pulmonary vascular system may contribute to left ventricle hypertrophy and remodelling, potentially increasing left-sided preload.

Abstract n SP6_5 - Presenting author**: Mirko Zoncapè**

Efficacy of a multidisciplinary clinic in improving cardiovascular and liver outcomes in Metabolic dysfunction-Associated Steatotic Liver Disease

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Aim: Cardiovascular disease (CVD) is the leading cause of mortality in Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD). Guidelines recommend a multidisciplinary approach, but real-world data are limited. This study evaluated the efficacy of a multidisciplinary MASLD clinic in optimising control of metabolic comorbidities and liver injury markers.
Methods: A retrospective analysis was conducted on 465 MASLD patients seen in a multidisciplinary clinic (June 2014 - June 2024). All participants were evaluated by both a hepatologist and a cardiovascular disease expert, and were referred directly from primary care or through the Camden and Islington MASLD Pathway (London, UK).
Patients underwent hepatological and cardiovascular evaluations, with dietary counselling as needed. Cardiovascular risk was assessed via QRISK-3, and statins were prescribed for patients with a ≥10% 10-year CVD risk or prior cardiovascular events. Changes in liver markers (transaminases, LSM) and metabolic comorbidities (e.g., blood pressure, HbA1c, lipids, QRISK-3) were primary endpoints.
Results: Patients had a mean age of 57±12 years; 56% were male, and 54% were Caucasian. Comorbid hypertension, diabetes, and dyslipidaemia were present in 66%, 56%, and 84%, respectively. At baseline, 65% had abnormal ALT, and the median LSM was 7.9 kPa (measured in 95%). Of 190 liver biopsies, 79% showed steatohepatitis, with bridging fibrosis in 29% and cirrhosis in 14%.
At a 15-month median follow-up, 61% of patients remained under secondary care, with significant improvements observed in ALT, AST, GGT, total cholesterol, LDL-c, TG, blood pressure, weight, BMI, LSM, and QRISK-3 (all $p<0.05$). Waist circumference decreased significantly in obese patients, with 12% achieving ≥10% weight loss. Therapy adjustments improved metabolic markers in diabetes, hypertension, and dyslipidaemia.
Conclusion: A multidisciplinary MASLD clinic significantly improved liver and CVD risk markers. Long-term collaboration between primary and secondary care is crucial to achieve and maintain these health improvements.

Abstract n SP6_6 - Presenting author**: Giada Di Betto**

Creatinine as a predictor of clinical events in metabolic dysfunction-associated steatotic liver disease

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Aim: Metabolic dysnfuction-associated steatotic liver disease (MASLD) is the leading cause of chronic liver disease, and liver fibrosis is the primary predictor of liver-related events and mortality. Identifying patients at higher risk of progression is crucial for improving outcomes. The aim of this study is to characterize patients referred for hepatic steatosis to the Metabolic Clinic of AOU Policlinico of Modena with a minimum follow-up of 10 years and to assess the incidence and predictors of clinical events of interest.
Methods: We prospectively enrolled all patients referred to the Metabolic Clinic for suspected NAFLD in the first years from its foundation (2011-2012). Retrospective data on cardiovascular events, liver-related events and mortality were collected. NITs for liver fibrosis were calculated and elastometric and histologic data were collected when available. Cox regression analysis was used to identify predictors of: 1) liver-related events, 2) cardiovascular events, 3) composite of death, hepatic decompensation, or cardiovascular events.
Results: The study population included 120 patients (33,3% females, mean age 53,32 ± 11,8 years). At baseline, 41 patients (37,3%) were obese (BMI of 29,02 ± 4,03), with T2DM, hypertension and dyslipidaemia prevalence of 14,2%, 26,7% and 76,7%, respectively. Over a mean follow-up of 11 years, 13 patients (10,8%) progressed to cirrhosis: 3 (5%) experienced hepatic decompensations, 3 developed HCC; 15 (12,5%) developed cardiovascular events, and 4 (3,3%) died.
Baseline Fib4 and APRI correlated with the composite outcome in univariate analysis, but not AGILE3. At the multivariate analysis, age, BMI and creatinine remained significant predictors (Figure 1).
Conclusions: Creatinine levels may serve as an additional marker for identifying patients with MASLD who are at higher risk of clinical events, highlighting the possible, often subclinical, organ damage in this patient group.

Figure 1

UNIVARIATE			MULTIVARIATE		
	HR 95% CI	p		HR 95% CI	p
Age	1,076 (1,031-1,123)	0,001	**MODEL1**		
BMI	1,13 (1,032-1,253)	0,009	Age	1,095 (1,010-1,187)	0,027
Hypertension	3,68 (1,493-9,083)	0,005	BMI	1,256 (1,040-1,515)	0,018
Diabetes	4,37 (1,717-11,17)	0,002	Hypertension	-	ns
CV events	5,30 (1,163-24,198)	0,031	N.Medications	-	ns
Comorbidities	1,887 (1,145-3,078)	0,013	Creatinin	197,0(2,56-15154,29)	0,017
N.Medications	1,37 (1,1,93-1,581)	<0,001	Platelets	-	ns
Statin	2,563 (1,006-6,531)	0,049	Glucose	-	ns
Creatinin	95,76 (2,92-313,05)	0,010	**MODEL 2**		
Platelets	0,99 (0,97-1,00)	0,084	BMI	1,55 (1,07-2,24)	0,021
Glucose	1,01 (1,00-1,02)	0,012	Hypertension	-	ns
Uric Acid	2,112 (0,99-4,605)	0,060	N.Medications	14,26 (1,14-178,57)	0,039
Fib4	7,29 (1,73-30,61)	0,007	Creatinin	138,96 (0,69-27713,88)	0,068
APRI	29,21 (1,89-449,57)	0,016	Fib4	-	ns
Never smoker	0,316 (1,49-9,08)	0,041	Diabetes	-	ns

Abstract n SP6_7 - Presenting author**: Daniele Tragni**

Longitudinal evaluation of clinical and biochemical parameters over a 5-year follow-up in a cohort of hypertensive patients

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Aim: The study aimed to evaluate the evolution of anthropometric, clinical, and laboratory parameters over a 5-year follow-up in a cohort of 30 hypertensive patients. The primary objective was to identify significant trends or changes in these variables and their potential clinical implications.
Methods: A total of 30 patients (19 males and 11 females) affected by hypertension were assessed at baseline (T0), after one year (T1), and after five years (T2), and were included in this preliminary analysis. Variables including weight, BMI, blood pressure, and biochemical markers were collected. Moreover all patients underwent physical examination, echocardiography, tonometry, electrocardiogram and carotid ecocolordoppler. Non-parametric repeated measures ANOVA (Friedman test) and descriptive statistics were applied to evaluate longitudinal changes and trends.
Results: The analysis showed no significant differences in weight, BMI, abdomen or neck circumference across the three time points ($p>0.05$). Furthermore, data demonstrated no discordances in blood pressure and heart rate. Among biochemical parameters, a significant reduction was observed in U-ACR ($p=0.02$) between T0 and T2. ABI values decreased significantly in both limbs between T0 and T2 ($p=0.017$). Overall, changes in most variables did not reach statistical significance, suggesting clinical stability over time.
Conclusions: This study highlights the stability of key clinical parameters over five years in a cohort of patients. The reduction in specific markers warrants further investigation to understand their long-term cardiovascular implications, relating these results also with drugs, physical activity and diet. These findings may guide tailored monitoring and intervention strategies in similar patient populations.

Abstract n SP6_8 - Presenting author: **Andrea Sablone**

Effect of SGLT2-i on hematocrit: A case series (trick or treat)

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Background and Aims: SGLT2 inhibitors are effective in managing type 2 diabetes (T2D), offering cardiovascular and renal benefits, partly by hematocrit (Hct) increase. However, high Hct levels may have clinical implications. This case series describes the management of SGLT2i therapy in patients with significant Hct elevation.
Materials and Methods: Out of 4,276 T2D patients undergoing SGLT2i therapy in 2024 at the Endocrinology and Metabolism Unit (UOC) of Pescara, 7 patients were identified with an increase in Hct levels during treatment, requiring a hematological specialist consultation. Among these, complete information was available for only 5 male patients (mean age 63.4±5.92 years, diabetes duration 11.6±2.88 years, 2 canagliflozin, 2 dapagliflozin, 1 empagliflozin). Blood parameters (Hct, hemoglobin [Hb], red blood cells [RBC], platelets [PLT], HbA1c), comorbidities, and ongoing therapies were collected from clinical patients charts.
Results: All patients had normal Hct (48.84±1.61%) and Hb (15.66±0.91 g/dl) before SGLT2i therapy. After 12.6±3.28 months, Hct and Hb increased to 54.4±1.04% and 18.3±0.36 g/dl, respectively. Two patients with severe obstructive sleep apnea (OSAS) and a smoking history and 1 with cardiovascular comorbidities required phlebotomy. Therapy discontinuation normalized blood parameters in all cases. In two patients, SLGT2i different from the previous was reintroduced, without effects on Hct elevation, still monitored.
Conclusions: This case series highlights the importance of monitoring hematocrit in patients on SGLT2 inhibitors, particularly those with risk factors. It remains to be clarified whether and when the discontinuation of SGLT2 inhibitors is necessary and whether switching the molecule could represent a useful solution.

Abstract n SP6_9 - Presenting author**: Alfredo Caturano**

Improvement of global longitudinal strain and myocardial work in type 2 diabetes patients on sodium–glucose cotransporter 2 inhibitors therapy

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Aim: Sodium–glucose cotransporter 2 inhibitors (SGLT2-i) are a novel class of oral hypoglycemic agents currently used among patients with type 2 diabetes mellitus (T2DM). The effects of SGLT2-i inhibitors on cardiac structure and function are not fully understood. The aim of this study is to evaluate the echocardiographic changes among patients with well-controlled T2DM treated with SGLT2-i in a real-world setting.
Methods: Thirty-five well-controlled T2DM patients (65±9 years, 43.7% male) with preserved left ventricular ejection fraction (LVEF) and 35 age - and sex-matched controls were included. T2DM patients underwent clinical and laboratory evaluation; 12-lead surface electrocardiogram; 2-dimensional color Doppler echocardiography at enrolment, before SGLT2-i administration, and at 6 months follow-up after an uninterrupted 10 mg once daily of empagliflozin (n: 21) or dapagliflozin (n: 14). Standard echocardiographic measurements, LV global longitudinal strain (LV-GLS), global wasted work, and global work efficiency were calculated.
Results: T2DM patients showed higher E/E' ratio (8.3±2.5 vs. 6.3±0.9; P<0.0001) and lower LV-GLS (15.8±8.1% vs. 22.1±1.4%; P<0.0001) and global myocardial work efficiency (91±4% vs. 94±3%; P=0.0007) compared with age- and sex-matched controls. At 6-month follow-up, T2DM patients showed a significant increase in LVEF (58.9±3.2% vs. 62±3.2%; P<0.0001), LV-GLS (16.2±2.8% vs. 18.7±2.4%; P=0.003), and global work efficiency (90.3±3.5% vs. 93.3±3.2%; P=0.0004) values; conversely, global wasted work values (161.2±33.6 vs. 112.72±37.3 mm Hg%; P<0.0001) significantly decreased.
Conclusions: Well-controlled T2DM patients with preserved LVEF who are treated with an SGLT2-i on top of guideline-directed medical therapy showed favorable cardiac remodeling, characterized by the improvement of LV-GLS and myocardial work efficiency.

Abstract n SP6_10 - Presenting author**: Alessandro Gezzi**

Bio-anthropometric indices of insulin resistance predict arterial hypertension and 24-hour blood pressure control in non-diabetic hypertensive patients

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Background and Aim: Insulin resistance (IR) promotes dyslipidemia and elevated blood pressure (BP) through various mechanisms. While the homeostatic model assessment (HOMA) is commonly used to quantify IR, alternative bio-anthropometric indices, such as TG/HDL-C, TyGi, TyGi-BMI, TyGi-WC, LAP, VAI, and METS-IR, have been validated against HOMA. Some indices have shown associations with hypertension risk and poor BP control evaluated using office BP (OBP). However, their relationships with 24-hour ambulatory BP monitoring (ABPM) and antihypertensive treatments remain unexplored. This study investigates the association between bio-anthropometric indices of IR and ABP in non-diabetic hypertensive outpatients.
Methods: This observational cross-sectional study included 1,336 outpatients assessed for hypertension using ABPM. Various IR indices were calculated, and when present antihypertensive therapy was evaluated using the number of medications and the treatment intensity score (TIS). Multivariate logistic regression models analysed the association between IR index quartiles and the prevalence of hypertension or uncontrolled 24-hour ABP. Subgroup analyses considered lipid-lowering therapy (LLT), sex, and age. A likelihood ratio test was used to assess the non-linearity of the association between the IR surrogate indexes and the outcome. And restricted cubic splines (RCS) analyses were performed to model non-linear relationship between the IR surrogate indexes and the odds of uncontrolled 24-hour BP.
Results: Mean age: 54.9 years (M 58.3%), mean BMI: 27.4 kg/m². Median values of key indices: TG/HDL-C (2.07), TyGi-BMI (234.9), TyGi-WC (832.8), LAP (41.4), VAI (71.3), and METS-IR (41). Patients with uncontrolled ABP: 64.2%. They were younger, predominantly male, and exhibited higher IR indices. In both adjusted and unadjusted models, higher METS-IR and TyGi-BMI quartiles were independently associated with uncontrolled ABP. Sensitivity analyses confirmed these associations regardless of LLT, sex, and age.
Conclusion: METS-IR and TyGi-BMI were the strongest predictors of uncontrolled ABP, independent of treatment status, LLT, sex, and age. These indices, derived from widely available parameters, offer practical tools for identifying patients with increased hypertension risk in real-life clinical settings.

Abstract n SP7_1 - Presenting author**: Carlo Maiorca**

Correlation between LDL cholesterol burden and coronary atherosclerosis in patients with Heterozygous Familial Hypercholesterolemia (HeFH)

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Aim: Heterozygous Familial Hypercholesterolemia (HeFH) is an autosomal dominant disorder causing high LDL cholesterol and increased risk of premature atherosclerosis and cardiovascular disease, including aortic stenosis. Cholesterol burden (CB) is key in developing atherosclerosis, though its exact relationship with atherosclerotic burden (AB) remains uncertain. Computed tomography coronary angiography (CCTA) is a valuable tool for assessing AB and aortic valve disease. Recent studies indicate that early lipid-lowering therapy reduces coronary plaque volume, linking CB to plaque size. The main objective of this study is to investigate the association between CB and AB in patients with genetically confirmed HeFH. Secondary objectives include the evaluation of the impact of lipid-lowering on the reduction of BA.
Methods: This is a retrospective-prospective, observational, non-randomized study on 250 patients with molecularly confirmed HeFH carrying pathogenic variants in LDLR, included in the LIPIGEN study and undergoing CCTA for routine clinical practice. Among these patients, 92 have already undergone CCTA and will be included in the present preliminary analysis. Medical records were retrospectively revised to collect clinical, biochemical, pharmacological and imaging data. AB was estimated by a comprehensive assessment of plaque phenotype, assessment of the degree of coronary stenosis by Coronary Artery Disease-Reporting and Data System (CAD-RADS score from 0 to 5) and evaluation of calcium quantity by Agatston score (expressed in HU, Hounsfield Units)].
Results: The cohort of patients undergoing CCTA (n=92, 59.8% male) had a mean LDL-C levels of 150,22 mg/dl corresponding to a CB equal to 6276 mg-year/dl (4769.25 - 8636.25). 44.6% (n=41) had a CAD-RADS score of 0, while more than half of the patients (n=51, 55.5%) had a CAD-RADS ≥1. The entire cohort of patients also had a median Agatston score of 8.85 (0 - 125.3). Regression analyzes highlighted a positive correlation between CB and CAD-RADS (Beta=0.26, P=0.009) which remained significant even after adjustment for major confounding factors, such as sex, BMI and smoking habits (Beta=0.33, P=0.001).
Conclusions: This preliminary analysis confirmed a positive correlation between LDL cholesterol burden and atherosclerotic burden. Further investigation will enable us to assess whether pharmacological modulation of LDL cholesterol can lead to a significant reduction in atherosclerotic plaque burden.

Abstract n SP7_2 - Presenting author**: Martina Ferrandino**

Evaluation of lipid profile, ApoB and Beta-lipoproteins distribution among patients with Familial Hypercholesterolemia

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Aim: Familial Hypercholesterolemia (FH) is a genetic disease characterized by high levels of LDL-cholesterol (LDL-c) and increased cardiovascular risk. We aim to characterize the differences of lipid profile, including the lipoproteins size, between FH patients with (FH/V+) and without pathogenic variants (FH/V-).
Methods: We analyzed by NGS (Devyser's FH kit) 192 patients (155 adults and 37 children) with clinical suspicion of FH, to identify variants in the main causative genes (*LDLR*, *APOB* and *PCSK9*). ApoB was quantified by nephelometry (Siemens) and other lipid parameters were measured by standard enzymatic methods. LDL-c/non-HDL-c and other lipid ratios were also calculated. Cholesterol of small-dense LDL (sdLDL-c) was estimated by Sampson equation.
Results: Higher levels of LDL-c and ApoB were observed in FH/V+ than in FH/V- patients, among both adults and children. In adults, we also observed higher levels of LDL-c/non-HDL-c ratio in FH/V+ (0.90 (0.85-0.94) than in FH/V- patients (0.84 (0.77-0.88); $p<0.001$), reflecting the greater prevalence of LDL among Beta-lipoproteins. Adult FH/V- patients showed slightly higher levels of triglycerides than FH/V+ patients (110 (82-175) and 78 (57-114), respectively; $p<0.001$), although mainly under the desirable values. We then calculated triglycerides/ApoB ratio that resulted higher in FH/V- than in FH/V+ patients (1.23 (0.91-1.55) and 0.72 (0.56-1.02), respectively; $p<0.001$), indicating the presence of triglycerides-rich lipoproteins in FH/V- patients. About LDL size, the ratio between the estimated sdLDL-c and estimated LDL-c values was higher in FH/V- than in FH/V+ patients (0.31 (0.27-0.36) and (0.24 (0.22-0.29); $p<0.001$), indicating a higher proportion of sdLDL in these patients, reflecting the higher levels of triglycerides.
Conclusions: We observed a different profile of distribution of Beta-lipoproteins among adult FH/V- and FH/V+ patients. Even a slight increase in triglycerides was associated with increased sdLDL and triglycerides-rich Beta-lipoproteins.

Abstract n SP7_3 - Presenting author**: Daniele Tramontano**

Fatty Liver Disease during long-term Lomitapide therapy in Familial Chylomicronemia Syndrome: a reversible outcome?

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Background and aim: Familial Chylomicronemia Syndrome (FCS) is a rare and life-threatening autosomal recessive disorder caused by mutations impairing lipoprotein lipase (LPL) activity, leading to severe hypertriglyceridemia (HTG) and an increased risk of acute pancreatitis (AP). Conventional triglyceride-lowering therapies are often ineffective in FCS, necessitating alternative treatments. Lomitapide, an inhibitor of microsomal triglyceride transfer protein (MTP), has shown efficacy in reducing triglyceride (TG) levels in FCS but is associated with hepatic side effects, including fatty liver disease (FLD). This study aimed to evaluate the long-term efficacy and hepatic safety of lomitapide in a patient with genetically confirmed FCS.
Methods: We describe the case of a 71-year-old woman with FCS treated with lomitapide for nearly five years, initiated during the LOCHNES study. Efficacy was assessed through reductions in triglyceride (TG) levels and prevention of AP episodes. Hepatic safety was monitored using ultrasound, FibroScan, and Magnetic Resonance Imaging (MRI), with radiologic images and biochemical data collected at regular intervals.
Results: Lomitapide therapy achieved a sustained reduction in TG levels by over 90%, effectively preventing recurrent AP. Hepatic monitoring through ultrasound, FibroScan, and Magnetic Resonance Imaging (MRI) during long-term lomitapide therapy revealed progressive FLD. Following treatment suspension due to hypertransaminasemia and increased liver stiffness (up to 15 kPa), repeat MRI after 70 days demonstrated complete resolution of FLD and normalization of liver stiffness (4.1 kPa).
Conclusion: This case highlights the efficacy of lomitapide in achieving significant TG reductions in FCS while underscoring the importance of rigorous hepatic monitoring. The reversibility of lomitapide-induced FLD and liver stiffness demonstrates the value of timely intervention and personalized dosing to balance efficacy and safety in long-term management.

Abstract n SP7_4 - Presenting author**: Tosin Paola**

The efficacy and safety of evinacumab in pediatric patients with homozygous familial hypercholesterolemia: Real-world experience of the Centre of Padua

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Aim: Homozygous familial hypercholesterolemia (HoFH) is a rare and severe genetic disease characterized by very high low-density lipoprotein cholesterol (LDL-C) associated to premature cardiovascular disease. The availability of novel lipid-lowering therapies (LLTs) has changed the clinical management of HoFH. This study evaluates the efficacy and safety of evinacumab, an inhibitor of angiopoietin-like 3 protein, combined with lomitapide in paediatric HoFH patients receiving standard-of-care LLTs in real-world clinical practice.
Methods: Three adolescents (mean age 11.4 years, 2 males and 1 female) with genetically confirmed HoFH were studied. Evinacumab was administrated intravenously (15 mg/kg every 4 weeks), with compassionate-use approval for patients under the age of 12. At each visit, patient underwent medical examinations, and blood samples were collected to assess lipid profiles and to evaluate liver and kidney function for safety monitoring.
Results: The mean pretreatment LDL-C concentration at diagnosis was 833±22 mg/dL (mean±standard deviation). The add-on therapy of evinacumab to high-intensity statin, ezetimibe, and Lomitapide, without the need for lipoprotein apheresis (LA), decreased LDL-C from 374±46.9 mg/dL at baseline to 139±33 mg/dL after 24 weeks of treatment. Therefore, evinacumab achieved a mean LDL-C reduction of 83±12% from LDL-C levels at diagnosis (Figure 1). No serious treatment-related adverse events occurred in any patient.
Conclusions: In this small cohort, evinacumab was associated with sustained reduction in LDL-C levels, demonstrating its potential as an effective LDL receptor-independent therapy. The combination of evinacumab and lomitapide eliminated the dependency on LA and offers a paradigm shift in the clinical treatment of HoFH.

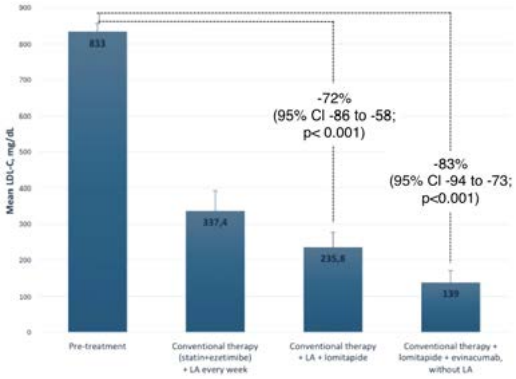

Figure 1: Mean LDL-C at each step intensified LLT.

Abstract n SP7_5 - Presenting author**: Sofia Castiglione**

Management of autosomal recessive hypercholesterolemia in real-world practice: a report of two Italian patients treated with evinacumab

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Aim: Autosomal recessive hypercholesterolemia (ARH) is a rare and severe form of hypercholesterolemia caused by mutations in the *LDLRAP1* gene. Similar to homozygous familial hypercholesterolemia, ARH is resistant to conventional LDL-lowering therapies and is associated with a significantly increased risk of atherosclerotic cardiovascular diseases (ASCVDs). Evinacumab, a monoclonal antibody targeting ANGPTL3, was recently introduced in Italy as a novel therapeutic option for achieving guideline-directed LDL-C control. However, limited data exist on its use in ARH.
Methods: We examined the short-time effectiveness and safety of evinacumab in two ARH patients treated at the Lipid Clinic in Milan, outside of a clinical trial setting.
Results: Two male patients (aged 60 and 42), carrying identical biallelic variants in *LDLRAP1* (c.432insA), were treated with evinacumab administered intravenously (15 mg/kg Q4W). Patient 1 has a BMI of 34.3 Kg/m^2 and a history of ASCVD. Previous treatments included evolocumab 420 mg Q2W, which proved ineffective, and lomitapide, which was discontinued due to AE. Evinacumab was added alongside ongoing lipoprotein apheresis, rosuvastatin 30 mg, ezetimibe and fenofibrate. At baseline, LDL-C was 549 mg/dL. Following just one administration, LDL-C levels decreased by 63.6%, and triglycerides were reduced from 276 mg/dL to 46 mg/dL. LDL-C levels at nadir was 92 mg/dL. Patient 2 has a BMI of 25.5 Kg/m^2 with stable coronary heart disease. Evinacumab was added to evolocumab 420 mg Q2W, rosuvastatin 40 mg/day, ezetimibe and bempedoic acid. Baseline LDL-C level was 103 mg/dL, which decreased by 79.6% after a single administration. Triglyceride levels also dropped, from 42 mg/dL to 20 mg/dL. HDL-C levels decreased by 50% in both patients. Evinacumab was well-tolerated, with no significant adverse events. Patient 1 reported only a mild headache after the first infusion, which resolved spontaneously.
Conclusions: In these two ARH patients, evinacumab demonstrated a profound and sustained LDL-C-lowering effect, with higher safety profile. Evinacumab is a potential game changer in the clinical management of HoFH, with predictable significant clinical cardiovascular benefits related to the magnitude of LDL-C reduction.

Abstract n SP7_6 - Presenting author**: Federica Galimberti**

Awareness and knowledge of Familial Hypercholesterolemia in Italy: results from a national survey among clinicians

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Aim: Familial Hypercholesterolemia (FH) is an inherited disease that can lead to early onset of coronary artery disease. Timely diagnosis and treatment are critical to ensure the best possible prognosis. While FH is usually managed by lipidologists, many healthcare professionals encounter this condition in their clinical practice, often without recognizing and diagnosing it. This study aimed to assess the level of awareness and knowledge of FH among Italian clinicians across different specialties.
Methods: An online survey, consisting of 21 anonymous questions, was designed and distributed starting on September 24, 2024 (i.e. FH Awareness Day), through the mailing lists of several national scientific societies.
Results: A total of 303 clinicians responded to the survey, including internists (35.3%), general practitioners (21.1%), and cardiologists (14.5%), with smaller proportions of paediatricians (5.0%) and diabetologists (1.7%). Overall, 28.4% had less than 5 years of clinical experience, while 41.6% had over 25 years. Although 43.5% of clinicians rated their knowledge of FH as above the average, and two-thirds of respondents reported diagnosing and managing patients with this condition, 18.8% were unaware of the disease's prevalence, 18.2% did not know FH-associated genes, 43.2% were unfamiliar with any of diagnostic algorithms, and 6.6% could not indicate first-line therapies to treat FH. In 20% of cases, no family screening was conducted; 15.8% did not consider genetic testing essential for diagnosis, and 40.3% did not find molecular diagnosis decisive for treatment choice. The mean FH knowledge and familiarity scores were higher among internists or diabetologists, as well as among respondents with more years of practice.
Conclusions: This survey among Italian clinicians identified significant gaps in knowledge, awareness, familiarity, and practice related to FH. Educational programs addressed to all healthcare professionals who are involved in the management of FH patients are essential to improve FH care, including systematic family screening to early identify at-risk individuals.

Abstract n SP7_7 - Presenting author**: Alessia Cipollone**

Clinical characteristics and genetic predisposition of dyslipidemic patients with statin intolerance

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Background: Statin therapy represents the gold standard in lipid lowering therapy, although it is associated with an increasing rate of therapeutic abandonment especially due to the onset of muscle symptoms (statin associated muscle symptoms SAMS). In literature, a higher incidence of SAMS in the female population has already been documented, probably attributable to differences in pharmacokinetics and pharmacodynamics between genders. A relevant element in this condition would seem to reside in the SLCO1B1 gene, responsible for the tissue transport of statins, whose mutation would determine an increased plasma concentration of the same with consequent development of SAMS.
Aim: The aim of our study was to evaluate the real-life prevalence of statin intolerance in patients referred at our Center and how this determines whether or not the 2019 ESC guideline's LDL target was reached. The influence of genetic factors (specifically the SLCO1B1 mutation) and of patients' general and clinical characteristics (gender, age, BMI) on the achievement of the target was also analyzed.
Methods: We selected a population of 185 patients attending our Center and enrolled in the LIPIGEN project (96 F; 89 M), of whom 131 FH+ (67 F; 64 M). In 97% of the total population it was possible to evaluate the SLCO1B1 gene, which was found to be mutated in 67 out of 179 patients (37 F; 30 M). The mean age of our patients was 35 years (18 to 74 years; 41 f, 30 m), the mean BMI was 24.2 (23.9 f; 24.5 m).
Discussion: In accordance with the literature, our data showed a greater statin intolerance in female (58% f vs 42% m). In particular, Atorvastatin was the worst tolerated, with predominantly SAMS development even in the absence of CPK elevation (only 2 patients). If intolerance was referred by the patient, we preferred to shift to Rosuvastatin, generally characterized by better tolerability.
Intolerance showed a continuous growth trend in relation to age in both sexes, more significant in female (5-fold increase from 35 to 75 years).
The evaluation of the BMI was affected by the different numerical representation between classes, given the prevalence of normal weight and overweight population. From our preliminary data, the BMI would seem to be directly correlated with the development of statin intolerance; less significant the correlation with the achievement of the target since the poor representation of some groups could determine confounding results.
Of the 179 patients analyzed for mutations of the SLCO1B1 gene, 37% presented its mutation. By stratifying the data based on sex, the influence of this mutation on the development of statin intolerance in female was confirmed, independently of the diagnosis of familial hypercholesterolemia, particularly in female FH+.
Conclusions: Statin intolerance still represents an obstacle to therapeutic compliance and the achievement of the LDL target. Particular importance seems to be related to age and the presence of SLCO1B1 mutations; the role of BMI/waist circumference is still uncertain.

Abstract n SP7_8 - Presenting author**: Riccardo Mattia Ricciardi**

SLCO1B1 mutation is a risk factor for statin intolerance and achieving lipid targets in patients with hypercholesterolemia independently from FH mutation

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Aim: Based on SCLO1B1 mutation, identify potential differences in achieving lipid targets and statin intolerance, in patients with hypercholesterolemia with and without FH, using real-life data.
Methods: The study involved 185 patients (96 females, 89 males), with and without familial hypercholesterolemia (FH+ and FH-). All patients underwent genetic analysis as part of the LIPIGEN project. Data was collected and analyzed to assess lipid target achievement and statin intolerance, comparing results by gender and SCLO1B1 mutation status.
Results: Females showed greater difficulty compared to males, associated with a higher rate of statin intolerance. Patients with a positive SCLO1B1 mutation demonstrated slightly more difficulty in achieving lipid targets.
• Men FH+ and SCLO1B1 mutation failed to achieve the target in 14.29% of cases, while those without the mutation failed in 11.63% of cases, with a significant increase in statin intolerance among men FH+ and the SCLO1B1 mutation compared to those without it (33% vs. 7%, respectively).
• Women FH+ and SCLO1B1 mutation failed to achieve the target in 43.48% of cases, compared to 22.73% in those without the mutation. However, the degree of statin intolerance was not significantly affected by the presence of the SCLO1B1 mutation, with 22% in mutated vs. 25% in non-mutated.
• Men FH-, the presence of the SCLO1B1 mutation led to greater difficulty in reaching the target (14% failed compared to 8% without the mutation). However, there was little difference in statin intolerance between those with and without the mutation (14% vs. 19%, respectively).
• Women FH- showed a similar rate of target achievement regardless of SCLO1B1 mutation (approximately 20% failing). However, the presence of the SCLO1B1 mutation significantly increased statin intolerance, with 50% of mutated experiencing intolerance compared to 30% of non-mutated.
Conclusions: Female gender and SCLO1B1 mutation are two independent risk factors both for achieving lipid targets and for the degree of statin intolerance. Further multicenter studies are needed to confirm these trends and improve dyslipidemia management in more vulnerable patient subgroups.

Abstract n SP7_9 - Presenting author**: Sara Soad Sheiban**

Empagliflozin in glycogen storage disease type Ib: a case report

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Aim: Glycogen storage disease type Ib (GSD-Ib) is a rare autosomal recessive disorder of carbohydrate metabolism, caused by mutations in glucose-6-phosphate translocase gene. Neutropenia and neutrophil dysfunction in GSD-Ib is known to result from the intracellular accumulation of 1,5-anhydroglucitol-6-phosphate (1,5-AG6P). Previous studies have shown that off-label treatment with empagliflozin, a sodium glucose co-transporter 2 (SGLT2) inhibitor approved for the treatment of type 2 diabetes, decreases blood levels of 1,5-AG6P precursor, 1,5-anhydroglucitol (1,5-AG), by increasing its urinary excretion. We report the case of an 18-year-old female affected by GSD-Ib presenting with recurrent oral aphthous lesions and long-lasting inguinal abscesses in relation to persisting neutropenia and neutrophil dysfunction, for which she had been chronically treated with subcutaneous granulocyte-colony stimulating factor (G-CSF).
Methods: From October 2020, additional treatment with empagliflozin was administered at the initial dose of 5 mg/day and progressively increased to 20 mg/day. The treatment was never discontinued and is still ongoing at present day. Furthermore, G-CSF dosage was gradually diminished until complete suspension.
Results: We observed a notable reduction in the frequency and severity of the oral and skin manifestations. In the 3 month-period following treatment initiation, blood 1,5-AG levels decreased from 52,9 to 12,2 µg/ml. Concomitantly, neutrophil counts increased from 130 to 880/µl, reaching 1170/µl in October 2023. In September 2024, the patient accepted the positioning of a flash glucose monitoring system in the two week-period prior to medical controls. Time below range (TBR) decreased from 11% (October 2024) to 2% (December 2024). No increases in urogenital infections were reported.
Conclusion: empagliflozin was a safe and effective alternative to G-CSF in the management of neutropenia and neutrophil dysfunction–related manifestations in a subject with GSD-Ib, obtaining amelioration of symptoms without increasing the hypoglycemic risk, thus suggesting a potential application as a first-line treatment in the affected population.

Abstract n SP8_1 - Presenting author**: Claudia Greco**

Relationship between cholesterol accumulation and cellular senescence in an *in vitro* model of human macrophage: Potential protective effects of resveratrol

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Aim: Cholesterol homeostasis seems impaired during ageing, but the interplay between these two processes has only been partially explored. The aim of this study was to investigate the reciprocal relationship between cellular senescence and cholesterol homeostasis, particularly in relation to atherosclerosis, using an in vitro model of human macrophages.
Methods: THP-1 derived macrophages were incubated with either doxorubicin [200nM, 24h], a well-established senescence inducer, acetylated LDL [50µg/ml, 24h] to induce macrophage cholesterol loading, or resveratrol [25µM, 12h], a polyphenol with potential anti-aging properties. Senescence-associated-β-Galactosidase (SA-β-Gal) expression, marker of senescent cells, was assessed by Western blot analyses, intracellular cholesterol by fluorometric assay and Sirt1 gene expression by RT-qPCR.
Results: Doxorubicin incubation had no significant impact on intracellular cholesterol levels ($p>0.05$ vs basal) but markedly increased SA-β-Gal expression (+78% vs basal, $p<0.0001$). acLDL caused a significant increase in intracellular cholesterol levels (+45% vs basal, $p<0.01$) which, interestingly, was paralleled by a significant increase in SA-β-Gal expression (+52% vs basal, $p<0.0001$). Co-incubation of doxorubicin with acLDL further enhanced SA-β-Gal expression (+27% vs. acLDL alone, $p<0.01$). Resveratrol induced a significant reduction of intracellular cholesterol content both in untreated cells (-28% vs basal, $p<0.01$) and in acLDL-loaded macrophages (-29% vs acLDL, p<0. 001); interestingly, ABCA1-mediated cholesterol efflux was significantly improved after resveratrol incubation (+31% vs. acLDL-loaded macrophages, $p<0.0001$), suggesting an increase in cholesterol efflux as a possible mechanism for the anti-atherosclerotic activity of resveratrol. Further strengthening the link between cellular cholesterol metabolism and senescence, acLDL incubation significantly reduced Sirt1 expression (-30% vs basal, $p<0.01$), which was in turn restored by resveratrol (+23% vs acLDL, $p<0.05$).
Conclusion: These findings reveal a strong link between macrophage cholesterol accumulation and cellular senescence and support a possible modulation exerted by resveratrol, thus suggesting cellular cholesterol metabolism as a possible pharmacological target to counteract negative effects of age-related cardiovascular diseases.

Abstract n SP8_2 - Presenting author**: Alessia Rubino**

Metabolic adaptations during feeding associate with phenotypic changes of neutrophils in circulation

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Background and aim: Feeding promotes the development of immune-inflammatory pathways. While this is well described in chronic pathological conditions, it is less clear if every time we eat inflammatory pathways, unique to a specific immune cell type, are activated. Here, we sought to find surrogate indicators of a cell-specific activation that emerge in the circulation during feeding.
Methods: In C57Bl/6j mice we characterized both the metabolic profile (inverse calorimetry, glycemia, insulinemia and triglyceridemia) and the blood immunophenotype (to detect cell-specific markers of leukocytes by flow-cytometry), either in prandial state (feeding a chow diet) or during two hours of refeeding ad libitum after fasting. We also sought to find enrichment of plasma proteins (by untargeted proteomics) that could represent surrogate indicators of immune cell-specific activation (by pathway clustering analysis) during refeeding.
Results: Chow feeding, which maintained higher prandial glycaemia, insulinemia and triglyceridemia compared to fasting, did not induce significant change in the immunophenotype, except for a tendency towards a higher abundance of CD19+ B cells. However, during re-feeding program, where glucose and triglycerides levels increased by two-to-three times more versus fasting unmasked a prominent increase in the blood count of Ly6G+ neutrophils, (which increased one-fold compared to fasting). Of note, the counts of other leukocytes (CD3+T, CD19+ B cells and Ly6c+ monocytes) did not change. Plasma proteomics revealed enrichment of immune pathways that connects with neutrophils activation and extra-vasation.
Conclusions: Our data suggest an innate, but acute, control of neutrophils in response to re-feeding. Further studies are needed to better understand the underlying mechanisms and the effect of more caloric diets.

Abstract n SP8_3 - Presenting author**: Giosiana Bosco**

Evaluations of metabolic and innate immunity profiles in subjects with familial hypercholesterolemia with or without subclinical atherosclerosis

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Aim: Familial hypercholesterolemia (FH) is a genetic condition characterized by high low-density lipoprotein cholesterol (LDL-C). The presence of risk modifiers could promote the atherosclerotic injury beyond LDLC. Our aim was to evaluate metabolic and innate immunity profiles in FH subjects with or without subclinical atherosclerosis.
Methods: In this cross-sectional observational study, we evaluated 211 genetically confirmed FH subjects on LDLC target and without cardiovascular diseases. Biochemical analyses, LDL-C burden (LCB) calculation and vascular profile evaluation were obtained from all subjects. Study population was divided into two groups according to subclinical atherosclerosis: the subclinical atherosclerosis (SA) group and non-subclinical atherosclerosis (NSA) group.
Results: SA group had higher LDL-C at diagnosis (288.35±24.52 vs 267.92±23.86, $p<0.05$) and LCB (13,465.84±3617.46 vs 10,872.63±3594.7, $p<0.001$) than NSA group. SA group had higher white blood cell count (WBCC, 6.9±1.66 vs 6.1±1.16), neutrophil count (NC, 4.2±1.3 vs 3.6±1.11), monocyte count (MC, 0.8±0.2 vs 0.4±0.1), triglyceride to high-density lipoprotein ratio (TG/HDL, 1.73±0.72 vs 1.45±0.69), triglyceride-glucose index (TyG, 8.29±0.35 vs 8.01±0.33) than NSA group (p value for all <0.01). Multivariate logistic regression analysis showed that LCB ($p<0.01$), WBCC ($p<0.01$), NC ($p<0.05$), MC ($p<0.05$) were associated with subclinical atherosclerosis. Simple linear regression analyses showed that LCB was associated with WBCC, NC, MC (p value for all <0.01).
Conclusion: An increased LCB and an impaired innate immunity profile were found in FH subjects with subclinical atherosclerosis and they were independently associated with atherosclerotic injury. LCB could modulate the innate immunity profile.

Abstract n SP8_4 - Presenting author**: Rosario Luigi Sessa**

Pharmacological intervention to target the pro-calcific phenotypic drift of myeloid cells: a pilot study

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Aims: Myeloid calcifying cells (MCCs), defined as monocytes expressing osteocalcin (OCN), have been shown to contribute to vascular disease in diabetes, while GLP1-RA improve cardiovascular outcomes in T2D. We hypothesize that treatment with GLP1-RA might impact on MCC, as a possible novel mechanism of cardiovascular protection.
Methods: In this prospective study, we measured circulating MCC levels in people with T2D treated with metformin and starting (group A, n=10) or not starting (Group B, n=34) a GLP1-RA therapy. Peripheral blood mononuclear cells (PBMC) were isolated from blood samples collected at baseline, 1 week (T1) and 3 months (T2) after enrollment and CD14+/OCN+ levels were evaluated by flow cytometry. PBMC from healthy volunteers (n=10) were also isolated and incubated in vitro for 24h with metformin (1 mmol/l) or exenatide-4 (10 nmol/l) and MCC levels were assessed by flow cytometry.
Results: Compared to baseline, CD14+/OCN+ cells significantly decreased at T1 in both groups ($p<0.05$ vs baseline), with a higher median [25th-75th percentile] reduction observed in Group A than in Group B (-53.1% [-79.3; -23.6] vs -16.8% [-49.0; -1.9], $p=0.038$). No further significant changes were observed in both groups from T1 to T2. In the in vitro study, CD14+/OCN+ cells significantly decreased after treatment with metformin (-70%±55,8%, $p=0.0001$), but not after treatment with GLP1-RA (-23%±18,6%, $p=0.114$).
Conclusions: Our data show an acute impact of GLP1-RA to decrease MCC levels in vivo. However, the negative results of the in vitro study suggest that such effects might not be mediated by a direct action of GLP1-RA on PBMCs, rather by pleiotropic actions yet to be investigated. On the contrary, a direct action of metformin on myeloid cells to decrease a pro-calcific drift can be hypothesized.

Abstract n SP8_5 - Presenting author**: Anna Colomba**

The emerging role of Left Atrial Strain in cardiovascular risk stratification for multiple myeloma patients undergoing carfilzomib therapy

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Objective: Carfilzomib (CFZ) is a proteasome inhibitor used in the treatment of multiple myeloma (MM) known for its cardiotoxic adverse events. Cardio-Oncology guidelines emphasize cardiovascular risk assessment during cardiotoxic therapy, with echocardiography as the first-line imaging technique. Evaluations typically include left ventricular ejection fraction (EF) and global longitudinal strain (GLS); left atrial strain (LAS), not currently included in the definition of cardiotoxicity, is emerging as a potential marker of cardiac dysfunction. Recent studies highlight LAS in early myocardial damage detection and as a mortality predictor in cancer patients, but its role in CFZ-induced hypertensive events in MM remains unclear. This study explores LAS as a predictor of CFZ-related hypertensive adverse events in MM patients, with or without pre-existing hypertension.
Design and method: 125 MM patients undergoing CFZ treatment were recruited at the Hypertension Centre, "Città della Salute e della Scienza" in Turin. Baseline assessments included medical history, clinical examination, office blood pressure measurement, 24-hour ambulatory blood pressure monitoring (ABPM), Pulse Wave Velocity (PWV), ECG, and transthoracic echocardiography (TTE). LAS values were analysed using Philips QLAB software. Patients were monitored for hypertensive events during CFZ therapy.
Results: Hypertensive events occurred in 52% of the population, primarily worsening of known arterial hypertension. LAS conduit was significantly worse in hypertensive vs. normotensive patients (-15.1 [8.32] % vs -21.0±7.59 %, p=0.002). In the normotensive population, LAS acted as a predictor of adverse hypertensive events (OR 2.37 [1.02; 5.50]). In the general population analysis LAS conduit was significantly reduced in the subgroup affected by hypertensive events (-16.2 [-20.75; -12.65] % vs. -20.8 [-26.3; 15.4] %, p=0.006); combined with variables such as PWV and Blood Pressure Variability at ABPM, LAS was able to predict risk of occurrence of hypertensive events during treatment (OR 0.96 [0.92-1.00]).
Conclusion: LAS conduit alteration is associated with increased risk of adverse hypertensive events during CFZ therapy. Its integration in current cardiovascular evaluation protocols dedicated to normotensive MM patients could be useful to identify early myocardial damage and allow better risk stratification in candidates for cardiotoxic therapies.

Abstract n SP8_6 - Presenting author**: Donatello Marziliano**

Glico-metabolic dysfunction relates to basal immune response but not with the outcome in patients with endocartitis

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Aim: The triglyceride-glucose (TyG) index is a novel marker of metabolic dysfunction based on glucose and triglyceride levels. This study investigates whether the TyG score can predict adverse clinical outcomes in patients with endocarditis or related to immune-dysfunction.
Methods: We conducted a preliminary analysis on 28 consecutive patients admitted with a diagnosis of endocarditis (14 males, mean age 61.15±14.95 years). Baseline evaluations included comprehensive blood tests, clinical assessment, and echocardiography upon admission. These parameters were reassessed at 7 days. Mortality was evaluated at discharge and one-year after, with survival measured from the day of admission. Statistical significance was set at $p<0.05$.
Results: The median survival was 164 days the median hospitalization duration was 20 days. Fourteen patients (50%) died during follow-up (median survival: 50 days), with 4 deaths occurring during hospitalization and the remainder in rehabilitation settings. Deceased patients showed significantly lower hemoglobin and monocyte counts and higher respiratory rates upon admission. No significant difference in basal TyG scores was observed between survivors and deceased patients. However, the TyG score correlated positively with gamma globulin percentage (r=0.40), calcium (r=0.37), lactates (r=0.42), mean arterial pressure (r=0.41), and systolic blood pressure (r=0.38), and inversely with HDL cholesterol (r=-0.66). These correlations were stronger in deceased patients, particularly with gamma globulins (r=0.60), calcium (r=0.66), and HDL cholesterol (r=-0.69).
Conclusions: Metabolic dysfunction, as assessed by TyG index, is associated with baseline immune and clinical parameters in patients with endocarditis but does not appear to predict mortality. This highlights the complex interplay between metabolic and immune systems in endocarditis. However, the small sample size and short follow-up period limit the generalizability of the findings. Larger multicenter studies are warranted to validate these preliminary results.

Abstract n SP8_7 - Presenting author**: Cristina Cargiolli**

Neutrophil-to-lymphocyte ratio at discharge predicts short and mid-term postoperative mortality in a cohort of elderly patients undergoing surgical treatment of femur fracture

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Aim: We aimed to identify biomarkers to aid risk stratification in elderly patients undergoing surgical treatment of hip fracture.
Methods: We consecutively enrolled n=147 elderly patients who underwent surgical treatment of traumatic femur fracture. All patients underwent a complete clinical-biochemical assessment at admission and at discharge, including comorbidities assessment at admission (CIRSc, BADL, IADL, CFS, social context) during hospitalization. Prognostic data were collected for each patient at 7 days and 1, 3, 6, 9 months post-discharge.
Results: Our cohort reflected a pre-frail population (mean age 85.2, CIRSc 1, CFS 5). We stratified subjects based on their survival status. Only the number of medications (p=0.015), and the neutrophil-to-lymphocyte (NLR) at discharge (p=0.004) were higher in the deceased. Accordingly, we stratified subjects based on the median value of NLR or at discharge (4.09). Subjects with NLR at discharge above the median value had a longer duration of hospitalization (8 vs 7 days, p=0.01) and delirium (4 vs 2 days, p=0.02), higher maximum PCR during hospitalization (13 vs 9 mg/dL, p=0.27), a reduced fT3/fT4 ratio (1.4 vs 1.7, p=0.049), a worse CIRSc (2 vs 1, p=0.11). Higher NLR at discharge identified a higher risk of post-discharge mortality at 9 months (OR 3.4, 95% CI 1.4-7.9, p=0.005) and at any time point (p<0.05), also after adjustment for confounders. This trend was confirmed also using NLR as linear variable: for each increase (1 unit) in NLR, the mortality risk was 25% higher (p=0.017).
Conclusions: Elevated NLR at discharge, a simple, inexpensive, easy-to-interpret biomarker, identifies an inflammatory phenotype at high risk of poor prognosis in the short-medium term independently of the individual's degree of frailty.

Abstract n SP8_8 - Presenting author**: Alfonso Ferrara**

Immune-mediated mechanisms of post-ischaemic cardiac remodeling

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Introduction: Cardiac remodeling after myocardial infarction is a complex process of altering myocardial architecture that can lead to ventricular failure. Inflammation and the immune response play a crucial role in this sophisticated process.
What we know about post-AMI cardiac remodeling is that it occurs in two main stages:
- A first inflammatory phase mediated by ly6Chi monocytes in the mouse (corresponding to human CD14+ CD16- monocytes which peak at 3 days).
- A second phase of cellular repair mediated by ly6Clo monocytes in the mouse (corresponding to human CD14+ CD16+ monocytes which peak at 5 days).
It has been demonstrated by the study of Atsushi et Al. that the switch between the two phases is regulated by dendritic cells: comparing mice with depletion of these cells and control mice, in the former, their lack caused an unfavorable remodeling and left ventricular dysfunction. This was accompanied by a prolonged inflammatory response and extracellular matrix degradation accompanied by suppression of myocardial neoangiogenesis. This alteration of tissue repair mechanisms was associated with increased infiltration of M1 inflammatory monocytes and, conversely, reduced recruitment of M2 anti-inflammatory monocytes in the post AMI phase.
Methods: In this study, we will select patients >18 years old, hospitalized for anterior IVA prox and median STEMI with TIMI 3 post-revascularization flow.
Patients with previous MI, already known cardiomyopathy, previous EF <55% will be excluded.
We will take blood samples at time 0 (within 12 hours) or arrival at the UTIC, 24 hours after the previous sample, on the 5th post-IMA day. The samples collected will be processed and subjected to flow cytometry. Cardiac color Doppler ultrasound will be performed within 12 h of arrival at the UTIC, on day 5, and at 12 months for evaluation of contractile function and global longitudinal strain.
Results: Increased M2 monocytes and a low M1/M2 ratio correlate with reduced LVEF probably due to a pronounced pro-fibrotic state, thus demonstrating that M1 and M2 monocyte expression can predict short-term post-STEMI systolic cardiac function.
Conclusions: The results of the 6- and 12-month follow-up will lead to further evaluation elements to clarify whether the inhibition of M2 monocytes could represent a turning point in the treatment of patients with myocardial infarction to prevent the evolution towards heart failure.

Abstract n SP8_9 - Presenting author**: Palma Carlucci**

Corticosteroids and cardiovascular risk in EGPA: Lipids and pressure in focus

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Aim: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic vasculitis often requiring glucocorticoid therapy. This study evaluated the impact of corticosteroids on lipid profile, arterial pressure, and cardiovascular risk (SCORE2/OP) in 33 patients treated at our centre.
Methods: This retrospective observational study included 33 EGPA patients receiving corticosteroids at baseline, with follow-ups at 1 year and 2 years. Lipid parameters (total cholesterol, LDL, HDL, triglycerides) and blood pressure (systolic, diastolic) were analyzed using appropriate statistical methods to assess changes over time. Effect sizes were calculated to evaluate the magnitude of observed changes.
Results: From T0 to T1, LDL ($p=0.032$, $d=-0.836$) and triglycerides ($p=0.048$, $d=-0.747$) significantly decreased, while HDL remained unchanged ($p=0.696$). Between T1 and T2, further reductions were observed in LDL ($p=0.003$, $d=-1.367$) and total cholesterol ($p<0.001$, $d=-1.698$), but triglycerides ($p=0.250$) and HDL ($p=0.619$) showed no changes.
Significant correlations were found between steroid dosage changes and variations in LDL ($r=0.485$, $p=0.004$) and triglycerides ($r=0.395$, $p=0.017$). Non-parametric ANOVA revealed group differences in LDL ($p=0.012$) and total cholesterol ($p=0.003$). Corticosteroid use negatively impacted cardiovascular risk (SCORE2/OP) ($p=0.031$, $d=-0.893$).
Conclusions: Corticosteroid therapy significantly impacts lipid metabolism and increases cardiovascular risk in EGPA patients, with dose-dependent effects on Cholesterol, LDL, triglycerides, and overall cardiovascular risk as measured by the SCORE2/OP. These findings highlight the need for careful cardiovascular risk management in patients undergoing long-term corticosteroid therapy. To mitigate these risks, steroid-sparing strategies should be prioritized, aiming to balance effective disease control with the reduction of long-term cardiovascular complications. Further prospective studies are warranted to refine treatment protocols, enhance cardiovascular risk assessment, and improve patient outcomes.

Abstract n SP8_10 - Presenting author**: Noemi Maggio**

Acute Kidney Injury during Sepsis (SA-AKI): A retrospective analysis of patients hospitalized in an internal medicine department

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Background: Sepsis is a heterogeneous condition characterized by a systemic inflammatory response triggered by the presence of pathogens. Its clinical course is highly variable, potentially progressing to septic shock, multiple-organ-failure (MOF), and death. Among the most feared complications is sepsis-associated acute kidney injury (SA-AKI), which significantly worsens patient prognosis.
Objective of the study: In this study we aimed to evaluate the prevalence of SA-AKI in hospitalized patients, factors predisposing its development, and its correlation with disease severity/outcomes.
Materials and methods: In a retrospective study, we analyzed the medical records of 1,283 patients consecutively hospitalized between January 2022-December 2023 at the Internal Medicine Unit of the University Hospital of Messina. From this cohort, 114 patients (65 men; 79 (IQR 13) years) presenting with sepsis (Sepsis-3 criteria) either at admission/during their hospital stay were selected. Data collected included demographics, hospitalization details (length of stay/discharge/death), and laboratory parameters [full blood count, high-sensitivity C-reactive protein (hs-CRP), procalcitonin (PCT), creatinine, and albumin]. Creatinine clearance (CKD-EPI), neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-lymphocyte-and-platelet ratio (NLP), and platelet-to-lymphocyte ratio (PLR), were calculated. SA-AKI definition was based on creatinine changes within 48 hours (early SA-AKI) or within 7 days (late SA-AKI) of sepsis diagnosis (KDIGO criteria).
Results: 14% of patients developed early SA-AKI, while 23.7% developed late SA-AKI. Mortality was significantly higher among SA-AKI patients (81.5%). Development of SA-AKI was associated with an increased risk of death [OR7.7, $p<0.0001$]. Factors significantly associated with SA-AKI onset included hospital stay length (BETA=-0.205, $p=0.042$), NLP ratio (BETA=-0.473, $p<0.001$), and PCT levels at diagnosis (BETA=-0.206, $p=0.049$). Conversely, no significant correlations were observed with age($p=0.099$), sex($p=0.236$), CKD-EPI ($p=0.186$), hs-CRP($p=0.726$), NLR($p=0.547$). Finally, sepsis development during hospitalization was associated with an increased risk of sAKI (OR2.17, $p=0.11$) and death (OR2.5, $p=0.044$).
Conclusions: Our study underscores the critical impact of SA-AKI on patient outcomes and highlights parameters (i.e., length of hospital stay, PCT levels at the time of diagnosis and NLP ratio) that could guide early identification of more-at-risk patients and intervention to improve prognosis.

Abstract n SP9_1 - Presenting author**: Francesco Di Giacomo Barbagallo**

Prevalence of extremely elevated Lp(a) levels in patients attended at a hospital lipid unit

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Background and aims: The development of treatments capable of reducing circulating Lp(a) levels has increased interest in the clinical significance of this lipid alteration and the prevalence of conditions that might be considered risky and therefore treatable At the Vascular and Metabolism Medicine Unit - Internal Medicine Department of the Sant Joan University Hospital, Reus (UVASMET), we have been evaluating Lp(a) levels in all patients attending for several decades. This study aims to evaluate the prevalence of hyper-Lp(a) among patients attending the lipid unit in the past two years, focusing on those with metabolic disorders and elevated cardiovascular risk and to assess their achievement of recommended LDL cholesterol targets.
Methods: We analyzed data from 1755 patients (mean age 56±19 years; 44.4% women), where Lp(a) was measured in nmol/L. Patients were grouped based on their Lp(a) levels, with specific attention to those with levels between 240 and 430 nmol/L and those exceeding 430 nmol/L. LDL cholesterol values were analyzed to evaluate the proportion of patients achieving recommended targets based on their cardiovascular risk profiles.
Results: Among the entire cohort, 608 patients (35%) had Lp(a) levels exceeding 120 nmol/L. Of these, 216 patients had Lp(a) levels between 240 and 430 nmol/L, and 49 patients had levels above 430 nmol/L.
In the group with Lp(a) between 240 and 430 nmol/L, 38 patients were classified as very high risk, and 78 as high risk. Whitin those at very high risk, only 25.4% achieved the target of LDL <55 mg/dL. Similarly, in the high-risk category, just 17.2% reached the LDL target of <70 mg/dL. For patients with Lp(a) >430 nmol/L, 20 were classified as very high risk, and 11 as high risk. In this group, 20% of the very high-risk patients achieved LDL <55 mg/dL, while 18.2% of high-risk patients reached LDL <70 mg/dL.
These findings highlight a failure to meet LDL targets in a substantial proportion of patients, particularly in the very high-risk category.
Additionally, we observed that 48% of patients with Lp(a) between 240 and 430 nmol/L, and 60% of those with Lp(a) >430 nmol/L, had documented atherosclerotic cardiovascular disease (ASCVD).
Conclusions: The prevalence of high Lp(a) levels is significant in this cohort, and these concentrations are strongly associated with atherosclerotic cardiovascular disease. However, a substantial proportion of patients fail to meet recommended LDL cholesterol targets, especially in the very high-risk category. These findings emphasize the need for more aggressive lipid-lowering strategies and tailored interventions to optimize cardiovascular risk management in this population.

Abstract n SP9_2 - Presenting author**: Daniele Pozzoli**

Evaluation of diagnostic accuracy of extreme cardiovascular risk definitions in acute coronary syndrome patients

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Aims: In 2022, the European Society of Cardiology published a consensus paper with six definitions of extreme cardiovascular (CV) risk. The gold standard for secondary prevention is definition 2: two cardiovascular events within two years. Commonly used alternative definitions are ACS combined with peripheral or polyvascular disease (definition 3), and ACS with multivessel coronary artery disease (definition 4). This study aimed to evaluate the diagnostic accuracy of definitions 3 and 4 compared to the gold standard in ACS patients.
Methods: The study included 1061 ACS patients admitted to the intensive cardiac care unit (ICCU) of our hospital between 2014 and 2020. The primary composite outcome was the time to the first ischemic event (myocardial infarction, stroke, or peripheral artery event) or CV death. Follow-up data were updated in June 2021, with events recorded within the first two years post-diagnosis.
Results: Of the 1061 ACS patients, 225 (21%) experienced the primary composite outcome, with a higher incidence in those meeting the criteria for definitions 3 and 4. Multivariate analysis showed a significant increased risk only for definition 4 (HR 1.44, p=0.031), while the risk for definition 3 was not significant (HR 1.31, p=0.114). When definitions 3 and 4 were compared to the gold standard (definition 2), both had poor predictive performance: definition 3 had sensitivity of 23.5%, specificity of 87.5%, and positive predictive value (PPV) of 35.7%, while definition 4 had sensitivity of 25.5%, specificity of 85.3%, and PPV of 32.1%. Both correctly classified 73% of patients.
Conclusion: Among the extreme CV risk definitions, ACS with multivessel coronary artery disease (definition 4) most effectively identifies patients at risk for early recurrence. However, both definitions had higher specificity than sensitivity, highlighting limitations in detecting all high-risk individuals. Refining these criteria is essential for improving prognostic accuracy and guiding targeted interventions.

Abstract n SP9_3 - Presenting author**: Filippo Egalini**

A pilot study on dyslipidemic patients with family history of early cardiovascular events: does coronary CT scan improve CV risk stratification?

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Aim: A family history of early cardiovascular disease (e-CVD) [before 55 and 60 years in men and women, respectively] modifies future CVD risk, nearly doubling the probability of developing coronary artery disease. Coronary CT angiography (CCTA) is a useful, non-invasive tool for detecting coronary atherosclerotic plaques (CAPs). Based on CCTA data, we aimed to reclassify the CV risk of subjects with dyslipidemia managed in primary prevention and a family history of e-CVD.
Methods: Individuals with dyslipidemia and a family history of e-CVD were retrospectively enrolled in two lipid clinics in Northern Italy ("City of Health and Science" Hospital of Turin and "Azienda Ospedaliera Universitaria Integrata" of Verona). Subjects with established CVD, age ≥70 years, genetically confirmed monogenic familial hypercholesterolemia (FH), diabetes, or kidney failure were excluded. Lipid profile, smoking status, BMI, and comorbid hypertension were recorded. All subjects had undergone CCTA and subsequently an invasive coronary angiography (ICA) if a ≥50% or critical stenosis was detected.
Results: The study included 20 individuals (10 women) classified as high CV risk. The mean age (±SD) was 51.8±8.5 years, mean untreated LDL-c 222.7±47.3 mg/dl, and mean Lp(a) 66.4±51 mg/dl. CCTA detected at least 1 CAP and critical CAPs in 14 (70%) and 6 (30%) subjects, respectively. ICA confirmed critical CAPs in 5 patients who underwent percutaneous coronary intervention with drug-eluting stent placement, anti-platelet treatment, and lipid-lowering therapy intensification.
Conclusions: This retrospective pilot study suggests that a family history of e-CVD is a major CV risk per se, even in the absence of FH or high Lp(a). CCTA showed a relatively high prevalence of critical CAPs that needed stent positioning and reclassified the CV risk of most patients, leading to treatment intensification. The implications of these findings require further investigation.

Abstract n SP9_4 - Presenting author**: Daniele Giannini**

Individual cardiovascular risk (CVR) assessment based on the SCORE2 and 2021 ESC guidelines using the validated web-based app www.humtelemed.it

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Aim: In 2022, we introduced a web application, www.humtelemed.it, based on the SCORE2/SCORE2-OP model and 2021 ESC Guidelines risk charts, to simplify CVR assessment. The application has recently been validated with a peer-reviewed published study, and we are reporting the first primary analyses of the dataset.
Methods: We performed a descriptive analysis based on the app data set; it has reached over 17 thousand accesses. Complete data of 7317 40-year-old or older individuals were available.
Results: The mean age was 59.4±11.8 years (male 55.3%). The mean BMI was 26.4±8.5. Actual smokers and past smokers were 20% and 17.3%, respectively; 90% were diabetics, 16% reported PAD, (plaque detection), and 46.4% were hypertensive. The mean systolic BP and diastolic BP, were 127.8±14.1 mmHg and 78.2 9.5 mmHg, respectively. The mean total cholesterol was 199.3±42.7 mg/dL, the mean HDL-C was 57.1±15.6 mg/dL, mean of triglycerides was 100 mg/dL (IQR 75-138 mg/dL); the mean LDL-C was 118.7±51.7 mg/dL and the mean non-HDL-C was 142.1±41.6 mg/dL. The median SCORE2 (or SCORE2-OP) was 6% (IQR 3-10%). The application classified 21.9%, 38%, 39.3%, and 0.8% patients into low-moderate, high, very high and extreme CV risk, respectively. In the overall sample, a risk-based LDL-C at goal was found only in 11.2%.
Conclusions: Our web application, was first designed to assist occasional users and busy clinicians in assessing individual CVR. It may also be considered a reliable epidemiological data source. Analysing the trends of the demographic, anthropometric, metabolic and therapeutical patterns in the general population is fundamental to asses CVR. Our data showed that most of the users had high and very high CVR with scarce CVR factor control, particularly LDL-C, underlining the necessity to increase CV prevention activity.

Abstract n SP9_5 - Presenting author**: Umberto Capece**

Differences between Friedewald and Martin Hopkins equations for LDL estimates and consequent effects on LDL-C target achievement in a diabetic population

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Introduction: Concordance of LDL-C estimating equations with direct enzymatic assay is lower in diabetes. Previous studies have demonstrated that the Martin-Hopkins (MH) equation provides better concordance than the Friedewald (F) equation. In our prior analysis of a population of inpatients, we found that LDL-C target achievement declines progressively in higher-risk categories, with only 32.1% of diabetic patients reaching their LDL-C targets.
Methods: Retrospective real-world data were extracted from the Hospital Information System using automated data extraction strategies and stored in a patient-centered repository (the Dyslipidemia Data Mart). Patients were excluded if triglycerides were >400 mg/dl. LDL-C was calculated using both the MH and F equations, and Pearson correlation was performed. Differences in LDL-C (ΔLDL-C) between the two equations were calculated for the entire population, as well as the diabetic and non-diabetic subgroups. LDL-C target achievement was assessed based on the 2019 ESC/EAS guidelines.
Results: The Pearson correlation coefficient between MH and F equations was 0.99 ($p<1x10-16$). The mean LDL-C was higher when calculated using MH compared to F. ΔLDL-C was 2.66 mg/dl, 2.16 mg/dl and 3.78 mg/dl ($p<0.001$) for the entire population, non-diabetic subgroup and diabetic subgroup, respectively. Overall, on-target patients were 35.8% with MH compared to 38.9% with F. The percentage of patients on-target (according to F) switching to off-target (according to MH) was significantly higher in diabetics compared to non-diabetics (5.1% vs 2.8%, $p<0.001$). Distance-to-target (DTT) was 21.8 mg/dl with MH and 18.1 mg/dl with F in patients with diabetes, while in non-diabetics was 11.9 mg/dl compared to 9.7 mg/dl respectively. The increase in DTT observed comparing MH vs F was higher in the diabetic subgroup than in non-diabetics (3.8 mg/dl vs 2.2 mg/dl, $p<0.001$).
Conclusions: Cardiovascular risk management is pivotal in diabetes and the methodology for LDL-C estimation could have a significant impact on LDL-C target achievement and therapeutic choices.

Abstract n SP9_6 - Presenting author**: Anna Boccali**

Lipoprotein(a) levels in chronic kidney disease: results from a single-center cross-sectional study

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Aim: Both lipoprotein(a) and chronic kidney disease (CKD) are cardiovascular risk factors. Several observational studies have explored the link between circulating Lp(a) levels and CKD, showing inconsistent results. In addition, it remains uncertain as to whether an interdependence exists between Lp(a) and CKD towards atherosclerosis. This study aimed to investigate 1) the correlation between circulating Lp(a) levels and estimated glomerular filtration rate (eGFR) within CKD range (i.e., <60 ml/min/1.73 m^2) and 2) to evaluate a possible joint impact of Lp(a) and CKD on carotid atherosclerosis.
Methods: Inpatients referring to an Internal Medicine Unit were consecutively recruited. Lp(a) levels were measured by an isoform-dependent biochemical test. The CKD-EPI formula was used to calculate eGFR and CKD was classified according to K-DOQI criteria. Carotid atherosclerosis was assessed by high-resolution ultrasonography, measuring maximum intima-media thickness (maxIMT) for each carotid vessel.
Results: One hundred patients (mean age 78.1±8.6 years old, M%/F% 76/24) were enrolled. Mean Lp(a) level was 30 mg/dl. Mean eGFR was 31±14.2 ml/min/1.73 m^2, with 39%, 48%, and 9% of patients having stage III/IV and V CKD, respectively. Median maxIMT was 2,6 (1,72-3,3) mm. No significant correlation was observed between Lp(a) levels and eGFR in the entire study population, with comparable Lp(a) levels across the K-DOQI groups. In addition, both Lp(a) and eGFR proved to be independent predictors of maxIMT (Lp(a): β=0.207, p=0.036; eGFR: β=-0.287, p=0.019), suggesting their independent contribution to atherosclerosis.
Conclusions: Lp(a) levels and GFR were not correlated and were independent predictors of carotid atherosclerosis. These results highlight 1) that the distribution of Lp(a) levels in CKD is almost comparable to that observed in the general population, and 2) that there is the need of monitoring Lp(a) levels in Internal Medicine wards, regardless of concomitant cardiovascular risk factors, to improve cardiovascular risk stratification and management.

Abstract n SP9_7 - Presenting author**: Aurora Merolla**

Low high-density lipoprotein cholesterol, but not high low-density lipoprotein cholesterol, associates with systemic metabolic alterations

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Aim: Dyslipidemia encompasses various forms of lipid abnormalities and represents a central component of metabolic syndrome. The relationship between dyslipidemia subtypes and broader metabolic profiles is poorly characterized in modern populations. This study provides a comprehensive metabolic characterization of patients presenting with distinct dyslipidemic patterns – low high-density lipoprotein cholesterol (HDL-c) and elevated low-density lipoprotein cholesterol (LDL-c) – at a dedicated tertiary-center outpatient clinic.
Methods: Patients evaluated at the Metabolic Health Clinic of San Raffaele Hospital, Milan, between January 2023 and October 2024, were included. Medical history, anthropometrics (i.e. body mass index, BMI, and waist circumference), serum lipids and liver enzymes were recorded. Patients with low HDL-c or high LDL-c, as defined according to current guidelines, were compared to patients with normal values. Network analysis identified patient distinct metabolic clusters.
Results: A total of 496 individuals were included. Patients with low HDL-c levels (n=193, 38.9%) exhibited higher BMI (28.6 vs 25.6 kg/m^2, p<0.001), waist circumference (100.0 vs 94.0 cm, p<0.001), ALT levels (28.0 vs. 23.0 U/L, p<0.001), and triglycerides (146.0 vs. 99.0 mg/dL, p<0.001), and a greater prevalence of fatty liver disease (33% vs. 21%, p 0.006) and arterial hypertension (51% vs. 39%, p 0.012) than those with normal HDL-c levels. HDL-c showed significant inverse correlations with both BMI (R coefficient -0.272, p<0.0001) and waist circumference (R coefficient -0.325, p<0.0001). Network analysis highlighted strong associations among HDL-c, triglycerides, ALT levels, BMI, and waist circumference. Conversely, high LDL-c levels, found in 382 (77%) patients, showed no association with metabolic parameters.
Conclusions: Low HDL-c was associated with obesity, central adiposity, hypertriglyceridemia, and fatty liver disease. In striking contrast, LDL-c appears to be independent of these metabolic alterations. These findings underscore the interconnectedness of HDL-c with the metabolic landscape, while emphasizing the importance of assessing LDL-c levels regardless of patient anthropometrics and metabolic phenotype.

Abstract n SP9_8 - Presenting author**: Alessia Riccio**

Association between IGF-1 and clinical features and outcomes in hospitalised patients

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Aim: Ageing is a complex physiological process that involves several changes in clinical parameters and physiological responses. Among these factors, Insulin-like Growth Factor 1 (IGF-1) plays a crucial role in the regulation of metabolism and the maintenance of muscle mass. The study aimed to explore the correlation of IGF-1 with several clinical features and outcomes in multimorbid elderly patients hospitalised in the Internal Medicine department enrolled in the Clinical Outcomes in HOspitalized patients Receiving Treatment at San Andrea Hospital (COHORTS) study.
Methods: Participants (n=190, 108 men and 82 women) were divided into three groups according to IGF-1 tertile levels. The biological age was calculated by the PhenoAge, including nine blood variables: albumin, alkaline phosphatase, creatinine, C-reactive protein (CRP), fasting glucose, mean cell volume, red cell distribution width, white blood cell count, and lymphocyte proportion.
The association between IGF-1 and clinical variables and outcomes was analysed by univariate analyses and a logistic regression model.
Results: Patients with lower levels of IFG-1 displayed higher values of age and CRP, and lower levels of fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and albumin. Moreover, in these patients, the rate of dementia (p=0.01) and death (p=0.02) was higher. In a univariate analysis levels of IGF-1 were inversely associated with the length of recovery (p=0.02); patients with lower levels of IGF-1 had a 4-fold risk of death (OR 4.0, 95%CI 1.5-10.2) and 3.9-fold risk of dementia (OR 3.9, 95%CI 1.52-10.03).
Conclusion: IGF-1 could serve as a useful biological marker for predicting recovery time and adverse outcomes in elderly multimorbid patients hospitalized. Further studies are needed to better understand the therapeutic potential of IGF-1 in pathological ageing.

Abstract n SP10_1 - Presenting author**: Beatrice Mattina**

In vivo MTD study of new potential inhibitors of Proprotein Convertase Subtilisin/Kexin 9 (PCSK9)

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Aim: This study aims to determine the *in vivo* safety of newly synthesized PCSK9 inhibitors (MR-compounds). PCSK9 controls peripheral and central cholesterol levels and it plays a crucial role in hypercholesterolemia, being a well-established pharmacological target to treat this pathology, while a possible involvement in the aetiopathogenesis of AD has been postulated. Currently, the available PCSK9i to counteract hypercholesterolemia are very expensive biotechnological drugs and only subcutaneously administrated. Based on these premises, orally bioavailable small-molecules may be a valuable addition to existing treatments.
Methods: After preliminary *in vitro* screening in human hepatocyte and neuroblastoma cells of 30 compounds, 4 compounds were selected to test tolerability and bioavailability *in vivo* in wild-type mice (C57BL/6J) at 12.5mg/kg, 25mg/kg, 50mg/kg, and 100mg/kg for 5 days. MR-532 and MR-533 were administered subcutaneously, while MR-3 and MR-644 both subcutaneously and orally. Body weight and phenotype analysis were assessed daily to evaluate tolerability and macroscopic toxicity. After the sacrifice, hepatic toxicity (histological analysis and ALT activity) and biodistribution (LC-MS/MS) were evaluated.
Results: All doses of compounds were well tolerated (no changes in body weight, food intake, coat; no lethargy was observed). The MR-532 and MR-533 at 100mg/kg did not show elevated levels of ALT activity compared to vehicle (66mU±55, 76mU±127, and 130mU±203, respectively) or inflammatory cell infiltration or necrosis in liver sections (histological analysis). Interestingly, MR-532 and MR-533 were detected at all doses in plasma (261-318nM; 159-192nM), liver (522-1063pmol/g; 2824-3135mol/g) and brain (513-779pmol/g; 457-380mol/g), respectively, without a dose-dependent trend. MR-3 and MR-644 analyses are in progress.
Conclusion: All tested compounds proved to be safe. MR-532 and MR-533 showed plasma and hepatic bioavailability. They can reach the CNS, although at low concentrations. Further investigations are needed to understand how the route of administration affects biodistribution and to evaluate the efficacy of these compounds in cardiovascular and neurodegenerative diseases.

Abstract n SP10_2 - Presenting author**: Giulia Cincotto**

Clinical implementation of bempedoic acid in blood lipid management: Real-world data from an Italian lipid clinic

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Objective: This study aims to evaluate the real-world clinical effectiveness and tolerability of bempedoic acid (BA) in an Italian cohort of dyslipidemic patients.
Methods: A retrospective analysis was conducted on patients from the Dyslipidemia Center at Niguarda Hospital, Milan, prescribed BA between April 2023 and October 2024. Lipid profiles were assessed at baseline and at 3, 6, and 12 months post-BA initiation. Data included adherence, lipid changes, and adverse events.
Results: Of 160 patients (82 men, 78 women; mean age 66.0±11.4 years), 122 completed at least one follow-up. According to ESC/EAS guidelines, 76 patients were at high risk, and 84 were at very high risk. Statin intolerance was reported in 97 patients (60.6%), and only 7 (4.4%) met LDL-C targets. BA was prescribed in combination with statins for 85 patients (53.1%), ezetimibe for 119 (74.3%), and PCSK9 inhibitors for 38 patients (23.8%), while it was used as monotherapy in 29 patients (18.1%). LDL-C reductions were 24.9%, 25.7%, and 24.5% at 3, 6, and 12 months, respectively, with a last-follow-up reduction of 24.4%. Differences in effectiveness were observed based on background therapy, with statin-treated patients showing a smaller LDL-C reduction (-20.5% vs -32.2% in non-statin-treated). The highest LDL-C reduction was -82.7% and the smallest was +39.2%. The 1-year drug discontinuation rate was 6.2%, primarily due to adverse events (4.4%), most commonly musculoskeletal complaints. An increase in uric acid was reported in 5 patients.
Conclusions: BA consistently reduced LDL-C in a real-world setting, with a manageable safety profile. Its effectiveness was influenced by background therapy, demonstrating utility as an adjunctive or alternative option for complex dyslipidemia, particularly in statin-intolerant patients. These findings support BA's role in achieving LDL-C targets in specialized lipid clinics.

Abstract n SP10_3 - Presenting author**: Marco Bellomare**

Pleiotropic effects of inclisiran on arterial structural and functional parameters

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Aim: Inclisiran is the latest PCSK9 inhibitor available for reducing LDL-cholesterol. Its effects on arterial structural and functional properties are not yet known. The purpose of our study is to longitudinally evaluate these properties in patients starting therapy with this new drug for dyslipidemia.
Methods: Prospective longitudinal study enrolling all patients who started Inclisiran therapy at our hospital. Inclisiran injections were administered at T0, after 3 months, and then every 6 months. Carotid-femoral Pulse Wave Velocity (PWV), carotid Intima-Media Thickness (IMT), and brachial Flow Mediated Dilation (FMD) were evaluated before the first injection, after 6 months (T1) and after 1 year (T2). Data from 15 patients at 1 year were analyzed.
Results: The mean age was 69±7.1 years, 72.7% of the subjects were men and the basal LDL-C was 102.7±49.6 mg/dL, while BP was 140.6±13.3/79.1±6.1 mmHg. 90.9% of patients were in secondary prevention (acute or chronic coronary syndrome). 86.4% were on high-intensity statin therapy and 81.8% on ezetimibe. At the 1 year's evaluation, a significant reduction of LDL-C (49.3±16.4 mg/dL, $p<0.001$) and BP (126.9±10.1/71.2±6.5 mmHg, $p<0.001$) was observed. Among the arterial biomarkers, only PWV showed a significant reduction (from 10.9±2.0 to 9.8±1.4 m/s, $p<0.001$) while the changes in IMT (from 705.9±151.3 to 696.0±202.1 µm, $p=0.333$) and FDM (from 7.5±8.9 a 6.9±8.0%, $p=0.449$) were not statistically significant.
Conclusions: Inclisiran has been confirmed as an excellent LDL-C lowering drug that also significantly reduces PWV. Studies with a larger number of patients are needed to confirm our findings.

Abstract n SP10_4 - Presenting author**: Ilaria Rossi**

High cardiovascular risk patients in primary prevention and stepwise strategy in real life: Economic impact of bempedoic acid therapy in achieving the target

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Background: The guidelines recommend a stepwise approach to improve statin tolerability and reach the target and currently the availability of new therapeutic approaches [PCSK9 inhibitors (PCSK9i) and Bempedoic Acid (BA)] is leading to ambitious LDL-C levels.
Aim: The aim of this study was to assess BA impact on target achievement and on costs for the Italian National Health System.
Methods: We evaluated 151 patients (61% females, mean age 70±10 years) who started BA therapy from March 2023 to September 2024. Only 85 patients in primary prevention with high and very high cardiovascular risk (CVR) were considered eligible for the analysis. All patients reported intolerance to statins or other lipid-lowering therapies (LLT).
Results: 96.5% of patients did not reach LDL-C target, with an average baseline LDL-C of 131±44 mg/dL and distance to target (DTT) of 45%. 20 patients stopped treatment before the follow-up visit (only 6 reported adverse events). At 3 months a mean LDL-C value of 88±26 mg/dl was reached with BA, with a mean reduction of 37%. 26% of patients reached the LDL-C target (mean DTT 31%). Sub-analyses were performed based on LLT: none of the patients treated with BA alone achieved the target; combination therapy with BA+Ezetimibe allowed to reach the target in 9.3% of patients (average LDL-C reduction of 40%); triple therapy (BA+Ezetimibe+low dose of high intensity statin) brought 16.7% of patients to the target. The cost analysis of LLT estimated that BA alone and BA+Ezetimibe cost on average 45-53 and 29-39 euros per year for each percentage point of reduction in LDL-C respectively, while therapy with PCSK9i costs 168-187 euros per year for each percentage point.
Conclusions: In patients with high CVR in primary prevention and intolerant to statins, and therefore potentially eligible for therapy with anti-PCSK9, the use of the stepwise strategy allows to reach the therapeutic goals with an effective cost-effective therapy.

Abstract n SP10_5 - Presenting author**: Giulia Serpente**

Management of hyperlipidemia with pcsk9i in cardiovascular patients: Effectiveness and safety

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Aim: The aim of this study was to evaluate the response of patients with different cardiovascular risk profiles to lipid-lowering therapy (LLT) with monoclonal antibodies targeting PCSK9 (Evolocumab and Alirocumab), in relation to their baseline therapy.
Methods: This monocentric, retrospective study included 164 patients currently followed by the Dyslipidemia Clinic of "D'Annunzio" University. All patients initiated LLT with PCSK9i monoclonal antibodies within the last 5 years: 105 patients (64%) received Alirocumab, and 59 (36%) received Evolocumab. Regarding baseline therapy, 66% of patients on Alirocumab and 68% of those on Evolocumab (overall, 66% of all participants) were already on maximal therapy (statin + ezetimibe) at the start of PCSK9i treatment.
Results: Patients treated with Alirocumab achieved better outcomes (62%) compared to those treated with Evolocumab (56%). Additionally, 72% of patients on Alirocumab underwent more frequent therapy titration and optimization than the 55% of Evolocumab patients. Notably, no cardiovascular events were observed from the initiation of PCSK9i treatment throughout the study period (7 years of follow up).
Conclusions: Our real-world data demonstrate the clinical efficacy and safety of LLT with monoclonal antibodies in cardiovascular patients. Furthermore, the findings underscore the importance of optimized background and combination therapy in achieving LDL-C targets.

Abstract n SP10_6 - Presenting author**: Greta Chiarelli**

Overcoming statin intolerance: Bempedoic acid's impact on LDL-C reduction

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Background: Statins continue to represent the cornerstone in the treatment of hypercholesterolemia. The introduction of ezetimibe and PCSK-9 inhibitors has facilitated the achievement of therapeutic targets set for various risk categories. Despite this, LDL targets are not always reached, particularly in high-risk or very high-risk patients, such as those with familial hypercholesterolemia or statin intolerance. In these cases, bempedoic acid offers a promising supplementary treatment. Bempedoic acid works by inhibiting ATP-citrate lyase, which leads to increased expression of LDL receptors in the liver, thereby enhancing the clearance of LDL particles and reducing LDL-C levels.
Methods: We conducted a real-world observational study to evaluate the efficacy and safety of bempedoic acid in patients with statin intolerance who had not achieved their therapeutic lipid targets. Lipid profiles, liver enzymes, and muscle enzymes were measured both at baseline and after 12 weeks of treatment.
Results: A total of 52 patients were enrolled in the study, with a mean age of 59 years. Of these, 69.2% had hypertension, 42.3% suffered from carotid atherosclerosis and hepatic steatosis, 13.5% were diabetic, and three patients had a history of cardiovascular events. After 12 weeks of treatment with bempedoic acid, a significant reduction in LDL-C was observed (from 134.63±42.083 mg/dl to 85.44±41.846 mg/dl, $p<0.001$). No adverse events were noted, including no significant increases in liver or muscle enzymes. However, an increase in triglyceride levels was observed (from 123.730±50.976 mg/dl to 142.08±72.116 mg/dl). While an increase in creatinine and uric acid levels, commonly reported in the literature, was noted, these changes were not statistically significant in our sample ($p>0.05$).
Conclusions: The preliminary findings suggest that bempedoic acid could serve as a valuable additional therapy for patients who have not achieved their cholesterol targets through other treatments, particularly those intolerants to statins. The absence of adverse events in our patient cohort, although the follow-up period was relatively short, indicates that bempedoic acid is a promising and safe option for lipid management in this patient group.

Abstract n SP10_7 - Presenting author**: Luigi Junior Valletta**

Effectiveness of bempedoic acid therapy in patients' treatment with non-target PCSK9 inhibitors

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Introduction: PCSK9 inhibitors are used in patients who do not reach the therapeutic target corresponding to their cardiovascular risk class. Bempedoic acid could be used especially in patients intolerant to ezetimibe due to IBD. The efficacy of bempedoic acid is evaluated in patients non-target treated for at least 6 months with PCSK9 inhibitors. We recruited 26 patients, 11 males (42.3%), 15 females (57.7%), the average age of 56.1±11.4 years.
Methods: Initial visit (V1): Remote pathological history, evaluating the presence of cardiovascular risk factors. First follow-up (V2): after prescription of BA, monitoring of total cholesterol (TOT-C), HDL, triglycerides (TGL) and LDL-c. Evaluation of uric acid (UA) and eGFR at both visits.
Results: At V1, mean TOT-C values were 196.8±53.1 mg/dl, with mean SCORE of 5.7±3.5% and mean LDL-C values of 121.5±52.2 mg/ dl; at V2 the mean CTOT values were 152.4±65.5 mg/dl, the LDL-c values were 80.5±58 mg/dl; there was a statistically significant reduction of 41.0±56.1 mg/dl in LDL-c (p value <0.05) and CTOT (p value <0.05).

Caratteristiche al basale (V1) e al follow-up (V2)

Variabili	Visita 1	Visita 2	Differenza	valore p
CTOT	196,8	152,4	44.4	0,007*
TGL	110.3	108.1	2.2	0,401
HDL	55.5	51.8	3.7	0,076
LDL	121.5	80,5	41.0	0,005*
Creatinina	0,82	0,86	-0,05	0,07
Acido urico	5.5	5.2	0,2	0,343

Conclusions: The association of bempedoic acid with PCSK9 represents a valid tool for the therapeutic target, resulting in a 20% reduction in LDL-c values and a reduction in cardiovascular risk.

Abstract n SP10_8 - Presenting author**: Fabio Troiano**

Effectiveness and tolerability of bempedoic acid and distance to LDL-target: Real-life data

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Background: Lipid-lowering therapy is a cornerstone in cardiovascular event prevention. Therapy with statins and ezetimibe often fails to reach LDL targets, partly due to poor tolerability.
Objective: To evaluate the effectiveness and tolerability of bempedoic acid (BA) in achieving LDL targets.
Methods: We included 151 patients (39% male, 61% female, mean age 70±10 years, mean BMI 28±5, waist circumference 100±11 cm) who started treatment with BA in March 2023. 89% were in primary prevention, with very high cardiovascular risk (CVR) in 26%, high in 46%, moderate in 20%, and low in 8%. 82% of patients reported intolerance to statins or previous lipid-lowering therapies. About 25% were not on treatment at baseline, mostly at high and very high CVR (73%). 90% of patients were not at target LDL-C levels. 122 patients had an initial evaluation after 1-3 months, and 32 had follow-up at 8-12 months. 26 patients (21%) discontinued treatment for reasons unrelated to drug efficacy or tolerability, due to bureaucratic issues, and only 6 (5%) stopped BA due to adverse events (myalgia, headache, gastrointestinal issues). The mean baseline LDL-C level was 132±42 mg/dl, with an average distance from target of 40%. 74% of patients continued BA therapy at 3 months, reaching a mean LDL-C level of 88±27 mg/dl, with a 35% reduction and an average distance from target of 28%. 36% fully reached the LDL-C target. Subgroup analyses showed that BA monotherapy reduced LDL-C by 34.5%, while combining BA with ezetimibe led to reductions of up to 50%.
Conclusions: Our study confirms that BA is effective and well-tolerated, achieving LDL targets in some dyslipidemic patients, particularly those with low or moderate cardiovascular risk. Despite its favorable tolerability profile compared to statins, BA is hindered by issues related to prescriptibility and market availability, which can impact therapeutic continuity and achievement of LDL targets.

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