SPRING 2026

Spring Meeting Giovani Ricercatori

SID SIGG SIIA SIMI SIPREC SISA

Spring of Minds: dalla genetica all'AI

Rimini 19-21 Aprile 2026

Young investigators meeting

European Atherosclerosis Journal

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SPRING 2026

Carissime Colleghe e Colleghi,

è con grande entusiasmo che vi invitiamo a partecipare all'**XI Edizione dello Spring Meeting Nazionale dei Giovani Ricercatori 2026**, che si terrà dal **19 al 21 aprile 2026** a Rimini. Quest'anno il Congresso si presenta con un tema di straordinaria attualità e rilevanza scientifica: l'intelligenza artificiale, filo conduttore dell'intera manifestazione.

L'edizione 2026, dal sottotitolo "**Spring of Minds: dalla genetica all'AI**", intende esplorare l'impatto crescente delle tecnologie digitali e delle strategie computazionali sulla ricerca cardiometabolica. Sarà un'occasione unica per discutere come l'AI stia trasformando la nostra capacità di interpretare dati complessi, comprendere i meccanismi biologici e sviluppare approcci innovativi per la diagnosi e la cura.

Anche quest'anno, il Meeting riunirà le sei Società Scientifiche coinvolte: **SID (Società Italiana di Diabetologia), SIIA (Società Italiana dell'Ipertensione Arteriosa), SIMI (Società Italiana di Medicina Interna), SIPREC (Società Italiana per la Prevenzione Cardiovascolare), SISA (Società Italiana per lo Studio dell'Aterosclerosi) e SIGG (Società Italiana di Geriatria e Gerontologia)**. La collaborazione interdisciplinare tra queste realtà continua a rappresentare la vera ricchezza del Meeting, favorendo un dialogo costruttivo tra ricerca clinica, di base e traslazionale.

Il programma seguirà il format ormai consolidato delle edizioni precedenti, con sessioni dedicate ai più recenti avanzamenti nella ricerca cardiometabolica, arricchite quest'anno da contributi specifici su algoritmi predittivi, intelligenza artificiale spiegabile, medicina di precisione e analisi dei big data. Ampio spazio sarà riservato alle comunicazioni orali, alle presentazioni poster e ai workshop metodologici, con un focus particolare sulle applicazioni pratiche dell'AI in ambito biomedico.

Come sempre, il Meeting offrirà un ambiente dinamico, inclusivo e stimolante, ideale per favorire il confronto tra giovani ricercatori, creare nuove sinergie e promuovere la crescita professionale e scientifica della nostra comunità.

Siamo certi che questa nuova edizione, proiettata verso il futuro della ricerca, rappresenterà un momento di grande ispirazione e innovazione per tutti noi.

Vi aspettiamo numerosi a Rimini per vivere insieme lo Spring Meeting 2026 – Spring of Minds!

Buon lavoro a tutte e a tutti!

Il comitato organizzatore

Domenica, 19 Aprile 2026

12.45-13.45 *Light Lunch*

13.45-14.00 Registrazione dei partecipanti

14.00-14.15 **Apertura lavori**
Vanessa Bianconi (SISA), Lorenzo Da Dalt (SISA), Damiano D'Ardes (SISA), Chiara Pavanello (SISA), Francesco Spannella (SIIA), Valeria Visco (SIIA), Rosa Curcio (SIMI), Mario Daidone (SIMI), Giovanna Gallo (SIPREC), Ludovico Di Gioia (SID), Luca D'Onofrio (SID), Francesco Salis (SIGG), Leonardo Bencivenga (SIGG).

14.15-14.45 **Saluto dei Presidenti**
Alberto Corsini (SISA), Raffaella Buzzetti (SID), Agostino Virdis (SIIA), Dario Leosco (SIGG), Nicola Montano (SIMI), Massimo Volpe (SIPREC)

14.45-16.45 **Sessione 1 – Tecnologia e medicina: sfide e opportunità**
Moderatori: Luca D'Onofrio (Roma), Francesco Spannella (Ancona)

L'impatto della tecnologia "intelligente" nella cura del diabete
- *Sara Coluzzi (Pescara)*

Abbiamo davvero la pressione sotto controllo?
Il Ruolo dei Wearable nel monitoraggio
- *Alessandro Croce (Milano)*

Discussione congiunta
Comunicazioni Orali (n.7)

16.45-17.15 *Coffee Break*

17.15-19.15 **Sessione 2 – Nuovi paradigmi terapeutici per la protezione d'organo e la riduzione del rischio cardiovascolare**
Moderatori: Ludovico Di Gioia (Acquaviva delle Fonti, Bari), Vanessa Bianconi (Perugia)

L'intelligenza dei nuovi farmaci: dalla glicemia alla protezione d'organo
- *Martina Chiriacò (Pisa)*

Strategie e tecnologie farmacologiche per ridurre il rischio residuo
- *Andrea Baragetti (Milano)*

Discussione congiunta
Comunicazioni Orali (n.7)

19.15-20.30 **AperiPoster - Sessioni Poster 01-05**

Sessione Poster 01: *Marta Biolo (Padova); Alessandro Gezzi (Ancona)*
Sessione Poster 02: *Francesco Giglioni (Perugia); Alessia Cipollone (Chieti)*
Sessione Poster 03: *Giovanna Gallo (Roma); Francesco Alfano (Firenze)*
Sessione Poster 04: *Lorenzo Da Dalt (Milano); Elena Levati (Roma)*
Sessione Poster 05: *Rosa Curcio (Taranto); Martina Chiriacò (Pisa)*

20.45 *Cena*

Lunedì, 20 Aprile 2026

08.15-08.30 Registrazione dei partecipanti

08.30-10.30 **Sessione 3 – Genetica ed epigenetica nelle malattie metaboliche: dal meccanismo biologico alla medicina di precisione**
Moderatori: Marco Perrone (Roma), Francesco Salis (Cagliari)

Metabolismo ed epigenetica dell'invecchiamento: dai meccanismi biologici alla pratica clinica
▪ *Luca Tagliafico (Genova)*

La genetica nel metabolismo lipidico: predire gli effetti a lungo termine dei target lipidici
▪ *Alessia Di Costanzo (Roma)*

Discussione congiunta
Comunicazioni Orali (n.7)

10.30-11.00 *Coffee break*

11.00-12.00 **WORKSHOP – Comprendere l'Intelligenza Artificiale nella medicina cardiometabolica: concetti, pratica e valutazione critica**
Comitato workshop: Marco Chierici, Monica Moroni (Fondazione Bruno Kessler, Trento), Elena Olmastroni (Milano), Leonardo Bencivenga (Napoli), Stefano Scotti (Milano)

Il contributo delle scienze omiche nelle malattie cardiovascolari
▪ *Elena Olmastroni e Stefano Scotti (Milano) per conto del gruppo OMIGEN*

Introduzione all'IA in medicina
▪ *Marco Chierici (Fondazione Bruno Kessler, Trento)*

12.00-13.30 *Lunch*

13.30-15.30 **WORKSHOP – Comprendere l'Intelligenza Artificiale nella medicina cardiometabolica: concetti, pratica e valutazione critica**

Dai dati alla modellazione: sessione pratica guidata dallo sviluppo all'interpretazione
▪ *Monica Moroni* e *Marco Chierici (Fondazione Bruno Kessler, Trento)*

Sessione tematica in sottogruppi (Parte 1)
▪ *Monica Moroni* e *Marco Chierici (Fondazione Bruno Kessler, Trento)*

15.30-16.00 *Coffee break*

16.00-18.00 **Sessione 4 – Complicanze internistiche del paziente oncologico**
Moderatori: Leonardo Bencivenga (Napoli), Rosa Curcio (Taranto)

Mismatch tra ricerca preclinica e clinica in cardiooncologia
▪ *Mario Stabile (Bruxelles)*

Oltre il mismatch: la cardiooncologia nella pratica clinica
▪ *Fabrizio Vallelonga (Torino)*

Modelli predittivi di tossicità nel paziente anziano oncologico candidato a terapia sistemica
▪ *Elena Page (Genova)*

Discussione congiunta
Comunicazioni Orali (n.5)

18.00-19.00 **AperiPoster - Sessioni Poster 06-10**
Sessione Poster 06: *Simone Bini (Roma); Ilaria Fucile (Napoli)*
Sessione Poster 07: *Giulio Francesco Romiti (Roma); Sara Coluzzi (Pescara)*
Sessione Poster 08: *Antonio Michele Bussu (Carbonia); Elena Olmastroni (Milano)*
Sessione Poster 09: *Giosiana Bosco (Catania); Ottavia Terenghi (Milano)*
Sessione Poster 10: *Ilaria Rossi (Chieti)*; *Maristella Belfiori (Cagliari)*

20.30 *Cena*

Martedì, 21 Aprile 2026

08.15-08.30 Registrazione dei partecipanti

08.30-10.30 **Sessione 5 – Nuove e vecchie sfide nella prevenzione cardiovascolare: fra avanzamento tecnologico e riscoperta della complessità biologica**
Moderatori: Mario Daidone (Palermo), Damiano D'Ardes (Chieti)

Ruolo dell'AI nella diagnosi della malattia coronarica
▪ *Stefano Benenati (Genova)*

Relazioni tra fragilità e malattie cardiometaboliche
▪ *Pasquale Mone (Campobasso)*

Discussione congiunta
Comunicazioni Orali (n.7)

10.30-11.00 *Coffee Break*

11.00-12.30 **WORKSHOP – Comprendere l'Intelligenza Artificiale nella medicina cardiometabolica: concetti, pratica e valutazione critica**

Sessione tematica in sottogruppi (Parte 2)
▪ *Monica Moroni* e *Marco Chierici (Fondazione Bruno Kessler, Trento)*

12.30-13.30 **Hai spiegato benissimo. Peccato che non ti abbia capito nessuno. (Effetti collaterali della comunicazione ai tempi dell'AI)**
▪ *Davide Gambardella (Rimini)*

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

Comitato organizzatore
Vanessa Bianconi (SISA), Lorenzo Da Dalt (SISA), Damiano D'Ardes (SISA), Chiara Pavanello (SISA), Francesco Spannella (SIIA), Valeria Visco (SIIA), Rosa Curcio (SIMI), Mario Daidone (SIMI), Giovanna Gallo (SIPREC), Ludovico Di Gioia (SID), Luca D'Onofrio (SID), Francesco Salis (SIGG), Leonardo Bencivenga (SIGG).

Relatori e moderatori
Francesco Alfano (Firenze)
Andrea Baragetti (Milano)
Maristella Belfiori (Cagliari)
Leonardo Bencivenga (Napoli)
Stefano Benenati (Genova)
Vanessa Bianconi (Perugia)
Simone Bini (Roma)
Marta Biolo (Padova)
Giosiana Bosco (Catania)
Antonio Michele Bussu (Carbonia)
Marco Chierici (Trento)
Martina Chiriacò (Pisa)
Alessia Cipollone (Chieti)
Sara Coluzzi (Pescara)
Alessandro Croce (Milano)
Rosa Curcio (Taranto)
Lorenzo Da Dalt (Milano)
Damiano D'Ardes (Chieti)
Luca D'Onofrio (Roma)
Mario Daidone (Palermo)
Alessia Di Costanzo (Roma)
Ludovico Di Gioia (Bari)
Ilaria Fucile (Napoli)
Giovanna Gallo (Roma)
Davide Gambardella (Rimini)
Alessandro Gezzi (Ancona)
Francesco Giglioni (Perugia)
Elena Levati (Roma)
Pasquale Mone (Campobasso)
Monica Moroni (Trento)
Elena Olmastroni (Milano)
Elena Page (Genova)
Chiara Pavanello (Milano)
Marco Perrone (Roma)
Giulio Francesco Romiti (Roma)
Ilaria Rossi (Chieti)
Francesco Salis (Cagliari)
Stefano Scotti (Milano)
Francesco Spannella (Ancona)
Mario Stabile (Bruxelles)
Luca Tagliafico (Genova)
Rosa Talerico (Roma)
Ottavia Terenghi (Milano)
Fabrizio Vallelonga (Torino)
Valeria Visco (Salerno)

SPRING 2026

Abstract

Sessioni Orali

Sessione 1 – Tecnologia e medicina: sfide e opportunità

Domenica 19 aprile - ore 14.45-16.45

Moderatori: Luca D'Onofrio (Roma), Francesco Spannella (Ancona)

Sessione 2 – Nuovi paradigmi terapeutici per la protezione d'organo e la riduzione del rischio cardiovascolare

Domenica 19 aprile - ore 17.15-19.15

Moderatori: Ludovico Di Gioia (Acquaviva delle Fonti, Bari), Vanessa Bianconi (Perugia)

Sessione 3 – Genetica ed epigenetica nelle malattie metaboliche: dal meccanismo biologico alla medicina di precisione

Lunedì 20 aprile - ore 11.00-13.00

Moderatori: Andrea Baragetti (Milano), Rosa Curcio (Taranto)

Sessione 4 – Complicanze internistiche del paziente oncologico

Lunedì 20 aprile - ore 16.00-18.00

Moderatori: Leonardo Bencivenga (Napoli), Rosa Curcio (Taranto)

Sessione 5 – Nuove e vecchie sfide nella prevenzione cardiovascolare: fra avanzamento tecnologico e riscoperta della complessità biologica

Martedì 21 aprile - ore 08.30-10.30

Moderatori: Mario Daidone (Palermo), Damiano D'Ardes (Chieti)

Sessioni Poster

Sessione Poster 1 - MASLD, NAFLD and hepatometabolic liver disease

Domenica 19 aprile: 19.15-20.30

Moderatori: Marta Biolo (Padova); Alessandro Gezzi (Ancona)

Sessione Poster 2 - Hypertension, vascular damage and secondary hypertension

Domenica 19 aprile: 19.15-20.30

Moderatori: Francesco Giglioni (Perugia); Alessia Cipollone (Chieti)

Sessione Poster 3 - Lipid disorders, lipoproteins and lipid-lowering therapy

Domenica 19 aprile: 19.15-20.30

Moderatori: Giovanna Gallo (Roma); Francesco Alfano (Firenze)

Sessione Poster 4 - Atherosclerosis, vascular biology and inflammation

Domenica 19 aprile: 19.15-20.30

Moderatori: Lorenzo Da Dalt (Milano); Elena Levati (Roma)

Sessione Poster 5 - Cardiovascular risk, biomarkers and prognostic indexes

Domenica 19 aprile: 19.15-20.30

Moderatori: Rosa Curcio (Taranto); Martina Chiriacò (Pisa)

Sessione Poster 6 - Diabetes, obesity, nutrition and endocrine metabolism

Lunedì 20 aprile: 18.00-19.00

Moderatori: Simone Bini (Roma); Ilaria Fucile (Napoli)

Sessione Poster 7 - Heart failure, arrhythmias and cardiac rehabilitation

Lunedì 20 aprile: 18.00-19.00

Moderatori: Giulio Francesco Romiti (Roma); Sara Coluzzi (Pescara)

Sessione Poster 8 - Aging, frailty and geriatric medicine

Lunedì 20 aprile: 18.00-19.00

Moderatori: Antonio Michele Bussu (Carbonia); Elena Olmastroni (Milano)

Sessione Poster 9 - Cognition, neuro-metabolism, digital health and AI

Lunedì 20 aprile: 18.00-19.00

Moderatori: Giosiana Bosco (Catania); Ottavia Terenghi (Milano)

Sessione Poster 10 - Rare diseases, genetics and clinical case reports

Lunedì 20 aprile: 18.00-19.00

Moderatori: Ilaria Rossi (Chieti); Maristella Belfiori (Cagliari)

Abstract n SO1_01 - Presenting author**: Stefano Scotti**

Targeted plasma proteomics discriminates patients with familial hypercholesterolemia from unaffected individuals

Stefano Scotti[1,2], Elena Olmastroni[1,2], Marco Chierici[3], Manuela Casula[1,2], Alberico L. Catapano[1,2]

[1]Epidemiology and Preventive Pharmacology Service (SEFAP), Department of Pharmacological Biomolecular Sciences, University of Milan, Italy
[2]IRCCS MultiMedica, Sesto San Giovanni, Italy
[3]Fondazione Bruno Kessler, Trento, Italy

Aim Familial hypercholesterolemia (FH) is characterized by lifelong elevated LDL-cholesterol (LDL-C) and increased cardiovascular risk. Many individuals remain undiagnosed when family history is absent or genetic testing is unavailable. We investigated whether Olink proximity extension assay-based proteomics could distinguish FH patients from unaffected individuals and compared its performance against current diagnostic criteria.
Methods Plasma samples from 702 healthy subjects and 101 FH patients from the Italian LIPIGEN registry were analyzed using three Olink Target 96 panels (Cardiovascular II, Cardiovascular III, Inflammation), harmonized via 16 bridging samples. After excluding assays with >30% values below detection limit, data were split into training (70%, n=563) and test (30%, n=240) sets. Feature screening employed linear models adjusted for age, sex, LDL-C, and lipid-lowering therapy, identifying differentially expressed proteins (FDR-corrected) for downstream modelling. Logistic regression with LASSO penalization was applied, with lambda hyperparameter tuned by 10-fold cross-validation maximizing AUC. Class imbalance was addressed through inverse-frequency weighting. Preprocessing included median imputation and z-score scaling within each cross-validation fold. LASSO selection robustness was evaluated through 1,000 bootstrap iterations (≥80% retention threshold), followed by unpenalized refitting. Performance was evaluated against Dutch Lipid Clinic Network (DLCN) score and LDL-C, with optimal threshold determined by Youden's J statistic.
Results Of 231 proteins, 109 were differentially expressed. LASSO with bootstrapping identified a stable 8-protein signature (HSP27, tPA, TRAP, TIE2, APN, AXIN1, MCP-4, CTSL1). On the test set, the model achieved AUC 0.970 (95%CI 0.920–1.000), accuracy 0.971, sensitivity 0.931, specificity 0.976, precision 0.844, F1-score 0.885, MCC 0.870. Performance was comparable to DLCN (AUC 0.951, p=0.56) and LDL-C (AUC 0.903, p=0.12). Combining proteomics with DLCN significantly improved prediction (AUC 0.999, p=0.005).
Conclusions Plasma proteomics enabled development of an interpretable and robust model discriminating FH patients from controls, highlighting proteomic biomarkers as complementary diagnostic tools. Future steps should assess possible discrimination between genetically confirmed and clinically diagnosed FH.

Abstract n SO1_02 - Presenting author**: Anna Maria Ciaccio**

Stroke at first sight: diagnosis and prognosis by a blood-based signature

Anna Maria Ciaccio[1,2], Gaetano Pacinella[1,2], Alessandra Casuccio[5], Mario Daidone[1,2], Tiziana Di Chiara[1,2], Vittoriano Della Corte[1,2], Rosaria Pecoraro[1,2], Valentina Arnao[6], Luisa Agnello[3,4], Domenico Di Raimondo[1,2], Marcello Ciaccio[3,4], and Antonino Tuttolomondo[1,2]

[1]Internal Medicine and Stroke Care Ward, AOUP "P. Giaccone", Palermo, Italy
[2]ProMISE Department, University of Palermo, Palermo, Italy
[3]Department of Biomedicine, Neurosciences and Advanced Diagnostics, Institute of Clinical Biochemistry, Clinical Molecular Medicine, and Clinical Laboratory Medicine, University of Palermo, Palermo, Italy
[4]Department of Laboratory Medicine, University Hospital "P. Giaccone", Palermo, Italy
[5]Department of Health Promotion, Maternal and Infant Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy
[6]Neurology and Stroke Unit, Azienda di Rilievo Nazionale ad Alta Specializzazione, Ospedali Civico Di Cristina Benfratelli, Palermo, Italy

Aim: Ischaemic stroke (IS) needs rapid diagnosis, but no blood test is in clinical use. We assessed the diagnostic and prognostic value of seven biomarkers reflecting inflammation, thrombosis, and neuronal/astrocytic injury, and their relationship with clinical features and TOAST subtypes.
Methods: In this case–control study, we enrolled 116 patients with acute IS and 59 controls at the University Hospital "Paolo Giaccone" in Palermo. We measured serum levels of osteopontin (OPN), platelet factor 4 (PF4), ubiquitin carboxy-terminal hydrolase L1 (UCHL1), interferon-γ–induced protein-10 (IP-10), soluble thrombomodulin (sCD141), glial fibrillary acidic protein (GFAP), and fatty-acid binding protein-3 (FABP3) using Enzyme-Linked Immunosorbent Assay (ELISA) upon admission and tested for associations with IS using univariate and multivariate logistic regression. We also evaluated diagnostic accuracy through ROC curves and examined relationships with clinical variables and National Institutes of Health Stroke Scale (NIHSS).
Results: OPN, PF4, and UCHL1 were significantly higher in IS patients than controls ($p < 0.001$). In multivariate models, all three biomarkers remained independently associated with IS (OPN OR = 1.015, PF4 OR = 1.005, UCHL1 OR = 1.002; $p < 0.01$). The individual diagnostic performance was fair to good for PF4 (AUC=0.67) and OPN (AUC=0.68), with the best performance for UCHL1 (AUC=0.77; specificity 92%). A combined UCHL1–PF4–OPN model showed improved discrimination (AUC=0.827), with high specificity (93%) and moderate sensitivity (60%). The biomarker profiles varied by TOAST subtype: PF4 and UCHL1 showed significant associations with large-artery atherosclerotic stroke. UCHL1 was strongly associated with lacunar stroke (AUC=0.88), while cardioembolic stroke exhibited weaker and less consistent associations with individual biomarkers.
Conclusions: A focused panel of PF4, OPN, and UCHL1 can reliably identify IS and provide valuable information for subtype classification, supporting its potential role in acute triage and clinical decision-making.

Abstract n SO1_03 - Presenting author**: Carini Tommaso**

Albumin-corrected anion gap in the prognostic stratification of septic patients admitted to internal medicine: a retrospective cohort study

Tommaso Carini, Filippo Figorilli, Francesco Maria Di Luca, Silvia Cardinali, Matteo Pirro

Università degli Studi di Perugia

Background and aim: Available studies on the prognosis of septic patients managed in Internal Medicine are limited. Anion Gap (AG) is a strong unfavourable prognostic marker in sepsis. However, hypoalbuminemia can cause significant underestimation of the traditional Anion Gap. Therefore, correction of AG for albumin level (ACAG) may overcome this limitation, providing additional prognostic information in patients with sepsis.
Materials and Methods: Data from 607 septic patients admitted to the Internal Medicine unit of the University of Perugia were analyzed. Arterial blood gas analysis at admission was available for 570 patients. The primary outcome was in-hospital mortality. The association between ACAG and mortality was assessed using univariate and multivariate Cox regression. Kaplan–Meier survival curves were analyzed by ACAG tertiles, a combined ACAG–SOFA variable, and a logistic regression model including an ACAG×SOFA interaction term.
Results: Among 570 analyzed patients, 140 (24.6%) died during hospitalization. ACAG was significantly associated with in-hospital mortality in univariate (HR 1.092; 95% CI 1.050–1.137; p<0.001) and multivariate analysis, remaining significant after adjusting for covariates, including SOFA (HR 1.061; 95% CI 1.015–1.109; p=0.009). Kaplan–Meier curves showed progressively lower survival in higher ACAG tertiles (log-rank p=0.016). The combined ACAG–SOFA variable revealed a 73% increased risk of death per risk category (OR 1.735; 95% CI 1.471–2.046; p for trend<0.001). No significant ACAG×SOFA interaction was observed, indicating an independent association of ACAG with in-hospital prognosis.
Conclusions: ACAG is an independent predictor of in-hospital mortality. Its prognostic value is particularly relevant in septic patients managed in Internal Medicine, generally characterized by low-to-moderate SOFA scores. ACAG may serve as a simple, readily available tool to enhance early prognostic stratification, beyond that provided by SOFA in septic patients.

Abstract n SO1_04 - Presenting author**: Jacopo Burrello**

A human 3d cardiac microtissue model to investigate aldosterone-induced fibrosis and electrical dysfunction

Jacopo Burrello[1], Giorgia Senesi[2,3], Claudia Altomare[2,3], Fabrizio Buffolo[1], Fabrizio D'Ascenzo[4], Lucio Barile[2,3], Paolo Mulatero[1], Carolina Balbi[5,6], Silvia Monticone[1]

[1]Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, Italy. [2]Institute for Translational Research (IRT), Faculty of Biomedical Sciences, Università della Svizzera italiana (USI) and Ente Ospedaliero Cantonale (EOC), Switzerland. [3] Laboratory for Cardiovascular Theranostics, Istituto Cardiocentro Ticino, Ente Ospedaliero Cantonale (EOC), Switzerland. [4]Division of Cardiology, Department of Medical Sciences, University of Torino, Italy. [5]Center for Molecular Cardiology, University of Zurich, Schlieren, Switzerland. [6]Department of Internal Medicine, Cantonal Hospital of Baden, Baden, Switzerland.

Aim – Aldosterone induces cardiac fibrotic remodelling and arrhythmogenic alterations. The lack of suitable pre-clinical models has hampered an in-depth investigation of the molecular mechanisms involved in aldosterone-induced cardiac damage. Our aim was to evaluate the effects of aldosterone on human 3D microtissue (hMT) cardiac organoids.
Methods – hMT were generated by co-culturing human cardiac fibroblasts, aortic endothelial cells and induced pluripotent stem cells-derived cardiomyocytes. hMT were treated with aldosterone, the mineralocorticoid receptor (MR) antagonist eplerenone, and serum from patients with primary aldosteronism (PA) or matched subjects with essential hypertension (EH). Immuno-fluorescence, histology, and western blot analyses were used to assess fibrosis; multielectrode array was employed to record extracellular field potentials of spontaneously beating human cardiomyocytes.
Results – Levels of profibrotic markers increased after incubation with serum from PA patients, compared to untreated organoids and hMT incubated with EH patient-derived serum. Aldosterone treatment reproduced the same pro-fibrotic effect, in a dose-dependent manner and co-administration of eplerenone blunted these effects. Aldosterone treatment increased corrected field potential duration (an estimate of QT interval) and downregulated the expression levels of *KCNQ1* and *ATP2A2*, responsible for the slow delayed rectifier potassium current and for calcium-handling in the sarcoplasmic reticulum. Eplerenone co- treatment reverted these electrical alterations.
Conclusions – 3D hMT organoids offer a relevant in vitro model to study aldosterone mediated cardiac effects. Aldosterone directly induces fibrosis and prolongation of QT interval in this model, which may partially explain the increase of cardiovascular risk in patients with PA and underscores the benefit of MR antagonist therapy

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Abstract n SO1_05 - Presenting author**: Michela Ricci**

Artificial intelligence in emergency department triage: standard methodology versus technological innovation

Michela Ricci[1], Michele Belardinelli[1], Marco Di Donato[2], Domenico Ventura[1], Stefania Rasori[1], Serena Frassini[1]

AST PU[1]; UNIVPM[2]

Aim The growing overcrowding of emergency departments(ED), together with the workload on nursing staff, has highlighted the need for innovative strategies to optimize the clinical assessment phase of triage.This study evaluate the performance of an AI system built on the GPT-5 ChatGPT architecture to support nurses in prioritizing patients presenting with non-traumatic chest pain, comparing its outputs with those obtained through standard triage performed by nurses.
Methods A single-center cross-sectional study was conducted in the ED Triage Area of Fano Hospital (AST PU) in Italy. Patients requiring immediate assistance and patients under 18 years of age were excluded from the study. For each case, the priority code assigned by the triage nurse was compared with the code produced by the AI chatbot. Statistical analyses included weighted Cohen's kappa, sensitivity, specificity, and overall accuracy.
Results 214 patients were enrolled. Analysis demonstrated a 67.3% concordance between priority codes assigned by the nursing staff and the codes generated by the AI system at the initial nursing evaluation, and 62.6% concordance during subsequent clinical reevaluation. Weighted kappa values were 0.57 and 0.56, indicating moderate agreement. The AI system underestimated clinical severity in 26% of cases, particularly within the deferrable emergencies (code 3), while maintaining good overall accuracy (≈0.78) and high specificity (≈0.84). Mean sensitivity was 0.67 at first assessment and 0.60 during nursing reevaluation.
Conclusions Findings suggest that AI chatbot may serve as a support tool to assist nurses in triage decision processes, contributing to improved efficiency in clinical prioritization. However, further refinement and targeted training are required to ensure safe and appropriate use in clinical practice.

Abstract n SO1_06 - Presenting author**: Francesco Giglioni**

Ultrasound evaluation of carotid perivascular adipose tissue thickness as a potential marker of atherosclerosis and cardiovascular risk

Francesco Giglioni[1], Vanessa Bianconi[1], Elena Cosentini[1], Filippo Figorilli[1], Cecilia Colangelo[1], Martina Corba[1], Giulia Cellini[1], Massimo Raffaele Mannarino[1], Matteo Pirro[1]

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Aim. Perivascular adipose tissue (PVAT) is widely recongnized as a metabolically active organ that possibly play a role in the development of atherosclerotic cardiovascular (CV) disease. Accordingly, PVAT thickness at different arterial districts could serve as a marker of atherosclerosis and CV risk. The aims of our study were 1) to evaluate the feasibility a non-invasive, ultrasound-based approach for measuring carotid PVAT thickness (cPVATt), and 2) to evaluate the association between cPVATt, carotid atherosclerosis burden, and CV risk.
Methods. We conducted an observational, cross-sectional, pilot study. Carotid PVAT was evaluated bilaterally by ultrasonography using a 10-MHz multifrequency linear probe positioned at the base of the neck in contact with clavicle, perpendicular to the skin and in a transverse orientation. The mean distance between the common carotid adventitia and the sternocleidomastoid muscle anteriorly and the longus colli muscle posteriorly, measured on both the right and the left sides, was used as a cumulative measure of cPVATt.
Results. A total of 465 patients were included in the study. The median value of cPVATt was 0.68 (0.58-0.85) cm. Significant direct correlations emerged between cPVATt and body mass index ($r=0.170$, $p<0.001$), waist circumference ($r=0.224$, $p<0.001$), neck circumference ($r=0.269$, $p<0.001$), uric acid ($r=0.106$, $p=0.031$), triglycerides ($r=0.095$, $p=0.048$), and hs-CRP ($r=0.202$, $p=0.019$). A significant inverse correlation was observed between cPVATt and HDL cholesterol ($r=-0.152$, $p=0.001$). No correlation was observed between cPVATt and any measure of carotid atherosclerotic burden. There was a significant increase in cPVATt across CV risk categories (p for trend=0.043).
Conclusions. The present study preliminarly demonstrates the feasibility of an ultrasound approach for assessing cPVAT, the reliability of cPVATt as a measure of adiposity and its potential value as a marker of increased CV risk. However, it does not show any significant correlation between cPVATt and carotid atherosclerotic burden.

Abstract n SO1_07 - Presenting author**: Carmine De Luca**

The role of point of care ultrasound (pocus) in ambulatorial hypertension mediated organ damage screening and detection

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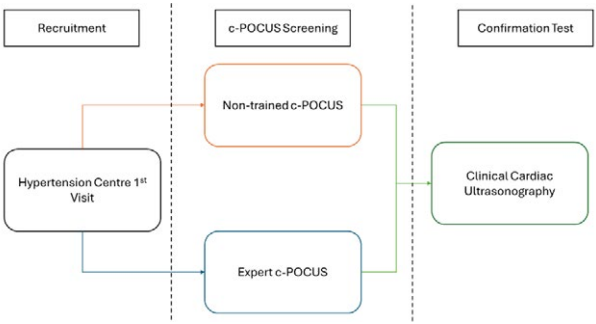
Introduction: European Society of Hypertension (ESH) guidelines for Arterial hypertension (IA) management suggest the evaluation of HMOD to stratify cardiovascular risk in patients affect by IA, even if it is not clearly described the role of cardiac ultrasonography during patient's first access to ambulatory.

Aim: to compare the difference in terms of performance between the non-trained and the expert ultrasonographic examination in HMOD detection.

Methods: We designed a cross-sectional study in a population of hypertensive patients that access for the first time to our ambulatory. Every patient undergoes to pressure measurement, cardiac-POCUS (c-POCUS) performed by a non-trained operator and by an expert, then clinical echocardiography performed by an expert. (Figure 1)

Aim: compare the difference in terms of performance between the non-trained and the expert ultrasonographic examination in HMOD detection.

Results: We recruited 193 consecutive hypertensive patients with characteristics reported in table 1. At the initial assessment, patients underwent to c-POCUS performed by the non-trained operator and the expert.



Discussion: Analyzing the performance indicators about the c-POCUS in HMOD detection we can see analogies between the two executors' approach accuracy, if we consider the ejection fraction (EF; IC95%: 94.4%-99.4% non-trained vs 95.2%-99.6% expert) and aortic dilatation (AD; IC95% 91.9%-98.2% non-trained vs 90.5%-97.4% expert). The most important differences found are about left atrial dilatation (LAD; IC95%: 73.7%-85.5% non-trained vs 83.5%-93% expert) and left ventricle hypertrophy (LVH; IC95%: 63.13%-76.55% vs 74.8%-86.4% expert), where diagnostic accuracy is different between two operators (table 2).

Conclusion: As shown by our data, c-POCUS could be suggested as HMOD screening test in patients that access the ambulatory for the first time, as a 1st level test, to determine more precisely their cardiovascular risk and start the right pharmacological treatment, even if executed by a non-expert operator.

Patients (N=193)	
Age (years)	55.4 ± 15.6
Male (n, %)	101 (52.6%)
BMI (kg/m^2)	28 ± 5
PAS (mmHg)	137.5 ± 12.4
PAD (mmHg)	81.8 ± 12.4
FC (bpm)	70.6 ± 11.3
Dyslipidaemia (%)	42.2 %
DM2 (%)	11.7 %
Stroke (%)	1.1 %
Cardiac Acute Disease (%)	5.7 %
Atrial Fibrillation (%)	4.2 %
OSAS (%)	2.6 %
Smoking habits (%)	28.6 %

Table 1: Patients characteristics at Baseline

	Diagnostic accuracy	
	Non trained	Expert
FE>55%	97.79%	98.33%
LVH	81.05%	70.16%
AD	95.81%	94.71%
LAD	80.10%	88.89%

Table 2: Diagnostic Accuracy

Abstract n SO2_01 - Presenting author**: Elisa Russo**

GLUTREPRO: A randomized controlled trial of SGLT2 inhibitors on renal senescence, inflammation, and tubulointerstitial injury in chronic kidney disease

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Aim: Dapagliflozin exerts significant cardiovascular and renal protection in patients with chronic kidney disease (CKD), irrespective of the presence of diabetes. The molecular mechanisms underlying this effect are multifaceted and not yet fully elucidated.
The aim of this study was to evaluate the effects of dapagliflozin treatment on proximal tubular epithelial cells (PTCEs) isolated from the urine of patients with CKD.
Methods: A total of 32 patients with CKD were enrolled in a randomized study. PTCEs were isolated from urine samples, establishing a primary cell line. Gene and protein expressions were assessed using real-time polymerase chain reaction (rtPCR) and western blotting, respectively.
Results: In urine-derived PTECs, dapagliflozin treatment was associated with significantly lower mRNA expression of vimentin (p=0.002), TGF-β (p<0.001), fibronectin (p=0.01), and DKK3 (p=0.04); while no significant differences were detected for collagen mRNA expression (p=0.88) and fibronectin protein expression (p=0.87), as shown in Figure 1. As for the parameters of inflammation, we observed a significant reduction in TLR4 protein expression (p=0.02), while MCP1 mRNA levels showed a reduction at 6 months (p=0.02) but not over the full study duration (p = 0.20). p16^INK4a protein expression was significantly decreased in the dapagliflozin group both at 6 months (p=0.02) and at study end (p=0.004, Fig). A trend toward reduction in SA-β-gal positivity in the treated group was observed, although it did not reach statistical significance.
Conclusions: The nephroprotective effect of dapagliflozin appears to be mediated by its action on mediators involved in inflammation and innate immunity, which contribute to tubular damage and fibrosis. Furthermore, dapagliflozin was found to inhibit the expression of key senescence markers, a phenomenon increasingly recognized as pivotal in the progression of CKD. These findings underscore the potential cardiovascular benefit of dapagliflozin, as inflammation and senescence are also critical contributors to cardiovascular risk in CKD patients.

Abstract n SO2_02 - Presenting author**: Carmen Tedesco**

The SGLT-2 inhibitor dapagliflozin rescues epicardial adipose tissue–driven cardiac progenitor cell dysfunction in human obesity via specific signaling pathways

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Aim: Sodium-glucose cotransporter 2 inhibitors (SGLT-2i) provide cardiovascular protection independently of glycemic control, although their direct effects on cardiac cells remain poorly understood. We previously demonstrated that conditioned medium (CM) derived from epicardial mature adipose cells of individuals with obesity induces apoptosis, JNK activation, and cytoskeletal disruption in human cardiac progenitor cells (hCPCs), effects that are prevented by dapagliflozin (DAPA). In contrast, CM obtained from epicardial adipocytes of subjects without obesity does not exert detrimental effects. This study aims to identify the intracellular mechanisms mediating DAPA-induced cardioprotection.
Methods: hCPCs were isolated from right auricle biopsies of healthy donors and exposed to CM derived from mature epicardial adipose cells of individuals with obesity (n = 11), in the presence or absence of DAPA. SGLT-2 expression was selectively silenced using a specific small interfering RNA (siRNA). Intracellular signaling pathways were investigated using a phospho-protein profiling approach to identify SGLT-2-dependent signaling pathways associated with DAPA treatment during exposure to the obesity-related adipose secretome.
Results: For the first time, we demonstrate that SGLT-2 is expressed in hCPCs. Functional relevance was confirmed by siRNA-mediated silencing, which abolished the protective effects of DAPA against CM-induced apoptosis and JNK-1/2 activation. Phospho-proteomic and gene set enrichment analyses revealed that, in SGLT-2-expressing hCPCs, DAPA activated receptor-associated and kinase-binding signaling pathways while suppressing stress-related pathways, including p53, JNK, and AP-1. These protective signaling responses were completely absent in SGLT-2-silenced cells.
Conclusions: DAPA directly counteracts obesity-related epicardial paracrine-induced dysfunction in hCPCs through specific SGLT-2-dependent signaling. These findings uncover a novel cell-autonomous role of SGLT-2 in hCPCs and support the concept that SGLT-2 inhibitors provide cardioprotection not only via systemic metabolic effects but also through direct cellular reprogramming of intracellular stress and survival pathways.

Abstract n SO2_03 - Presenting author**: Isabella Calderoni**

Protective effects of tirzepatide against lipotoxic stress in human cardiac progenitor cells

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Aims: The viability of human cardiac stem and progenitor cells (hCPC) is essential for constant tissue repair and renewal in the adult heart. Defective hCPC number and pro-angiogenic capacity contribute to diabetes- and obesity-related heart failure in humans. Evidence supports beneficial cardiovascular effects of the dual GIP/GLP-1 receptor agonist tirzepatide in humans. The aim of this study was to evaluate whether hCPC express functional GLP-1R and GIPR, and to investigate the ability of tirzepatide to prevent palmitate-induces apoptosis, autophagy and senescence in hCPC.
Methods: hCPC were obtained from right auricle biopsies of non-obese and non-diabetic subjects undergoing elective cardiac surgery. GLP-1R and GIPR mRNA and protein expression were demonstrated by quantitative real-time PCR and immunoblotting, respectively. hCPC were exposed to 100 nM tirzepatide for different times. hCPC, pretreated or not with 100 nM tirzepatide for 1 h, were exposed to 0.25 mM palmitate for 16 h. CREB phosphorylation was evaluated by immunoblotting. Apoptosis, autophagy, and senescence were evaluated by cleaved caspase-3, LC3-II and p21Cip1/WAF1 immunoblotting, respectively.
Results: hCPC express both functional GLP-1R and GIPR. Exposure of hCPC to tirzepatide for different times induces CREB phosphorylation starting from 5 min ($p<0.05$). Treatment of hCPC with palmitate induced apoptosis, autophagy and senescence ($p<0.05$). Pretreatment of hCPC with tirzepatide prevented palmitate-induced apoptosis, autophagy and senescence ($p<0.05$).
Conclusions: hCPC express functional GLP-1R and GIPR. Tirzepatide prevents palmitate-induced apoptosis, autophagy and senescence of hCPC. Therefore, tirzepatide could confer cardioprotection against lipotoxic damage in hCPC.

Abstract n SO2_04 - Presenting author**: Giosiana Bosco**

Effect of inclisiran on lipid and mechanical vascular profiles in familial hypercholesterolemia subjects: results from a single lipid center real-world experience

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Aim: Familial hypercholesterolemia (FH) is characterized by elevated LDL-C and an increased risk of premature cardiovascular events. Inclisiran is a small interfering RNA that inhibits hepatic PCSK9 synthesis and promotes LDL-C clearance by enhancing LDLR expression on hepatocytes. This study aimed to evaluate the efficacy of six-months add-on inclisiran on lipid profile and PWV in FH; furthermore, we investigated the association between LDL-C reduction and PWV variation.
Methods: This prospective observational study involved 78 genetically confirmed FH subjects with an LDL-C off target despite high-intensity statins plus ezetimibe. All subjects obtained biochemical analysis and PWV evaluation at baseline and after six months add-on inclisiran.
Results: After six months add-on inclisiran, 41 % of subjects achieved LDL-C targets. Significant reductions of LDL-C (- 41.5 %, $p < 0.001$), ApoB (- 33.7 %, $p < 0.01$), Non-HDL-C (- 35.9 %, $p < 0.001$), and Lp(a) (- 18 %, $p < 0.01$) were observed, while PWV improved by 14.4 % ($p < 0.001$). In a secondary analysis, the study population was divided in two groups according to the cardiovascular history: FH subjects without ASCVD (Primary prevention group) and FH subjects with ASCVD (Secondary prevention group). The Primary prevention group showed a higher prevalence of subjects on LDL-C target than the Secondary prevention group (59 % vs 23.1 %, $p < 0.001$). Both groups exhibited significant improvements of lipid profile and PWV (Δ - 14.1 %, $p < 0.01$ and Δ - 14.6 %, $p < 0.001$, respectively). Linear regression showed a significant association between ΔPWV and ΔLDL-C in the whole study population as well as in the Primary and Secondary prevention groups (p for all < 0.001).
Conclusions: Inclisiran significantly improved lipid profile and PWV in a cohort of FH subjects. ΔPWV was significantly associated with ΔLDL-C.

Abstract n SO2_05 - Presenting author**: Valerio Galasso**

Irisin as potential mediator of GLP-1 receptor agonists action

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Aim: Irisin is a hormone secreted by skeletal muscle following physical activity or excess saturated fatty acids, promoting energy expenditure and metabolic homeostasis. Circulating irisin levels are reduced in patients with type 2 diabetes (T2D), while exogenous irisin administration improves glycemic control in diabetic mice. Interestingly, irisin and GLP-1 share pleiotropic effects and activate similar intracellular pathways at both pancreatic and extra-pancreatic sites. This study investigated whether irisin mediates the metabolic effects of GLP-1 receptor agonists (GLP-1RAs).
Methods: 190 T2D patients (age 18-70 years) were stratified by anti-diabetes therapy: diet; metformin; metformin plus GLP-1RAs; metformin plus DPP-4 inhibitors; metformin plus SGLT2 inhibitors; other therapies. 36 sex- and BMI-matched normoglycemic individuals (ND) served as controls. In addition, human skeletal muscle cells (hSkMCs) were exposed in vitro to semaglutide (1–100 nM) for 24 h to assess its ability to induce irisin secretion. Irisin levels in serum and culture media were measured by ELISA. Intracellular signalling was evaluated in hSkMCs treated with semaglutide (50 nmol/L, 24 h) using a Proteome Profiler™ Array to assess phosphorylation status of 37 signaling proteins, with key findings confirmed by immunoblotting. Signalling activation and irisin release were also analysed in the presence of 5 µmol/L PKA inhibitor (H89).
Results: As expected, T2D patients showed lower irisin levels than controls, whereas patients receiving metformin plus GLP-1RAs exhibited an increase in irisin levels, reaching values observed in ND subjects. *In vitro*, semaglutide treatment (50 nmol/L, 24 h) induced CREB phosphorylation in hSkMCs. Consistently, inhibition of PKA with H89 significantly reduced semaglutide-induced CREB activation and irisin secretion.
Conclusions: GLP-1RA treatment in T2D patients significantly increases serum irisin levels to those observed in ND subjects. This effect appears to be mediated by direct stimulation of skeletal muscle cells through PKA/CREB signalling. These findings identify irisin as a potential mediator of GLP-1RAs effects.

Abstract n SO2_06 - Presenting author: **Luigi Savino**

SGLT2 inhibition improves cognitive impairment in frail older adults with HFpEF and diabetes

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Aim: Heart failure with preserved ejection fraction (HFpEF) is a common condition among patients with multiple comorbidities, particularly older adults. HFpEF is associated with an increased risk of adverse outcomes, including frailty, which involves both cognitive and physical decline. Type 2 diabetes mellitus (T2D) contributes to endothelial dysfunction, inflammation, atherosclerosis, and oxidative stress, potentially driving the development and progression of HFpEF. Sodium-glucose cotransporter 2 inhibitors (SGLT2-I) have demonstrated efficacy in the management of both T2D and HFpEF. This study aimed to evaluate the effects of SGLT2-I on cognitive function in a population of older adults.
Methods: We conducted a prospective observational study with a one-year follow-up, enrolling consecutive frail older adults with confirmed diagnoses of T2D and HFpEF. Inclusion criteria were: age >65 years; confirmed diagnoses of T2D, frailty, and HFpEF; and a Montreal Cognitive Assessment (MoCA) score <26. All participants received metformin in combination with either an SGLT2-I, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), or insulin. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA). It is a quick, 30-point screening tool used to detect mild cognitive impairment (MCI), assessing memory, attention, executive functions, language, visuoconstruction, and orientation. Completed in about 10 minutes, a score of 26 or higher usually indicates normal function, while lower scores suggest cognitive issues.
Results: A total of 423 patients were screened. Of these, 54 did not meet the inclusion criteria, 32 discontinued treatment due to drug intolerance, and 17 declined to provide clinical information, resulting in 321 enrolled participants. Patients were stratified into four treatment groups based on their antidiabetic therapy: SGLT2-I (82 patients), GLP-1 RA (76 patients), insulin (80 patients), and metformin alone (83 patients). Treatment with SGLT2-I was associated with significant improvements in cognitive function (p=0.0095), while no significant changes were observed in the other treatment groups.
Conclusions: These findings indicate that SGLT2-I may confer anti-frailty and potentially anti-aging benefits in older adults with T2D and HFpEF. The observed improvements in cognitive domains suggest pleiotropic effects of SGLT2-I that extends beyond glycemic control. Further large-scale, randomized studies are warranted to confirm these results and elucidate the underlying mechanisms linking SGLT2 inhibition to improved frailty outcomes.

Abstract n SO2_07 - Presenting author**: Greta Chiarelli**

A gender medicine approach to PCSK9-targeted therapy: differential response to siRNA and monoclonal antibodies

Greta Chiarelli, Miriam Giovanna Mazzone, Martina Romeo, Guido D'errico, Raffaele Russo, Carmine De Luca, Luigi Jr Valletta, Vincenzina Palermo, Sofia Donnarumma, Ilenia Lorenza Calcaterra, Gabriella Iannuzzo, Matteo Di Minno

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Objective: To evaluate the efficacy and safety of anti-PCSK9 therapies, comparing siRNA and monoclonal antibodies (mAb), and assess sex-based differences in high cardiovascular risk patients.
Methods: This prospective observational study included 72 patients (34 males, 38 females; mean age 52.6 years). Genetic testing identified 35 heterozygous FH, 21 polygenic, and 16 non-causative variants. Comorbidities included prior myocardial infarction or stroke (n=22), hepatic steatosis (n=22), diabetes (n=15), thyroid disorders (n=19), hypertension (n=37), smoking (n=30), and carotid atherosclerosis (n=33); 23 were statin-intolerant. Concomitant therapies included statins (n=49), ezetimibe (n=67), and bempedoic acid (n=15). Evaluated parameters included lipid panel and hepatic, renal, glucose, and CPK values at baseline and after 6 months. Changes were expressed as percentages from baseline and analyzed using paired t-tests or Wilcoxon tests; $p<0.05$ was considered significant.
Results: Overall, LDL decreased −28.7%, total cholesterol −14.7%, triglycerides −5.1%, and HDL increased +1.5%. Both sexes showed similar LDL reductions (women −28.4%, men −28.7%), with slightly more favorable HDL increase in women. Among women, siRNA produced the greatest LDL reduction (−35.3%) with consistent improvements in total cholesterol and HDL, and a tendency to stabilize hepatic and renal parameters. Women treated with mAb also had significant LDL reduction (−18.9%) and stable liver, kidney, and CPK values. In men, mAb therapy led to greater LDL reduction than siRNA (−30.4% vs −24.5%), while siRNA-treated men showed favorable triglyceride reductions, slight HDL increase, and stable glucose and CPK. Overall, renal and hepatic function remained stable in all groups, confirming excellent safety. mAb therapy produced a more uniform lipid-lowering effect, while siRNA showed potential advantages in women at high cardiovascular risk.
Conclusions: Both siRNA and mAb anti-PCSK9 therapies significantly improved lipid profiles with excellent tolerability. SiRNA was more effective in women, mAb produced greater LDL reduction in men, highlighting the importance of personalized, gender medicine–oriented therapy.

Abstract n SO3_01 - Presenting author**: Cosma Riccardo**

A proof-of-concept pharmacogenetic trial of fenofibrate in type 2 diabetes: lipids and beyond for cardiovascular prevention

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Objectives: Pharmacogenetics may optimize cardiovascular prevention by identifying subgroups deriving greater benefit from drugs with heterogeneous trials results, such as the PPAR-α agonist fenofibrate. In post-hoc analyses of large studies, we identified and validated a common PPARA variant (rs6008845) that marks individuals with type 2 diabetes (T2D) who experience a substantial (~50%) reduction in cardiovascular events when treated with fenofibrate. This benefit was also observed in patients without dyslipidemia, and the underlying mechanisms remain unknown. The aim of this study was to investigate the pathophysiological basis of this genetically modulated response.
Methods: We conducted at Padua University Hospital, 200 patients with T2D on active statin treatments, well controlled lipid and metabolic profile and preserved renal function. Participants were randomized to fenofibrate or placebo for 12 weeks. The rs6008845 variant and a genetically determined score (eQTL-GS) for PPARA expression across multiple tissues were analyzed. Changes in endothelial function (reactive hyperemia index-RHI), arterial stiffness (PWV-cf), lipid and apolipoprotein profiles, and inflammatory, hepatic, and renal parameters were assessed.
Results: A total of 180 patients completed the study with well-controlled cardiovascular risk factors (mean age 66 years; 23% women; LDL-c 62 mg/dl, TG 102 mg/dl; HbA1c 6.6%). Fenofibrate did not significantly affect RHI or PWV-cf, nor were these parameters modified by genetic background. Fenofibrate significantly reduced TG and apoC-III and increased apoA-II, LDL-c, and the LDL/ApoB ratio, consistent with a shift toward larger, less atherogenic LDL particles. Both rs6008845 and the eQTL-GS modulated LDL-c and ApoB responses (interaction $p<0.05$), with larger benefit in genetic groups with larger CV benefit from fenofibrate.
Conclusions: This proof-of-concept pharmacogenetic study supports the use of variants in the gene coding the fenofibrate pharmacological target to identify subjects with favorable response. However, changes in apolipoproteins alone do not fully explain the previously observed CV benefit, suggesting additional mechanisms involved.

Abstract n SO3_02 - Presenting author**: Francesca Protopapa**

Leukocyte telomere length in hypercholesterolemic patients: differential dynamics between clinical and genetic familial hypercholesterolemia

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Aim: Aging is a major risk factor for several diseases, including cardiovascular disease (CVD). Clonal hematopoiesis of indeterminate potential (CHIP), an age-related condition, has emerged as an independent contributor to CVD. This condition develops when HSCs acquire somatic mutations in driver genes, like DNMT3A**,** TET2**,** ASXL1 and JAK2 in individuals without hematologic malignancies. Both CHIP and leukocyte telomere shortening represent age-related hallmarks linked to cardiovascular dysregulation. Reduced leukocyte telomere length (LTL) is associated with cardiovascular risk factors and with the onset of CVD. The aim of this study was to assess telomere dynamics in hypercholesterolaemic individuals with clinically diagnosed or genetically confirmed familial hypercholesterolaemia.
Methods: 95 hypercholesterolaemic subjects (over than 50 years), either untreated or receiving lipid-lowering therapy, from the LIPIGEN Registry (Milan) underwent clinical evaluation, biochemical profiling, Dutch Lipid Clinic Network Score assessment and cardiovascular history collection. Genetic testing distinguished heterozygous familial hypercholesterolaemia (He-FH) (n=56) from clinically diagnosed FH without pathogenic variants (CD-FH) (n=39). Genomic DNA was isolated from leukocytes and LTL was measured by qPCR, calculating the telomere-to-single-copy gene ratio. All samples were analysed in triplicate, normalized to internal controls, re-tested for extreme values and evaluated by melting curve analysis to confirm specificity. Operators were blinded to clinical data.
Results: In hypercholesterolaemic subjects who were not receiving lipid-lowering therapy, LTL showed no significant difference between CD-FH and He-FH ($p = 0.3725$, Mann–Whitney test). Conversely, among participants undergoing lipid-lowering treatment, He-FH individuals showed significantly shorter LTL compared with CD-FH subjects ($p = 0.0029$, Mann–Whitney test), indicating that the divergence in TL emerged only in the treated subgroup.
Conclusions: LTL was comparable between CD-FH and He-FH untreated individuals, whereas a significant reduction emerged in He-FH treated patients as compared to CD-FH treated patients. These findings suggest that genetic background and lipid-lowering treatment may modulate telomere dynamics in FH.

Abstract n SO3_03 - Presenting author**: Daniele Tramontano**

High-parameter spectral phenotyping of platelets in Familial Chylomicronemia Syndrome

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Aim: *Familial chylomicronemia syndrome* (FCS) is a rare monogenic disorder of lipid metabolism leading to severe hypertriglyceridemia and to increased risk of pancreatitis. Thrombocytopenia has been observed in FCS patients. However, the relationship between triglyceride (TG)-rich lipoproteins, platelet function and thrombosis are not fully understood. To perform a detailed, multi-parametric analysis of platelet phenotype and functionality in patients with genetically confirmed severe chylomicronemia syndromes.
Methods: Eight FCS with a median [interquartile range] TG concentration of 1389 [936-2704] mg/dL and a platelet count of 160 [120.5-168.8]x10^3/l, were compared to an age- and sex-matched cohort (n=16) of *Multifactorial Chylomicronemia Syndrome* (MCS) patients with a TG concentration of 269 [174-530] mg/dL and a normal platelet count (276 [214.5-295.8]x10^3/l). Platelet responsiveness to agonists (ADP, TRAP6, convulxin) and phosphatidylserine exposure were measured by conventional flow cytometry. The platelet phenotype was characterized by spectral flow cytometry with a newly developed 16-color panel (Figure).
Results: FCS displayed a significantly larger fraction of circulating phosphatidylserine-positive and P-selectin negative platelets, i.e. apoptotic platelets (FCS: 14.8 [6.8-29.3]% *vs* MCS:0.4 [0.1-3.2]%). The percentage of apoptotic platelets was inversely related to the platelet count (p=.014), independently of age, TG and mutation burden. Upon stimulation, FCS platelets displayed an impaired response to all tested agonists. Multiparametric spectral phenotyping detected significantly higher platelet expression of CD44, CD36, CD42b, CD31 in FCS compared to MCS. Elevated CD31 and CD42b were the most distinctive features in FCS with higher frequency of apoptotic platelets (Figure). The platelet hypo-responsiveness to agonists and the frequency of apoptotic platelets associated with a higher incidence of splenomegaly and pancreatitis.
Conclusions: In FCS the reduced platelet count is associated to an increase of apoptotic death, reduced responsiveness and a phenotypical shift of the circulating platelet pool. Ongoing mechanistic studies may provide insight on the relationship between TG-rich lipoproteins, platelets and the clinical outcomes of hypertriglyceridemia.

Abstract n SO3_04 - Presenting author**: Giovanni Pennisi**

Impact of dietary habits on inflammatory and metabolic profiles and subclinical atherosclerosis in patients with familial hypercholesterolemia

Giovanni Pennisi[1], Francesco Di Giacomo Barbagallo[1,2], Giosiana Bosco[1,2], Vanessa Di Francesco[1], Maurizio Di Marco[1], Sabrina Scilletta[1], Antonino Di Pino[1], Salvatore Piro[1], Roberto Scicali[1]

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Backgroung and Aim Familial hypercholesterolemia (FH) is characterized by lifelong exposure to elevated LDL cholesterol and a markedly increased risk of premature atherosclerotic cardiovascular disease. Despite the genetic background, residual cardiometabolic and inflammatory risk may be modulated by lifestyle-related factors. This study evaluated the association between adherence to the Mediterranean diet, assessed using the Pyramid-based Mediterranean Diet Score (PyrMDS), and metabolic, inflammatory, and vascular parameters in individuals with familial hypercholesterolemia (FH).
Methods In this cross-sectional study, 120 adult subjects with clinically or genetically confirmed FH, free from lipid-lowering therapy and without atherosclerotic cardiovascular disease, were enrolled. Adherence to the Mediterranean diet was assessed using the validated PyrMDS questionnaire and participants were classified into high (PyrMDS ≥9) and low (PyrMDS <9) adherence groups. Metabolic and inflammatory parameters were measured after fasting. Arterial stiffness was assessed by carotid–femoral PWV, while subclinical atherosclerosis was defined by CAC score >0 and/or carotid or femoral plaques.
Results 72 subjects (60%) showed high adherence to the Mediterranean diet. Compared to the low-adherence group, they had a lower body mass index (24.1 ± 2.8 vs 26.2 ± 3.5 kg/m², $p < 0.05$), fasting plasma glucose (86.4 ± 9.7 vs 89.8 ± 10.2 mg/dL, $p < 0.05$), and hs-CRP levels (0.72 ± 0.46 vs 0.93 ± 0.51 mg/L, $p < 0.05$). Lipid parameters (LDL-C, ApoB, triglycerides, HDL-C) were similar between groups. PWV was lower in the high-adherence group (8.2 ± 1.2 vs 8.3 ± 1.3 m/s). Subclinical atherosclerosis was lower compared with subjects with low adherence (32.9% vs 41.7%).
Conclusions Higher adherence to the Mediterranean diet in FH subjects not receiving lipid-lowering therapy was associated with a better metabolic and inflammatory profile and improved vascular parameters. These findings support the potential role of dietary habits as a complementary strategy for addressing residual cardiometabolic and vascular risk in individuals with FH.

Abstract n SO3_05 - Presenting author**: Martina Ferrandino**

Estimation of sdLDL-cholesterol and other lipid parameters in patients with clinical suspicion of Familial Hypercholesterolemia

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Aim: Familial Hypercholesterolemia (FH) is a common genetic disorder characterized by increased cardiovascular (CV) risk, mainly due to the high burden of LDL-cholesterol (LDL-c). We aim to evaluate the distribution of ApoB and E-sdLDL-c levels in patients with clinical suspicion of FH with (FH/V+) and without pathogenic variants (FH/V-).
Methods: The main causative genes of FH were analyzed in 205 unrelated patients by NGS (Devyser's kit). ApoB was quantified by nephelometry (Siemens), while other lipid parameters were measured by standard methods. Small dense LDL-c was estimated by Sampson equation (E-sdLDL-c).
Results: Higher levels of LDL-c and ApoB and lower levels of triglycerides were observed in FH/V+ than in FH/V- patients. To assess the portion of LDL-c contained in small dense LDL (sdLDL) particles, E-sdLDL-c/E-LDL-c ratio was calculated. This ratio was higher in FH/V- (0.31 (0.27-0.36)) than in FH/V+ patients (0.25 (0.22-0.30); $p<0.0001$), reflecting the association of sdLDL particles to non-genetic hypercholesterolemia. To evaluate the possible additional role of E-sdLDL-c in defining residual CV risk, a discordance analysis with ApoB was performed. Univariate linear regression showed similar beta-coefficients (0.871 in FH/V- and 0.838 in FH/V+), but different intercept values (31.3 in FH/V- and 42.9 in FH/V+), depending on the presence of a pathogenic variant. A similar ApoB level is associated with higher E-sdLDL-c levels in FH/V- than in FH/V+, indicating the presence of larger LDL particles in FH/V+ patients. Greater discordance was observed in presence of higher triglycerides, that were associated with higher E-sdLDL-c levels, independently from the presence of pathogenic variants.
Conclusions: Despite similar ApoB levels, different E-sdLDL-c levels were observed in FH/V+ and FH/V- patients. Adding sdLDL-c to the other lipid parameters, already used as therapeutic targets, may improve CV risk stratification and patients' management.

Abstract n SO3_06 - Presenting author**: Francesco Di Giacomo Barbagallo**

Evaluation of glycemic status and subclinical atherosclerosis in familial hypercholesterolemia subjects with or without LDL receptor mutation

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Aim: Familial hypercholesterolemia (FH) is a genetic condition characterized by elevated LDL-C and increased cardiovascular risk. Beyond LDL-C levels, the impact of genotype on glucose homeostasis has not been well evaluated. We aimed to evaluate the impact of genotype on glycemic status and on atherosclerotic injury in FH subjects.
Methods: We conducted a cross-sectional study on 322 FH subjects not on lipid-lowering therapy and without history of cardiovascular disease. Biochemical and genetic analyses as well as vascular profile assessment were obtained from all subjects. The study population was divided into two groups according to genotype: LDL receptor (LDLR) group and non-LDLR (NLDLR) group.
Results: The LDLR group exhibited a higher prevalence of low glycemic status (LGS) than the NLDLR group (44.1% vs. 26%, $p < 0.01$), whereas a high glycemic status (HGS) was more prevalent in the NLDLR group compared with LDLR group (74% vs. 55.9%, $p < 0.01$). The NLDLR group exhibited a higher prevalence of peripheral atherosclerotic plaques than the LDLR group (93.4% vs. 73%, $p < 0.05$), while coronary artery calcification (CAC) presence was more prevalent in the LDLR group compared with the NLDLR group (74.7% vs. 48%, $p < 0.01$). In a secondary analysis the study population was stratified into three groups based on LDLR genotype: NLDLR, LDLR defective, LDLR null groups. The prevalence of LGS progressively increased from the NLDLR to the LDLR null group, while HGS showed an inverse trend (p for trend < 0.05). Peripheral atherosclerotic plaque prevalence decreased from the NLDLR to the LDLR null group (p for trend < 0.05), while CAC prevalence increased progressively in the three groups (p for trend < 0.01). Logistic regression analysis showed that FH groups with an LDLR mutation were inversely associated with HGS (p for both < 0.01) and the LDLR null group exhibited the strongest association.
Conclusions: FH subjects with NLDLR mutations exhibited a worse glycemic profile, while null LDLR mutations showed the strongest inverse association with HGS. The integrations of genetic, lipid and glucose data could be useful to better identify the metabolic profile and the atherosclerosis distribution in FH subjects.

Abstract n SO3_07 - Presenting author**: Riccardo Rizzo**

Lipoprotein-bound PCSK9: structural and functional insights

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Introduction: PCSK9 promotes the degradation of the low-density lipoprotein receptor (LDLR), thereby reducing plasma LDL clearance. Monoclonal antibodies (mAbs) and small interfering RNA (siRNAs) targeting PCSK9 are approved for the treatment of hypercholesterolemia. We and others have shown that a fraction of circulating PCSK9 associates with LDL. This study aimed to investigate the PCSK9–lipoprotein interaction.
Methods: Lipoproteins were isolated by density gradient ultracentrifugation with iodixanol from patient plasma (n=50 hypercholesterolemic individuals) before and after mAb or siRNA treatment. Lipoprotein composition was characterized using spectrophotometric, lipidomic, and proteomic approaches. PCSK9 subspecies and secretion mechanisms were studied by Western blotting and cell culture experiments.
Results: siRNA therapy reduced LDL cholesterol from 103 ± 50 to 42 ± 17 mg/dL, while mAbs reduced LDL cholesterol from 126 ± 50 to 57 ± 31 mg/dL (both $p < 0.01$). Circulating PCSK9 levels decreased by 65% following siRNA treatment and increased by approximately 1000% after mAb therapy ($n = 20$ and 30, respectively). In both treatment groups, approximately 15% of PCSK9 associated with LDL ($n = 50$; $p < 0.01$), a finding also confirmed in control subjects. Immunoblot analyses demonstrated that the active form of PCSK9 interacts preferentially with LDL. Lipidomic and LC–MS analyses showed that PCSK9 associates with a less dense LDL subfraction enriched in ApoE, ApoC, and triglycerides, exhibiting IDL-like characteristics. Particle size assessed by electron microscopy was consistent with this data.
Conclusions: An IDL-like LDL subpopulation was identified as the main carrier of circulating PCSK9. The interaction may occur directly in plasma or originate from co-secretion with VLDL; studies are ongoing to test this hypothesis. Despite marked therapy-induced changes in LDL-C and PCSK9 circulating levels, the proportion of LDL-bound PCSK9 remains constant, suggesting a non-saturable mechanism.

Abstract n SO4_01 - Presenting author**: Giorgia Laureti**

The impact of dehydration on in-hospital, medium-term, and long-term mortality in hospitalized older adults

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Aim: Dehydration constitutes a potentially negative prognostic factor in older patients admitted for acute conditions. In a population of older patients hospitalized for acute conditions, we want to evaluate the relationship between dehydration at hospital admission and an increase of in-hospital mortality, as well as medium- and long-term mortality.
Materials and methods: The study was conducted on 3540 patients, from the REPORT-AGE database, ≥65 years old, consecutively admitted to one of the hospital facilities of IRCCS INRCA in Italy during the period from 2011 to 2024. Patients were classified according to plasma osmolarity values obtained at hospital admission. Patients with plasma osmolarity ≥ 300 mOsm/l were classified as "dehydrated." The impact of dehydration on in-hospital mortality, as well as mortality at three months and one year after hospital admission, was evaluated independently of other confounding prognostic factors.
Results: The mean age was 86±6 years, with female prevalence (59%). 73% of patients was dehydrated. We found a correlation between dehydration and mortality across all three periods examined, with a statistically significant difference between the two patient groups ($p < 0.001$) in terms of in-hospital mortality and mortality at 3 months after discharge, as well as at 1 year ($p = 0.001$).
Multivariate analysis showed a statistically significant correlation between dehydration and mortality in all three periods analyzed, with a decreasing strength over time but a consistently significant association even after adjustment for potential confounding factors.
Conclusions: Dehydration in older patients hospitalized for acute conditions represents an independent determinant of early, subacute, and long-term mortality.
Frailty, as a reflection of reduced functional reserve and diminished ability to adapt to the clinical stress associated with hospitalization, represents a very strong negative prognostic factor.

Abstract n SO4_02 - Presenting author**: Marialuisa Sveva Marozzi**

Analysis of the impact of environmental factors on emergency department visits: a longitudinal observational study (2014–2024)

Marialuisa Sveva Marozzi[1,2], Vanessa Desantis[3], Cristina Piarulli[1], Angelo Vacca[1], Sebastiano Cicco[1,2]

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Aim: Climate factors and air pollution are relevant determinants of emergency care demand, yet the Mediterranean context remains underrepresented in literature. Most studies focus on single clinical outcomes without integrated analysis, and the interaction between climate variables and pollutants has been rarely explored, risking erroneous causal attributions due to seasonal confounding. This study aimed to evaluate the association between environmental variables and Emergency Department (ED) visits at a Southern Italian university hospital, focusing on cardiometabolic outcomes including hypertensive crises, cardiovascular diagnoses, and pregnancy-related hypertension.
Methods: A retrospective observational study was conducted on monthly aggregated data over 132 consecutive months (January 2014–December 2024) at Policlinico di Bari. Environmental variables included temperature, humidity, NO_2, PM2.5, PM10, ozone, and benzene. Multiple linear regression models were constructed including seasonal variables and temporal trends to assess associations with total visits, triage codes, and cardiometabolic outcomes.
Results: Mean monthly ED visits were 5358±1090. NO_2 (25.71±5.75 μg/m³) emerged as the pollutant with most consistent associations, showing positive correlations with total visits (β=122–199, p<0.001), green codes (β=72–109, p<0.001), and hypertensive crises (β=0.23–0.30, p≤0.003). Cardiovascular diagnoses showed no significant associations with pollutants. Comparative analysis revealed seasonal pattern inversion: summer months appeared protective in climate-only models (July: β=-4274, p=0.001) but associated with increased visits in pollutant-adjusted models (August: β=+3538, p<0.001), indicating confounding by NO_2. All outcomes exhibited negative temporal trends except red triage codes proportion, which progressively increased.
Conclusions: The atmospheric environment significantly affects ED workload with effects modulated by diagnostic category. NO_2 emerges as the main pollutant associated with visits and hypertensive crises, while cardiovascular diagnoses appear less sensitive. The seasonal pattern inversion between models represents an original methodological contribution, providing empirical basis for resource planning and AI-based predictive systems.

Abstract n SO4_03 - Presenting author**: Roberto Emolo**

Comparison of prognostic risk stratification scores in patients with pulmonary embolism and active oncohematological disease presenting to the emergency department

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Aim Cancer-associated pulmonary embolism is frequently diagnosed in the ED and increasingly detected as *incidental PE (IPE)* on oncologic CT scans, making short-term risk stratification crucial for management decisions. This study compared EPIPHANY Index, POMPE-C, and HESTIA criteria for predicting 30-day adverse outcomes in oncologic patients with PE, including a dedicated analysis in the IPE subgroup.
Methods Retrospective, single-center ED study including adults with active malignancy and imaging-confirmed PE (2015–2019 and 2023; 2020–2022 excluded). The 30-day composite endpoint was death and/or acute respiratory failure and/or PE-related hospitalization. Prognostic accuracy (Se/Sp, NPV, LR−) and discrimination (ROC-AUC) were calculated for each score; subgroup analysis was performed for IPE.
Results Among 404 patients, 207 (51.2%) had IPE. The 30-day composite outcome occurred in 34.9% overall and was lower in IPE (15.5%) than in symptomatic PE (55.3%). Overall discrimination favored POMPE-C (AUC 0.874) vs EPIPHANY (AUC 0.795). In IPE, POMPE-C provided the strongest rule-out profile (NPV 95.4%, LR− 0.263), while HESTIA also supported low-risk identification (NPV 92.2%, LR− 0.46); EPIPHANY was less discriminative in IPE (NPV 89.6%, LR− 0.633).
Conclusions In ED patients with active cancer and PE—particularly those with IPE—POMPE-C showed the best prognostic performance for short-term adverse outcomes, with HESTIA offering a practical discharge-oriented screen. These tools may support safer triage decisions, provided they are integrated with clinical judgment and follow-up capability.

Abstract n SO4_04 - Presenting author**: Marta Iaia**

Survivors of childhood acute lymphoblastic leukemia (ALL) present an altered immune, vascular and metabolic profile

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Background and aims: ALL is the most common childhood blood cancer, is treated with chemotherapy and, for high-risk or relapsed patients, total body irradiation followed by stem cell transplantation (TBI-HSCT). Although survival now exceeds 90%, ALL survivors show increased cardiovascular and metabolic risk. This project aims to investigate metabolic and inflammatory sequelae after TBI-HSCT and how these changes affect mature immune cells derived from transplanted stem cells.
Methods: A cohort of 14 disease-free cALL survivors who received TBI-HSCT (median age at HSCT: 13 years) (recipients) about 10 years prior to the enrolment, along with 14 matched sibling donors with an average age of 23.7 were recruited. Clinical profiling, blood sampling for immunophenotyping, transcriptomics, proteomics and telomere analysis, and ultrasound assessment of supra-aortic trunks for carotid intima-media thickness (IMT) were performed.
Results: Hematopoietic stem cell transplantation (HSCT) in recipients showed accelerated telomere shortening in leukocytes (slope −0.009 vs −0.0008), reduced HSCs ($CD34^+$), and increased B cells ($CD19^+$) compared with donors. scRNA-seq revealed inflammation and impaired B-cell functions. IgM levels were lower in recipients (58,62 SE±4,062 vs 49,23 SE±3,188), while IgG remained similar (329.7 SE±16.43 vs 350.6 SE±14.49). Recipients also had higher cholesterol (171.9 SE±10.43 vs 157.5 SE±9.19), triglycerides (105.0 SE±11.31 vs 65.57 SE±5.22), insulin (15.23 SE±2.95 vs 8.46 SE±1.87), and HOMA index (2.98 SE±0.62 vs 1.59 SE±0.37), despite comparable anthropometrics. Proteomics showed increased acute-phase proteins (CRP, APS) and dyslipidaemia-related proteins (APOB, APOC4-APOC2). Clinically, recipients showed accelerated carotid IMT progression (0.0083 vs 0.0034) and a 14.3% prevalence of metabolic syndrome.
Conclusions: TBI-HSCT is associated with an impaired B-cell phenotype and metabolic profile, potentially increasing long-term cardiovascular risk of cALL survivors. Ongoing B-cell subsets analyses aim to clarify functional impairments. Together this evidence suggests the need to optimize the clinical follow-up strategies to mitigate the increased cardiometabolic risk in cALL survivors.

Abstract n SO4_05 - Presenting author**: Noemi Maggio**

Unlocking the predictive power of nutritional scores in septic patients

Arianna Toscano[1], Federica Bellone[1], Noemi Maggio[1], Maria Cinquegrani[1], Francesca Spadaro[1], Francesca Maria Bueti[1], Giuseppe Lorello[1], Herbert Ryan Marini[1], Alberto Lo Gullo[2], Giorgio Basile[3], Giovanni Squadrito[1], Giuseppe Mandraffino[1], and Carmela Morace[1]

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Aim: Sepsis is a critical condition characterized by severe immune dysregulation, ranking among the leading causes of morbidity and mortality in Internal Medicine Units. Malnutrition is frequently observed in septic patients and is strongly associated with worse clinical outcomes, including increased mortality, prolonged hospital stays, and greater complication rates. Nutritional scoring systems have emerged as valuable tools to evaluate patients' nutritional status and predict clinical trajectories. Since a direct comparison of their performance has never been conducted, we aimed to evaluate the effectiveness of various nutritional scores as predictive tools for clinical outcomes in septic patients.
Methods: A retrospective analysis was conducted on 143 patients diagnosed with sepsis or septic shock, admitted to an Internal Medicine Unit. Key variables included clinical and laboratory parameters, comorbidities, and nutritional scores at the time of diagnosis. The modified Glasgow Prognostic Score (mGPS), Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT) score, modified Nutrition Risk in Critically Ill (mNUTRIC) score, and the blood urea nitrogen-to-albumin ratio (BAR) were evaluated in forecasting mortality and clinical outcomes in patients with sepsis.
Results: A total of 143 patients with sepsis/septic shock were included (median age 79.3 years), An in-hospital mortality rate of 49% was observed. In stepwise multivariable regression analysis, only the mNUTRIC score emerged as an independent predictor of in-hospital mortality. ROC curve analysis demonstrated good discriminative ability for the mNUTRIC score (AUC 0.814; 95%CI: 0.737–0.891), with an optimal cut-off value of 4.5 points for mortality risk stratification. The other nutritional scores did not show significant predictive value in this clinical setting.
Conclusions: The study highlights the mNUTRIC score's practicality and reliability in assessing nutritional and inflammatory risks in septic patients, particularly in non-ICU settings. These findings suggest its potential utility in guiding nutritional interventions and improving clinical outcomes, emphasizing the importance of integrating nutritional assessment into sepsis management.

Abstract n SO5_01 - Presenting author**: Sergio Ferrantelli**

The impact of NOACS versus VKAS on absolute and relative cognitive function decline over time: a machine learning approach

Sergio Ferrantelli, Mario Daidone, Giuseppe Armentaro, Gaetano Pacinella, Stefania Scaglione, Anna M. Ciaccio, Edoardo Pirera, Carlo D. Maida, Giuseppe Miceli, Giuliana Rizzo, Vittoriano Della Corte, Domenico Di Raimondo, Daniele Pastori, Angela Sciacqua, Antonino Tuttolomondo

Università degli studi di Palermo

Aim: Atrial fibrillation (AF) is independently associated with a higher incidence of cognitive impairment and dementia. While Non-vitamin K antagonist oral anticoagulants (NOACs) demonstrate a superior safety profile regarding stroke prevention compared to Vitamin K antagonists (VKAs), their potential role in mitigating cognitive decline remains uncertain. This study employs a machine learning-driven approach within a multicenter prospective cohort to investigate whether NOACs attenuate the progression of cognitive decline relative to VKAs in elderly AF patients.
Methods: This multicenter prospective cohort study included 983 AF outpatients enrolled between 2008 and 2022 at the University of Catanzaro and the University of Palermo. Stroke and bleeding risks were assessed using CHA2DS2-VASc and HAS-BLED scores. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), with cognitive decline defined as a decrease in score between baseline and follow-up. Patients with prior anticoagulant therapy, severe dementia, or comorbidities affecting cognition were excluded. We employed multivariable logistic regression and a Random Forest classifier to assess if anticoagulant type independently predicted decline.
Results: At baseline, cognitive performance was comparable between groups ($p=0.11$). After a mean follow-up of 7.2 ± 3.4 years, MMSE scores declined significantly more in VKA-treated patients (-1.7 vs. -0.3 points, $p < 0.001$). In logistic regression, NOAC use was independently associated with a lower risk of cognitive decline (OR: 0.322; 95% CI: 0.221–0.469; $p < 0.0001$). The Random Forest classifier achieved a mean cross-validated AUC of 0.8719 and a test-set AUC of 0.880. Permutation importance analysis identified anticoagulant therapy type as the top predictor. Predicted probabilities of cognitive decline were significantly higher in VKA users (median=0.70) than in NOAC users (median=0.09; $p < 0.001$).
Conclusions: NOAC use is associated with a significantly reduced risk of cognitive decline compared to VKAs, suggesting clinical benefits extending beyond stroke prevention.

Abstract n SO5_02 - Presenting author**: Maristella Belfiori**

Data-driven identification of frailty and resilience phenotypes in older adults: insights from a large comprehensive geriatric assessment cohort

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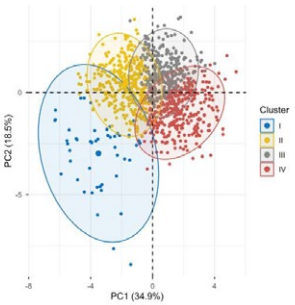
Aim: Population aging is characterized by increasing clinical heterogeneity, requiring multidimensional approaches, such as Comprehensive Geriatric Assessment (CGA), to accurately describe frailty and resilience in older adults. This study aimed to leverage CGA data using multivariate and data-driven analytical approaches, Principal Component Analysis (PCA) and cluster analysis, to identify distinct and clinically meaningful frailty and resilience phenotypes in a large cohort of older outpatients.

Methods: We conducted a cross-sectional analysis of 1,055 outpatients aged ≥65 years consecutively evaluated at the Geriatric Outpatient Service of the University Hospitalof Monserrato, Cagliari, Italy, between 2020 and 2024. All participants underwent a standardized CGA. PCA was applied to key CGA domains to reduce dimensionality and identify latent constructs. The resulting components were used to perform hierarchical cluster analysis.

Results: PCA identified four principal components explaining 73.5% of total variance. The first component reflected a global Frailty Dimension, while the second captured Reserve Capacity. Cluster analysis based on these components revealed four distinct phenotypes: (I) **Vulnerable Low-Complexity**, characterized by younger age, low comorbidity burden, and pronounced cognitive, nutritional, and functional impairments; (II) **Resilient High-Reserve**, showing preserved multidomain function, low comorbidity, and higher educational attainment; (III) **Resilient Frailty**, marked by high comorbidity and functional and nutritional deficits despite preserved cognitive reserve; and (IV) **Globally Frail**, comprising older individuals with high comorbidity burden and impairments across all CGA domains (*Figure 1 and 2*).

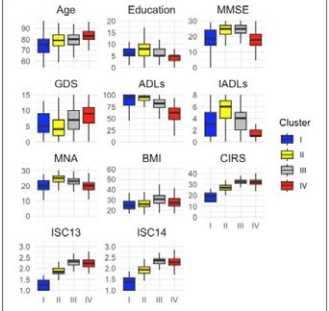
Conclusions: This large CGA-based study demonstrates that a multidimensional analytical combined with PCA- informed clustering approach can uncover distinct and clinically relevant frailty and resilience phenotypes in aging populations. These findings support refined risk stratification and more individualized geriatric care pathways.

Figure 1: Cluster distribution of individuals according to Principal Components.



Abbreviations: PC, Principal Component

Figure 2: Boxplots of the variables included in the PCA, stratified by cluster.



Abbreviations: ADLs, Activities of Daily Living; BMI, Body Mass Index; CIRS, Cumulative Illness Rating Scale; CIRS ISC, Cumulative Illness Rating Scale Severity Index; GDS, Geriatric Depression Scale; IADLs, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; PC, Principal Component; PCA, Principal Component Analysis.

Abstract n SO5_03 - Presenting author**: Chiara Chinigò**

Monocyte-to-HDL ratio and mortality risk stratification in older adults with chronic kidney disease using data-driven models

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Aim: Risk stratification in older adults with chronic kidney disease (CKD) remains challenging due to complex inflammatory–metabolic interactions and multimorbidity. Data-driven and artificial intelligence–oriented analytical approaches enable integration of immune-metabolic biomarkers with traditional clinical variables to identify predictors from large-scale data. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR), integrating immune activation and lipid metabolism, is a promising biomarker. The aim of this study was to evaluate whether MHR improves all-cause and renal mortality risk stratification in older adults with CKD beyond established kidney measures using data-driven analytical strategies.
Methods: We analyzed 5,115 adults aged ≥70 years with CKD from NHANES 1999–2018, with external validation in 1,684 participants from the 2016 Health and Retirement Study. CKD was defined by estimated glomerular filtration rate <60 mL/min/1.73 m² and/or albumin-to-creatinine ratio ≥30 mg/g. All-cause and renal-specific mortality were assessed via linkage to the National Death Index. Associations between the monocyte-to-HDL cholesterol ratio (MHR) and mortality were evaluated using survey-weighted Cox and Fine–Gray models, supported by data-driven approaches including penalized regression (LASSO) and survival random forest with Boruta selection.
Results: During a mean follow-up of 82 months in NHANES, higher MHR was independently associated with increased all-cause (HR 1.32, 95% CI 1.20–1.45) and renal-specific mortality (sub-distribution HR 1.43, 95% CI 1.12–1.82), after adjustment for eGFR, ACR, and clinical factors. Feature selection using LASSO and the Boruta algorithm identified MHR as a stable predictor of both outcomes, ranking alongside eGFR and ACR and outperforming traditional lipid and immune markers. Associations were consistent in the HRS cohort, with stronger links to all-cause mortality in moderate CKD and renal mortality in advanced CKD.
Conclusion: In older adults with CKD, the monocyte-to-HDL cholesterol ratio is independently associated with all-cause and renal-specific mortality and adds prognostic information beyond traditional kidney measures. These findings support integrating immune-metabolic biomarkers into data-driven risk stratification frameworks to improve prognostic assessment in CKD.

Abstract n SO5_04 - Presenting author**: Caroline Lopa**

Association of mitofusin 2 polymorphic variants with left ventricular hypertrophy in human hypertension

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Aims: Previous experimental studies showed that dysfunctions of mitofusin 2 (Mfn2) are associated with the development of left ventricular hypertrophy (LVH). We examined the association of *MFN2*/rs2336384 and *MNF2*/rs2236057 polymorphic variants with the development of LVH in hypertensive patients.
Methods and results: Three-hundred-fourty-five hypertensive subjects (199 male, 57.6%) were studied, 113 with LVH. Patients carrying the GG genotype at the *MFN2*/rs2336384 had a significant increase of echocardiographically assessed septal thickness (p=0.001), posterior wall thickness (p=0.001), relative wall thickness (RWT) (p=0.003), LV mass/ body surface area (BSA) (p=0.001), LV mass/height$^{2.}$(p=0.001), left atrium volume index (LAVi) (p=0.001) compared to subjects carrying either TT or TG genotypes. With regard to *MNF2*/rs2236057, hypertensive subjects carrying the mutant A allele had a significant increase of septal thickness (p=0.001), posterior wall thickness (p=0.002), RWT (p=0.01), LV mass/BSA(p=0.001), LV mass/height$^{2.7}$(p=0.002) and LAVi (p=0.001) compared to wild-type homozygotes (GG genotype) and heterozygotes (GA genotype). The results maintained significance also after adjustments for age, gender, body mass index (BMI), office blood pressure (BP), antihypertensive treatment with a combination of 2 or more drugs and the number of BP-lowering agents as covariates.
Multivariable logistic regression analysis, assuming the development of LVH as the dependent variable and both SNPs with the above-mentioned covariates as independent variables, demonstrated that the carrier status of both G allele at rs2336384 and AA genotype at s2236057 was associated with an increased risk of LVH (OR=2.175 [95% confidence interval, 1.27–3.71]; P=0.004 and OR=1.617 [95% confidence interval, 1.13–2.31]; P=0.009, respectively).
Conclusions: Our results demonstrate a significant association of *MFN2* variants with LVH in hypertensives and highlight a role of MFN2 dependent mitochondrial dysfunction on increased susceptibility to cardiac damage in human hypertension. This study paves the way of a new pathophysiological mechanism of LVH which may lead to new clinical strategies.

Abstract n SO5_05 - Presenting author: **Isabella Fichtner**

Extracellular vesicles isolated from patients with heart failure retain proinflammatory features

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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 of the present project was to characterize EVs in HF patients, investigating their potential as biomarkers and tools to discriminate between HFrEF and HFpEF clinical phenotypes.
Methods The study included 39 HF patients (13 HFpEF and 26 HFrEF) and 28 volunteers (CTR). EVs were isolated from plasma by size-exclusion chromatography and ultracentrifugation, then characterized using nanoparticles tracking analysis, transmission electron microscopy (TEM), Western blot (WB) and flow cytometry (FACS). Functional assays using patient-derived EVs were performed on cellular models of monocyte (THP-1) and cardiomyocyte (H9C2).
Results Diagnosis of HF relied on echocardiographic (e.g. E/e' ratio) and biochemical parameters (e.g. NT-proBNP). Isolation of EV was confirmed by FACS and WB analyses (e.g. the presence of CD63, CD9, CD81, Alix and β1 integrin), while integrity by TEM. EV size was increased in HF (nm: 202 vs 181). Among different subpopulations of EVs, those from monocytes (CD14+), macrophages (CD206+), neutrophils (CD66b+), endothelial cells (CD202b+), activated endothelial cells (CD62E+), cardiomyocytes (CD172a+), platelets (CD41a+), were significantly reduced in HF. Conversely, EVs released by T helper lymphocytes (CD4+) were significantly increased in HF patients when compared to controls. Treatment of THP-1 and H9C2 cells with EVs derived from HF patients led to an increased expression of proinflammatory cytokines (i.e. IL-1α, IL-1β, IL-6), when compared to cells treated with EVs isolated from CTR subjects. This change was mostly driven by EVs derived from HFpEF patients.
Conclusions EVs derived from HF patients exhibit a distinct profile that reflects the hemodynamic characteristics of the condition and possess proinflammatory properties.

Abstract n SO5_06 - Presenting author**: Agnese Fontana**

ChatGPT-Based AI workflow for low-cost body composition estimation: proof-of-concept study

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Background: Accurate assessment of body composition is crucial for diagnosing metabolic disorders and guiding nutritional interventions. Traditional tools such as body mass index (BMI) and bioimpedance analysis (BIA) often provide limited information or lack precision, whereas dual-energy x-ray absorptiometry (DEXA) is expensive, requires ionizing radiation and specialized equipment. Large language models such as ChatGPT can process diverse inputs including text and images and may offer an accessible alternative for estimating body composition.
Methods: In this exploratory proof-of-concept study, 21 adult volunteers underwent anthropometric measurements, standardized smartphone photography and reference DEXA scanning. Three ChatGPT-based AI configurations were compared: AI1 used anthropometric data alone; AI2 used anthropometric data plus front- and side-view images; AI3 added back-view images and additional variables. The ChatGPT-5 model with deterministic settings (temperature = 0) was prompted once per participant to generate estimates of body fat percentage (FM%). Estimates were compared with DEXA and BIA using intraclass correlation coefficients (ICC), Bland–Altman analysis and mean absolute percentage error (MAPE).
Results: Participants (median age 35 years, interquartile range [IQR] 28–42; 48 % female) had a mean BMI of
27.1 ± 4.7 kg/m² and DEXA-measured FM% of 31.4 ± 9.6. AI2 produced FM% estimates with excellent agreement to DEXA (ICC = 0.95, 95 % CI 0.90–0.98; bias < 1 % and MAPE 7 %), outperforming both AI1 and AI3 and providing more accurate estimates than BIA (ICC = 0.78). A plateau in performance was observed with AI3 despite the additional inputs**.**
Conclusions: In this small proof-of-concept study, ChatGPT-5 generated body composition estimates with excellent agreement to DEXA when provided with anthropometric data and two standardized images. While results suggest that AI2 may serve as an accessible and radiation-free adjunct for body composition assessment, larger multicenter studies are required to validate its use in diverse populations.

Abstract n SO5_07 - Presenting author**: Francesco Alfano**

Markers of inflammation and hypofibrinolysis are associated with cognitive dysfunction and motor performances in atrial fibrillation patients on oral anticoagulant therapy: insights from the Strat-AF Study

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Aim: Atrial fibrillation (AF) is the most common supraventricular arrythmia and one of the most commonly encountered heart conditions in clinical practice. Emerging evidence suggests a significant role of inflammation in the pathogenesis of AF. Population studies have also suggested an association between AF and cognitive impairment and dementia. The aim of this study is therefore to assess, in a population of AF patients on oral anticoagulant therapy, the association between circulating biomarkers involved in the pathogenesis of AF and the cognitive and motor performances of the enrolled patients.
Methods: The Strat-AF study is an observational, prospective, single-center, hospital-based study enrolling elderly patients with AF. Results refer to 180 subjects who underwent a complete clinical, biohumoral, cognitive, and functional evaluation.
Results: At multivariate logistic regression, Clot Lysis Time (CLT) and circulating levels of von Willebrand Factor (vWF) remained significantly associated with pathological performances at the Stroop test (expressed as execution time) [OR 95% CI 1.54 (1.02-2.35), p = 0.042 and 1.75 (1.08-2.82), p = 0.023, respectively]. With regard to the Short Physical Performance Battery (SPPB), the circulating levels of IL-8 remained significantly associated with the clinical endpoint [OR 95% CI 2.19 (1.13-4.25), p = 0.020].
Conclusions: Our results suggest a potential innovative tool able to identify AF patients at risk of worse prognosis in terms of cognitive and motor performances. The clinical relevance of these results is due to the fact that we have no efficient methods to predict a deterioration in the cognitive performance and, consequently, the possible onset of dementia in AF patients undergoing oral anticoagulant therapy.

Abstract n SP01_1 - Presenting author**: Marta Peccarisi**

Gut-derived endotoxemia and dyslipidemia as predictors of sarcopenia in older patients with metabolic dysfunction–associated steatotic liver disease (MASLD)

Marta Peccarisi, Chiara Greco, Nicholas Cocomello, Vittoria Cammisotto, Federica Moscucci, Pasquale Pignatelli, Francesco Baratta, Giovambattista Desideri

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Background and aims: Sarcopenia frequently coexists with metabolic dysfunction and may worsen prognosis in patients with metabolic-associated fatty liver disease (MAFLD). Gut-derived endotoxemia, reflected by circulating lipopolysaccharide (LPS), has been implicated in systemic inflammation and muscle impairment, but longitudinal data in older adults with hepatic steatosis are limited. Objectives were to investigate the longitudinal association between muscle strength, metabolic profile, and gut permeability markers—particularly LPS—in older patients with hepatic steatosis.
Methods: This retrospective longitudinal study was conducted within the PLINIO cohort (ClinicalTrials.gov Identifier:NCT04036357). Patients aged ≥65 years with persistent ultrasound-confirmed hepatic steatosis and preserved functional autonomy were included. Handgrip strength was assessed at follow-up and correlated with baseline clinical, biochemical, and instrumental data collected at PLINIO enrollment. Sarcopenia was defined according to EWGSOP2 handgrip cut-offs. LPS and zonulin were measured on stored serum samples by ELISA. Correlation analyses (Spearman) and multivariable Cox regression models were performed to identify independent predictors of sarcopenia.
Results: Seventy-one patients (mean age 71.6±5.9 years; 39.4% women) were included; sarcopenia prevalence was 36.6%, higher in women. Among 53 patients with complete baseline data, sarcopenic individuals had lower BMI but significantly higher total cholesterol, LDL, non-HDL cholesterol, and LPS levels. Handgrip strength was inversely correlated with LPS (rS −0.428, p=0.001) and total cholesterol (rS −0.257, p=0.049). In multivariable Cox regression adjusted for age and sex, LPS (aHR 1.017 per unit; p=0.007) and total cholesterol (aHR 1.012; p=0.046) were independent predictors of sarcopenia. Categorizing LPS above the median markedly increased risk (aHR 6.48; p=0.006). LPS strongly correlated with zonulin (rS 0.560, p=0.001).
Conclusions: In older patients with hepatic steatosis, sarcopenia is common and independently associated with elevated LPS and adverse lipid profile. These findings support a potential role of gut permeability and endotoxemia in muscle decline, warranting prospective mechanistic studies.

Abstract n SP01_2 - Presenting author**: Gaetano Leo**

Lipoprotein(a) levels across histological severity in metabolic dysfunction–associated steatotic liver disease

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Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) encompasses a spectrum ranging from simple steatosis to metabolic dysfunction–associated steatohepatitis (MASH) and cirrhosis. Lipoprotein(a) [Lp(a)] is a well-established atherogenic risk factor, but its relationship with MASLD and its histological severity has been poorly investigated. The aim of this study was to describe plasma Lp(a) levels across different histological stages and features of MASLD.
Methods: Eighty-eight patients enrolled in the PLINIO study (ClinicalTrials.gov Identifier: NCT04036357) who underwent liver biopsy were included. Plasma Lp(a) levels were measured using a specific ELISA kit. Patients were stratified according to histological diagnosis into simple steatosis (MASLD-SS), MASH, and cirrhosis. In a subgroup of 29 patients, immunohistochemical analysis was performed to assess hepatic Lp(a) expression on liver biopsy samples.
Results: Plasma Lp(a) levels increased progressively with histological severity (MASLD-SS: 22.1 [20.2–26.6] mg/dL; MASH: 28.7 [24.2–32.8] mg/dL; cirrhosis: 31.1 [29.4–33.1] mg/dL; p=0.001). Plasma Lp(a) correlated positively with fibrosis stage (rS=0.401, p<0.001), inflammation grade (rS=0.214, p=0.045), hepatocellular ballooning (rS=0.383, p<0.001), and NAFLD Activity Score (rS=0.410, p<0.001). In multivariable regression analysis including demographic and clinical variables, plasma Lp(a) was independently associated with LDL cholesterol (β=0.003, p=0.012) after adjustment for age, sex, ALT, and diabetes. At immunohistochemical analysis, no overall correlation was found between hepatic and plasma Lp(a) or histological features. However, after excluding cirrhotic patients, hepatic and plasma Lp(a) levels correlated significantly (rS=0.436, p=0.033). Among patients with MASH, hepatic Lp(a) expression was higher in those with more severe ballooning (p=0.043).
Conclusions: In this histologically characterized MASLD cohort, Lp(a) levels increased with disease severity and correlated with fibrosis and activity parameters. These findings suggest a potential role for Lp(a) in MASLD progression and warrant further studies to clarify its contribution to liver disease pathogenesis and cardiovascular risk in this population.

Abstract n SP01_3 - Presenting author**: Mirko Parasiliti-Caprino**

Evaluating steroid profiles through sexual dimorphism to define metabolic phenotypes and identify advanced fibrosis in patients with MASLD

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Aim. Sex-related differences in metabolic dysfunction-associated steatotic liver disease (MASLD) are increasingly recognised, yet the endocrine mechanisms underlying disease progression remain poorly understood. We aimed to explore sexual dimorphism in MASLD and to predict advanced hepatic fibrosis through a targeted steroidomic approach.
Methods. In this cross-sectional study, we enrolled 463 patients with biopsy-proven MASLD from two tertiary Liver Units in Italy. Steroid hormones were quantified using a newly validated method. Associations with sex, metabolic comorbidities, PNPLA3 genotype, and liver fibrosis were analysed. A predictive tool (FaSter model) for advanced fibrosis (F≥3) was derived in the Turin cohort (n=313) and externally validated in the Palermo cohort (n=150). A subgroup of 32 patients underwent hepatic gene expression analysis for key steroidogenic enzymes.
Results. Steroid profiling revealed significant sex- and age-related differences, with distinct patterns associated with obesity, type 2 diabetes, arterial hypertension, and PNPLA3 genotype. In men, advanced fibrosis was associated with reduced androgen sulfation and glucuronidation. In women, alterations reflected menopausal status and metabolic phenotype. The FaSter model, integrating clinical parameters and ten steroid biomarkers, showed high diagnostic accuracy for advanced fibrosis (AUC 0.88 in training cohort; 0.82 in validation cohort), outperforming FIB-4 and NFS, and approaching Vibration-Controlled Transient Elastography performance (VCTE). Combining model with VCTE further improved accuracy (AUC up to 0.91). Gene expression data supported a pathophysiological role for impaired hepatic steroid inactivation in advanced disease.
Conclusions. Steroid metabolism is tightly linked to sexual dimorphism and fibrosis progression in MASLD. FaSter model represents a novel, non-invasive tool for risk stratification, with potential application in personalised hepatology. Future longitudinal and multi-ethnic studies are warranted.

Abstract n SP01_4 - Presenting author**: Andrea Bagnato**

Age-related differences in lipid profile and insulin resistance markers in patients with metabolic dysfunction–associated steatotic liver disease (MASLD

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Background and Aims: Metabolic dysfunction–associated steatotic liver disease (MASLD) is a leading cause of chronic liver disease worldwide. Its prevalence increases with age but declines in the oldest age groups, suggesting the presence of survivorship bias. Aging is accompanied by changes in lipid metabolism and insulin resistance, which may contribute to differences in metabolic profiles between younger and older patients with MASLD.
Methods: This cross-sectional study included patients with MASLD enrolled in the PLINIO study (ClinicalTrials.gov Identifier:NCT04036357). Participants were divided into two age groups (<65 and ≥65 years) and matched by propensity score for sex, statin use, antihypertensive therapy, antiplatelet therapy, and type 2 diabetes.
Results: A total of 404 patients were analyzed (202 per group). Compared with patients <65 years, those ≥65 years had a significantly lower BMI (28.8 ± 4.4 vs 31.3 ± 5.4 kg/m²; p<0.001) and a more favorable lipid profile, with higher HDL cholesterol (53.4 ± 15.0 vs 48.4 ± 12.6 mg/dL; p<0.001), lower triglycerides (129.4 ± 55.1 vs 148.8 ± 67.9 mg/dL; p=0.002), lower VLDL (25.9 ± 11.0 vs 29.8 ± 13.6 mg/dL; p=0.002), and lower remnant cholesterol (25.9 ± 11.0 vs 29.8 ± 13.6 mg/dL; p=0.002). The total-cholesterol/HDL ratio was significantly lower in older patients (3.74 ± 1.21 vs 4.20 ± 1.19; p<0.001). Insulin resistance, assessed by the TyG index, was also slightly but significantly lower in patients ≥65 years (4.72 ± 0.24 vs 4.78 ± 0.26; p=0.031). No significant differences were observed in total cholesterol, LDL cholesterol, or fasting glucose levels.
Conclusions: Older patients with MASLD display a more favorable lipid profile and lower insulin resistance compared with younger patients, despite similar cardiometabolic comorbidities. These findings support the presence of survivorship bias in MASLD and suggest that individuals reaching older age may represent a metabolically “resilient” subgroup characterized by reduced atherogenic dyslipidemia and insulin resistance.

Abstract n SP01_5 - Presenting author**: Michele Tafuro**

Dyslipidemia in patients with primary biliary cholangitis (PBC) is less atherogenic than in patients with primary polygenic hypercholesterolemia

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Aim: Patients with primary biliary cholangitis (PBC) display various degrees of dyslipidemia, with a frequent disconnect between lipid levels and cardiovascular risk. In this study, we compared high-density lipoprotein (HDL) functionality (cholesterol efflux capacity, CEC) and whole-serum atherogenicity (cholesterol loading capacity, CLC) in patients with PBC versus patients with polygenic hypercholesterolemia (PH).
Methods: Single-center prospective study including 36 adults (23 PBC; 13 PH) propensity score matched 2:1 on demographics, anthropometrics, and baseline lipids. CEC was quantified with radioisotopic systems and CLC was measured in macrophages exposed to patients' serum.
Results: Groups were similar for age (66 vs 65 years), sex (23/23 vs 12/13 female), anthropometrics, and lipid profile. Patients with PBC showed higher ALP (99 vs 78 U/L; p=0.031), AST (26 vs 20 U/L; p=0.011), and γ-globulins (15.1 vs 12.6; p=0.002), while bilirubin, ALT, GGT, albumin were similar to patients with PH. Passive-diffusion was higher in PBC (13.30 vs 12.67 %/4 h; p=0.008), whereas there were no significant differences in other CEC characteristics: ABCA1-CEC (p=0.093), ABCG1-CEC (p=0.281), SR-BI-CEC (p=0.820), and total CEC (p=0.361). CLC was significantly lower in patients with PBC (35.20 vs 43.76 µg/mg; p=0.001). After adjustment for body mass index and baseline low-density lipoproteins, PBC status remained associated with a lower CLC (p=0.008), while higher CLC was independently associated with cardiometabolic family history (p=0.002).
Conclusions: Dyslipidemia in patients with PBC seems to be less atherogenic than in those with PH, helping to explain the observed disconnect between hyperlipemia and cardiovascular risk in patient with PBC.

Abstract n SP02_1 - Presenting author**: Simona Persia**

The sinuses of valsalva/ascending aorta diameter ratio as a marker of subclinical cardiovascular damage in hypertension

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Aim: Dilatation of the ascending thoracic aorta is a parameter closely associated with arterial hypertension and increased cardiovascular risk, as demonstrated by the higher prevalence of this echocardiographic finding in hypertensive patients.Most clinical studies focused on assessing the diameter of the ascending aorta in patients with established aortic ectasia.This study aimed to evaluate whether, in hypertensive patients without dilatation of the ascending aorta, the ratio between the thoracic aortic diameter at the sinuses of Valsalva and at the tubular ascending aorta(SoV/AoAsc)could represent a potential marker of organ damage.
Methods: This single-center observational study included 288 patients(mean age 62.5 ± 11.7 years) undergoing outpatient evaluation comprising medical history, physical examination, anthropometric measurements, blood pressure assessment, blood tests, electrocardiography, echocardiography, and indices of endothelial dysfunction. The SoV/AoAsc ratio was calculated and patients were classified into two groups: Group 1 with a ratio <1 and Group 2 with a ratio >1.
Results:_ Group 1 showed higher systolic blood pressure values(p = 0.016)and LDL cholesterol levels(p = 0.001), a greater prevalence of smoking habit(p = 0.021),and more frequent proteinuria(p = 0.046).From an electrocardiographic and echocardiographic standpoint, Group 1 exhibited QTc prolongation(p = 0.036) and signs of cardiac remodeling, including increased left ventricular internal diameter(p = 0.044)and higher indexed left ventricular mass(LVMi, p = 0.003; LVM_27, p = 0.0013).In addition, advanced diastolic dysfunction(p = 0.0001)and an increased right ventricular diameter(p = 0.0001)were observed.
Conclusions: n hypertensive patients without ascending aortic dilatation, a SoV/AoAsc ratio <1 is associated with a worse cardiovascular profile, characterized by a higher burden of risk factors,early signs of cardiac remodeling, and markers of subclinical target organ damage.This echocardiographic ratio may represent an early marker of cardiovascular risk, allowing a more refined prognostic stratification than isolated aortic diameter measurements.Further prospective studies are needed to confirm its independent prognostic value and to define its role in clinical practice.

Abstract n SP02_2 - Presenting author**: Gabriele Leone**

Small-RNA characterization of circulating extracellular vesicles from patients with adrenal-producing adenomas

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Aim Primary aldosteronism (PA) is associated with an increased burden of vascular target-organ damage, including endothelial dysfunction, inflammation, fibrosis, and accelerated atherosclerosis. Extracellular vesicles (EVs) are key mediators of intercellular communication and transport biologically active molecules, such as small non-coding RNAs. This study aimed to investigate the small RNA content of circulating EVs in patients with aldosterone-producing adenoma (APA) compared with essential hypertension (EH), and to explore their potential involvement in disease-specific vascular pathways.
Methods Circulating EVs were isolated by ultracentrifugation from serum samples of 12 APA patients and 12 EH patients matched for cardiovascular risk factors. Small RNA sequencing was performed to compare EV-associated miRNA profiles between groups and in APA patients before and after adrenalectomy. Bioinformatic and network-cluster analyses were applied to identify enriched signaling pathways. Selected miRNA–mRNA interactions were functionally validated in vitro using human microvascular endothelial cells (HMECs), including aldosterone and eplerenone treatments.
Results Nineteen miRNAs were differentially expressed in EVs from APA patients compared with EH patients, with 6 upregulated and 13 downregulated. Pathway analyses revealed enrichment of MAPK-related pro-inflammatory signaling in APA, whereas TGFβ-associated pathways predominated in EH. In HMECs, inhibition of miR-769-5p increased MAPK1 expression, while overexpression of miR-486-5p reduced SMAD2 levels, consistent with enhanced TGFβ signaling in APA patients. Circulating EV levels of miR-486-5p significantly decreased after adrenalectomy. Aldosterone treatment increased miR-486-5p expression in HMECs, an effect reversed by eplerenone addition.
Conclusions The EV-associated small RNA signature in APA is linked to pro-inflammatory and anti-fibrotic pathways, potentially promoting vascular inflammation and plaque instability, and contributing to the elevated cardiovascular risk observed in APA patients.

Abstract n SP02_3 - Presenting author**: Lara Ponsa**

Prevalence and predictors of intolerance to calcium channel blocker in an italian hypertensive outpatient cohort

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Aim Calcium channel blockers (CCBs) treat hypertension, but their use can cause side effects, reduce adherence and necessitate alternative therapies.
The aim is to evaluate intolerance to CCBs and identify related independent clinical predictors in an Italian hypertensive outpatient cohort.
Methods We retrospectively analysed 14629 hypertensives evaluated at a tertiary care hypertension centre.
Results Among 14,629 hypertensives, 8,004 (54.71%) were treated with CCBs (56% with amlodipine). CCB intolerance was observed in 2,299 patients (15.7%), mainly to amlodipine (34,02%). Intolerants were more often female (57.1% vs 48.4%, $p<0.001$), allergic (33.4% vs 25.9%, $p<0.001$), with secondary hypertension (10.9% vs 6.5%, $p<0.001$), low education (45.4% vs 39.2%, $p<0.001$), higher BMI (27 vs 26, $p<0.001$), and showed more visits, medications and diagnostic tests ($p<0.001$). Multivariate analysis identified female (OR 1.30 [1.15–1.46]), allergy (OR 1.50 [1.32–1.69]), secondary hypertension (OR 2.00 [1.66–2.42]), low education (OR 1.10 [1.04–1.18]), SBP (OR 1.01 [1.01–1.01]), and BMI (OR 1.03 [1.01–1.04]) as independent predictors of CCB intolerance. Among 1,527 intolerants to amlodipine, 16.2% were also intolerant to other CCBs, 36.9% switched to another CCB, and 30.8% tolerated the switch. Compared to tolerants, those intolerant amlodipine were more often female (53.8% vs 38.3%, $p<0.001$), allergic (32.3% vs 22.6%, $p<0.001$), and had secondary hypertension (10.9% vs 8.4%, $p=0.004$), with a higher number of visits, medications and diagnostic tests. A multivariate analysis on amlodipine intolerance showed the same results of those of CCB intolerance. No significant differences in BP control were found between amlodipine and other CCB treatments, despite patients assuming amlodipine reached BP control with fewer drugs ($p<0,001$).
Conclusions CCB intolerance is linked to female sex, allergies, secondary hypertension, and higher BMI. These factors can help to personalize therapy. Switching to other CCBs may reduce the side effects despite being equally effective in terms of BP control.

Abstract n SP02_4 - Presenting author: **Jessica Goi**

Predictors of treatment response to mineralocorticoid receptor antagonist therapy in primary aldosteronism: data from the SPAIN-ALDO Registry

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Aim – Data on factors predicting successful response to targeted medical therapy in primary aldosteronism (PA), based on PAMO criteria, remain limited. The aim of this study was to identify baseline parameters independently associated with clinical and biochemical outcomes after mineralocorticoid receptor antagonist (MRA) therapy after at least 6 months of treatment.
Methods – PA patients from the national, multicenter SPAIN-ALDO Registry, treated with MRA (or amiloride) and with available clinical and/or biochemical follow-up data after ≥6 months of therapy were included.
Results – A total of 402 patients (38.3% women; mean age 57 years) were analyzed. Median follow-up duration was 30 months (IQR 20–76). At last visit, 55% of patients were receiving spironolactone, 44% eplerenone, and 1.2% amiloride. Among 389 patients with clinical follow-up data, 16.2% achieved complete clinical success, 65.5% partial response, and 18.3% absent response. Complete clinical response was more likely in women, in patients with lower BMI, fewer antihypertensive drugs, and higher potassium levels at baseline. Among 261 patients with biochemical follow-up data, 50.1% had complete biochemical response, 21.5% partial, and 28.4% absent. Predictors of complete biochemical response included lower baseline plasma aldosterone, higher baseline renin levels, use of spironolactone rather than eplerenone, and higher MRA doses.
Conclusion – Timely initiation of targeted therapy and optimized MRA titration, particularly with eplerenone, are essential to achieve optimal clinical and biochemical outcomes, especially in patients with more severe PA.

Abstract n SP02_5 - Presenting author**: Sara Moriglia**

Renin-to-aldosterone ratio is mechanistically associated with ambulatory blood pressure levels and control in treated hypertensive patients with overweight or obesity

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Aim: Combination therapy with a renin–angiotensin system inhibitor (RASi) and a thiazide/thiazide-like diuretic (TZD) or a calcium channel blocker (CCB) is the first-line approach in hypertension management and modulates circulating markers of the RAAS. Since excess adiposity, through different mechanisms, may induce RAAS dysregulation and contribute to blood pressure variability and treatment resistance, this study aimed to evaluate the association between the renin-to-aldosterone ratio (RAR) and ambulatory blood pressure (ABP) in treated hypertensive patients with central overweight (OW) or obesity (OB).
Design and method: In a cross-sectional design, 97 adults with essential hypertension and OW/OB on stable RASi + TZD and/or CCB therapy were matched with 97 normal-weight hypertensive controls (Fig 1). All participants underwent 24-hour ABP monitoring and orthostatic direct renin concentration (DRC) and plasma aldosterone concentration (PAC) measurements.
Results: RAR and DRC were inversely associated with 24-hour, daytime, and night-time BP in controls but not in OW/OB patients; however, higher RAR and DRC values were linked to greater odds of achieving ABP control across all subgroups, whereas PAC showed no significant associations (Fig 2, Fig 3).
Conclusions: RAR, primarily driven by higher DRC levels secondary to the pharmacologic response to RAS inhibition, may reflect a mechanism-based association with ABP control in treated hypertension regardless of BMI.

Abstract n SP02_6 - Presenting author**: Giuseppe Simone Falcone**

Renal denervation in resistant hypertension: short-term blood pressure effects and the role of potential predictive markers of response

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Aim: Renal denervation (RDN) represents a therapeutic strategy for true resistant hypertension. However, the identification of predictive markers of response remains a relevant clinical challenge. Proposed parameters include arterial stiffness, electrocardiographic indices, and biochemical markers of inflammation and vascular damage.
Methods: Eight patients with resistant hypertension undergoing RDN were enrolled. Clinical, biochemical, and instrumental assessments were performed at baseline (T0) and at 3-month follow-up (T1), including blood pressure, heart rate, renal function, arterial stiffness assessed by non-invasive carotid–femoral pulse wave velocity (PWV) measurement, electrocardiography, and glyco-metabolic and electrolyte profiles. Patients achieving a reduction in systolic blood pressure (SBP) ≥10 mmHg were classified as responders.
Results: The mean age was 60.4 ± 12.5 years, and 75% of patients were male. At 3 months after the procedure, a mean SBP reduction of −15 ± 22.6 mmHg was observed, with a responder rate of 75%. Mean PWV decreased from 11.8 ± 3.2 m/s to 7.2 ± 1.9 m/s, without a significant correlation with blood pressure changes. Responders showed a significantly shorter PR interval compared with non-responders, with high discriminative ability (AUC >0.99). Moreover, lower uric acid levels and a lower platelet-to-lymphocyte ratio (PLR) were associated with a higher likelihood of response (AUC = 0.83 for both). Renal function and serum electrolytes remained overall stable during follow-up.
Conclusions: Renal denervation appears to be an effective and safe procedure in the short term for patients with resistant hypertension. In our cohort, PWV did not emerge as a predictive marker of response, whereas simple and easily obtainable parameters such as PR interval, PLR, and serum uric acid levels showed potential value in patient selection, possibly reflecting increased baseline sympathetic activity, systemic inflammation, and arterial stiffness. Prospective studies in larger populations with longer follow-up are warranted to validate integrated predictive models.

Abstract n SP02_7 - Presenting author**: Vanessa Desantis**

Sex-specific pharmaco-epidemiology in hypertensive patients

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Aim: Biological sex plays a substantial role in hypertension through differences in vascular physiology, pharmacological response, and risk profiles. This study aimed to describe sex-specific differences in antihypertensive treatment patterns to assess their association with markers of arterial stiffness.
Methods: We conducted a cross-sectional observational study (536 patients, 297 male, mean age 62.7±9.6, 239 female, mean age 63.15±11.2). For each participant, we collected age, sex, BMI, blood pressure (BP), therapy (antihypertensive, antiplatelet and lipid-lowering). Arterial stiffness was assessed through carotid–femoral pulse wave velocity (cfPWV) and Augmentation Index (IAS), measured according to international standards.
Results: Men exhibited higher systolic BP than women (132±16 vs 129±17 mmHg; p=0.01) and lower BMI (28.0±4.8 vs 29.1±5.6 kg/m²; p=0.05). Clear sex-specific differences in pharmacological management were observed: ACE inhibitors (29% vs 21%; p=0.035), indapamide (7.4% vs 2.1%; p=0.013), and acetylsalicylic acid (18% vs 11%; p=0.012) were more frequently prescribed to men, whereas thiazide diuretics were more commonly prescribed to women (33% vs 42%; p=0.034). No significant sex-based differences were observed in statin prescription (p=0.73). Mean cfPWV (9.0±2.0 men vs 9.0±2.1 women m/s; p=0.71) and IAS (10.7±8.8 men vs 10.4±8.5 women; p=0.60) did not differ significantly between the sexes. In adjusted models, no antihypertensive class demonstrated a clinically meaningful independent association with cfPWV or IAS.
Conclusions: In this cohort of hypertensive patients, substantial sex-specific differences were observed in antihypertensive treatment patterns. Despite these differences, arterial stiffness markers were comparable between men and women, suggesting that distinct therapeutic strategies may compensate for sex-based differences in cardiovascular risk profiles.

Abstract n SP02_8 - Presenting author**: Annalisa D'Alfonso**

Atherosclerotic renovascular hypertension: when CT angiography underestimates disease severity

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Aim: To describe a case of resistant hypertension in which conventional imaging underestimated renal artery disease, and to highlight the diagnostic and therapeutic value of invasive angiography in selected patients.
Methods: A 71-year-old former smoker with long-standing, poorly controlled arterial hypertension and peripheral artery disease was referred to our Hypertension Centre for resistant hypertension despite multidrug therapy (nebivolol/hydrochlorothiazide, spironolactone, amlodipine, torasemide). Secondary hypertension was investigated by renal artery Doppler ultrasound, abdominal CT angiography, and renal scintigraphy. Anti-hypertensive therapy was optimized, including irbesartan 300 mg daily, and 24-hour ambulatory blood pressure monitoring (ABPM) was performed. Due to persistent hypertension and worsening renal function, renal arteriography was subsequently undertaken.
Results: Initial imaging revealed a non–hemodynamically significant right renal artery stenosis with reduced ipsilateral kidney size, without relevant lesions of the left renal artery. After therapy optimization, mean 24-hour BP remained elevated (152/75 mmHg), with an increase in serum creatinine from 1.10 to 1.40 mg/dL. Renal arteriography demonstrated complete occlusion of the right renal artery and critical stenosis of the left renal artery (Fig 1), not previously detected by CT angiography. Bilateral angioplasty and stenting were performed, followed by marked polyuria and significant BP reduction, consistent with volume-dependent hypertension. Antihypertensive therapy was therefore reduced, achieving good BP control (24-hour mean BP: 127/65 mmHg). At one-month follow-up, Doppler ultrasound confirmed stent patency, and renal scintigraphy showed a GFR of 11 mL/min (right kidney) and 29.9 mL/min (left kidney). Renal function remained stable (creatinine 1.3 mg/dL).
Conclusions: This case illustrates that CT angiography may underestimate the severity of renal artery disease. In this patient with resistant hypertension and inconclusive non-invasive imaging, angiography revealed clinically relevant atherosclerotic bilateral renal artery lesions.

Abstract n SP03_1 - Presenting author**: Marco Bellomare**

ELASTIC (Effect of new Lipid-lowering therApies on arterial STructural and funCtIonal properties) study: no significant effects on arterial structural and functional properties of PCSK9 inhibitory monoclonal antibodies

Marco Bellomare[1] Chiara Tognola[2], Giorgio Toscani[1], Filippo Brucato[1], Beatrice Invernici[1], Francesca Daus[2], Marco Biolcati[2], Mariaelena Catarinacci[1], Marta Campana[1], Cristina Giannattasio[1,2], Alessandro Maloberti[1,2]

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Aim: Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) inhibitor antibodies reduce the frequency of new cardiovascular (CV) events through Low-Density Lipoprotein Cholesterol (LDL-C) reduction and plaque stabilisation. However, only a few studies have evaluated whether this effect is also determined by an improvement in arterial functional and structural parameters. We aimed to evaluate aortic stiffness (carotid-femoral Pulse Wave Velocity - PWV), arterial structure (carotid Intima-Media Thickness - IMT), and endothelial function (brachial Flow Mediated Dilatation - FMD) in patients treated with Alirocumab and Evolocumab.
Methods: This is a monocentric, prospective, longitudinal study on patients who received antibody-based PCSK9-i therapy at the cardiac rehabilitation and CV prevention outpatient clinic of our hospital. All patients starting a PCSK9-i on a clinical basis were enrolled and underwent PWV, FMD, and IMT measurement at three timepoints: the same day of the first injection (T0), after 6 months (T1), and after 12 months (T2).
Results: 84 patients concluded the 12-months period. The population's mean age was 67±8.2 years, and most of them were male (70.2%). LDL-C had a significant reduction during the follow-up (117.6±35.6 vs 37.5±26.2 mg/dL, p<0.001). However, there were no significant changes in PWV (10.6±2.8 vs 10.6±2.3 m/s, p=0.124), FMD (7.0±8.6 vs 8.3±10.8%, p=0.474) and IMT (719.2±184.9 vs 740.9±170.2 µm, p=0.386) values.
Conclusions: In our population, PCSK9 inhibitors showed neither significant benefits nor changes in vascular properties; however, the stability of these parameters may indicate a deceleration in the progression of atherosclerotic disease, which might otherwise have worsened in this high-risk population.

Abstract n SP03_2 - Presenting author**: Camilla Portinari**

Real-world experience with lipoprotein apheresis for elevated Lipoprotein(a): insights from the Padua cohort

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Background and aim. Lipoprotein(a) [Lp(a)] is a causal independent risk factor for atherosclerotic cardiovascular disease (ASCVD). Pharmacological strategies to reduce Lp(a) remain limited, while lipoprotein apheresis (LA) represents the most effective option in selected very high-risk patients. To evaluate the effectiveness of LA in lowering Lp(a) levels and preventing recurrent cardiovascular (CV) events in a real-world cohort.
Methods. This retrospective single-centre study included 8 patients (7 men, 1 woman; mean age 57.1 ± 7.7 years) with markedly elevated Lp(a) and recurrent ASCVD events despite maximally tolerated lipid-lowering therapy. Demographics, lipid profile, CV history and adverse reactions (ARs) were collected at baseline and during follow-up. Pre- and post-apheresis lipid values and ARs were recorded.
Results. All patients had coronary artery disease, with multivessel involvement in 87.5%. Peripheral arterial disease affected 37.5%; one patient had prior ischaemic stroke and one aortic stenosis. The first CV event occurred at a mean age of 52.8 ± 10.6 years. LA inter-session interval was 7–21 days, and the overall median duration of LA was 4.7 years. Six patients were treated with DALI and two with HELP. Median Lp(a) decreased from 289 to 117 mg/dL (−57.6%; $p<0.001$), while the time-averaged concentration was 236 mg/dL (−18%; $p<0.001$). Mean LDL-c decreased from 42.2 to 14.7 mg/dL (−65.2%; $p<0.005$), and the time-averaged mean was 34.4 mg/dL (−18%; $p<0.001$). Before LA, 22 CV events occurred over 35 patient-years (0.62 events/year), whereas during therapy only one acute myocardial infarction occurred over 41 patient-years (0.02 events/year; $p<0.01$). LA was well tolerated, with an AR rate of 1.1% per session and 0.29 AR/patient-year.
Conclusions. In this analysis LA produced time-averaged reductions in Lp(a) and LDL-c, but the main clinical result was the marked decrease in CV events. Despite procedural burden, LA remains a valuable and tolerated option for patients at extremely high ASCVD risk until targeted Lp(a)-lowering therapies become available.

Abstract n SP03_3 - Presenting author**: Ilaria Rossi**

Lipoprotein(a) and residual cardiovascular risk: evidence from a real-world lipid clinic cohort

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Background/Aims: Lipoprotein(a) [Lp(a)] is increasingly recognized as a genetically determined cardiovascular risk factor with established atherothrombotic properties. However, its prognostic value and clinically relevant cut-off levels in clinical settings remain unclear.
Materials and methods: This study included 155 patients (mean age 49.8 ±14.4 years; 55.5% male) referred to the Lipid Clinic of Chieti during a period of ten years between 2015 and 2025. Data regarding demographic characteristics, cardiovascular risk factors, laboratory and imaging tests were collected. The mean follow-up period was 5 years.
Participants were categorized according to Lp(a) levels into three groups: Low (<30 mg/dL, n=60), Moderate (30–50 mg/dL, n=22), and High (>50 mg/dL, n=73) group. The occurrence of cardiovascular, cerebrovascular, and thromboembolic events was evaluated during the follow-up period.
Results: The average Lp(a) level in the study population was 76.2 ± 92.24 mg/dL. Overall, 32 patients (20.6%) experienced clinical events, including 24 (15.5%) cardiovascular, 5 (3.2%) cerebrovascular, and 3 (1.9%) thromboembolic events. Individuals with Lp(a) concentrations ≥30 mg/dL had a higher rate of cardiovascular events compared with those with levels <30 mg/dL (19 vs 5 events, p=0,037). All thromboembolic events were observed exclusively in patients with high Lp(a) levels (>50 mg/dL). Conventional cardiovascular risk factors (age, BMI, hypertension, dyslipidemia, diabetes, and smoking status) similarly distributed across groups, indicating a potential independent contribution of Lp(a).
Discussion and conclusion: Higher Lp(a) concentrations were associated with an increased risk of cardiovascular and thromboembolic events, independently of traditional risk factors, reinforcing the concept of Lp(a) as a residual cardiovascular risk factor. The association between adverse outcomes and Lp(a) levels in the 30–50 mg/dL range suggests a continuous risk relationship, with clinically relevant risk also present below the 50 mg/dL threshold.

Abstract n SP03_4 - Presenting author**: Elisa Acitelli**

Bempedoic acid: real-world data and sex-specific analysis from an Italian cohort

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Aim: Bempedoic acid (BA) is a novel lipid-lowering agent, often used in statin-intolerant patients. Previous studies[1] suggested women may experience greater LDL-c reductions than men in ASCVD/HeFH populations. This study aimed to evaluate real-world lipid-lowering efficacy of BA and to describe baseline characteristics of patients prescribed BA, with a focus on sex-specific differences in therapy initiation and response.
Methods: We conducted a retrospective study at the Internal Medicine and Metabolic Diseases Unit of Policlinico Umberto I, Rome. Demographic, clinical, anthropometric, and laboratory data were collected from medical records at BA initiation (T0) and first follow-up (T1). Parametric and nonparametric comparisons were performed using T-tests and Wilcoxon tests; binary variables were analyzed with McNemar tests; ANCOVA and multivariate linear regression were used to assess determinants of LDL reduction.
Results: Data from 120 patients were analyzed. The majority of patients were females (63.3%), statin-intolerant (67.7%) in primary cardiovascular prevention (80.7%). Median follow-up was 105 days (range 30–161), and no treatment discontinuations due to adverse events were recorded. Mean age was 64.6 ± 11.4 years, with females significantly older than males (66.5 ± 10.5 vs 61.3 ± 12.4 years; $p = 0.019$); other baseline characteristics and concomitant therapies were similar between sexes. LDL reduction did not differ significantly by sex. In multivariate linear regression, baseline LDL ($\beta = 0.628$, $p < 0.001$), BMI ($\beta = 1.85$, $p = 0.007$), and statin discontinuation ($\beta = -25.84$, $p = 0.017$) independently predicted LDL reduction, whereas sex, age, and statin intolerance did not.
Conclusions: BA is effective in lowering LDL-c in hypercholesterolemic patients, particularly statin-intolerant females. No sex differences in LDL response were observed after adjustment for baseline characteristics and therapy factors, partly contrasting prior literature. Differences in baseline LDL, BMI, and statin discontinuation may explain apparent sex-related disparities.

Abstract n SP03_5 - Presenting author**: Michela Algeri**

Achievement of LDL cholesterol targets in HIV-positive patients

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Background and objectives: People living with HIV (PLWH) face an increased cardiovascular (CV) risk due to the interaction of traditional risk factors, chronic inflammation and cumulative antiretroviral therapy (ART) adverse metabolic effects. However, standard risk models often underestimate this burden, limiting effective prevention. This study evaluates LDL cholesterol target achivement in PLWH, based on European Society of Cardiology guidelines, and explores its association with clinical, immunological, and therapeutic HIV-related variables.
Methods: A retrospective analysis was conducted on 246 HIV-positive patients, aged ≥40, on ART at Niguarda Hospital. Clinical, laboratory, and therapeutic data were extracted from the hospital's electronic registries, while ten-year CV risk was assessed using SCORE2 from which each patients LDL cholesterol target was defined.
Results: Only 27.2% of the analyzed cohort achieved the recommended LDL cholesterol targets; a significantly higher prevalence of uncontrolled profiles was observed among patients belonging to the "high" or "very high" SCORE2 risk categories (29.3 and 14.6% of the population, respectively). 35.4% of the patients take statins, 12.2% ezetimibe while only the l'11.4% take their association. Univariate analysis showed that lower value of total cholesterol (r=-0.490, p<0.0001), triglycerides (r=-0.188, p=0.003), systolic blood pressure (r=-0.190, p=0.003), and SCORE2 risk class (r=0.270, p<0.0001) were significantly associated with an increased likelihood of achieving the LDL cholesterol target, whereas no significant relation was found with HIV-specific variables.
Conclusions: LDL cholesterol target achievement in PLWH remains suboptimal. A refined predictive model integrating HIV-specific variables, could be useful to enhance individualized risk stratification and to optimize therapeutic strategies tailored to PLWH.

Abstract n SP03_6 - Presenting author**: Andrea Sablone**

Clinical management and outcomes of bempedoic in type 2 Diabetes: a retrospective cohort study

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Background and Aims: Dyslipidaemia is a major cardiovascular risk factor in individuals with type 2 diabetes (T2D), in whom achievement of recommended lipid targets often remains suboptimal. This study aimed to describe the clinical profile of individuals with T2D initiating bempedoic acid therapy and to evaluate its effectiveness in a real-world clinical setting.
Materials and Methods: This retrospective, single-centre observational study was conducted at the outpatient Unit of Endocrinology and Metabolism of the Pescara Health Service (Italy) in accordance with the Declaration of Helsinki. Adults with T2D who initiated bempedoic acid between May 2023 and July 2025 were included. Demographic, clinical, and laboratory data, comorbidities, concomitant therapies, and statin intolerance were collected at baseline and at first follow-up. Data are presented as mean ± SD or frequency (%). Changes from baseline are reported as estimated mean differences with 95% CI. Analyses were performed using Stata/SE 17.0, with $p < 0.05$ considered statistically significant.
Results: Of the 200 identified patients, data from 105 individuals (mean age 68 ± 8.8 years; 43% male; BMI 29.5 ± 6.3 kg/m²) were analysed, with a first follow-up at 5.4 ± 2.2 months. Common comorbidities included hypertension (70%), obesity (41%), microangiopathy (38.5%), and macroangiopathy (22%). At baseline, mean HbA1c was 6.9 ± 2.1%, none of the patients had LDL-C levels within the recommended target range; 59% reported statin intolerance, and only 19% were receiving the maximum tolerated statin dose. At follow up, bempedoic acid treatment significantly reduced LDL-C (−25.8%, 95% CI −37.8 to −13.7), total cholesterol (−20.1%, 95% CI −28.7 to −11.3), and non–HDL cholesterol (−22.6%, 95% CI −32.8 to −12.4), with no significant changes in HDL cholesterol or triglycerides. LDL-C targets were achieved in 50% of patients at moderate cardiovascular risk and in 40% at high risk. Treatment discontinuation due to gastrointestinal adverse events occurred in 8% of patients.
Conclusions: In routine clinical practice, bempedoic acid was effective and well tolerated, supporting its role as a therapeutic option for lipid management in patients with T2D inadequately controlled with other lipid-lowering therapies.

Abstract n SP03_7 - Presenting author**: Simone Mattivi**

Efficacy and safety of bempedoic acid in clinical practice: real-world analysis and predictors of response

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Introduction: Bempedoic acid is a novel ATP citrate lyase inhibitor introduced for the treatment of hypercholesterolemia, particularly in patients with inadequate response or intolerance to statins. The management of dyslipidemic patients with high cardiovascular risk remains challenging, especially when first-line lipid-lowering therapies are poorly tolerated. In this context, bempedoic acid represents a potential therapeutic alternative aimed at improving lipid control and reducing residual cardiovascular risk. However, real-world evidence regarding its efficacy and safety remains limited, particularly in heterogeneous clinical populations.
Objectives: The aim of this study was to evaluate the efficacy and safety of bempedoic acid in a real-world cohort of dyslipidemic patients, assessing changes in lipid parameters, achievement of LDL-c therapeutic targets, and the occurrence of adverse events during follow-up. Additional analyses explored clinical and demographic predictors of lipid target achievement or treatment failure.
Methods: We conducted a retrospective observational study including 90 patients treated with bempedoic acid at a lipid clinic. The mean age was 61 ± 12.7 years, with 48.9% male subjects. Most patients were in primary prevention (83.3%), and 71.1% reported statin intolerance, while 22.2% were also intolerant to ezetimibe. The mean follow-up duration was 310 ± 176.8 days. Baseline and follow-up data included anthropometric, biochemical, and clinical variables. Changes in lipid and laboratory parameters were analyzed using appropriate statistical tests, with significance set at $p < 0.05$.
Results and Conclusions: Bempedoic acid therapy resulted in a significant reduction in LDL cholesterol (-15.8% vs. baseline, $p < 0.001$) and total cholesterol ($p < 0.001$), with no significant changes in HDL or triglycerides. LDL-c therapeutic targets were achieved in 21.1% of patients, with a higher success rate among those at moderate cardiovascular risk compared with high or very high-risk individuals. Multivariate analysis identified older age ($p = 0.017$) and familial hypercholesterolemia ($p = 0.037$) as independent predictors of non-achievement of LDL-c goals. Adverse events were generally mild, with muscle-related symptoms (26.7%), gastrointestinal complaints (11.1%), and skin rash (5.6%) being the most common. Treatment discontinuation occurred in 18.9% of cases, mainly due to myalgia or gastrointestinal intolerance. From the renal point of view, a slight increase in creatinine was observed ($p=0.003$) while a non-statistically significant increase was observed for uric acid levels ($p=0.081$).
Overall, bempedoic acid demonstrated a favorable efficacy and safety profile in dyslipidemic patients, particularly in those intolerant to statins. Despite a moderate reduction in LDL-c compared to traditional agents, its good tolerability, safety, and ease of combination therapy support its role as a valuable option in the personalized management of residual cardiovascular risk.

Abstract n SP03_8 - Presenting author: **Iliana Iemmolo**

Efficacy of dual therapy (evinacumab and lomitapide) in a HoFH patient

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Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder characterized by extremely high LDL cholesterol levels from birth, associated with a very high risk of premature atherosclerotic cardiovascular disease. Despite the use of conventional lipid-lowering therapies, lipid control in these patients is often inadequate, as they carry mutations that impair the function of the LDL receptor, requiring the use of innovative therapeutic strategies.
The aim of this work is to evaluate the efficacy and tolerability of the combination of third- generation lipid-lowering therapies in the treatment of HoFH patients with missense or nonsense mutations, on LDL cholesterol levels, and the safety profile in the context of real-world clinical practice. Available therapeutic options, including traditional pharmacological therapies, include molecules directed to novel molecular targets, such as PCSK9, ANGPTL3, and MTTP.
We present a case report of five patients with severe HoFH with severe LDL receptor mutations and residual activity less than 2%, treated with therapeutic combinations including new- generation drugs, particularly lomitapide and evinacumab, sometimes in combination with LDL apheresis.
The observed results, consistent with the ELIPSE HoFH study, compared with data from the Italian ELIPSE HoFH cohort, show a significant reduction in LDL cholesterol levels compared to baseline, with an overall favorable tolerability profile. Specifically, third-generation therapies achieved previously unachievable cholesterol levels, reducing the fluctuating trend observed between apheresis periods, and sometimes even achieving the therapeutic target established by guidelines. Our case report represents a significant portion of the Italian cohort and among the most significant real-world data at an international level.
In conclusion, the combination of third-generation lipid-lowering therapies represents a fundamental therapeutic strategy in the treatment of homozygous familial hypercholesterolemia, allowing for better control of cardiovascular risk and opening new perspectives in the management of this complex disease.

Abstract n SP04_1 - Presenting author**: Amirbahman Zeynali**

Plasma proteomics to differentiate FH patients from hypercholesterolaemic patients

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Background: Familial hypercholesterolemia (FH) is a genetic disorder characterized by lifelong exposure to elevated low-density lipoprotein cholesterol and an increased risk of premature cardiovascular disease. Although the genetic determinants of FH are well understood, the associated systemic proteomic alterations remain incompletely defined. Exploratory plasma proteomics may provide preliminary insights into disease-related protein patterns and generate hypotheses for further investigation. This study reports preliminary proteomic data comparing patients with FH and subjects with non-familial hypercholesterolemia.
Material and Methods: Baseline assessment was conducted on both subjects (n=10), including clinical and lifestyle data, as well as plasma proteomics profiling which was performed using untargeted and targeted liquid chromatography-mass spectrometry (LC–MS/MS) approaches. Integrated datasets were analysed using supervised machine learning (ML) models, including random forest, gradient boosting machines, support vector machines, and deep neural networks. Model performance was evaluated against traditional risk scores, with interpretability ensured through explainable AI methods.
Results: Preliminary untargeted plasma proteomic profiling was performed, quantifying 3,472 proteins across the two groups. Statistical comparison between FH and hypercholesterolemic subjects did not identify proteins reaching statistical significance after correction for multiple testing (false discovery rate, FDR < 0.05). At the nominal level, 174 proteins showed p-values < 0.05, 36 proteins p-values < 0.01, and 5 proteins p-values < 0.001; however, all corresponding q-values remained > 0.6, reflecting the exploratory nature of the analysis and the multiple-testing burden. Several proteins exhibited consistent trends toward differential abundance with large effect sizes. For example, ASCL4 showed lower levels in FH compared with controls while CP4X1 displayed higher levels in FH. Similar trend-level differences were observed for AK1D1, F90AR, CLIC5, and EPYC.
Conclusion: This findings represent preliminary, hypothesis-generating analysis highlights candidate proteins and pathways that may merit further investigation. A larger population of FH is currently being studied to confirm these findings.

Abstract n SP04_2 - Presenting author: **Chiara Comi**

Effects of gliflozins on lecithin:cholesterol acyltransferase

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Introduction: Lecithin:cholesterol acyltransferase (LCAT) is a key enzyme in lipoprotein metabolism, being responsible for the synthesis of cholesteryl esters. LCAT activity is required for the maturation of high-density lipoproteins (HDL). Mutations in the *LCAT* gene causes a rare dyslipidemia characterized by very low HDL-cholesterol levels. In this context, LCAT-activating compounds have been explored as potential therapies for coronary heart diseases and LCAT deficiency. *In silico* and *in vitro* experiments conducted in our laboratories have recently identified gliflozins, potent antidiabetic drugs, as potential LCAT activators.
Aim: This study aims to evaluate the in vivo effects of glifozins on cholesterol esterification.
Methods: Sixteen patients with coronary artery disease and type 2 diabetes were enrolled and randomized 1:1 to dapagliflozin or placebo for 4 weeks. Plasma lipid and lipoprotein profiles were analyzed before and after treatment with dapagliflozin or placebo. Cholesterol esterification was assessed using analytical methods developed in our laboratory.
Results: Total cholesterol, HDL cholesterol, and apolipoprotein A-I levels were comparable between groups after 4 weeks. The unesterified-to-total cholesterol ratio (UC/TC), a proxy of plasma cholesterol esterification, showed a modest decrease following drug administration (0.30 ± 0.05 at baseline vs 0.28 ± 0.07 post-treatment), while remaining unchanged in the placebo group (0.26 ± 0.05 vs 0.26 ± 0.03). Similarly, a trend toward increased plasma LCAT activity was observed after treatment compared with baseline (35.4 ± 9.9 vs 39.2 ± 14.3 nmol/mL/h), whereas no change was detected in the placebo group (39.9 ± 9.1 vs 37.6 ± 8.5 nmol/mL/h). Interestingly, changes in the UC/TC were positively associated with changes in fasting plasma glucose ($r = 0.752$, $p = 0.03$).
Conclusions: These findings indicate that gliflozins may modestly enhance cholesterol esterification. If confirmed in a larger ongoing study, these results would suggest that the LCAT activation induced by treatment contributes to the beneficial effect of this class of drugs.

Abstract n SP04_3 - Presenting author**: Martina Zampoleri**

Arterial functional and structural effects of PCSK9 Inhibitors: a comparison between antibody and small interfering RNA

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Background and Objectives: Proprotein Convertase Subtilisin/Kexin type 9 inhibitors (PCSK9-i) are a drug class used to reduce LDL cholesterol in patients with dyslipidemia who do not adequately respond to traditional therapies. PCSK9 could be inhibited through monoclonal antibodies (Alirocumab and Evolocumab) or siRNA (Inclisiran). While their lipid-lowering efficacy is well established, their effects on vascular structure and function remain uncertain. The aim of this study was to evaluate if these properties change after initiation of PCSK9-I during a 1-year follow-up comparing Inclisiran to antibodies.
Methods: This prospective longitudinal study enrolled all patients who began treatment with Evolocumab, Alirocumab, or Inclisiran at the Cardiology 4 Department of Niguarda Hospital (Milan, Italy). Evolocumab and Alirocumab were self-administered every 2 weeks while Inclisiran was administered by healthcare professionals at baseline, at 3 months, and every 6 months thereafter. Carotid-femoral Pulse Wave Velocity (cf-PWV), carotid Intima-Media Thickness (cIMT), and brachial Flow-Mediated Dilation (FMD) were assessed at T0 (the day before PCSK9-inhibitions start), 6 months (T1), and 12 months (T2). Statistical analysis was conducted on 42 patients treated with PCSK9 monoclonal antibodies and 42 patients treated with Inclisiran, matched by age, sex, and BMI.
Results: Both groups had a mean age of 69.1±8.8 years, with 78.6% male and a mean BMI of 26.9±3.2 kg/m². LDL-C levels significantly decreased in both groups (Inclisiran: Δ(T0-T2) = 60.6±37.2 mg/dL; PCSK9i-Ab Δ(T0-T2) = 71.1 mg/dL±10.0 mg/dL; p<0.001). A borderline increase in HDL-C (from 49.4±14.7 to 52.5±14.5 mg/dL; p=0.032) was observed with antibodies, while a borderline decrease in triglycerides (from 115.3±48.2 to 100.8±36.6 mg/dL; p=0.048) was observed with Inclisiran. Systolic blood pressure decreased in the Inclisiran group (from 131.8±15.3 to 125.5±11.2 mmHg; p=0.001), while diastolic blood pressure decreased in the PCSK9i-Ab group (from 80.1±13.1 to 75.2±9.3 mmHg; p=0.020). While no significant changes were observed in IMT or FMD, PWV significantly decreased in the Inclisiran group (10.9±2.4 m/s at T0, 10.4±2.5 m/s at T1, 10.3±1.8 m/s at T2; p=0.013), but not in the antibody group.
Conclusions: PCSK9 inhibitors confirm their efficacy in reducing LDL-C while only Inclisiran seems to be able to reduce arterial stiffness. However, this evidence was associated with the finding of a significant decrease in systolic blood pressure (the main determinant of PWV). So, further studies with larger populations are needed to reach definitive conclusions on PCSK9-inhibitions effects on vascular structure and function.

Abstract n SP04_4 - Presenting author**: Elisa Nespoli**

The role of runt-related transcription factor1 (Runx1) in the phenotypic switch of vascular smooth muscle cells during atherosclerosis

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Background: Vascular smooth muscle cells (VSMCs) switch from contractile to synthetic phenotype during the most critical phases of atherosclerosis, when plaque instability leads to the clinical manifestation of cardiovascular diseases (CVD). Multiple transcription factors regulate this phenotypic switch in VSMCs and, Runt-related transcription factor 1 (Runx1), primarily studied in hematopoiesis, could also be a key player in this context, although not explored so far.
Aim: This study aimed to characterize Runx1 expression in VSMCs under atherogenic conditions and to evaluate the effects of its deletion in VSMCs on atherosclerosis development.
Methods: Both primary mouse and human VSMCs were isolated from aortas and stimulated with PDGF-β to assess RUNX1 expression under atherogenic conditions, along with other markers of VSMCs proliferation and differentiation that we have a priori considered at this moment (COL1A1, COL3A1, MKI67, TBX18, EGR1, SM22). In vivo, tamoxifen-inducible VSMC-specific Runx1 homozygous and heterozygous mice (Myh11-CreERT2^{+}; Runx1^flox/flox; LDLR$^{-/-}$, "Runx1-SMC-iKO") were fed 16 weeks a cholesterol enriched (0.15%) western-type diet ("WTD"), compared to LDLRKO mice only to assess the progression of hypercholesterolemia associated to atherosclerosis.
Results: In mouse VSMCs, Runx1 expression increased by 1.771±0.947-fold, 1 hour after PDGF-β stimulation, along with the up-regulation of EGR-1 (7.100±1.069-fold; p-value=0.001) and SM22 (2.562±0.664-fold; p-value=0.036). In human VSMCs, Runx1 also increased, similarly doubled after 1 hour stimulation (1.929±0.216-fold; p-value=0.002). The expression of other genes, including COL1A1, COL3A1, MKI67, TBX18, only moderately changed (1.23-1.26 folds) in both cell lines. Upon WTD feeding homozygous Runx1-SMC-iKO mice developed less hypercholesterolemia (1009.38±222.68 mg/dl) vs heterozygous Runx1-SMC-iKO (1378.80±400.12 mg/dl; p-value=0.02) and LDLRKO mice (1410.74±202.14 mg/dl; p-value=0.016), independent from other gluco-metabolic alterations (insulin resistance and glucose intolerance).
Conclusions: On this premise, we are now studying if the ablation of Runx1 in VMSCs results into a different evolution and characteristics of atherosclerosis.

Abstract n SP04_5 - Presenting author**: Daniele Pozzoli**

Effects of bempedoic acid on arterial structural and functional parameters

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Background and Objectives: Bempedoic Acid (BA) is a recently approved agent for LDL-C reduction. Its effects on arterial structural and functional parameters are unknown. We longitudinally evaluated these properties in patients initiating BA and compared them with a matched cohort receiving PCSK9-inhibitors (PCSK9i).
Methods: Patients starting BA were enrolled. Carotid-femoral Pulse Wave Velocity (PWV), carotid Intima Media Thickness (IMT) and brachial Flow Mediated Dilation (FMD) were assessed at baseline (T0), 6 months (T1) and 1 year (T2). Twenty BA patients with a 1-year follow-up were analyzed and compared with 20 sex-, age- and Body Mass Index (BMI)-matched PCSK9i patients.
Results: Mean age in the BA group was 65.3±7.9 years, 55.0% were male and BMI was 25.7±2.9 kg/m². Baseline LDL-C was lower with BA than with PCSK9i (101.5±36.9 vs 122.0±31.4 mg/dL); the more frequent indication was primary prevention for BA (65.0%) and secondary prevention for PCSK9i (75.0%). Statins were used by 45.0% and 40.0% in the BA and PCSK9i groups, respectively, and ezetimibe by 80.0% in both groups. After 1 year, LDL-C was 77.6±37.3 mg/dL with BA and 46.1±30.4 mg/dL with PCSK9i ($p<0.001$). No statistically significant changes were observed in PWV (9.7±2.3 to 9.4±1.2 m/s, p=0.466), FMD (6.7±5.2 to 6.3±5.9%, p=0.071), or IMT (715.2±153.4 to 678.6±180.9 µm, p=0.239) in the BA group. Similarly, no significant changes were found in the PCSK9i group for PWV, FMD, or IMT over the same 1-year follow-up when compared to baseline values, and no statistically significant differences emerged in the between-group comparison at 6 months (T1) or 1 year (T2) overall.
Conclusions: BA was confirmed to be a highly effective LDL-C–lowering agent. However, no significant improvements were observed in arterial structural or functional parameters, either within the BA group or in comparison with the PCSK9i group.

Abstract n SP04_6 - Presenting author**: Davide Barbarossa**

Postprandial VLDL and endothelial inflammatory activation: *in vitro* studies

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Aim: Elevated postprandial triglyceride (TG) levels are recognized as an independent and causal cardiovascular risk factor. After a meal, triglyceride-rich lipoproteins (TRLs), mainly chylomicron remnants and very-low-density lipoproteins (VLDL), accumulate and interact with the vascular endothelium, promoting low-grade inflammation and endothelial activation. This study investigated the endothelial responses induced by physiologically relevant postprandial VLDL concentrations and explored potential early molecular biomarkers of TRL-driven vascular inflammation.
Methods: VLDL fractions were isolated from plasma collected four hours after an oral fat load in normolipidemic individuals using an 8% iodixanol density-gradient ultracentrifugation. Lipoproteins were standardized to final TG concentrations of 10, 25, and 100 µg/mL. Human umbilical vein endothelial cells (HUVEC) were serum-starved for two hours and subsequently exposed to VLDL for four hours. Gene expression of IL-6, MCP-1, ICAM-1, P-selectin, ELAM-1, and VCAM-1 was quantified by RT-qPCR and normalized to RPL13A. Lipopolysaccharide (LPS, 30 ng/mL) served as a positive inflammatory control.
Results: VLDL induced a dose-dependent endothelial inflammatory response (n = 5). At 100 µg/mL TG, significant increases were observed for IL-6 (1.45 ± 0.54 vs 1.02 ± 0.02; p = 0.03) and MCP-1 (1.95 ± 0.81 vs 1.02 ± 0.02; p = 0.02). Adhesion molecules were also up-regulated: ICAM-1 (1.86 ± 1.01 vs 1.00 ± 0.05; p = 0.02), P-selectin (2.07 ± 0.59 vs 1.12 ± 0.13; p = 0.02), and ELAM-1 (1.63 ± 0.59 vs 1.01 ± 0.01; p = 0.02). VCAM-1 showed no significant variation (1.19 ± 0.71 vs 1.00 ± 0.06). As expected, LPS markedly activated all analyzed genes.
Conclusions: Postprandial VLDL concentrations induced a modest endothelial inflammatory activation, characterized by cytokine induction and increased expression of adhesion molecules. These preliminary results support existing evidence and offer a controlled in-vitro model to further investigate the molecular mechanisms through which postprandial VLDL modulate endothelial function. Future studies will apply this model to postprandial VLDL from healthy, prediabetic, and type 2 diabetic subjects to compare endothelial activation across groups.

Abstract n SP04_7 - Presenting author**: Clara Rossi**

VEGFA/VEGFR2 axis regulate crosstalk between senescent vascular smooth muscle cells and intraplaque neovessels in atherosclerosis

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Aim: Atherosclerosis, the leading cause of cardiovascular disease, progresses from early fatty streaks to unstable rupture-prone plaques that trigger thrombotic events. A key feature of plaque instability is intraplaque angiogenesis (IPA), characterized by the formation of fragile, leaky neovessels that promote intraplaque hemorrhage (IPH) and inflammation. Although hypoxia is a known driver of angiogenesis, additional pro-angiogenic mechanisms remain poorly understood. As an age-related disease, atherosclerosis is marked by the accumulation of senescent vascular smooth muscle cells (VSMCs), which are non-proliferative but metabolically active and acquire a senescence-associated secretory phenotype (SASP) that promotes chronic inflammation and tissue remodeling.
Despite increasing evidence for a detrimental role of senescent VSMCs in atherosclerosis, whether their SASP directly promotes IPA and IPH has remained unexplored.
Here, we investigated the relationship between VSMC senescence, SASP production, and angiogenesis, and assessed whether SASP-related pathways represent therapeutic targets.
Methods and results: Re-analysis of a scRNASeq dataset identified a distinct population of senescent VSMCs in atherosclerotic lesions, identified by expression of CDKN1A, CDKN2A, TP53, and GLB1. Moreover, gene ontology and gene enrichment analyses revealed that senescent VSMCs exhibit an enrichment of angiogenesis-related pathways. Importantly, immunohistochemical analyses confirmed that senescent VSMCs are significantly more abundant in unstable human carotid plaques compared with stable lesions.
Using replicative and doxorubicin-induced in vitro models of VSMC senescence, we found that senescent VSMCs secrete markedly increased levels of pro-angiogenic factors, particularly VEGFA. Conditioned media from senescent VSMCs significantly enhanced angiogenic responses in HUVECs. Pharmacological inhibition of VEGFR2 in HUVECs abolished these effects, identifying the VEGFA/VEGFR2 axis as a central mediator of senescence-driven angiogenesis.
Conclusions: Together, our findings demonstrate that senescent VSMCs may facilitate plaque progression and instability through a strongly pro-angiogenic SASP production. Targeting vascular senescence and the VEGFA/VEGFR2 pathway may represent a promising strategy to limit IPA and stabilize high-risk atherosclerotic plaques.

Abstract n SP04_8 - Presenting author**: Paola Bonicco**

Colonic (poly)phenol metabolites as promising tools to control inflammation and prevent cardiovascular disease

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Aim: Chronic inflammation underlies numerous diseases, including atherosclerosis. The identification of anti-inflammatory agents, particularly from dietary sources, is of great interest for the development of functional products targeting early stages of chronic inflammatory conditions. This study investigated the *in vitro* anti-inflammatory activity of chiral phenyl-γ-valerolactones, the main colonic metabolites of flavan-3-ols.
Methods: Human dermal fibroblasts were treated with 10 phenyl-γ-valerolactones (1 μM) for 48 hours. Compounds included pure enantiomers and methylated or sulfated derivatives, tested at concentrations representative of plasma levels following dietary intake. During the first 24 hours, cells were treated under basal conditions; during the second 24 hours, treatments were repeated in the presence or absence of lipopolysaccharide (LPS, 1 μg/mL). Cytotoxicity was assessed by MTT and lactate dehydrogenase assays (LDH). Anti-inflammatory activity was evaluated by measuring IL-6 and IL-8 secretion using ELISA, with data normalized to protein content (bicinchoninic acid assay). To investigate the underlying mechanism of action, NF-κB activation was assessed by western blot analysis of p65 expression, normalized to β-actin. A 24-hour pharmacokinetic study was conducted to evaluate compound biotransformation and to characterize metabolic products, monitoring 31 phenyl-γ-valerolactones.
Results: None of the tested compounds induced cytotoxicity. (4*R*)-5-(4'-hydroxyphenyl)-γ-valerolactone (R-CC01) reduced IL-6 and IL-8 secretion by 76% (p<0.001) and 70% (p<0.01), respectively, while its enantiomer (S-CC01) inhibited IL-6 by 89% (p<0.001) and IL-8 by 86% (p<0.01). (4*R*)-5-(3',4'-dihydroxyphenyl)-γ-valerolactone (R-CC02) reduced both IL-6 and IL-8 by 83% (p<0.001). (4*S*)- and (4*R*)-5-(3'-hydroxy-4'-methoxyphenyl)-γ-valerolactones (CC03) reduced IL-6 by 90% and 78% (p<0.001), and IL-8 by 87% and 71% (p<0.01), respectively. Western blot analysis showed reduced NF-κB activation, with p65 levels decreased by 37% (R-CC01, p<0.05), 61% (R-CC02, p<0.01), and 73% (R-CC03, p<0.001). The analysis of cellular metabolism revealed that within 24 hours R-CC01 remained unmodified, whereas R-CC02 and R-CC03 formed sulfate metabolites in a time-dependent manner.
Conclusions:
Phenyl-γ-valerolactones significantly reduced pro-inflammatory cytokine secretion in LPS-stimulated human fibroblasts, partly through NF-κB inhibition. These findings support their potential role in dietary or nutraceutical strategies targeting chronic inflammation.

Abstract n SP05_1 - Presenting author**: Guendalina Vizza**

Sex-and age-specific prognostic value of serum uric acid for cardiovascular events: insights from the URRAH Study

Vizza Guendalina[1], Francesco Baratta[1], Federica Moscucci[1], Edoardo Casiglia[2], Guido Grassi[3], Maria Lorenza Muiesan[4], Roberto Pontremoli[5], Agostino Virdis[6], Giovambattista Desideri[1], Claudio Borghi[7] on behalf of Working Group on Uric Acid and Cardiovascular Risk of the Italian Society of Hypertension (SIIA)

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Background: Increasing epidemiological evidence suggests a potential role for serum uric acid (SUA) in cardiovascular disease (CVD), although this association remains controversial due to strong correlations with cardiometabolic risk factors. Moreover, sex- and age-related differences may modify the prognostic impact of SUA but have been insufficiently explored. Objective: To evaluate the prognostic value of SUA for major CVEs according to sex and age, identify group-specific prognostic cut-offs.
Methods: This post-hoc analysis used data from the Italian multicenter observational URRAH (Uric Acid Right for Heart Health) study promoted by the Italian Society of Hypertension. A total of 20,051 participants without prior cardiovascular events, gout, or urate-lowering therapy were included. Participants were stratified into four groups: women <50 years, women ≥50 years, men <60 years, and men ≥60 years, based on age-related SUA patterns. The primary endpoint was a composite of major CVEs.
Results: Over a median follow-up of 10.2 years (183,588.8 person-years), 2,244 CVEs occurred (1.2 per 100 person-years). In women<50 years, SUA showed strong prognostic performance (AUROC=0.71). A cut-off of 4.2 mg/dL was associated with a markedly increased CVEs risk (adjusted HR [aHR] 3.58; 95% CI 2.19–5.86; p<0.001) and high sensitivity (91.2%). In women≥50 years, a higher cut-off (5.7 mg/dL) predicted increased risk (aHR 1.36; 95% CI 1.19–1.56; p<0.001), though with attenuated discrimination. Similarly, in men≥60 years, SUA ≥5.7 mg/dL (AUROC=0.56) was associated with higher CVE risk (aHR 1.36; 95% CI 1.18–1.57; p<0.001). No significant association was observed in men<60 years.
Conclusions: The cardiovascular prognostic value of SUA is strongly sex- and age-dependent. In presumably premenopausal women, SUA predicts CVEs even at levels considered normal. Enhanced xanthine oxidase activity may underlie these findings. Sex- and age-specific SUA cut-offs should be considered, and prospective studies are warranted to test personalized preventive strategies targeting xanthine oxidase activity.

Abstract n SP05_2 - Presenting author**: Filippo Figorilli**

Increased plasma C-reactive protein levels predicts unfavourable cardiovascular prognosis in subjects at increased ASCVD risk and impaired kidney function: longitudinal results from the IMPROVE study

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Background and Aim: Chronic Kidney Disease (CKD) is a detrimental condition that leads to an increased risk of cardio-, cerebro-, and peripheral-vascular events (VEs). High-sensitivity-C-Reactive Protein (hsCRP) >2 mg/L is considered a reliable marker of systemic low-grade inflammation. The impact of hsCRP>2 mg/L on the VEs incidence among patients at increased cardiovascular risk but with no previous VEs, has been examined across estimated glomerular filtration rate (eGFR) strata in the IMT-Progression-as-Predictors-of-VEs (IMPROVE) study.
Methods: Among 3,040 IMPROVE participants, plasma hsCRP levels were available for 2.072 subjects without inflammatory disease or ongoing anti-inflammatory therapy. The prevalence of high hsCRP levels across different eGFR strata [group A:≥79 mL/min (median) and group B:<79 mL/min; group A1:>90 mL/min, group B1:60-90 mL/min, group C1:<60 mL/min] was estimated. The prognostic impact of high hsCRP levels on incident VEs was explored at 3 and 8.5 years, after correction for confounders.
Results: The median hsCRP levels were 1.63 mg/L and 2.02 mg/L in group A and B (p=0.001), respectively, and 1.46 mg/L, 1.89 mg/L and 2.42 mg/L in groups A1, B1 and C1 (p for trend=0.001). During a follow-up of 3.0 and 8.5 years, 97 and 209 VEs were recorded. HsCRP >2 mg/L was associated with an increased VEs risk in short and long follow-up (HR 2.05, 95%-CI:1.32-3.17 and HR 1.59. 95%-CI:1.20-2.12), irrespective of confounders. A significant interaction has been found between hsCRP>2 mg/L and below-median eGFR in predicting VEs risk both in the short and long follow-ups (p=0.018 and p=0.029). HsCRP>2 mg/L was associated with increased short-term and long-term VEs risk in group A [HR 3.05(1.63-5.69) and HR 2.01(1.40-3.17)] but not in group B [HR 1.28(0.66-2.50) and HR 1.21(0.80-1.84)]. Elevated hsCRP predicted an increased VEs risk in group C1 and B1 [short follow-up: HR 4.66 (1.35-16.12) and HR 1.90 (1.10-3.32)]&[long follow-up: HR 2.87 (1.21-6.83) and HR 1.48 (1.04-2.10)], but not in group A1 [short follow-up: HR 1.60 (0.62-4.12)]&[long follow-up: HR 1.64 (0.87-3.12)].
Conclusions: Approximately half of subjects at increased cardiovascular risk with impaired kidney function have an elevated plasma hsCRP level. An increase in hsCRP level is longitudinally associated with an increased VEs risk in subjects with lower kidney function, in both the short-term and long-term follow-ups. Conversely, elevated hsCRP levels were not associated with an increased VEs risk in subjects with normal GFR.

Abstract n SP05_3 - Presenting author**: Francesco Maria Di Luca**

Total-cholesterol-to-triglycerides ratio as a predictor of 30-day mortality and cardiovascular complication in patients with sepsis: a retrospective cohort study

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Background and aim: previous studies described the association between total cholesterol (TC) reduction or triglycerides (TG) increase and sepsis prognosis. However, the prognostic value of their combination, expressed by TC/TG ratio, remains unexplored. This study evaluated the association between the TC/TG ratio at the admission, 30-day mortality, and the risk of acute congestive heart failure (aCHF) development during hospitalization for sepsis.
Methods: data from 497 adult patients hospitalized for infectious disease who met the Sepsis 3.0 criteria and for whom a complete lipid profile was available within the first 48 hours of admission, were retrospectively analyzed. Death within 30 days of admission and intercurrent aCHF, defined as the need for parenteral diuretic therapy at doses higher than those used at home, were assessed. The association between CT/TG and outcomes was investigated using logistic regressions, Kaplan–Meier curves, and contingency analysis based on the combination of median CT/TG values and SOFA scores. The discriminatory capacity of the combined SOFA+CT/TG model was analyzed using ROC curves.
Results: Of the patients analyzed X (23.1%) died within 30 days. CT/TG was significantly lower in patients who died, and a unit reduction in the ratio was associated with a significative 4.8% increase in 30-day mortality (OR: 0.952 IC-95%: 0922-0.984 p=0.003). CT/TG below the median (13.72) was associated with a significant increase in 30-day mortality risk, irrespective of confounding factors. The combined SOFA+CT/TG model showed a better discriminatory ability than SOFA alone (AUC vs AUC). In addition, a low CT/TG was associated with a significant 3.3% increase in the risk of developing aCHF during hospitalization (OR: 0.967 IC-95%: 0.939-0.996 p=0.027).
Conclusions: A reduced CT/TG ratio is an independent prognostic factor for 30-day mortality and intercurrent aCHF in patients with sepsis.

Abstract n SP05_4 - Presenting author**: Arianna Toscano**

PRedictive Evaluation of Cardiovascular rIsk Scores for subclinical damage in Early inflammatory joint disease: the PRECISE study

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Aim: Patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) carry a higher cardiovascular (CV) risk than the general population, nearly one third of which could be attributable to disease-specific mechanisms. Early identification of subclinical CV involvement is crucial, but current risk calculators were developed for the general population and may not adequately capture inflammation-driven damage.
Methods: We enrolled 106 (mean age= 46 years, 84% female), newly diagnosed, treatment-naïve RA/PsA patients with no traditional CV risk factors and 43 age- and gender-matched healthy controls. All participants underwent carotid ultrasound for IMT evaluation and pulse wave velocity (PWV) estimation, and speckle-tracking echocardiography for global longitudinal strain (GLS) analysis. Cardiovascular risk was estimated by using SCORE2, Framingham Risk Score (FRS), ProgettoCuore, Reynolds Risk Score (RRS), the Expanded Risk Score for RA (ERS-RA) and its adapted version for PsA (ERS-PsA). Predictors of subclinical CV damage were identified through regression and ROC curve analyses.
Results: Compared with controls, patients showed significantly increased cIMT ($p=0.011$), higher PWV ($p=0.047$), and impaired GLS ($p<0.001$). Subclinical alterations were present in 53%, 43%, and 59% of patients for cIMT, PWV, and GLS, respectively, despite the absence of overt CV risk factors. Traditional scores showed modest associations, mainly with cIMT, while their predictive accuracy for PWV and GLS was limited. In contrast, ERS-RA demonstrated consistent associations across vascular and myocardial surrogates and superior discriminatory ability in ROC analyses (cIMT: AUC 0.770; GLS: AUC 0.786).
Conclusions: Subclinical cardiovascular injury is already detectable at the time of RA/PsA diagnosis, even in patients without traditional risk factors, and remains largely unrecognized by conventional risk calculators, even after validated adjustments. ERS-RA performed better but requires recalibration to capture early disease-related risk. These findings emphasize the need for tailored strategies integrating and developing alternative approaches to improve CV risk stratification in inflammatory arthritis.

Abstract n SP05_5 - Presenting author**: Beatrice Invernici**

Lipoprotein(a) does not correlate with hypertensive mediated organ damage and subsequent cardiovascular events in a primary prevention cohort

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Aim: Elevated lipoprotein(a) [Lp(a)] levels have been strongly related to cardiovascular (CV) risk. However, its association with Hypertension Mediated Organ Damage (HMOD) and CV events in the primary prevention setting remains unclear. The aim of our study is to evaluate in these patients the correlation between Lp(a) levels and: (i) heart, vessels and kidney HMOD and; (ii) CV events and all-cause mortality in a primary prevention setting.
Methods: 747 low CV risk subjects were recruited between 2009 and 2014. HMOD was assessed through Pulse Wave Velocity (PWV), carotid Intima-Media Thickness (IMT), presence of carotid plaques, Left Ventricular Hypertrophy (LVH), Ejection Fraction (EF) and glomerular filtration rate (GFR). All-cause mortality and CV events up to 2021 were retrieved by electronic health records, for a median follow-up time of 10 years (I-III quartiles 9.6-11.1).
Results: Mean age was 50.8 ± 13.0 years and 63.5% of the subjects were men. The prevalence of hypertension was 37.9%, dyslipidemia 67.2%, smoking 17.8%, and diabetes mellitus 8.7%. Median Lp(a) value was 17 mg/dL (5.9–56.0), and 26.5% of patients had values above 50 mg/dL. Regarding HMOD, 10.3% subjects had arterial stiffness, 7.2% increased IMT, 19.8% carotid plaques while only 0.7% had LVH. No significant correlation was found between Lp(a) levels and indices of subclinical HMOD. Furthermore, no relationship was found between CV events and all-cause mortality and Lp(a) levels.
Conclusions: In this primary prevention cohort, elevated Lp(a) levels were not associated with significant structural damage to the heart, carotid arteries, or increased aortic stiffness and were not associated with CV events and all-cause mortality.

Abstract n SP05_6 - Presenting author**: Simone Pugnaloni**

High cardiovascular risk and poor risk factor control in patients living with COPD: real-world evidence

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Background: Chronic obstructive pulmonary disease (COPD) is a major global health burden and is frequently associated with cardiovascular (CV) comorbidities. Although COPD patients experience higher CV morbidity and mortality, the disease itself is not explicitly included in traditional CV risk prediction algorithms. Shared risk factors, such as smoking habit, hypertension, diabetes mellitus (DM), and dyslipidemia, as well as disease-specific mechanisms—including chronic hypoxia, oxidative stress, vascular remodeling—may contribute to the elevated CV burden in COPD. This study aimed to assess CV risk in COPD patients, based on SCORE2/SCORE2-OP risk charts (using the recently validated HUMTELEMED web-application), and to identify clinical and biochemical variables associated with higher CV risk.
Methods: We conducted an observational study including 198 consecutive COPD patients referred to the Respiratory Medicine Office of IRCCS INRCA and the Regional Hypertension and Cardiovascular Disease Centre (Ancona, Italy), between January 2013 and May 2024. Inclusion criteria were confirmed diagnosis of COPD and availability of parameters required for CV risk calculation. Demographic, clinical, biochemical, and functional data were collected, including age, sex, body mass index (BMI), blood pressure (BP), lipid profile, renal function, comorbidities, smoking status, COPD Assessment Test (CAT), and Modified Medical Research Council (mMRC) dyspnea score. CV risk was estimated by the www.humtelemed.it validated web-app, according to SCORE2/SCORE2-OP charts. Statistical analyses were performed using SPSS version 23, with significance set at $p<0.05$.
Results: Characteristics of the study population (65.7% M): mean age of 72.2±9.4 years, mean BMI 28.9±5.3 kg/m². The study population showed an high prevalence of comorbidities: current or former smokers (77.8%), hypertension (97.5%), DM (25.8%), dyslipidemia (80.8%), heart failure (12.1%), atherosclerotic cardiovascular disease (ASCVD, 36.4%), and chronic kidney disease (CKD, 17.7 %). Mean CAT score was 16.0±5.6, and mMRC scores indicated moderate-to-severe dyspnea in most patients. According to SCORE2/SCORE2-OP, 10.6% of participants were classified at high risk and 89.4% at very high risk, while none were at low-to-moderate CV risk. Factors associated with very high risk included older age (70.3±8.8 vs 60.5±6.2 years, $p<0.001$), presence of ASCVD (40.7% vs 0%, $p<0.001$), peripheral artery disease (72.3% vs 4.8%, $p<0.001$), DM (28.8% vs 0%, $p=0.004$), and CKD (19.8% vs 0%, $p=0.025$). Higher systolic BP, lower total cholesterol, and lower non-HDL cholesterol were also associated with very high risk. Symptom severity correlated with risk stratification: patients with CAT ≥17 or mMRC score of 3 were consistently at very high risk ($p<0.05$). Alarmingly, 76.3% of participants failed to achieve BP targets and 86.9% were not at LDL cholesterol goal according to ESC 2021 guidelines, with no significant difference between high and very high-risk groups.
Conclusions: The vast majority of COPD patients in this cohort exhibited an elevated CV risk profile, mainly driven by advanced age, cardiometabolic comorbidities, and atherosclerotic burden. Symptom severity appeared to be associated with increased risk, suggesting a possible interplay between respiratory impairment and CV disease. Despite their elevated risk, most participants did not meet recommended BP and serum lipid targets, underscoring a substantial gap in preventive care. These findings highlight the urgent need for comprehensive, integrated CV risk assessment and aggressive management strategies in COPD populations.

Abstract n SP05_7 - Presenting author**: Isabella Soliman**

Vitamin D levels in a population of healthy subjects and its association with metabolic derangement and cardiac and carotid target organ damage

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Introduction: while vitamin D is primarily recognized for its role in intestinal calcium absorption and bone mineralization, it had numerous extra-skeletal effects also regarding the cardiovascular (CV) systems.
Aim: to evaluate the correlation between vitamin D levels and cardiovascular risk factors and Target Organ Damage (TOD) in a healthy population.
Methods: we enrolled 311 healthy participants from a CV risk assessment program at Niguarda Hospital. Medical history, physical exams, Blood Pressure (BP), Body Mass Index (BMI) and laboratory tests (glucose, lipids, creatinine, eGFR) were collected. TOD was evaluated by echocardiography and carotid ultrasound.
Results: at multivariable models with age, sex and kidney function as covariates, vitamin D was significantly associated with BMI (β=-0.142, p=0.007), SBP (β=-0.116, p=0.039), triglycerides (β=-0.239, p<0.001) and HDL (β=0.141, p=0.007). Furthermore, vitamin D deficiency (<12 ng/mL) was significantly associated with hypertriglyceridemia (> 150 mg/dL) with an HR of 5.984 (p<0.001). No significant association with TOD was found.
Conclusions: our study found that low vitamin D levels are linked to metabolic disturbances, including lower HDL and higher TG, BP, and BMI, but showed no significant association with heart or carotid TOD. One could speculate that in an otherwise healthy population metabolic derangement determined by low vitamin D levels could precede TOD development.

Abstract n SP06_1 - Presenting author**: Noemi Cimbalo**

Dietary carbohydrate restriction affects hepatic glucose production and intestinal glucose absorption independently of body weight loss

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Background and aims: Low-carbohydrate diets (LCD) improve body weight and glycaemic control in the short term. Carbohydrate restriction may modulate hepatic glycogenolysis, duodenal glucose absorption, and peripheral glucose disposal. However, how LCD distinctly influences glucose handling remains unclear. This study evaluated the impact of LCD compared to an energy-matched Mediterranean diet (MED) on post-load glucose metabolic fluxes in overweight individuals.
Materials and methods: In this randomized cross-over study, 20 individuals (age 53.5±7.4 years, BMI 30.8±3.5 kg/m2) were assigned to a 4-week hypocaloric LCD (20% carbohydrate, 50% fat, 30% protein) and an energy-matched 4-week MED (50% carbohydrate, 20% fat, 30% protein). After each diet, an OGTT with two stable glucose isotopes (intravenous [6,6-2 H2] glucose and oral [U-13C] glucose) was performed to measure endogenous glucose production (EGP), rate of appearance of oral glucose (RaO), and glucose clearance (GCl). Insulin secretion rate (ISR) was estimated by modelling C-peptide concentrations.
Results: By design, LCD and MED led to a similar weight reduction (-2.8±2.3 and -2.7±2.4 kg, respectively, p=0.398) but differed in self-reported daily carbohydrate intake (29.7±5.3% and 47.2±6.3%, p<0.0001) and CGM-derived average glucose levels. Plasma glucose, insulin and ISR profiles during OGTT were similar after the two diets. EGP was more suppressed by the oral glucose load after LCD than MED, showing reduced hepatic resistance to portal insulin (EGP×ISR AUC 113±43 and 125±41 µmol min-1 kg-1× nmol/m2×min, p=0.026). Furthermore, RaO was significantly delayed by the LCD compared with MED (time to peak 30±12 and 21±7 min, p=0.001), although not reduced over the 180-min observation. There were no differences in post-load GCl between the two diets.
Conclusion: Carbohydrate restriction enhances suppression of EGP and delays intestinal glucose absorption after an oral glucose load without affecting peripheral glucose disposal. These mechanisms may underlie the beneficial effects of LCD on postprandial glycaemic control in overweight individuals.

Abstract n SP06_2 - Presenting author**: Stefania Scaglione**

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

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Background: A randomized clinical trial to evaluate the effect of a Mediterranean-style diet on vascular health indices such as endothelial function indices, serum lipid and ceramide plasma and some adipokine serum levels. We recruited all consecutive patients at high risk of cardiovascular diseases admitted to the Internal Medicine and Stroke Care ward at the University Hospital of Palermo between September 2017 and December 2020.
Materials and methods: The enrolled subjects, after the evaluation of the degree of adherence to a dietary regimen of the Mediterranean-style diet, were randomised to a Mediterranean Diet (group A) assessing the adherence to a Mediterranean-style diet at each follow up visit (every three months) for the entire duration of the study (twelve months) and to a Low-fat diet (group B) with a dietary "counselling" starting every three months for the entire duration of the study (twelve months).The aims of the study were to evaluate: the effects of adherence to Mediterranean Diet on some surrogate markers of vascular damage, such as endothelial function measured by means of the reactive hyperaemia index (RHI) and augmentation index (AIX), at the 6-(T1) and 12-month (T2) follow-ups; the effects of adherence to Mediterranean Diet on the lipidaemic profile and on serum levels of ceramides at T1 and T2 follow-ups; the effects of adherence to Mediterranean Diet on serum levels of visfatin, adiponectin and resistin at the 6- and 12-month follow-ups.
Results: A total of 101 patients were randomised to a Mediterranean Diet style and 52 control subjects were randomised to a low-fat diet with a dietary "counselling". At the six-month follow-up (T1), subjects in the Mediterranean Diet group showed significantly lower mean serum total cholesterol levels, and significantly higher increase in reactive hyperaemia index (RHI) values compared to the low-fat diet group. Patients in the Mediterranean Diet group also showed lower serum levels of resistin and visfatin at the six-month follow-up compared to the control group, as well as higher values of adiponectin, lower values of C24:0, higher values of C22:0 and higher values of the C24:0/C16:0 ratio. At the twelve-month follow-up (T2), subjects in the Mediterranean Diet group showed lower serum total cholesterol levels and lower serum LDL cholesterol levels than those in the control group. At the twelve-month follow-up, we also observed a further significant increase in the mean RHI in the Mediterranean Diet group, lower serum levels of resistin and visfatin, lower values of C24:0 and of C:18:0,and higher values of the C24:0/C16:0 ratio.
Discussion: The findings of our current study offer a further possible explanation with regard to the beneficial effects of a higher degree of adherence to a Mediterranean-style diet on multiple cardiovascular risk factors and the underlying mechanisms of atherosclerosis. Moreover, these findings provide an additional plausible interpretation of the results from observational and cohort studies linking high adherence to a Mediterranean-style diet with lower total mortality and a decrease in cardiovascular events and cardiovascular mortality.

Abstract n SP06_3 - Presenting author: **Rocco Amendolara**

Distinct interplay between β-cell function and insulin sensitivity in latent autoimmune diabetes in adults and type 2 diabetes

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Aim. To elucidate the interplay between β-cell function and indexes of peripheral insulin sensitivity, comparing individuals with latent autoimmune diabetes in adults (LADA) and type 2 diabetes (T2D) with similar body mass index (BMI) and disease duration.
Methods. Thirty-one people with LADA were matched 1:1 for gender, BMI and disease duration with 31 people with T2D. Insulin resistance was estimated using established surrogate indexes. Visceral adipose tissue (VAT) was assessed by dual-energy X-ray absorptiometry. Serum C-peptide levels were measured by ELISA. Clinical data were collected from medical records.
Results. Individuals with LADA exhibited significantly lower C-peptide levels and reduced insulin resistance scores in several indexes (TG-HDL, TyG-Waist, lipid accumulation product (LAP), visceral adiposity index (VAI), VAT; $p < 0.05$ for all) than those with T2D. TyG-BMI and metabolic score for insulin resistance (METS-IR) were also numerically lower in LADA group. Patients with LADA consistently showed reduced β-cell function compared to the T2D group, even at similar insulin sensitivity. C-peptide levels were associated with the majority of insulin sensitivity indexes exclusively within the T2D group (p-value for interaction < 0.05 for triglycerides/HDL ratio, TyG-BMI, TyG-Waist, METS-IR, LAP, VAI, VAT).
Conclusions. Our data demonstrates that individuals with LADA exhibit a markedly blunted insulin response compared to those with T2D, even at comparable insulin sensitivity, being unable to mount a meaningful compensatory response to insulin resistance. This pronounced defect in insulin secretion places patients with LADA at a significantly higher risk of impaired glycemic control to their non-autoimmune counterparts, highlighting the critical need for early accurate diagnosis of adult-onset diabetes.

Abstract n SP06_4 - Presenting author**: Soheil Houshan**

Real-world efficacy and safety of SGLT2-inhibitors in an elderly population

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Aim: Sodium–glucose cotransporter 2 inhibitors (SGLT2-i) demonstrated cardiovascular and renal benefits, likely mediated by their natriuretic action. However, evidence regarding their effectiveness and safety in very old patients remains limited. The aim of this study was to evaluate the clinical and laboratory impact of SGLT2-i therapy in patients aged ≥80 years with a clinical indication for treatment.
Methods: 77 patients aged ≥80 years referred to the Internal Medicine and Geriatrics (IRCCS INRCA, Ancona, Italy) were included. Clinical, laboratory, and functional scores (including blood pressure, renal function, metabolic parameters, NT-proBNP, comorbidities, Activity of Daily Living (ADL), and Geriatric Index of Comorbidity (GIC)) were collected. Assessments were performed before initiation of SGLT2 inhibitor therapy (T0) and at subsequent follow-up visits (T1, T2).
Results: Seventy-seven patients were included (mean age 86.8 ± 4.6 years, F 54.5%). Dyslipidemia 83.1%, atrial fibrillation 64.9%, chronic obstructive pulmonary disease 42.9%, ischemic heart disease 37.7%, valvular heart disease in 42.9%, and type 2 diabetes mellitus 36.4%. Partial or total dependence by ADL was observed in 88.4%. During follow-up, initiation of SGLT2-i therapy was associated with a significant reduction in NT-proBNP levels ($p<0.05$) (Fig.1). Both systolic and diastolic blood pressure showed a reduction during follow-up ($p<0.001$). At T0, most patients were in classified in NYHA 3–4 (64,9%), whereas at T1 a significant shift toward lower classes was observed, with a marked increase in class 2 and reduction in classes 3–4 ($p<0.05$) (Fig.2). Moreover, we observed a reduction in NT-proBNP in HFmrEF ($p<0.001$) and HFpEF ($p<0.001$), while in HFrEF not statistically significant (Fig.3).
Conclusions: In very elderly patients, SGLT2-i therapy was associated with significant improvements in NT-proBNP, blood pressure, and heart failure symptoms. Reduction in NT-proBNP was more pronounced in HFmrEF and HFpEF phenotypes. Our findings may support the use of SGLT2-i in real-world geriatric populations and warrant confirmation in larger prospective studies.

Abstract n SP06_5 - Presenting author**: Artenca Shehu**

Management of polypharmacoterapy in hypercholesterolemic patients treated with bempedoic acid: a monocentric, real-world observational study

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Background: Low-density lipoprotein cholesterol (LDL-C) plays a causal and cumulative role in atherosclerotic disease genesis and cardiovascular (CV) events For this reason, several drugs and therapeutic strategies have been developed to reduce LDL-C levels, but, despite this, achievement of the therapeutic target (TT) and retention in therapy remain low, especially in patients with multiple comorbidities and polypharmacy.
In this context, bempedoic acid (BA) appears to be a good therapeutic option for reducing LDL cholesterol, achieving the TT, and overcoming statin intolerance, but it is increasingly being used in combination therapies.
Aim: The objective of our study was to observe 1) real-life use of BA as a means of achieving the LDL-C target in polypharmacy when other treatment strategies are not possible; 2) adherence and retention in therapy; 3) tolerability; and 4) develop strategies to reduce potential adverse effects by adjusting concomitant medications.
Methods: Patients prescribed BA therapy at our center were monitored from March 2023 (when BA therapy became available in Italy) to June 2025 according to AIFA prescription criteria. Data were collected from 215 patients (M 34.88%, F 65.12%, mean age 66.9 years, weight 71.79 kg, BMI 27.91, waist circumference 98.39 cm). Cardiovascular risk (CVR) was calculated based on the SCORE2, SCORE2-OP, and SCORE2-DIABETES charts and the physician's clinical assessment; patients were then divided into: low CVR 8.37%, moderate 21.86%, high 46.51%, and very high 23.26%. Background therapies were analyzed at baseline, 1-3 months, and 6-12-24 months, as well as achievement of LDL-C and non-HDL-C goals at baseline, 1-3 months, and 6-12-24 months.
All patient comorbidities and concomitant medications were recorded. Lipid-lowering therapies were analyzed at baseline, 1-3 months, and 6-12-24 months, as well as achievement of LDL-C goals at the same time points. Adverse events and/or reasons for discontinuation, creatinine and uric acid levels, were recorded at each follow-up.
Results: At baseline, 68 patients (31.63% of the entire sample of 215) were not taking any therapy, 65 (30.23%) were on monotherapy, and 82 (38.14%) were on polypharmacy. We analyzed data from 174 patients who returned for follow-up after 1–3 months. Of these, 140 (82.8%) continued therapy: 29.29% were on BA monotherapy and 70.71% on combination therapy with two or more drugs (40% BA + ezetimibe; 3.57% BA + statin; 24% BA + ezetimibe + statin; 3.57 BA + other drugs). The remaining 34 patients (17.2%) discontinued therapy: 9 (5.2%) due to drug-related adverse events, while 25 patients (14.4%) discontinued therapy for administrative, non-drug-related reasons and did not return for follow-up visits. Of the latter, 19 (75%) were lost in the first year of observation and only 6 (25%) in the second year. LDL-C and non-HDL-C targets were assessed: at baseline, only 5.58% of patients had already reached the LDL-C target (9.77% for non-HDL-C) but had to modify therapy due to poor tolerability, while at the 1-3 month follow-up, the LDL-C target was reached by 35.7% (43.57% for non-HDL-C). Sub-analyses were also performed to evaluate target achievement based on risk classes. Nineteen patients (11%) reported adverse effects: 8 (42%) musculoskeletal disorders, 3 (15.8%) gastrointestinal disorders, 3 (15.8%) elevated uric acid, and 5 (26.3%) other disorders (impotence, headache, fatigue); only 9 patients (5.2%) discontinued therapy due to adverse events. These results were substantially confirmed at 12-24 month follow-up visits, although they were not reported due to the progressive reduction in the observed sample size and the lack of significance of the data.
Conclusions: BA has proven to be an effective, fast-acting, safe, and well-tolerated drug in the general population, but also in the elderly, allowing LDL-C targets to be reached in a portion of patients with no other therapeutic strategies. In light of what has also been observed in younger patients, we have developed a strategy to reduce uric acid elevations. We evaluated all concomitant therapy, including antihypertensives, seeking to promote the use of drugs with a lower metabolic impact.
Our project plans to monitor the patients in whom we have applied this strategy to verify whether this has resulted in a reduction in the BA discontinuation rate.

Abstract n SP06_6 - Presenting author**: Celeste Lauriola**

Free fatty acids impair steroidogenesis and promote apoptosis in leydig cells: A new link between metabolic dysfunction and hypogonadism

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Excess circulating fatty acids contributes to the association between metabolic disorders and hormonal alterations. Indeed, obesity and diabetes mellitus are frequently associated with functional hypogonadism characterised by reduced testosterone levels. Although a high-fat-diet is known to negatively affect testicular function, its specific impact on steroidogenesis remains unclear. Therefore, the aim of this study has been to investigate the effects of different FFAs, with or without human chorionic gonadotropin (hCG) stimulation, on steroidogenesis and apoptosis in a murine Leydig cell line (mLTC1).
mLTC1 cells were exposed with increasing concentrations of palmitate (PA) or oleate (OA), in the presence or absence of 0.2 IU/mL hCG. The expression of the Steroidogenic Acute Regulatory (STAR) protein, a key marker of steroidogenesis, was evaluated by immunoblotting. Testosterone secretion was measured by ELISA, while apoptosis was evaluated by cleaved caspase-3 (C3C) protein expression using immunoblotting.
Exposure to PA significantly reduced hCG-induced STAR protein expression in a dose-dependent manner after 6h and 15h, respectively, compared with PA-free conditions. Similarly, exposure to OA reduced STAR protein expression at all concentrations tested (0.4-1 mM). Prolonged treatment with PA (96 hours) further compromised steroidogenic capacity, leading to a reduction in testosterone production. Furthermore, PA significantly increased C3C levels. Notably, hCG stimulation during the last 6h of incubation significantly reduced PA-induced C3C levels at all concentrations.
In conclusion, both PA and OA impair hCG-induced steroidogenesis, while PA additionally promotes Leydig cell apoptosis. These findings suggest a direct detrimental role of excess FFAs on testicular function in obesity and indicate a potential protective role of hCG in preserving Leydig cell viability under conditions of metabolic stress.

Abstract n SP06_7 - Presenting author**: Maria Luisa D'Onghia**

Glycemic levels correlate with inflammation in burn patients

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Background: Burns are a significant global health issue. Prior studies have shown an increase in C-reactive protein and other inflammatory biomarkers in burn patients. Additionally, these patients often experience hyperglycemia, likely as a result of the inflammatory response. Blood glucose levels above 140 mg/dL may serve as a nonspecific indicator of an underlying infectious process and warrant heightened clinical attention. When glycemic values exceed 200 mg/dL, burn patients experience a markedly increased susceptibility to infectious complications. Our study aimed to investigate the relationship between glycemic levels and C-reactive protein in burn patients.
Methods: We enrolled 18 burn patients who were referred to our burn division from September 2025 to December 2025. We used an age criterion of over 18 years for inclusion. We conducted routine blood tests for each patient, focusing on inflammation and glycemia.
Results: We observed the following mean age: 51.2±18.1, glycemic values: 124±27 and c-reactive protein values: 23.0±31.1. We found a strong correlation between glycemic levels and C-reactive protein in burn patients ($r = 0.707$, $p = 0.0011$).
Discussion: Our results indicate a significant relationship between the inflammatory burden and glycemic values. Inflammation at the injury site is essential for wound healing and innate immune defense. In this context, a cytokine storm may lead to changes in glycemic levels, which in turn increases inflammation and oxidative stress. This chain reaction can contribute to negative outcomes, such as increased mortality and longer hospital stays

Abstract n SP06_8 - Presenting author**: Rosario Mare**

Citrus waste-derived flavonoids as potential agents for diabetes and obesity management

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Aim: The increasing focus on food waste valorization emphasizes citrus by-products as valuable matrices due to their high content of bioactive constituents. Notably, flavonoids contained in *Citrus spp.* species cultivated in Southern Italy may represent an effective resource for the prevention and management of metabolic disorders. The present study investigates the biological effects of citrus-derived biomolecules obtained from food waste on obesity and type-2 diabetes.
Methods: Sustainable extraction techniques, namely maceration, ultrasound-assisted extraction, and supercritical CO_2 extraction, were compared to obtain bioactive compounds from 11 species belonging to the *Citrus* genus. All extracts were characterized using UV–Vis spectrophotometric assays and high-performance liquid chromatography (HPLC). The most effective extracts were subsequently evaluated for antioxidant capacity, α-amylase inhibitory activity, and their ability to modulate glucose metabolism and triglyceride accumulation in differentiated 3T3-L1 adipocytes.
Results: Ultrasound-assisted extraction proved to be the most efficient method for flavonoid recovery, particularly for naringin and hesperidin. The resulting extracts exhibited marked antioxidant activity, reaching up to 56.18 ± 0.87 %I, and significantly inhibited α-amylase activity up to 22.14 ± 0.98 %. Moreover, selected extracts approximately doubled glucose uptake, especially those derived from late-ripening orange, and almost completely suppressed the adipocyte differentiation process.
Conclusions: *Citrus* processing wastes emerge as promising sources of flavonoids with potential protective effects against metabolic disorders. Flavonoids obtained from citrus by-products, especially those showing high antioxidant efficacy, may be exploited for the development of nutraceuticals and dietary supplements with adjuvant roles in the prevention and management of metabolic-nutritional diseases such as obesity and diabetes.

Abstract n SP06_9 - Presenting author**: Annalisa Giosuè**

Reproducibility of Continuous Glucose Monitoring-derived postprandial glucose features and their potential use as predictors of glycemic control in type 2 diabetes

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Aim: Targeting postprandial glucose response (PPGR) is more effective than lowering fasting glucose in improving glycemic control and reducing cardiovascular risk in individuals with T2D. This study aims to evaluate the within-subject reproducibility of CGM-derived dynamic parameters of PPGR and their potential as independent predictors of glycemic control in T2D.
Methods: A total of 102 individuals with T2D underwent a 7-day CGM and consumed a standardized breakfast twice to assess the 4-hour glucose response, described by: glucose peak; time to peak; delta glucose max – the difference between the peak and fasting glucose; nadir – the lowest post-peak glucose value; incremental area under the glucose curve; mean postprandial glucose – the average interstitial glucose concentration. Intraclass correlation coefficients (ICCs) with 95% CIs were calculated to assess the reproducibility of PPGR parameters. Multivariable linear regression models were used to evaluate the predictive value of PPGR parameters, fasting glucose, and 2-hour postprandial glucose on 7-day CGM metrics and HbA1c.
Results: Good to moderate reproducibility emerged for mean glucose (ICC: 0.78, 95% CI 0.69–0.84), glucose peak (ICC: 0.69, 95% CI 0.57–0.78), and glucose nadir (0.74, 95% CI 0.64–0.82). Mean postprandial glucose was the strongest predictor of 7-day TIR (β= -0.772, p<0.001), 7-day mean glucose (β=0.800, p<0.001) and HbA1c (β=0.434, p<0.001). The glucose peak was the main predictor of short-term glycemic variability, as reflected by the 7-day coefficient of variation (β=0.258, p=0.006) and mean amplitude of glucose excursions (β=0.613, p<0.001).
Conclusions: CGM-derived PPGR parameters are reproducible in T2D and could represent a practical tool to uncover meaningful information about glucose control, which 2-hour postprandial glucose fails to predict.

Abstract n SP07_1 - Presenting author**: Marco Savino**

SGLT2 inhibition ameliorates physical function in frail older adults with HFpEF and diabetes

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Background: Heart failure with preserved ejection fraction (HFpEF) is a common condition among patients with multiple comorbidities, particularly older adults. HFpEF is associated with an increased risk of physical decline. Type 2 diabetes mellitus (T2D) contributes to endothelial dysfunction, inflammation, atherosclerosis, and oxidative stress, potentially driving the development and progression of HFpEF. Sodium-glucose cotransporter 2 inhibitors (SGLT2-I) have demonstrated efficacy in the management of both T2D and HFpEF. This study aimed to evaluate the effects of SGLT2-I on physical function, in a population of older adults.
Methods: We conducted a prospective observational study with a one-year follow-up, enrolling consecutive frail older adults with confirmed diagnoses of T2D and HFpEF. Inclusion criteria were: age >65 years; confirmed diagnoses of T2D, frailty, and HFpEF and a Montreal Cognitive Assessment (MoCA) score <26. All participants received metformin in combination with either an SGLT2-I, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), or insulin. Physical frailty was assessed using the Fried criteria, with frailty defined as the presence of at least three of five components: low physical activity, unintentional weight loss, exhaustion, weakness, and slowness.
Results: A total of 423 patients were screened. Of these, 54 did not meet the inclusion criteria, 32 discontinued treatment due to drug intolerance, and 17 declined to provide clinical information, resulting in 321 enrolled participants. Patients were stratified into four treatment groups based on their antidiabetic therapy: SGLT2-I (82 patients), GLP-1 RA (76 patients), insulin (80 patients), and metformin alone (83 patients). Treatment with SGLT2-I was associated with significant improvements in physical performance ($p<0.0001$), while no significant changes were observed in the other treatment groups.
Discussion: These findings indicate that SGLT2-I may confer anti-frailty and potentially anti-aging benefits in older adults with T2D and HFpEF. The observed improvements in physical domains suggest pleiotropic effects of SGLT2-I that extends beyond glycemic control. Further large-scale, randomized studies are warranted to confirm these results and elucidate the underlying mechanisms linking SGLT2 inhibition to improved frailty outcomes.

Abstract n SP07_2 - Presenting author**: Emanuele Valeriani**

Age-Related Enhancement of COX-1–Mediated Thromboxane Production in Patients with Atrial Fibrillation

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Background: Enhanced platelet activation contributes to the increased cardiovascular risk of elderly patients with atrial fibrillation. The biological mechanisms underlying this phenomenon are not fully clarified. This study investigated whether age-related increases in serum thromboxane B_2 (TxB_2) are associated with platelet cyclooxygenase-1 (Cox-1) upregulation in older individuals.
Methods: Serum levels of Cox-1 and TxB_2 were assessed in patients with atrial fibrillation enrolled between 2022 and 2023. A subset of participants underwent in vitro analyses to evaluate the inhibitory effect of aspirin on platelet TxB_2 generation and to quantify platelet Cox-1 expression across different age groups (<65 vs. ≥65 years). The relationship between Cox-1 expression and aspirin-mediated inhibition of TxB_2 was also explored. Associations were analyzed using Spearman correlation, and mediation analysis was performed to assess indirect effects.
Results: The study included 134 patients. Age showed a positive correlation with both Cox-1 expression ($R = 0.42$, $p < 0.01$) and TxB_2 levels ($R = 0.44$, $p < 0.01$). Additionally, Cox-1 expression was positively associated with TxB_2 concentrations ($R = 0.50$, $p < 0.01$). Mediation analysis demonstrated that Cox-1 partially mediated the relationship between age and TxB_2 levels ($\beta = 5.23$, 95% CI: 2.33–8.63). In vitro experiments revealed a reduced sensitivity to aspirin in older patients, as reflected by higher IC_{50} values for inhibition of platelet TxB_2 production (96.78 µM in ≥65 years vs. 48.92 µM in <65 years). This reduced response was accompanied by increased platelet Cox-1 expression in the elderly group. Moreover, higher Cox-1 levels were inversely correlated with aspirin-induced inhibition of platelet TxB_2 ($R = -0.64$, $p < 0.01$).
Conclusions: Advancing age is associated with increased thromboxane production, driven in part by platelet Cox-1 upregulation. This alteration is accompanied by a reduced capacity of aspirin to suppress Cox-1 activity, potentially contributing to the heightened thrombotic risk observed in elderly patients.

Abstract n SP07_3 - Presenting author**: Clara Musarò**

Heart failure with preserved ejection fraction in hospitalized older adults: guidelines and diagnostic uncertainties

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Aim: Heart failure with preserved ejection fraction (HFpEF) is increasingly suspected in older adults, yet diagnosis remains uncertain in routine clinical practice. Nonspecific symptoms, age-related cardiac remodeling, and comorbid conditions often overlap with HF manifestations, while diagnostic algorithms are largely derived from younger populations. This study aimed to estimate HFpEF prevalence in older hospitalized patients according to ESC 2021 criteria and to assess the diagnostic performance of established probability scores.
Methods: In this prospective, single-center cohort study, consecutive inpatients aged >75 years admitted to acute Geriatrics were enrolled if presenting signs suggesting HF without prior diagnosis. HFpEF was defined per ESC 2021 criteria (LVEF ≥50%, structural/functional abnormalities, age-adjusted NT-proBNP >1800 pg/mL). The H-FPEF and HFA-PEFF scores were calculated, and diagnostic accuracy assessed. A modified HFA-PEFF score with geriatric-specific cut-offs for NT-proBNP and septal e' was also tested. Confounding comorbidities were recorded.
Results: Among 200 patients (median age 86.6 years; 58% women), 96% fulfilled ESC 2021 criteria. Echocardiographic abnormalities were universal (95%), mainly left atrial enlargement (70%) and increased wall thickness (66.5%), whereas only 52% showed elevated age-adjusted NT-proBNP. Nearly all (98%) had confounding comorbidities, primarily chronic kidney disease (60%) and acute infections (40%). The H-FPEF score showed low sensitivity (0.07) despite perfect specificity (1.00; AUROC 0.676). The HFA-PEFF score demonstrated higher accuracy (sensitivity 0.69, specificity 0.75; AUROC 0.856), while the geriatric-adapted HFA-PEFF improved discrimination (AUROC 0.908) by increasing specificity to 1.00.
Conclusions: In very old, complex inpatients, ESC 2021 criteria may overestimate HFpEF prevalence due to age-related changes and comorbidity burden. While standard H-FPEF and HFA-PEFF scores provided discordant results, geriatric-adapted algorithms integrating specific biomarker and imaging thresholds enhanced specificity. These findings suggest that adapted algorithms support more precise, personalized clinical decision-making, representing a necessary step toward data-driven care in older adults.

Abstract n SP07_4 - Presenting author**: Sara d'Alesio**

Eligibility for icosapent ethyl in patients undergoing cardiac rehabilitation: a real-world cohort study

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Aim: Despite optimal lipid-lowering therapy, many patients with established cardiovascular disease (CVD) maintain elevated triglyceride (TG) levels, contributing to residual risk. Icosapent ethyl (IPE) has shown clinical benefit in patients with moderate hypertriglyceridemia. This study aimed to evaluate eligibility for IPE treatment based on REDUCE-IT and Italian Drugs Administration (AIFA) eligibility criteria.
Methods: We retrospectively analyzed 1129 patients referred to a cardiac rehabilitation program for a recent acute coronary syndromes or with a chronic coronary syndromes between 2012 and 2025. Fasting TG and LDL were assessed at admission and discharge. We identified patients eligible for IPE treatment based on REDUCE-IT (TG 135–499 mg/dL, LDL 40–100 mg/dL, statin therapy) and AIFA eligibility criteria (TG ≥200 mg/dL, LDL <70 mg/dL, BMI ≥27 kg/m², statin + ezetimibe therapies, age 18–80).
Results: Median TG values significantly decreased from 117 (IQR 86–159) mg/dL at admission to 99 (79–132) mg/dL at discharge ($p<0.001$). LDL also decreased from 106.7 ± 40.1 to 62.8 ± 24.8 mg/dL ($p<0.001$). Based on REDUCE-IT criteria, 117 patients (10.4%) were eligible for IPE while only 6 patients (0.53%) met all AIFA eligibility criteria.
Conclusions: In a large real-world cohort of acute and chronic coronary syndrome undergoing cardiac rehabilitation, over 10% of patients were theoretically eligible for IPE based on clinical trial criteria. However, less than 1% met current AIFA eligibility conditions due to added restrictions, highlighting a significant barrier to implementation in clinical practice.

Abstract n SP07_5 - Presenting author**: Michela Cecchini**

SGLT2-inhibitors and GLP1-receptor agonists decrease Plasma NT-proBNP in patients with type 2 diabetes mellitus and heart stress: a longitudinal multicenter real-life study

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Aims: We investigated the effect of a short-term treatment with sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP1-RA) on N-terminal pro-brain natriuretic peptide (NT-proBNP) levels in asymptomatic T2DM patients without known heart failure, but with elevated blood pressure and heart stress (HS), subclinical cardiac damage.
Methods: Multicenter observational longitudinal "real-life" study on 100 consecutive patients. Plasma NT-proBNP was assessed at baseline, before starting SGLT2i/GLP1-RA and after a 3-month follow-up. For the analyses, NT-proBNP levels were adjusted for estimated glomerular filtration rate (eGFR) in SGLT2i group and for body mass index (BMI) in GLP1-RA group.
Results: Mean age: 73.3±7.7 years. Baseline median NT-proBNP: 192.5 (114.0-966.0) pg/mL. At follow-up, we found a slight reduction in adjusted NT-proBNP in the SGLT2i group (n°57 patients) (-2.3%; p=0.049) (Fig. 1). Adjusted NT-proBNP showed a statistically significant decrease (-6.5%; p=0.002) (Fig. 1) within the entire GLP1-RA group (n°43 patients), with a significant greater reduction in patients with higher baseline NT-proBNP (-13.3%; p<0.001). In both subgroups, patients aged >70 years showed a greater reduction in NT-proBNP (Fig. 2).
Conclusions: In asymptomatic patients with T2DM and HS, SGLT2i and especially GLP1-RA led to a slight but significant improvement in cardiac wall stress, as evidenced by the NT-proBNP decrease.

Abstract n SP07_6 - Presenting author**: Danilo Menichelli**

Pharmacological rhythm control strategy and outcomes in very elderly atrial fibrillation patients: an analysis of the nationwide Italian START registry

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Aim: Evidence on antiarrhythmic drug (AAD) use in very elderly patients with atrial fibrillation (AF) is limited. We investigated clinical characteristics and outcomes associated with AAD use in this population.
Methods. 4,244 very elderly (age ≥80 years) AF patients from the nationwide START registry were included. Patients were divided into 3 groups: no AADs (n=3,573), class 1c-AAD (n=207), Amiodarone (n=464). Factors associated to class 1c-AAD and Amiodarone were evaluated by multivariable logistic regression models. Risks of all-cause mortality and Cardiovascular Events (CVEs) were analysed according to AAD use using Cox regression and Fine-Gray model, respectively.
Results: Mean age was 84.8±3.8 years; 54.9% were women. AADs were used in 15.8% of patients (Amiodarone 10.9%, Class 1c 4.9%).
Class 1c-AADs use was inversely with older age, female sex, diabetes, heart failure, digoxin, COPD/OSAS, beta-blockers and lack of familial/social support. Amiodarone use was directly associated with the presence of coronary artery disease, wheelchair use, and inversely associated with age, peripheral artery disease, living alone, digoxin use, beta-blockers and lack of familial/social support.
Over a mean follow-up of 685,6±537.7 days, 492 all-cause deaths, and 548 CVEs events occurred. In univariable Cox analysis, Class 1c AADs were associated with lower mortality (HR 0.371, 95%CI 0.191-0.717) and CVEs (sHR 0.443, 95%CI 0.250-0.786), while amiodarone was not. These associations did not persist in multivariable analysis.
Conclusions: Among very elderly AF patients, the choice of rhythm control strategy is influenced by frailty elements. AADs use has no association with clinical outcomes.

Abstract n SP07_7 - Presenting author**: Nicola Osti**

Lipoprotein(a) plasma levels and coagulation biomarkers: results from a comprehensive laboratory assessment in an angiographically-controlled cardiovascular cohort

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Aim: Lipoprotein(a) [Lp(a)] is a causal risk factor for coronary artery disease (CAD), with proposed prothrombotic properties in addition to its proatherogenic effects. However, the association between Lp(a) and coagulation remains controversial so far. This study examined this relationship in subjects with or without angiographically documented CAD.
Methods: Plasma levels of Lp(a) and coagulation biomarkers were assessed in clinically stable subjects undergoing elective coronary angiography. Subjects taking any anticoagulant therapy were excluded. The coagulation panel included coagulant activities of factors II, V, VII, VIII, IX, X, XI and XII, thrombin generation assay (TGA) and activated factor VII-antithrombin (FVIIa-AT) complex. Lp(a) threshold values were defined according to the European Atherosclerosis Society consensus statement: normal <30 mg/dL, intermediate 30-50 mg/dL, and high >50 mg/dL.
Results: Complete laboratory data were available for 383 subjects (males 75.3%; mean age 68.2±9.7 years): 65 subjects had normal coronary arteries, 51 subjects had coronary lesions with stenosis <50%, and 267 subjects had coronary lesions with stenosis ≥50%. A modest yet significant increase in coagulant activity of FV (FV:C) from low to high Lp(a) plasma levels was found and confirmed after adjustment for potential confounding factors, including gender, age, angiographic CAD diagnosis, renal function, and apolipoprotein B. No difference was observed for all the other coagulant activities, neither FVIIa-AT levels nor TGA parameters.
Conclusions: In this pilot study, no major contribution of Lp(a) plasma levels was detected in modulating coagulation phenotype. High Lp(a) plasma levels were associated with only a mild increase of FV:C.

Abstract n SP07_8 - Presenting author**: Francesca Monego**

High prevalence of advanced cardiovascular-kidney-metabolic syndrome in cardiac rehabilitation patients and therapeutic implications: a single-day observational study

Francesca Monego, Chiara Milan, Laura Severino

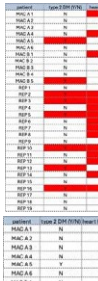
ASST Brianza (Carate Brianza), ASST Grande Ospedale Metropolitano Niguarda (Milano), IRCSS San Gerardo dei Tintori (Monza)

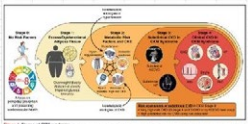
Background: Cardiovascular-Kidney-Metabolic Syndrome (CKM syndrome) is a clinical entity with major prognostic implications, characterized by a complex interrelationship between cardiac, renal, and metabolic dysfunctions, for which several therapeutic strategies have proven highly effective. Though often associated with advanced chronic kidney disease (CKD), its prevalence among cardiac patients without severe renal impairment may be underestimated. This study aimed to assess the prevalence and severity of CKM syndrome and the potential for treatment optimization in patients admitted to a Cardiac Rehabilitation Unit.

Methods: We conducted an observational study on the thirty patients enrolled in a cardiac rehabilitation program at Carate Brianza Hospital on a chosen day (September 24th 2025), both as outpatients (MAC A/B) and inpatients (REP). Clinical and biochemical data were collected at admission, pharmacological data at admission and discharge. Patients were classified based on CKM syndrome stages, according to the 2023 American Heart Association presidential advisory, and CKD severity, according to the 2024 KDIGO classification. We focused of key drugs for CKM syndrome management: RAS blockers, SGLT2 Inhibitors, GLP-1 agonists, cholesterol-lowering agents.

Results: Out of the 30 patients, 26 (86.7%) presented with advanced CKM syndrome, ie. stage 4 (fig.1). Only 7 (23%) had moderate-to-severe CKD (fig.2). Metabolic and cardiovascular disorders were highly prevalent: type 2 diabetes was present in 8 (26.7%), heart failure in 15 (50%), hypertension in 19 (63.3%), dyslipidemia in 25 (83.3%). An optimization of CKD treatment was possible for 11 patients (36.7%) (fig.3).

Conclusions: Our findings reveal a strikingly high prevalence of advanced CKM syndrome, even without severe renal impairment. The use of spot urine albumin instead of albumin-to-creatinine ratio may have contributed to underestimating CKD severity. Despite recent hospitalization in acute care settings, therapeutic optimization remained feasible in a substantial proportion of patients, underscoring the importance of early diagnosis, a holistic approach, and timely multidisciplinary management.





patient	therapy at admission	therapy at discharge	optimization
MAC A 1	canrenone, empagliflozin, valsartan, atorvastatin/ezetemibe	canrenone, empagliflozin, valsartan, atorvastatin/ezetemibe	no
MAC A 2	ramipril	ramipril	no
MAC A 3	sacubitril/valsartan, epelerenone, rosuvastatin/ezetemibe	sacubitril/valsartan, epelerenone, rosuvastatin/ezetemibe	no
MAC A 4	canrenone, dapagliflozin, sacubitril/valsartan, rosuvastatin	canrenone, dapagliflozin, sacubitril/valsartan, rosuvastatin	no
MAC A 5	empagliflozin, semaglutide, rosuvastatin/ezetemibe	empagliflozin, semaglutide, rosuvastatin/ezetemibe	no
MAC A 6	ramipril, canrenone, atorvastatin/ezetemibe	ramipril, canrenone, atorvastatin/ezetemibe	no
MAC B 1	ramipril, rosuvastatin/ezetemibe	ramipril, empagliflozin, rosuvastatin/ezetemibe	si
MAC B 2	canrenone, rosuvastatin/ezetemibe	canrenone, rosuvastatin/ezetemibe	no
MAC B 3	canrenone	canrenone	no
MAC B 4	aldactone, sacubitril/valsartan, rosuvastatin/ezetemibe	aldactone, sacubitril/valsartan, empagliflozin, rosuvastatin/ezetimibe	si
MAC B 5	valsartan, dapagliflozin, dulaglutide, rosuvastatin/ezetemibe	valsartan, dapagliflozin, dulaglutide, rosuvastatin/ezetemibe	no
REP 1	ramipril	ramipril, canrenone, empagliflozin	si
REP 2	canrenone, valsartan, rosuvastatin/ezetemibe	canrenone, sacubitril/valsartan, empagliflozin, rosuvastatin/ezetemibe, dulaglutide	si
REP 3	spironolactone, sacubitril/valsartan, empagliflozin, semaglutide, rosuvastatin/ezetemibe	canrenone, sacubitril/valsartan, empagliflozin, semaglutide, rosuvastatin/ezetemibe	no
REP 4	spironolactone	canrenone, empagliflozin, rosuvastatin	si
REP 5	ramipril, simvastatin	ramipril, simvastatin	no
REP 6	eplerenone, rosuvastatin	canrenone, rosuvastatin/ezetemibe	si
REP 7	ramipril, atorvastatin	ramipril, canrenone, atorvastatin	si
REP 8	canrenone, ramipril, rosuvastatin/ezetemibe	canrenone, ramipril, rosuvastatin/ezetemibe	no
REP 9	spironolactone, furosemide, ezetemibe	rosuvastatin	no
REP 10	empagliflozin, dulaglutide, atorvastatin/ezetemibe	semaglutide, atorvastatin/ezetimibe	no
REP 11	canrenone, valsartan, rosuvastatin/ezetemibe	canrenone, sacubitril/valsartan, rosuvastatin/ezetemibe	si
REP 12	rosuvastatin/ezetemibe	ramipril, rosuvastatin/ezetemibe	si
REP 13	dapagliflozin, zofenopril, rosuvastatin	dapagliflozin, zofenopril, rosuvastatin	no
REP 14	canrenone, atorvastatin	canrenone, atorvastatin	si
REP 15	ramipril, atorvastatin/ezetemibe	ramipril, atorvastatin/ezetemibe	no
REP 16	valsartan, empagliflozin, atorvastatin/ezetimibe	valsartan, empagliflozin, dulaglutide, atorvastatin/ezetimibe	si
REP 17	valsartan, canrenone, rosuvastatin/ezetimibe	valsartan, canrenone, rosuvastatin/ezetimibe	no
REP 18	olmesartan, atorvastatin/ezetimibe	valsartan, atorvastatin/ezetimibe	no
REP 19	atorvastatin	atorvastatin	no

Abstract n SP08_1 - Presenting author**: Elena Levati**

Does the use of benzodiazepine influence the effectiveness of lifestyle intervention? Secondary analysis from the Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies (SPRINTT) trial

Elena Levati[1], Maria Beatrice Zazzara[1,2], Daniele Giuli[3], Emanuele Marzetti[1,2], Anna Picca,[4] Riccardo Calvani[2], Francesco Landi[1,2], Roberto Bernabei[5], Graziano Onder[1,2]

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Purpose. Benzodiazepine use is prevalent among older adults despite its recognized negative effects. Lifestyle interventions can preserve physical function and reduce the risk of disability. This study investigates whether benzodiazepine use reduces the effectiveness of lifestyle-based interventions on mobility disability.
Methods. We performed a secondary analysis of the *SPRINTT* trial. The lifestyle intervention consisted of physical exercise and nutritional counselling. Benzodiazepine use was assessed based on baseline or longitudinal exposure. Cox regression models were used to ascertain the association between benzodiazepine use and mobility disability incidence. A separate analysis was conducted among participants with a SPPB score 3 to 7.
Results. Among the 1,506 participants included (mean age 78.9 years; 71.5% female; 753 intervention vs. 753 control), 211 (14.0%) reported benzodiazepine use at baseline. Overall, 55.0% of baseline benzodiazepine users and 43.6% of non-users developed mobility disability (p=0.003). When baseline benzodiazepine use was considered, no significant effect associated with MCI was shown among non-users (HR = 0.87; 95% CI 0.73–1.04) and users (HR = 0.98; CI 0.64–1.51). In the subgroup of participants with SPPB scores 3 to 7, a significant effect of the MCI was observed only among non-users (HR = 0.81, 95% CI 0.67–0.98), while no effect was detected among users (HR = 1.06; 95% CI 0.66–1.70, p for interaction= 0.045). When longitudinal benzodiazepine exposure was considered, similar results were observed. In particular, in the SPPB score 3 to 7 subgroup, the beneficial effect of the MCI was observed only among non-users (HR = 0.80; 95% CI 0.66 – 0.98), while no effect was detected among users (HR = 1.16; 95% CI 0.62–2.17, p for interaction= 0.033).
Conclusion. In frail older adults, benzodiazepine use blunts the effectiveness of lifestyle interventions for preventing mobility disability. These findings support a prudent approach to benzodiazepine use.

Abstract n SP08_2 - Presenting author: **Alessandro Perencin**

Sex-specific prognostic performance of the CALLY index in hospitalized older adults

Alessandro Perencin[2]; Mario Virgilio Papa[1,2]; Chiara Ceolin[1,2,3]; Veronica Liberati[2]; Vittorio Acunto[2]; Margherita Vergadoro[4,5]; Cristina Simonato[2]; Sara Cazzavillan[2]; Giulia Salerno Trapella[2]; Chiara Curreri[2]; Bruno Micael Zanforlini[2]; Anna Bertocco[2]; Giulia Gasparini[2]; Maria Devita[2,6]; Alessandra Coin[1,2]; Paolo Simioni[7]; Giuseppe Sergi[1,2]; Marina De Rui[2]

[1]Department of Medicine (DIMED), University of Padua, Italy. [2]Geriatrics Division, University Hospital of Padua, Padua, Italy [3]Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Aging Research Center, Stockholm, Sweden [4]Department of Medicine, First Chair of Internal Medicine, Padova University Hospital, Italy [5]Department of Women's and Children's Health, School of Community Medicine and Primary Health Care, University of Padua, Italy [6]Department of General Psychology (DPG), University of Padua, Italy [7]First Chair of Internal Medicine & Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine (DIMED), University of Padova, Padova, Italy.

Aim: In older adults hospitalized with coronavirus disease 2019 (COVID-19), systemic inflammation, immune dysregulation, and nutritional impairment are major determinants of short-term outcomes. The CRP–Albumin–Lymphocyte (CALLY) index integrates these biological domains into a single laboratory-based score and has shown prognostic value in oncology and critical illness. However, evidence in geriatric patients with COVID-19 is scarce, and potential sex-specific differences remain poorly defined.

Methods: We conducted a retrospective cohort study including 363 adults aged ≥65 years hospitalized for COVID-19 in a tertiary geriatric unit between 2020 and 2023. The CALLY index was calculated at hospital admission using serum albumin, lymphocyte count, and C-reactive protein. Short-term mortality was the primary outcome. Discriminative performance was assessed using receiver operating characteristic (ROC) curve analysis overall and stratified by sex, with comparison of areas under the curve (AUCs) using DeLong's test. Survival was evaluated using Kaplan–Meier curves and time-dependent Cox regression models. Analyses were adjusted for age, sex, medication burden, and the Multidimensional Prognostic Index (MPI). Clinical utility was assessed through decision curve analysis, and calibration using bootstrap-corrected methods.

Results: The CALLY index showed moderate overall discrimination for short-term mortality (AUC 0.68), with higher prognostic accuracy in men (AUC 0.76) than in women (AUC 0.65; p <0.05). Lower CALLY values were associated with reduced survival, particularly early during hospitalization. Time-dependent Cox models demonstrated a strong early protective effect of higher CALLY values that attenuated over time, independent of age, sex, medication burden, and MPI. Decision curve analysis indicated improved net clinical benefit, with good calibration between predicted and observed mortality.

Conclusions: In hospitalized older adults with COVID-19, the CALLY index provides clinically meaningful prognostic information for short-term mortality, with stronger performance in men, supporting its use as a rapid risk stratification tool in acute geriatric care.

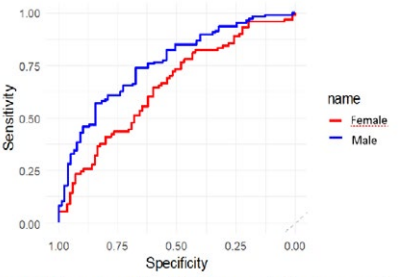

Figure 2. ROC curves of the CALLY score stratified by sex, with separate curves for females and males, highlighting potential differences in discriminatory performance between sexes.

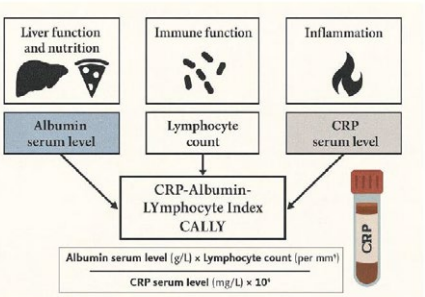

Figure 1. CALLY Index (CRP-Albumin-Lymphocyte Index) and its calculation formula: albumin serum level (g/L) × lymphocyte count (per mm³) divided by CRP serum level (mg/L) × 10⁴.

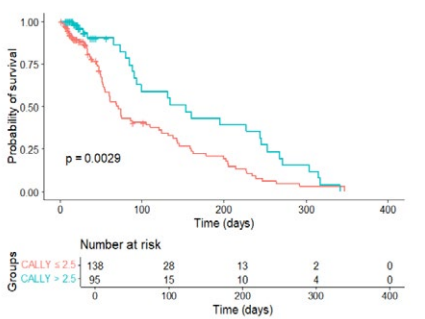

Figure 3. Kaplan--Meier survival curves stratified according to the CALLY score. Patients were classified into two groups based on the predefined cut-off value (CALLY ≤ 2.5 vs. CALLY > 2.5). The figure shows a significantly lower probability of survival over time in patients with lower CALLY values compared with those with higher CALLY values. The p value was calculated using the log-rank test. The number of patients at risk at each time point is reported below the plot. Lower CALLY values correspond to a worse inflammatory--nutritional profile and higher short-term mortality risk.

Abstract n SP08_3 - Presenting author**: Carlotta De Nuntiis**

Prognostic Value of the C-reactive protein-triglyceride glucose index in older hospitalized patients

Alessia Riccio, Chiara M. A. Cefalo, Carlotta De Nuntiis, Teresa Vanessa Fiorentino, Giorgio Sesti

Sapienza, University of Rome

Aim Metabolic inflammation represents a pivotal mechanism in the development of chronic and age-related diseases. C-reactive protein (CRP) is a well-established biomarker of systemic inflammation, whereas the triglyceride–glucose (TyG) index is a validated surrogate of insulin resistance and metabolic dysfunction. The combined CRP/TyG index integrates inflammatory and metabolic pathways and has been proposed as a marker of metabolic inflammation; however, its prognostic value in non–critically ill hospitalized patients remains insufficiently explored. This study aimed to evaluate the association between the CRP/TyG index and adverse clinical outcomes in older, non–critically ill patients enrolled in the Clinical Outcomes in Hospitalized Patients Receiving Treatment at Sant'Andrea Hospital (COHORTS) study.
Methods A total of 229 patients aged 65 years or older were included. The CRP/TyG index was calculated at hospital admission, and patients were stratified into tertiles according to index values. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI). Associations between the CRP/TyG index and clinical variables were evaluated using univariate analyses. Clinical outcomes across tertiles were compared using logistic regression models adjusted for age, sex, and CCI.
Results Patients in the highest CRP/TyG index tertile showed significantly higher levels of white blood cells, fibrinogen, and alanine aminotransferase, along with lower levels of albumin and high-density lipoprotein cholesterol, compared with those in the lower tertiles. Higher CRP/TyG index values were associated with a greater prevalence of type 2 diabetes ($p = 0.003$), chronic pulmonary disease ($p = 0.02$), and a longer length of hospital stay ($p = 0.02$). After adjustment for potential confounders, elevated CRP/TyG index values remained independently associated with an increased risk of in-hospital mortality (OR: 3.6; 95% CI: 1.4–9.3; $p = 0.02$).
Conclusion The CRP/TyG index appears to be a practical and easily obtainable tool for early risk stratification in non–critically ill hospitalized patients. Further prospective studies are warranted to confirm its prognostic value and support its implementation in routine clinical practice.

Abstract n SP08_4 - Presenting author**: Laura Andreea Ceparano**

Identification of potential circulating biomarkers of frailty in hospitalized older adults

Laura Andreea Ceparano[1], Laura de Lisio[1], Mohd Rashid Khan[3], Domenico Iervolino[3], Chiara Di Lorenzo[1], Leonardo Cristinziano[1], Antonio Di Maio[1], Alessandro Orrera[1], Giuseppina Gambino[1], Raffaele Formisano[1], Grazia Daniela Femminella[1], Pasquale Dolce[2], Danila Azzolina[2], Leonardo Bencivenga[1], Giuseppe Rengo[1]

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Aim: Frailty represents a major clinical challenge due to its multidimensional and heterogeneous nature, which limits the applicability of standardized diagnostic and therapeutic algorithms. Understanding the biological mechanisms underlying frailty may aid in the early identification of high-risk patients and guide personalized interventions. Although Comprehensive Geriatric Assessment (CGA) remains the gold standard, it is time-consuming and not always feasible in routine clinical practice. Moreover, frailty diagnostic criteria encompass multiple clinical domains, including physical, cognitive, and social assessments; accordingly, the identification of blood-based molecular biomarkers could help facilitate and enhance frailty detection. Therefore, the aim of this study was to investigate the association between aging-related biomarkers and frailty in a population of hospitalized older adults.
Methods: A total of 248 patients aged ≥60 years, were recruited from the Geriatric ward of Federico II University Hospital, Naples, Italy. All participants underwent a CGA and venous blood sampling. Frailty was assessed using a CGA-derived Frailty Index (FI). Plasma concentrations of potential frailty biomarkers (FGF-21, GDF-15, sRAGE, BDNF, and NfL) were measured using the Ella™ automated microfluidic immunoassay platform. Multivariable beta regression models were used to evaluate the associations between biomarker levels and FI.
Results: The mean age of the study population was 76.1±8.01 years, 64.1% male. Frail individuals were significantly older, more frequently female, and exhibited worse functional, cognitive, and physical performance compared with non-frail participants. Plasma levels of FGF-21, GDF-15, and NfL were significantly higher in frail individuals, whereas BDNF and sRAGE showed no differences in unadjusted analyses. In multivariable models, only NfL and sRAGE concentrations were significantly associated with FI, while FGF-21 and GDF-15 showed a trend to significance.
Conclusions: Our results indicate that NfL and sRAGE are independently associated with frailty beyond chronological age, supporting their potential role as biomarkers of biological vulnerability. Combining biomarker profiling with CGA may enable earlier frailty detection.

Abstract n SP08_5 - Presenting author**: Barbara Fioretti**

Serum Creatinine variations in hip fracture patients: is muscle mass loss the culprit?

Barbara Fioretti[1], Giulio Maria Mannarino[1], Alessandro Cartei[1], Alice Ceccofiglio[1], Anna Giannolo[1], Gianluca Polidori[1], Gaia Rubbieri[1], Elisa Fabbri[1], Cristina Vilucchi[1], Giuseppe Dario Testa[1], Andrea Ungar[1,2,*], Giulia Rivasi[1,2,*]
* shared last authorship

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Aim Renal function estimates based on serum creatinine levels may be inaccurate in hospitalized elderly patients due to multiple factors, including acute mass muscle loss (acute sarcopenia). This study examined the relationship between changes in serum creatinine levels and variations in muscle vastus lateralis thickness, measured by point-of-care ultrasound (POCUS), in orthogeriatric patients during hospital stay.
Materials and methods This prospective, longitudinal, observational study enrolled patients aged 65 years and older with proximal femoral fractures at Careggi Hospital from January 2024 to July 2025. Exclusion criteria included complex or metastatic fractures. Upon admission, comprehensive assessments were performed, including evaluations of frailty (CFS and Barthel Index), nutritional status (MNA and BMI), and serum creatinine. VL thickness was measured using POCUS before surgery and on postoperative day 5. The primary analysis compared the change in serum creatinine (ΔCr) with the change in VL muscle thickness (ΔVL). Correlations were evaluated using Pearson's correlation coefficient.
Results The study enrolled 335 elderly patients with a mean age of 85 years and a prevalence of female subjects (68%). Renal dysfunction (GFR <60 ml/min) was highly prevalent, affecting 38% of the cohort. Hospitalization was associated with improvement in renal function, as evidenced by a significant decrease in creatinine and an increase in eGFR. In addition, VL thickness significantly decreased postoperatively. Despite this data, no statistically significant correlation was found between VL thickness and creatinine values nor between ΔVL and ΔCr.
Conclusion While the in-hospital decline in both creatinine serum levels and VL muscle thickness reached statistical significance, no correlation was observed between creatinine values and VL muscle thickness either at admission or on postoperative day 5 or on their variations.

Abstract n SP08_6 - Presenting author**: Alessandro Gezzi**

Predictors of mortality in hypertensive older patients with obstructive sleep apnea: the role of intermittent hypoxia

Alessandro Gezzi[a], Francesco Spannella[a,b], Silvia Sarnari[a,b], Federico Giulietti[b,c], Simone Pugnaloni[a,b], Michela Cecchini[a,b], Matteo Landolfo[a,b], Riccardo Sarzani[a,b]

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Aim: Obstructive sleep apnea (OSA) is highly prevalent in older adults and is associated with hypertension and adverse cardiovascular, metabolic, and neurocognitive outcomes. However, the prognostic significance of OSA severity in the elderly remains controversial. The Apnea–Hypopnea Index (AHI), traditionally used to define disease severity, prognostic value in older patients may be attenuated due to aging-related physiological changes and a high prevalence of cardiovascular (CV) comorbidities. Increasing evidence suggests that parameters reflecting intermittent hypoxia may better represent the biological impact of OSA in this population.
Methods: We conducted a retrospective cohort study including patients aged ≥65 years with a diagnosis of OSA established by nocturnal cardiorespiratory monitoring, evaluate between January 2015 and July 2018, referred to the IRCCS INRCA Respiratory Medicine Outpatients Centre. AHI, oxygen desaturation index (ODI), mean nocturnal oxygen saturation (SpO_2), SpO_2-nadir, mean of minimum oxygen saturations, and the percentage of recording time spent with SpO_2 <90% (T90%), were evaluated. Clinical characteristics, cardiovascular and metabolic comorbidities, laboratory data, and ongoing pharmacological therapies were collected. The primary endpoint was all-cause mortality, assessed after a median follow-up of 92,5 months [IQR 76,7 – 111,0].
Results: Study population=194 (mean age 74,1±6,4 years; M 68.6%). During follow-up, 62 deaths (32.0%) occurred. Mean BMI was 31,4±5,8 kg/m². Mean AHI= 28,9±17,0 events/hour and ODI 38,8±20,3 events/hour. Mean Systolic Blood Pressure 140,4±14,6 mmHg and Diastolic Blood Pressure 77,1±10,0 mmHg. SCORE2/SCORE2-OP was 20,5±8,5%. Mean Total Cholesterol (TC)=179,7±37,0 mg/dL, HDL=45,7±12,2 mg/dL, LDL-C=11,5±34,0 mg/dL, and median triglycerides 100 mg/dL [IQR 77–137]. Hypertension was present in 88,6% of participants, hypertensive heart disease in 70,1%, dyslipidemia in 87,9%. OSA severity defined by AHI was not associated with mortality in univariate analyses (p=0,651) or Kaplan–Meier curves (p=0,971) (Fig.1). No oximetric parameter independently predicted mortality, although T90% >15% showed a near-significant association (HR 1,64; p=0,052) (Fig.2). Age (HR 1,11; p<0.001), coronary artery disease (HR 2,05; p=0,015), and atrial fibrillation (HR 2,35; p=0,005) were independent predictors of mortality.
Conclusions: In older patients with OSA, long-term mortality is primarily driven by cardiovascular comorbidities rather than by conventional indices of sleep apnea severity such as AHI. Although intermittent hypoxia parameters did not reach statistical significance as independent predictors, their consistent association with increased risk suggests a potential biological role in modulating prognosis. Larger studies should be conducted to evaluate these emerging parameters as predictors of mortality in older patients with OSA.

Abstract n SP08_7 - Presenting author**: Alessia Riccio**

Phenoage is associated with in-hospital mortality in non-critical patients

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Aim Biological ageing has emerged as a major risk factor for age-related diseases and mortality. PhenoAge, a recently developed biological ageing model based on routinely available laboratory parameters, provides an estimate of biological age beyond chronological age. This study aimed to investigate the association between PhenoAge and clinical outcomes in multimorbid older patients hospitalized in the Internal Medicine Department and enrolled in the Clinical Outcomes in Hospitalized Patients Receiving Treatment at Sant'Andrea Hospital (COHORTS) study.
Methods A total of 267 patients aged ≥65 years were enrolled and stratified into tertiles according to PhenoAge. PhenoAge was calculated using chronological age and nine biomarkers: albumin, creatinine, fasting glucose, log-transformed C-reactive protein, lymphocyte percentage, mean corpuscular volume, red cell distribution width, alkaline phosphatase, and white blood cell count. Multimorbidity was quantified using the Charlson Comorbidity Index (CCI). Associations between PhenoAge and clinical parameters were assessed using univariate analyses, while logistic regression models were applied to evaluate the association between PhenoAge and in-hospital mortality.
Results Patients in the highest PhenoAge tertile were older and more frequently female. They exhibited significantly higher levels of haemoglobin, blood urea nitrogen, uric acid, lactate dehydrogenase and CCI, along with lower blood pressure, estimated glomerular filtration rate, D3 vitamin, total protein, and total and low-density lipoprotein cholesterol, compared with patients in the lower tertiles. Higher PhenoAge values were also associated with a greater prevalence of polypharmacy ($p = 0.02$), type 2 diabetes ($p = 0.003$) and chronic kidney disease ($p < 0.001$). Importantly, individuals in the highest PhenoAge tertile had a 4.1-fold increased risk of in-hospital mortality (OR 4.1; 95% CI 1.6–10.5), independent of sex and CCI.
Conclusion PhenoAge appears to be a promising predictor of adverse clinical outcomes in hospitalized, multimorbid older patients. Further studies are warranted to validate its prognostic value across different healthcare settings.

Abstract n SP09_1 - Presenting author**: Chiara Di Lorenzo**

SGLT2 inhibitors and cognitive decline: a systematic review and meta-analysis

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Aim: Heart failure (HF) is a condition that is continuously growing globally, with incidence and prevalence increasing with age and life expectancy. It is estimated that approximately 40 million people worldwide are affected, with a growing trend due to the aging population and the rise in cardiovascular risk factors. Sodium-glucose cotransporter 2 inhibitors (SGLT-2I) initially developed for the treatment of type 2 diabetes, have also proven effective in the treatment of heart failure, reducing the risk of hospitalization and mortality. Frailty is a state of physiological vulnerability associated with aging, caused by an alteration in the body's homeostatic reserve capacity and a reduced ability to cope with stress, such as acute illnesses. Cognitive decline is an important element of aging and one of the crucial domains of frailty. This systematic review and meta-analysis aimed to determine the association between cognitive frailty and the use of SGLT-2I in patients with HF.
Methods: We searched for the most recent scientific literature on the main biomedical databases: PubMed/MEDLINE and Scopus about the use of SGLT-2I in patients with HF up to April 2025. We focused on selecting original articles found in the literature regarding the study of the effects of this class of drugs on cognitive decline in patients with HF.
Results: A total of 336 patients with HF treated with SGLT2I were identified.
The improvement in cognitive decline assessed at the end of the follow-up period measured using the Montreal Cognitive Assessment (MoCA) and compared to baseline was (Mean Differences:1.03, 95% CI: 0.03–2.04 I^2=93.80% p=0.04).
Conclusions: This systematic review and meta-analysis indicate a potential role of SGLT2I in ameliorating cognitive domain of frailty in patients with HF. However, the heterogeneity was high, which suggests that future studies are necessary to explore the role of SGLT2I in cognitive frailty among HF patients.

Abstract n SP09_2 - Presenting author**: Gaetano Pacinella**

Adipo-neuroinflammation, cognitive impairment and surrogate markers of cardiovascular risk in patients with MASLD

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Aim. The epidemiological burden MASLD have been slowly increasing in recent years. Starting from a background of metabolic dysfunction, we evaluated the associations between adipo-neuroinflammation markers (LCN2), indicators of cognitive impairment (MMSE score), surrogate cardiovascular risk indicators (RHI, IMT and MMEE), and MASLD.
Methods. In this cross-sectional study, we enrolled a group of 40 patients with a recent diagnosis of MASLD and a control group of 40 patients with no history of liver disease.
Results. Compared with the controls, patients with MASLD had higher serum levels of LCN2, lower RHI and MMEE values, and lower MMSE scores; univariate analysis also revealed that the differences between the groups in terms of heart rate, body weight, body mass index, body surface area, glycated haemoglobin, and echocardiographic variables (interventricular septal thickness, LVPWT, EF, LAVI, and E/A ratio) were statistically significant. Multinomial regression revealed that the presence of MASLD was significantly positively associated with LVPWT and LCN2, and significantly negatively associated with the RHI. With regards to assessments of cognitive impairment, the presence of MASLD was significantly negatively associated with the MMSE score. We also performed ROC curve analysis to explore the ability of RHI to predict MASLD; the results yielded an AUC of 0.826 (95% CI: 0.72–0.90; $p<0.0005$) at an optimal cut-off value of 1.87 (sensitivity=72.5%, specificity=90%), suggesting that the RHI can serve as a marker of endothelial dysfunction and thus as an indirect indicator of cardiovascular risk in patients with MASLD.
Conclusions. Patients with MASLD have greater cognitive impairment than controls; they also have higher serum levels of LCN-2 and greater endothelial dysfunction. These results imply that subjects with MASLD have a worse cardiovascular risk profile in addition to more pronounced cognitive impairment than controls do, thus suggesting that liver plays a greater role than simply serving as the metabolic centre.

Abstract n SP09_3 - Presenting author: **Vito de Filippis**

Executive cognitive impairment in individuals with severe hypertriglyceridemia independent of cardiovascular risk factors: a cross-sectional study

Vito de Filippis[1]*, Rosario Mare[2]*, Alessia Placanica[1], Valeria Rizzo[3], Yvelise Ferro[2], Francesca Curcio[2], Giusy Torchia[2], Fabio Michelangelo Pirrotta[2], Gennarina Arabia[2], Arturo Pujia[2,3], Tiziana Montalcini[1,3]
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Aim: Patients with hypertriglyceridemia often report dizziness and confusion, especially during triglyceride spikes. Some studies suggest a potential link between triglyceride levels and cognitive function, but the causal relationship between dyslipidemia and neurodegeneration or cognitive decline remains uncertain and debated. Our objective was to explore the association between triglyceride levels and cognitive performance in individuals with hypertriglyceridemia.
Methods: This study included 36 adults (aged: 30-55 years) of both genders. Exclusion criteria included: neurological/psychiatric diagnoses, uncorrected hearing/vision deficits, brain injury and diabetes. Participants were classified into three groups based on their fasting triglyceride levels: severe hypertriglyceridemia (≥500 mg/dL), moderate hypertriglyceridemia (150-500 mg/dL) and control group (<100 mg/dL). All participants underwent neuropsychological assessments. In addition, the publicly available dataset of the 'Leipzig Study for Mind/Body/Emotion Interactions' (LEMON) was used extracting data on biochemical analyses and assessments of cognitive to explore the relationship between triglyceride levels and cognitive function.
Results: Patients with severe hypertriglyceridemia exhibited significantly reduced performance compared to controls in executive and working memory domains, as measured by the Frontal Assessment Battery (p=0.03), the Digit Symbol Test (p=0.01), and the Digit Span Backward (p=0.004). Severe executive dysfunction was observed in 36% of individuals with severe hypertriglyceridemia, in 6% of those with moderate hypertriglyceridemia, and in none of the control group (p=0.004). There were no significant associations between Frontal Assessment Battery scores, hypertension, creatinine, and LDL cholesterol. The population analysed from the LEMON study showed that participants with highest triglyceride values had significantly lower mean scores in test evaluated working memory compared to participants with lower levels of triglyceride.
Conclusions: These findings suggest that severe hypertriglyceridemia is linked to impaired cognitive performance in adults, independent of cardiovascular risk factors. Similar results were obtained analyzing the LEMON dataset. Further research is needed to confirm our results.

Abstract n SP09_4 - Presenting author**: Salvatore Distaso**

MESALAB: an integrated digital platform for cardiorenal-hepatometabolic patients

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Aim: Cardiovascular, renal, hepatic, and metabolic (CRHM) syndrome represents a global epidemic. Cardiovascular diseases, chronic kidney disease (CKD), metabolic dysfunction–associated steatotic liver disease (MASLD), and metabolic disorders such as obesity and type 2 diabetes mellitus share common hemodynamic and metabolic abnormalities, as well as a state of chronic systemic inflammation. The management of CRHM syndrome requires a multidisciplinary approach, and eHealth solutions may play a pivotal role. We implemented an integrated digital platform to improve the management of patients with CRHM syndrome.
Methods: The platform integrates general (age, weight, height) and clinical, biochemical, and imaging data from cardiology (blood pressure, heart rate, electrocardiography, echocardiography, B-type natriuretic peptide, high-sensitivity C-reactive protein), nephrology (serum creatinine, blood urea nitrogen, estimated glomerular filtration rate, urinalysis, electrolytes, mineral and bone metabolism, anemia), hepatology (liver function tests, data from imaging techniques, scores of fibrosis such as Fibrosis-4 index/NAFLD fibrosis score, vibration controlled transient elastography/shear wave elastography, liver histology), and metabolic care (body mass index, waist circumference, fasting plasma glucose, hemoglobin A1c, lipids). Data are continuously collected from electronic health records and updated to reflect therapeutic changes, as well as patient-reported symptoms and events. Artificial intelligence algorithms support risk stratification, early detection of disease progression, and personalized clinical decision-making. The system enables multidisciplinary data sharing through a secure digital interface.
Expected results: The integrated digital platform is expected to improve early detection of clinical deterioration, optimize therapeutic decision-making, and enhance coordination among specialists. Additional anticipated benefits include improved adherence to guideline-directed medical therapy and reduction in unplanned hospitalizations.
Conclusions: An AI-driven integrated digital platform represents a promising strategy for the multidisciplinary management of CRHM syndrome. By enabling data integration, personalized risk assessment, and coordinated care, such platforms may improve clinical outcomes and support a value-based, patient-centered approach.

Abstract n SP09_5 - Presenting author**: Pardini Noemi**

Short term blood pressure variability is associated with physical and cognitive frailty in older adults with arterial hypertension

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Aim: We aimed to characterize ambulatory BP monitoring (ABPM)-assessed short term blood pressure (BP) variability in older adults with hypertension.
Methods: We analyzed cross-sectional data from the Italian multicentric longitudinal HYPER-FRAIL study. Individuals ≥75 years and suffering from arterial hypertension underwent a comprehensive geriatric assessment, measurement of office, home and ABPM BP. Short-term BP variability was defined as the standard deviation of the daily systolic BP divided by the daily systolic BP mean (dCV).
Results: In the study cohort (n=278 patients of 81±4 years, 58% women), we observed a positive correlation between dCV and age (p=0.0013), social support score (p=0.0020), Fried frailty phenotype (p=0.0306), frailty index (p=0.0234), clinical frailty scale (CFS; p=0.0271), and a negative correlation with iADL (p=0.0039), number of anti-hypertensive drugs (p=0.0063). dCV was higher in patients with a miniCog test impaired (p=0.0256). In fit-to-mild frail subjects (CFS≤5) the positive correlation with social support scale (p=0.0031) and the negative correlation with iADL (p=0.0237) and number of anti-hypertensive drugs (p=0.0183) were confirmed. In fit-to-mild frail subjects on BP target according to ESH guidelines and without orthostatic hypotension, all these correlations were lost. In these individuals dCV was negatively correlated with Mini Mental State Examination (MMSE; p=0.0140) and higher in subjects with a positive miniCog (p=0.0484). If stratified for the median value (12%), subjects with higher dCV had lower MMSE (23 vs 28, p=0.01048); 1% increase in dCV was associated with an increased risk of 1.7 (95% CI 1.0-2.7, p=0.03647) of having a MMSE below 24.
Conclusions: In older adults with hypertension dCV seems correlated with overall frailty. However, in non-moderate/severe frail subjects on BP target, it identifies a phenotype associated with worse cognitive performance.

Abstract n SP09_6 - Presenting author**: Claudia Giglione**

Trimethylamine N-Oxide (TMAO): HPLC-MS/MS-based quantification of circulating levels and machine learning-driven integration to predict personalized CVD risk profiles

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Aim: Trimethylamine N-oxide (TMAO) has been recently identified as an independent predictor of Cardiovascular Diseases (CVDs), including atherosclerotic CVD (ASCVD). Currently, TMAO clinical reference ranges have not yet been defined since standard requirements to measure TMAO are still an unmet need. Moreover, circulating TMAO levels have been mainly measured by high performance liquid chromatography (HPLC) coupled to mass spectrometry (MS), considered the gold standard approach to measure analytes from complex matrices. Recently, machine learning (ML) algorithms are being exploited to improve ASCVD risk prediction by integrating multiple clinical parameters, including TMAO, and omic data.
Hence, this study aimed at quantifying circulating TMAO levels in a sub-cohort of subjects in CVD primary prevention from the PLIC study, applying a newly validated and highly reproducible HPLC-MS/MS method. Then, clinical and biochemical data were integrated, including TMAO, in a supervised ML model to predict personalized ASCVD risk profiles.
Methods: TMAO was measured exploiting a novel HPLC-MS/MS method in plasma samples from a sub-sample (n=327) of the PLIC study. Clinical and biochemical measurements were thereby integrated in a newly designed predictive ML model based on forward feature selection coupled to supervised logistic regression algorithm to assess ASCVD risk.
Results: TMAO median (Q1-Q3) value was 258 (176-417) ng/mL. TMAO contributed to ASCVD risk prediction with an accuracy of 0.687 in the ML predictive model (accuracy: 0.724; area under the curve: 0.743; CI lower-upper: 0.689-0.79). Systolic (accuracy: 0.721) and diastolic (accuracy: 0.715) blood pressures were revealed among stronger ASCVD risk predictors compared to TMAO.
Conclusions: It is concluded that TMAO is a weaker predictor of ASCVD risk in the sub-cohort of patients from the PLIC study in CVD primary prevention, based on ML predictive model. Further assessments exploiting patients in secondary CVD prevention may help in better defying the predictive value of TMAO in ASCVD.

Abstract n SP09_7 - Presenting author: **Anna Parolini**

CXCR4-dependent neutrophil peripheral dynamics coordinate immunometabolic responses to short-term high fat diet

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Aim: Impaired metabolic adaptations to high fat diets (HFD) are crucial during the first stages of cardiometabolic diseases evolution. Chronic high-fat diet (HFD) primes granulocyte–monocyte progenitors (GMPs) toward heightened inflammasome activity and enhanced granulopoiesis in the bone marrow (BM). However, the peripheral adaptations to short-term HFD remain poorly understood. Given that neutrophil trafficking from BM to peripheral tissues is tightly controlled by CXCR4 receptor, we investigated whether CXCR4 signaling coordinates this immune-metabolic interplay.
Methods: WT mice were fed HFD (60% Kcal from fat) for seven days to induce short-term dysmetabolic adaptations. We characterized their immunophenotypic profile by integrating flow cytometry-based assessment of circulating neutrophil activation and migration, plasma proteomics, and bulk RNA-sequencing of BM-derived GMPs. To explore the involvement of CXCR4 signaling, we compared these immune-metabolic responses between mice with neutrophil-specific CXCR4 deletion (CXCR4fl/flMrp8Cre+, characterized by constitutive neutrophilia due to impaired BM retention) and their WT counterpart (CXCR4fl/flMrp8Cre-).
Results: Short-term HFD induced metabolic alterations along with increased plasma levels of proteins indicative of activated inflammatory and innate immune pathways, also reflected by altered neutrophil membrane expression of CXCR2, CD62L and CD11b, suggesting increased neutrophil activation and migration. An altered BM progenitor transcriptomic profile after short-term HFD, followed by seven-day switch to chow diet, partially explained immune phenotype. Moreover, short-term HFD feeding further aggravated neutrophilia in CXCR4fl/flMrp8Cre+ compared to controls, independently of metabolic adaptations and neutrophil membrane expression of activation and mobilization markers. Notably, we observed altered neutrophil peripheral dynamics in CXCR4fl/flMrp8Cre+ mice, with CXCR4-defective neutrophils moving towards key metabolic tissues (liver) during HFD feeding. Besides, CXCR4-dependent immune alterations seem to associate with the adverse metabolic adaptations to HFD.
Conclusions: We propose that immunometabolic adaptations to short-term HFD, and the consequent increase in cardiometabolic risk, are modulated by CXCR4-dependent alterations in neutrophil dynamics across circulation and peripheral tissues.

Abstract n SP10_1 - Presenting author**: Stella Covino**

Reclassification of the LDLR p.Ser123Pro as a FH pathogenic variant by using ex vivo flow cytometry method

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Background and Aim: The c.367T>C (p.Ser123Pro) missense *LDLR* variant is frequently detected in FH patients. Its pathogenicity has been debated, fluctuating between likely pathogenic and uncertain significance, with ClinVar currently listing it as VUS. Previous functional data came from a compound heterozygote, limiting assessment of its direct effect. We evaluated the variant's impact on LDLR activity using an optimized flow-cytometry assay in autologous activated $CD4^+$ T-lymphocytes.
Methods: Twenty-two heterozygous FH patients carrying the p.Ser123Pro variant were enrolled. PBMCs were isolated from 11 individuals. Six known pathogenic *LDLR* variants served as positive controls, and T-lymphocytes from healthy donors as negative controls. PBMCs were stimulated with CD3/CD28 beads in lipoprotein-deficient serum. LDLR expression, LDL binding, and uptake were measured by flow-cytometry using Bodipy-labeled LDL and expressed as the geometric mean fluorescence intensity ratio between patient and control $CD4^+$ T-cells. Following ClinGen FH Expert Panel criteria, the variant was classified as defective if activity was <85% of control in at least one parameter (PS3_Supporting). In vitro assays and family segregation studies were performed to support pathogenicity.
Results: At flow-cytometry, compared with healthy donors, heterozygous carriers of the p.Ser123Pro variant exhibited a ~30% reduction in LDLR expression, with no differences in LDL-binding or uptake. In contrast, *site-directed* mutagenesis in the homozygous state resulted in a complete absence of LDLR expression, demonstrating a more pronounced effect than observed in heterozygotes and confirming the flow-cytometry findings. In this model, LDL uptake was reduced by 60% relative to LDLR wild-type cells ($P = 0.002$). Cascade screening across five families demonstrated segregation in 8 informative meioses. Collectively, these data fulfil the PS3_Supporting criterion for functional evidence and PP1_strong for segregation, supporting pathogenic classification of the variant.
Conclusions: These findings support the pathogenicity of c.367T>C and highlight flow-cytometry as a robust tool for functional assessment of LDLR VUS.

Abstract n SP10_2 - Presenting author**: Alice Franco**

Role of dyslipidemia in Alagille Syndrome on cardiovascular and renal outcomes

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Aim: Alagille syndrome (ALGS) is a rare, autosomal dominant disease characterized by abnormal development of intrahepatic bile ducts, heart, arteries and kidneys due to disrupted Notch signaling. Although hypercholesterolemia is a hallmark feature of ALGS, data on lipid and lipoprotein profiles remain limited. The aim of the study is to characterize the lipid and lipoprotein profiles in ALGS and explore their relationship to disease phenotype focusing on liver involvement, renal and cardiovascular outcomes.
Methods: Twenty-five subjects affected by ALGS were enrolled with a median age of 13 years (IQR: 4.0–16.75), 20 patients with native livers and 5 liver transplant recipients. Lipid and lipoprotein profile was characterized in plasma samples, IMT and PWV were measured to assess cardiovascular risk, biochemical markers of cholestatic liver disease and renal function were measured in plasma. In vitro studies were performed in podocytes and tubular cells (HK2) to assess plasma and lipoprotein toxicity.
Results: ALGS patients exhibited a distinctive lipid profile, characterized by high total cholesterol (42%), elevated free cholesterol (FC, 47.6%) and phospholipids (52%). LpX was identified in 62% of the cohort and was associated with markers of cholestatic liver disease. ALGS patients had IMT and PWV values exceeding the 95th percentile for age in 60% and 38% of cases, however, were not associated with dyslipidemia. In vitro, plasma from LpX-positive patients induced significant podocyte necrosis ($p=0.03$) and apoptosis ($p=0.050$), compared to LpX-negative patients. Additionally, LpX reduced the expression of podocin ($p=0.005$).
Conclusions: The results showed that ALGS patients present with a distinctive LpX-driven dyslipidemia, which reflects altered cholesterol homeostasis, likely due to increased FC release from the cholestatic liver and reduced LpX catabolism due to low LCAT activity. ALGS-associated dyslipidemia does not appear atherogenic. However, in vitro findings indicate a nephrotoxic role for LpX, with potential contribution to renal complications in ALGS.

Abstract n SP10_3 - Presenting author**: Marcella Palumbo**

Effect of elexacaftor/tezacaftor/ivacaftor therapy on serum lipoproteins functions in adults with cystic fibrosis

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Cystic fibrosis is a genetic and multisystemic disease associated with a very poor quality and expectancy of life. The introduction of the combined treatment with elexacaftor/tezacaftor/ivacaftor (ETI, Kaftrio) has extended the life expectancy of adults with cystic fibrosis (awCF), which could have an impact on the prevalence of certain chronic diseases such as cardiovascular (CV) diseases. In this regard, in a recent work it was observed that treatment with Kaftrio has a heterogeneous effect on CV risk factors, ameliorating some of them, such as chronic inflammation and worsening others. Among the relevant factors determining CV risk, the capacity of HDL to promote cholesterol efflux (HDL-CEC), one of the main functions of this class of lipoproteins, has proven to be a better predictor as compared to plasma HDL concentrations. In addition, the serum capacity to load macrophages with cholesterol (cholesterol loading capacity, CLC) represents an index of serum lipoproteins' pro-atherogenic potential.
This work aimed to evaluate the effect of six months therapy with Kaftrio on serum lipoprotein functions, namely HDL-CEC and serum CLC, in 16 awCF, and in 8 sex and age matched healthy controls. HDL-CEC through the main pathways was evaluated with a radioisotopic cell-based assay in specific cell models, and serum CLC was assessed fluorimetrically in human monocyte-derived macrophages THP-1.
Concerning plasma lipid profile, after treatment with Kaftrio, total cholesterol, LDL-C and HDL-C significantly increased as compared to baseline ($p<0.001$, $p<0.001$, and $p=0.023$ respectively), reaching values comparable to those of healthy controls. Regarding HDL function, HDL-CEC mediated by the transporter ABCA1 was significantly lower in awCF at baseline compared to healthy controls (-14%, $p=0.0142$). Treatment with Kaftrio increased ABCA1 HDL-CEC compared to awCF at baseline (+7%, $p=0.02499$). Similarly, ABCG1 HDL-CEC was significantly lower in awCF at baseline compared to healthy controls (-22%, $p=0.0218$) while significantly higher after treatment compared to not treated awCF (+18%, $p=0.0255$). In both cases, Kaftrio restored HDL-CEC levels to values comparable to those of healthy controls.
No significant differences were found for serum CLC in awCF compared to healthy controls. Kaftrio did not have any significant impact on this parameter, despite the increased LDL-C levels observed after treatment.
In conclusion, Kaftrio treatment had a positive impact on the functional lipid profile as it increased ABCA1 and ABCG1 HDL-CEC without negatively affecting serum CLC. All these effects may contribute to reduce the CV risk in awCF.

Abstract n SP10_4 - Presenting author**: Chiara Moschetti**

LDL-C target achievement after adding evinacumab in two patients with autosomal recessive hypercholesterolemia

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Aim: Autosomal recessive hypercholesterolemia (ARH) is a rare inherited hypercholesterolemia caused by biallelic pathogenic variants in LDLRAP1, resulting in defective internalization of the low-density lipoprotein receptor (LDL-R). ARH is characterized by markedly elevated LDL-C levels and a high risk of premature atherosclerotic cardiovascular disease (ASCVD). As conventional lipid-lowering therapies act through LDL-R–dependent mechanisms, their efficacy in ARH is often limited, and many patients require lomitapide or long-term lipoprotein apheresis (LA). Evinacumab, a monoclonal antibody targeting angiopoietin-like protein 3 (ANGPTL3), lowers LDL-C via an LDL-R–independent pathway, but evidence in ARH remains limited. We report two ARH patients with a marked response to evinacumab.
Methods: Short and mid-term effectiveness and safety of evinacumab were evaluated in two male patients with genetically confirmed ARH followed at a tertiary lipid clinic. Both carried the same biallelic LDLRAP1 variant (c.432dupA). Evinacumab was administered intravenously at 15 mg/kg every four weeks on top of maximally tolerated lipid-lowering therapy. Lipid profile and liver function were monitored.
Results: Patient 1, a 60-year-old man with obesity (BMI 34.6 kg/m²) and advanced ASCVD, had a baseline LDL-C of 549 mg/dL despite intensive therapy and biweekly LA. Evinacumab led to a mean LDL-C reduction of 69.8% and triglyceride reduction from 276 to 57 mg/dL; after one year of treatment, time-average post-apheresis LDL-C values fell by 82%, with nadir values as low as 26 mg/dL.
Patient 2, a 42-year-old man, with earlier diagnosis, more intensive lifelong lipid-lowering therapy and stable coronary artery disease, experienced a mean LDL-C reduction of 74.8%, reaching and maintaining LDL-C target (<55 mg/dL), which enabled adjustment of background therapies. Triglycerides decreased from 42 to 20 mg/dL. HDL-C declined by approximately 50% in both patients. Treatment was well tolerated with only mild adverse effects.
Conclusions: Evinacumab achieved rapid and profound reductions in LDL-C and triglycerides in two patients with ARH supporting ANGPTL3 inhibition as an effective LDL-R-independent therapeutic option that may reduce reliance on LA.

Abstract n SP10_5 - Presenting author**: Riccardo Mattia Ricciardi**

Extreme Dyslipidemia Revealing Underlying MGRS: A Case of IgG-Lambda MGUS with Rapidly Progressive Nephrotic Syndrome

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Background: Severe dyslipidemia is a characteristic yet often underestimated manifestation of nephrotic syndrome. In the presence of monoclonal gammopathy (MGUS), such a profile may represent the earliest clinical clue to an underlying monoclonal gammopathy of renal significance (MGRS) or AL amyloidosis. We present a case in which extreme dyslipidemia served as the primary clinical alert for an unrecognized systemic disorder.
Case report: A 73-year-old woman with known IgG-λ MGUS was admitted for rapidly worsening renal function and nonspecific symptoms (nausea, vomiting, weight loss, fatigue). Laboratory evaluation revealed severe mixed dyslipidemia: total cholesterol 597 mg/dL, LDL 301 mg/dL, triglycerides 714–812 mg/dL. Concurrent findings included hypoalbuminemia (2.4 g/dL), proteinuria of 10 g/24h, and moderate renal impairment (creatinine 2.2 mg/dL), outlining a picture of full-blown nephrotic syndrome. Serum and urine electrophoresis confirmed a monoclonal IgG-λ component with urinary λ light-chain positivity (Bence Jones). CT imaging showed reduced renal size with signs of chronic nephropathy. Nephrology evaluation raised strong suspicion for MGRS/AL amyloidosis with renal involvement, and renal biopsy was deemed necessary for diagnostic confirmation.
Discussion: The lipid abnormalities observed align with the classical profile of nephrotic syndrome: marked elevations in LDL and VLDL, increased apoB-containing lipoproteins, reduced hepatic clearance, and compensatory overproduction of lipoproteins. In this case, the monoclonal gammopathy acted as the pathogenic trigger for the nephropathy, producing a secondary but clinically dominant dyslipidemic syndrome.
Conclusion: Severe dyslipidemia may be the most prominent clinical manifestation of nephrotic syndrome driven by MGUS complicated by MGRS or AL amyloidosis. Early recognition of the link between extreme dyslipidemia and monoclonal light-chain–related kidney disease is essential to guide timely hematologic and nephrologic evaluation and may significantly alter patient prognosis.

Abstract n SP10_6 - Presenting author**: Francesca Fabiani**

Abdominal aortic aneurysm in familial chylomicronemia syndrome: a case report

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Aim: Familial chylomicronemia syndrome (FCS) is a rare autosomal recessive disorder caused by biallelic loss-of-function variants affecting the lipoprotein lipase pathway, leading to lifelong severe hypertriglyceridemia and recurrent episodes of acute pancreatitis. While pancreatitis represents hallmark clinical complication, long-term vascular manifestations of chronic hyperchylomicronemia remain poorly defined, and an association with aneurysmal disease has not been previously reported.
Methods: We report the case of a 57-year-old Italian male with genetically confirmed familial chylomicronemia syndrome (FCS), followed at the Lipid Clinic of Policlinico Umberto I, Sapienza University of Rome.
Results: The patient presented with lifelong severe hypertriglyceridemia, refractory to dietary interventions and all available conventional lipid-lowering therapies, complicated by recurrent episodes of acute pancreatitis. Owing to the severity and persistence of the phenotype and the absence of effective approved therapeutic options, the patient was granted access over time to clinical trials evaluating innovative investigational therapies. He was initially enrolled in the APPROACH trial and treated with volanesorsen, achieving a partial biochemical response, but treatment was discontinued due to significant injection-site reactions and arthralgia. Lomitapide was subsequently initiated and later discontinued because of progressive hepatic steatosis. More recently, the patient participated in the BALANCE trial with olezarsen, which was stopped following a severe hypersensitivity reaction. Despite multiple therapeutic attempts, the patient continues to exhibit persistent severe hypertriglyceridemia and remains at high risk for further episodes of acute pancreatitis.
During long-term clinical follow-up (25 years), vascular screening investigations were undertaken as part of a comprehensive assessment of potential systemic complications. Imaging performed in 2017 incidentally revealed mild infrarenal aortic ectasia, which progressively evolved into a fusiform abdominal aortic aneurysm with additional aneurysmal involvement of visceral arteries, including the origin of the celiac trunk, as well as splenic and femoral arteries. In 2024, the patient underwent endovascular abdominal aortic aneurysm repair and surgical femoral revascularization, with a favorable outcome. In 2025, a small intracranial aneurysm was detected and is currently managed with regular radiological surveillance. The patient had a history of arterial hypertension since 2010, consistently well controlled with pharmacological therapy, and was a former smoker since 1990, having transitioned to electronic cigarettes after abdominal revascularization and subsequently achieved complete smoking cessation following intracranial aneurysm diagnosis.
Conclusion: This case suggests that FCS may be associated with previously unrecognized aneurysmal involvement, expanding its clinical spectrum beyond pancreatitis and highlighting the need for awareness of potential vascular complications in this population. However, larger studies in broader patient populations are required to confirm this observation and to clarify its clinical relevance.

Abstract n SP10_7 - Presenting author**: Fabio Troiano**

Use of evinacumab in real-life: a paradigmatic clinical case

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Background: Familial hypercholesterolemia (FH) is a genetic disorder characterized by markedly elevated LDL cholesterol (LDL-C) and increased risk of premature cardiovascular (CV) events. Severe phenotypes—such as homozygous or compound heterozygous forms—are often refractory to conventional LDL-lowering strategies, requiring advanced and resource-intensive management. In this context, organizational innovations that enhance continuity of care and support patient-centered treatment delivery are increasingly relevant.
Case report: We describe the clinical course of a 77-year-old woman with a strong family history of FH and premature myocardial infarction. Diagnosed with Fredrikson type IIa hypercholesterolemia at a young age, she consistently showed extremely high lipid levels between 2005–2012 (total cholesterol >500 mg/dL, LDL-C 337–435 mg/dL) despite multiple therapeutic attempts (resins, high-dose statins, ezetimibe, and simvastatin 40 mg + ezetimibe), all discontinued for poor efficacy or statin intolerance. At first evaluation in 2012 (age 64), she presented tendon xanthomas and carotid atheromasia; the Dutch Lipid Score was 21, confirming definite FH. Genetic testing identified two LDLR variants consistent with compound HeFH, and she was referred for LDL apheresis due to treatment failure and very-high CV risk.
In the following years, she received maximal LLT (rosuvastatin 40 mg/d, ezetimibe 10 mg/d), LDL apheresis every 7–21 days and lomitapide 5–10 mg (discontinued for intolerance), with partial benefit. Evolocumab 145 mg/month (phase II RCT, 2014) was added without achieving target LDL-C (nadir 132 mg/dL). During this period, several CV events occurred: left carotid TEA (2013), TAVI and coronary stenting (2023), and right TEA (2024). According to ESC/EAS 2025, she is now in secondary prevention with extreme CV risk.
In 2025, evinacumab 15 mg/kg every 28 days was initiated, with five well-tolerated infusions in day-hospital and no adverse events. LDL-C decreased markedly and remained around 40 mg/dL (−69%), meeting guideline targets. After the fifth infusion, a home-based infusion program was activated, ensuring safe monitoring, continuity of therapy, and excellent adherence.
Discussion: This case illustrates how evinacumab, with its superior tolerability compared with prior therapies such as lomitapide, substantially improved adherence. The introduction of a home-based infusion model further reinforced long-term engagement, reducing treatment burden and supporting sustained achievement of LDL-C goals. Together, pharmacological efficacy and organizational innovation reshaped the care pathway of this severe FH phenotype.

Abstract n SP10_8 - Presenting author**: Miriam Giovanna Mazzone**

Case of familial hypercholesterolemia refractory to maximal lipid-lowering therapy associated with Cushing's disease

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Familial hypercholesterolemia (FH) is a common genetic disorder characterized by elevated low-density lipoprotein cholesterol (LDL-C) and increased cardiovascular risk. Although lipid-lowering therapies such as statins, ezetimibe, and PCSK9 inhibitors are effective in most patients, a subset fails to reach therapeutic targets.

We describe a 22-year-old patient referred to our lipid clinic for severe hypercholesterolemia refractory to maximal lipid-lowering therapy with evolocumab, rosuvastatin, and ezetimibe. The patient carried heterozygous LDL receptor and PCSK9 variants of uncertain significance and had a medical history of type 2 diabetes mellitus and gastric perforation. Laboratory evaluation revealed neutrophilic leukocytosis without signs of infection. Physical examination showed central obesity (BMI 32), violaceous abdominal striae, and borderline hypertension, raising suspicion of hypercortisolism.

Endocrine assessment demonstrated markedly elevated 24-hour urinary cortisol levels, elevated morning ACTH, and lack of cortisol suppression following low-dose dexamethasone testing. Pituitary MRI identified a 3 mm microadenoma. Bilateral inferior petrosal sinus sampling confirmed ACTH-dependent hypercortisolism of pituitary origin, leading to the diagnosis of Cushing's disease.

Excess cortisol impairs hepatic LDL-C clearance by reducing LDL receptor expression and function. In this patient, cortisol excess likely amplified the underlying genetic LDL receptor defect, explaining the marked resistance to lipid-lowering therapy. The coexistence of FH and Cushing's disease substantially increases cardiovascular risk.

This case highlights the importance of investigating secondary causes of dyslipidemia in patients with treatment-resistant hypercholesterolemia. A multidisciplinary approach targeting both cortisol excess and lipid abnormalities is essential to optimize cardiovascular risk reduction in this high-risk population.

Abstract n SP10_9 - Presenting author**: Serena Amato**

Abetalipoproteinemia: an italian case

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We present the case of an Italian male of 41 years old with an abetalipoproteinemia diagnosed when he was 1 years old. He came to our attention in September 2024 with a weight of 45 kg and a height of 152 cm (BMI of 19.48). He has a mutation of MTTP ***c.1392delA*** in homozygosis. He had poor growth in height and weight, reduced bone mass at the vertebral level and reduced tolerance to effort. From a psycho-intellectual point of view, we can observe mild deficit in cognitive and intellectual performance, described in the past as attention disorders and a picture of psychomotor agitation and behavioral alterations. At the neurological evaluation, he presents mild weakness in segmental strength tests and mild paratonia in the evaluation of muscle tone; patellar and biceps ROT present, unexcitable styloid and achillea reflexes. From the ocular point of view, corneal micro-deepithelializations are present. His medications are vitamin E, vitamin A, vitamin B12, vitamin K, 25 OH vitamin D and vitamin B9. His last exams were: total cholesterol 22 mg/dl, HDL-c 21 mg/dl, CLDL–C <1 mg/dl, triglycerides 3 mg/dl, total bilirubin 4,4 mg/dl (indirect 3,9 mg/dl), creatine 0,77 mg/dl, folic acid 4,8 mg/dl, vitamin B12 327 mg/dl, vitamin A 0,23 mg/dl (low), vitamin E 0,94 mg/dl (low), 25 OH vitamin D 47, hemoglobin 14,6 g/dl. Last abdominal echography (2022) showed a liver with bigger dimensions, mild hyper echogenicity, diffusely inhomogeneous and with inhomogeneous fat distribution, areas of focal steatosis. Last ophthalmic visit (2024) showed bilateral partial vitreous detachment and mild bilateral vitreous organization.
Conclusion: Genetic test allowed us to make a diagnosis of a rare disease which must be monitored. If left untreated, ABL patients start manifesting systemic complications related to fat-soluble vitamin deficiencies. Early diagnosis and adequate supplementation of vitamin E, A, and other fat-soluble vitamins may prevent, delay, or alleviate the complications and improve the prognosis, enabling some patients to live to the eighth decade of life. More studies are needed to unravel the pathogenesis, genotype-phenotype relationship, burden of disease, and unmet needs.

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