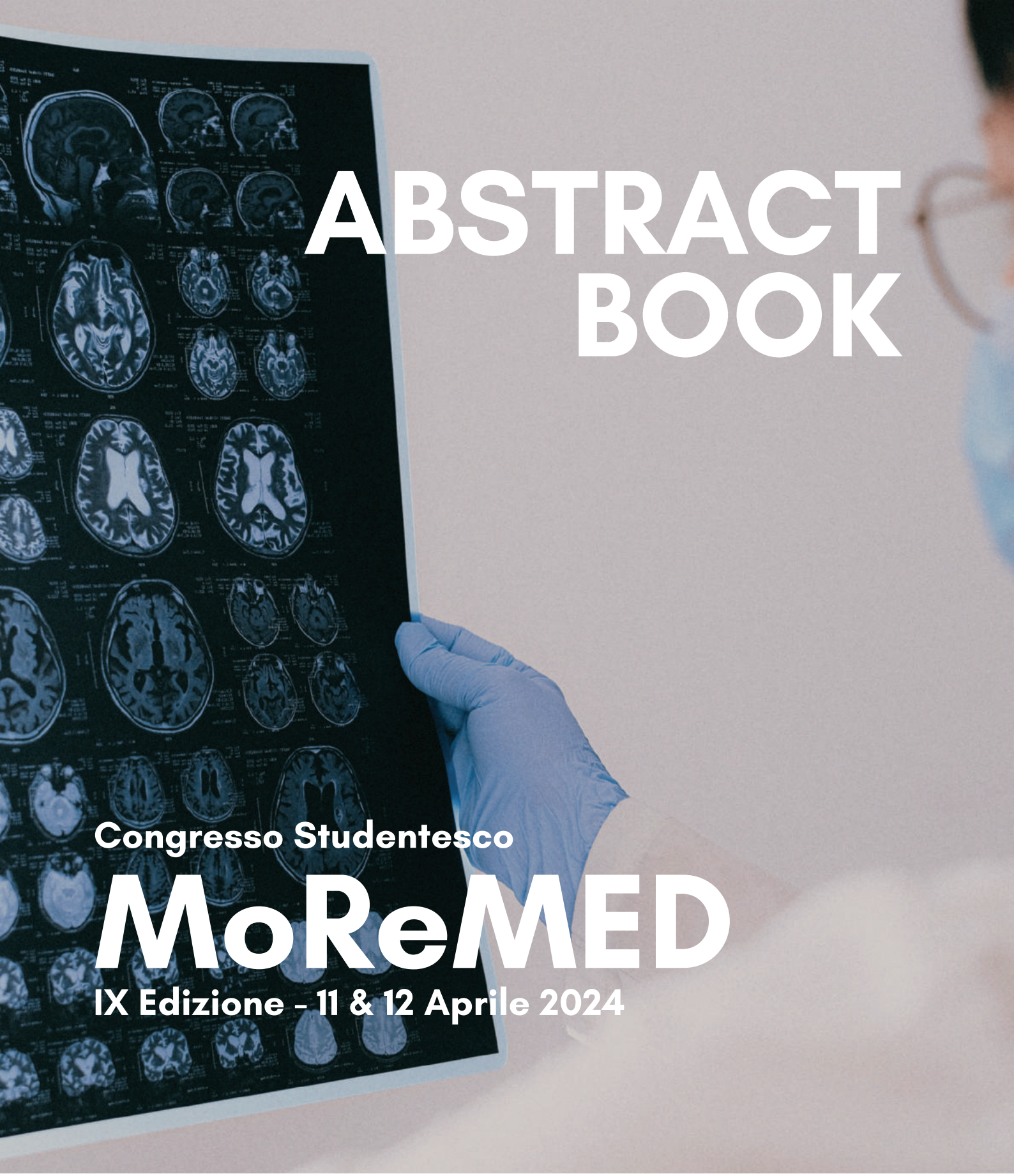

ABSTRACT BOOK

Congresso Studentesco

MoReMED

IX Edizione - 11 & 12 Aprile 2024

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

MoReMED

Ringraziamenti

È con immensa felicità ed onore che vi presentiamo il Congresso Studentesco MoReMED, giunto alla sua IX Edizione.
Nella sua evoluzione il progetto si è ampliato, arricchito, innovato; nonostante questo, non possiamo non ringraziare chi, prima di noi, ha dato vita al nostro congresso: esprimiamo quindi la nostra gratitudine ai fondatori del Congresso Studentesco MoReMED: il Dott. Emiliano Barbieri e il Dott. Giuseppe Esposito.

Da studenti, il nostro entusiasmo e le nostre idee non sono ancora sufficienti da soli per poter portare a termine un progetto così ambizioso; ci teniamo quindi a ringraziare i Professori della Facoltà di Medicina e Chirurgia che, con la loro esperienza e i loro consigli, ci hanno aiutato e ci aiutano da diversi anni ad organizzare MoReMED.
Pertanto, ringraziamo i membri della Segreteria Scientifica, in particolare il Professore Antonello Pietrangelo e il Professore Alexis Grande. Un ringraziamento speciale va anche ai membri del Comitato di Selezione, in particolare il Professore Alexis Grande, la Professoressa Chiara Mussi e il Professore Alessandro Stefani.
Un ulteriore grazie lo rivolgiamo ai membri del Comitato di Valutazione e a tutti i Professori che si impegneranno a trasmettere le loro conoscenze e competenze in maniera diretta agli studenti durante i Workshop.

MoReMED rappresenta un punto di riferimento nell'ambito della formazione universitaria anche per l'elevato contributo scientifico e culturale che portano i nostri ospiti. Ci teniamo a ringraziare loro, che rendono il Congresso ancora più interessante e dinamico, permettendo di conoscere da vicino temi per noi estremamente importanti e fondamentali per la formazione e la vita professionale di Medico o di Sanitario.

Il nostro Congresso non si potrebbe tenere senza il supporto organizzativo, ed in parte economico, dell'Università degli Studi di Modena e Reggio Emilia, della Facoltà di Medicina e Chirurgia, e del Corso di Laurea in Medicina e Chirurgia. Per questo motivo, ringraziamo il Magnifico Rettore, Professore Carlo Adolfo Porro, il Preside della Facoltà, Professore Michele Zoli, e il Presidente del Corso di Laurea, Professore Paolo Ventura.

In ultimo, ci teniamo a ringraziare coloro che rappresentano il cuore del nostro congresso: gli studenti. Ci auguriamo infatti che queste due giornate possano essere per loro un motivo di confronto, riflessione, studio e, soprattutto, relazione.
Con l'augurio che questo Congresso rimanga parte integrante del percorso di formazione universitario, vi ringraziamo ancora per la calda partecipazione a queste giornate congressuali.
Il Comitato Organizzatore MoReMED

Il Progetto MoReMED

Storia e caratteristiche del progetto
Il "Congresso Studentesco MoReMED", giunto quest'anno alla sua IX Edizione, avrà luogo nelle giornate di giovedì 11 e venerdì 12 aprile 2024. Sarà possibile seguire l'evento in presenza e online, in diretta sul nostro canale Youtube.
La I Edizione, svoltasi ad aprile 2016, ha visto la partecipazione di oltre 500 spettatori e circa 150 sincronizzazioni alla diretta streaming su tv.unimore.it. Partendo da questi ottimi risultati e facendo tesoro di quanto imparato durante l'organizzazione dell'evento, il Comitato Organizzatore si è allargato e nelle successive edizioni sono state raggiunte cifre ancora più importanti: oltre 1000 presenze in Aula Magna e 1800 sincronizzazioni alla diretta streaming. Il progetto gode dell'appoggio e del contributo dell'Università degli Studi di Modena e Reggio Emilia, in particolar modo della Facoltà di Medicina e Chirurgia, con i suoi Dipartimenti di Area Medica e i Corsi di Laurea afferenti. Nelle precedenti edizioni, il Congresso ha potuto vantare il Patrocinio dell'Azienda Ospedaliero-Universitaria di Modena, della Città di Modena, del Comune di Reggio-Emilia, della Provincia di Modena, dell'Ordine dei Medici, della Regione Emilia-Romagna e del Ministero della Salute.

Unicità del progetto
Il progetto si ispira ai cosiddetti "Congressi degli Studenti" delle più importanti Università degli Studi iberiche e si propone di figurare in Italia come la prima esperienza di tale portata: un evento completamente organizzato dagli studenti e rivolto agli studenti stessi. Ancora oggi il "Congresso Studentesco MoReMED" costituisce un evento unico nel panorama delle Università italiane, rappresentando per lo studente di area medica e sanitaria un'opportunità davvero straordinaria per poter acquisire esperienze fondamentali per la propria carriera futura - opportunità che nessun altro Ateneo in Italia è al momento in grado di offrire.

Finalità
Il "Congresso Studentesco MoReMED" nasce dall'esigenza percepita dagli studenti di Medicina e Chirurgia di dare vita ad un nuovo approccio formativo – integrativo e non sostituibile a quello tradizionale, atto a fornire, con modalità innovative, competenze al momento trascurate dal manifesto degli studi. Il fine è quantomeno duplice: scientifico e pedagogico. Da un lato la promozione della ricerca scientifica e degli strumenti necessari al suo compimento, nonché l'insegnamento di una corretta divulgazione grafica e oratoria della scienza. Dall'altro l'opportunità offerta a tutti gli studenti di divenire divulgatori tra pari – e non più soltanto fruitori della ricerca scientifica con un sistema tutelato e impostato sulla "peer education", in grado di garantire qualità e serietà al progetto. Il fine del progetto è ulteriormente amplificato dalla richiesta mandatoria di tematiche extra-curricolari (non trattate in ambito di didattica frontale) su cui sviluppare le presentazioni. L'esperienza congressuale consente così agli studenti la possibilità di ampliare l'offerta formativa prevista dal Corso di Laurea incentivando la formazione e l'interesse su specifici campi medici, stimolando riflessioni critiche su tematiche altresì neglette e incoraggiando lo sviluppo di competenze nella ricerca autonoma delle fonti scientifiche, nel lavoro di gruppo, nella presentazione e nell'efficace comunicazione di informazioni scientificamente comprovate.

Le novità della IX Edizione
La IX Edizione del Congresso Studentesco MoReMED verrà svolta al Centro Servizi della Facoltà di Medicina e Chirurgia di Modena. Gli studenti espositori saranno invitati a presentare il loro lavoro in presenza. Gli studenti non espositori potranno seguire il congresso sia in online sia in presenza. Nella IZ Edizione verranno mantenute le presentazioni degli elaborati in Sessione Plenaria e in Sessione Poster, nonché lo svolgimento di Workshop interattivi.

La vera novità della IX Edizione riguarda l'internazionalizzazione del congresso: per la prima volta più della metà degli interventi e delle tavole rotonde verrà svolto in lingua inglese, dando ampio respiro al progetto e inserendo di diritto il congresso all'interno di un panorama non solo italiano ma europeo.

L'obiettivo della IX Edizione è inoltre quello di inserire la nostra realtà in un contesto globale in continuo rinnovamento. Riconosciamo l'importanza e la centralità che la corretta divulgazione della scienza sulle piattaforme digitali avrà per la futura classe medica. Con sempre maggiore frequenza, infatti, i medici di domani dovranno interfacciarsi a realtà di comunicazione con il pubblico in formato digitale e dematerializzato. Questo implica l'abilità di saper adottare ed utilizzare correttamente degli schemi comunicativi adatti alle piattaforme web e ai canali di informazione online.

Obiettivi Futuri
Il progetto si propone di rappresentare una tappa stabile e fondamentale all'interno dell'Anno Accademico e coltiva l'ambizione di divenire un evento di sempre maggior rilievo nel panorama universitario italiano. Proprio per questo il "Congresso Studentesco MoReMED" è divenuto nazionale, perseguendo l'obiettivo di rappresentare una rivoluzione nel campo della didattica in area medica e sanitaria, di cui potranno beneficiare gli studenti del presente, i medici del futuro e i pazienti sia di oggi che di domani. Allo stesso tempo, la IX Edizione del Congresso Studentesco MoReMED vuole rappresentare un graduale inizio ad affacciarsi verso la creazione di un evento di carattere internazionale.

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Prof. Paolo Ventura: Presidente del Corso di Laurea Medicina e Chirurgia presso l'Università di Modena e Reggio Emilia

Lectures

Let's do a Surgery Together: Clipping a Cerebral Aneurism.

Prof. Saleem Albdulrauf, Clinical Professor of Neurosurgery at George Washington University, Washington D.C., U.S.A

Supermicrochirurgy in Treatment of Lymphedema

Prof. Juame Masia, Chief of Plastic Surgery Department at Hospital de Santa Creu I Sant Pau and Hospital del Mar at Barcelona, Professor in Plastic Surgery at Universitat Autonoma de Barcelona, Director of Microsurgery and Breast Reconstructive Unit at Clinica Planas in Barcelona

Attraversare il Confine: il fine vita nella pratica medica

Moderatore **Prof. Leonardo Potenza,** Professore Associato di Ematologia presso UNIMORE, Responsabile Ambulatorio Cure Palliative Precoci presso UOC Ematologia, AOU Policlinico di Modena, Direttore del Master in Cure Palliative Precoci presso UNIMORE
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Climate Change and its Impact on Health

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Generazione di Cellule Staminali Pluripotenti Indotte per ottenere Modelli di Malattia in vitro

Dott.ssa Piera Trionfini, PhD e Ricercatrice del Dipartimento di Ricerca di Medicina Molecolare presso l'Istituto Mario Negri

Sessione Plenaria

Giovedì 11 Aprile 2024

Metodologie didattiche innovative: uno studio quasi-sperimentale a metodo misto sull'introduzione dell'ecografia al Corso di Studi in Infermieristica

Chiara Diambri - Università degli Studi di Modena e Reggio Emilia

Background: L'ecografia è una metodologia di diagnostica per immagini che negli ultimi anni ha acquisito un grande successo grazie ai suoi innumerevoli vantaggi. In letteratura, è stato osservato che l'impiego degli ultrasuoni (US) in campo infermieristico permette di migliorare gli outcome clinici e la qualità di vita dei pazienti, di ridurre le complicanze, i tempi e le risorse, oltre a incrementare la soddisfazione dei professionisti e degli assistiti. Dati i considerevoli benefici, il presente studio quasi-sperimentale desidera indagare l'efficacia di una nuova offerta didattica, proposta agli studenti del Corso di Studi (CdS) in Infermieristica di Modena, basata sull'acquisizione di nuove competenze di ecografia infermieristica. Nello specifico, sono state valutate l'evoluzione delle conoscenze e l'autoefficacia percepita

Methods: Hanno partecipato alla ricerca quasi-sperimentale 118 studenti (tasso di risposta: 100%) frequentanti il 3° anno di corso. A seguito di una lezione teorico-pratica sull'utilizzo degli US in ambito pelvico e vascolare, ai partecipanti sono stati somministrati dei test pre- e post-formazione, predisposti in base alla letteratura di riferimento dai ricercatori. Lo strumento indagava dati socio-anagrafici e si componeva di due questionari: uno sulle conoscenze teoriche e uno sull'autoefficacia percepita, in cui lo studente aveva la possibilità di rispondere indicando il suo grado di self-confidence su una scala likert da 1 a 5; entrambi erano composti da 5 item. Infine, veniva esplorata la soddisfazione, nonché la percezione sull'eventuale valore aggiunto dalla formazione ed eventuali commenti liberi.

Results: Dall'analisi del questionario sulle conoscenze teoriche, è emerso un aumento nelle risposte corrette dal 48,1% al 93,4% nel test finale. È stato rilevato un netto incremento anche per l'autoefficacia percepita, con una differenza nella media delle risposte pre e post-test, indagata con il test t di Student, statisticamente significativa su tutti gli item. Infine, l'86,4% dei partecipanti si è dichiarato "completamente soddisfatto". Nelle 116 risposte alle domande aperte, è stato confermato l'interesse e l'apprezzamento per l'opportunità fornita della quale è stata riconosciuta l'utilità, consigliando di riproporre questo tipo di formazione, riconosciuto dai partecipanti come un valore aggiunto, poiché permetterebbe, oltretutto, di giungere al tirocinio clinico con maggior preparazione.

Conclusions: Il presente studio dimostra l'efficacia della formazione proposta agli studenti del CdS in Infermieristica nell'accrescere i contenuti teorici e l'autoefficacia percepita, aumentando la loro consapevolezza rispetto all'importanza di questa metodica, sia per aumentare il comfort del paziente che per aumentare le competenze e l'autonomia del professionista. Viene inoltre riscontrata una forte soddisfazione dei partecipanti che richiedono di proseguire ed implementare la formazione negli anni accademici futuri.

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A Mathematical Network Model of the Pre-Botzinger Complex to Simulate the Activity and the Modulation of the Respiratory Central Pattern Generator

Lorenzo De Toni, Federica Perricone – Università degli Studi di Modena e Reggio Emilia

Introduction: Central pattern generators (CPG) are neuronal networks that in absence of rhythmic inputs generate repetitive motor patterns, such as walking, breathing or chewing. The neural circuits driving breathing movements are spatially and functionally organized brainstem neural circuit including the respiratory CPG that triggers muscle contraction through the autonomous generation of bursts of action potentials. Although the cellular and anatomical organization of CPG has been identified, the mechanisms underlying neuronal synchronization leading to population dynamics have yet to be fully understood. Different studies evidenced that only the preBötzinger complex (preBotC) is essential and sufficient to generate the respiratory rhythm. Still, the question of how the rhythm is generated remains unanswered and indeed the two main hypotheses on rhythmogenesis which could be due to pacemaker neurons activity or to synaptic inhibition arising at the circuit level have never been demonstrated.

Aim: According to a recent theory, a key element is a network-level mechanism residing within the preBotC microcircuit. To test this hypothesis, we chose to simulate a computational model of the circuit. Simulating neuronal circuits is paramount to investigate action mechanisms otherwise poorly testable in experimental
conditions.

Method: We developed a circuit of thousand "integrate and fire" neurons reproducing the main electrophysiological behaviors of preBotC neurons such as regular firing and burst firing. Neurons were connected according to probabilistic rules through excitatory synapses to form two distinct populations with different sizes. The smaller population (rhythm population; 250 neurons) received external repeated and asynchronous stimuli with a variable average frequency in the range of 1-6 Hz.

Results: Following a Poisson stimulation the whole network was progressively engaged in synchronous bursting activity. Noteworthy, single neurons showed a transition from regular to bursting firing generating electrophysiological activity similar to the one observed in experimental recordings. Furthermore, the oscillatory behavior of the neuronal population could be tuned according to the input pattern and the I/O relationship was a saturating exponential. The modulation of incoming input has been designed to mimic an external perturbation such as changes in blood gases concentration. Interestingly, the range of output frequency was distributed among physiological values (0.2-0.7) with a saturation value (0.7 Hz) that was assessed independently from the limits imposed by pulmonary mechanics.

Conclusion: These results show that a hierarchical network of purely excitatory neurons can be used to simulate the PreBotzinger Complex shading light on the physiological mechanisms underlying the neuronal control of respiration activity, providing insight on the pathogenesis of dysfunctions and eventually leading to therapeutic and pharmacological intervention.

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Role of TAPSE/PAPs Ratio for Pulmonary Arterial Hypertension Screening in Sjogren Syndrome. Is it Appropriate to Introduce it?

Cecilia Campani - Università degli Studi di Modena e Reggio Emilia

Introduction: Although it does not represent the main cause of comorbidity, pulmonary arterial hypertension (PAH) still represents a cause of death related to Sjogren's syndrome, which is further aggravated by a late diagnosis. Unlike other connective tissue diseases, there are no screening algorithms for this pathology.
From this perspective, the TAPSE/PAPs ratio has recently emerged as a new predictive risk factor for PH, cardiovascular events and mortality, however its role in SJ, in association with common screening systems for pulmonary hypertension, is still poorly studied in this syndrome. The aim of this study was to bring this comorbidity to attention in the classification of the patient with Sjogren's syndrome and to correlate the TAPSE/PAPs ratio with some parameters (mPAP, PVR, Wedge pressure, RAP) of the Right heart catheterization and clinical parameters.

Materials and methods: In this single-centre prospective study, we analysed 50 patients affected by SJ at Unit of the Cardiology Modena Polyclinic from November 2022 to January 2024. All patients underwent clinical evaluation with laboratory and instrumental tests (ECG/Color Doppler echocardiography) looking for indirect signs of pulmonary hypertension and in those where important signs were found, a right heart catheterization was done.

Results: 50 patients (44F/6M) were enrolled in the study and one pulmonary hypertension was found, showing a prevalence of the pathology of 2%. In this subgroup we have found interstitial lung disease at HRTC and a significant correlation between the TAPSE/PAPs ratio <0.6 mm/mmHg and the mPAP/ PVR/ RAP at RHC.

Conclusion: This study demonstrates how the prevalence of Sjogren's syndrome is no negligible and how TAPSE/PAPs ratio < 0.6 mm/mmHg is a predictive risk factor for the diagnosis of PAH and correlates with PAP/ PVR/ PAD at RHC. Furthermore, we demonstrate the correlation between PAH and Sjogren's Syndrome complicated with ILD. Consequently, these patients should be monitored with serial echocardiography to look for indirect signs of pulmonary hypertension, in particular in those with TAPSE/PAPs ratio less than 0.7 (11/50).

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Novel therapeutic candidates for pancreatic cancer: Targeting epigenetic modifications induced by the tumor microenvironment

Viviana Cortiana - Università degli Studi di Bologna

Background: Pancreatic ductal adenocarcinoma (PDAC), the most common subtype of cancer, is predicted to become the second leading cause of cancer-related deaths by 2040. Many factors contribute to its high mortality, and the current 5-year survival rate is about 13%. A unique feature of the disease is the abundance of tumour microenvironment (TME), constituting 90% of tumour mass. Recent unpublished data from our lab reveals that inflammatory (iCAFs) and myofibroblastic cancer-associated fibroblasts (myCAFs) induce differential protein expression and modulate chromatin accessibility in PDAC cells. Therefore, we aim to understand how the TME modulates epigenetic processes shaping tumour behaviour and progression with the ultimate goal of addressing the critical need for more effective PDAC therapeutic strategies.

Methods: Utilizing Rapid Immunoprecipitation of Endogenous Proteins (RIME), a technique developed in our lab that allows the study of protein complexes, we identified unique interactors recruited towards FOXA1 and FOXA2 complexes when PDAC cells are co-cultured with iCAFs or myCAFs. These are two pioneer factors driving gene expression of particular interest as the former is involved in PDAC liver metastases, while the latter exhibits stage-dependent plasticity, varying its impact on tumour behaviour. Based on these results, the project aimed to evaluate the role of selected interactors (STAT1, KDM2A, PPARG) in the presence of conditioned media derived from iCAFs and myCAFs populations as a strategy to target FOXA1 and FOXA2. Viability assays (IC50), colony formation, and proliferation assays for PDAC cells (FC1245) were performed. Gemcitabine or inhibitors of the respective interactors (Fludarabine, KDM2A/7A-IN-1, Soyasaponin Ab) were administered and cells were cultured in normal, iCAF-derived, or myCAF-derived media.

Results: We observed that conditioned media is sufficient to induce significant behavioural differences in PDAC cells. Cancer cells become more sensitive to some of the inhibitors when cultured in conditioned media, exhibiting a considerably diminished viability, colony formation in both count and average area, and proliferation in the presence of the drugs compared to the control. Additionally, iCAF and myCAF-derived media increase the proliferation and colony formation potential of PDAC cells and decrease responsiveness for Gemcitabine.

Conclusions: These findings underline how we could be underestimating the impact of the TME on malignant cells. Our results reveal that CAFs-conditioned media enhance resistance to Gemcitabine, the standard of care, and stimulate increased proliferation of cancer cells, thereby promoting primary tumour growth. Moreover, as expected, cancer cells exhibit heightened sensitivity to the inhibitors when cultured in conditioned media. Therefore, these molecules emerge as promising options to target FOXA1 and FOXA2 transcription factors in the context of either CAF population.

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Role of NLRP3 Inflammasome in a Three-day Model of Alcohol Binges and High Fat-Sucrose-Cholesterol Diet

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Background and Aims: The prevalence of Alcohol-associated Hepatitis (AH) is increasing globally and this coincides with the obesity epidemic. The coexistence of obesity and alcohol use is associated with increased liver injury, progression to chronic liver disease, and liver-related death and is now clinically recognized as MetALD. Previous studies have shown the role of NLRP3 inflammasomes in the progression of Alcohol-associated Liver Disease (ALD) and Metabolic dysfunction-associated Steatohepatitis (MASH). In this study, we aim to identify the role of NLRP3 inflammasome in MetALD using a combined liver injury model of alcohol binges and a high fat-cholesterol-sugar diet (HF-HC-HS or MASH diet) in mice.

Methods: 8-10 weeks old male C57BL/6 (WT) mice were fed on either Chow or HF-HC-HS diet for 3 days with daily alcohol binges (5g/kg). Some mice received MCC950, an NLRP3 inflammasome inhibitor. ALT was measured to assess liver damage. Liver tissue was analyzed for liver injury markers, steatosis, and inflammation markers by ELISA and RT-qPCR.

Results: In the three-day model of MASH diet plus alcohol binges levels of NLRP3, cleaved-caspase1, and IL-1B were significantly elevated as compared to control Chow diet-fed mice, suggesting inflammasome activation in this model. Mice that received in vivo administration of NLRP3 inflammasome inhibitor, MCC950, showed significantly attenuated liver damage as measured by ALT. Therefore, we assessed the relative mRNA expression of various inflammatory genes such as CCL-2, TNF-a, and IL-1b, which was increased in the alcohol binges plus MASH diet group and was significantly attenuated in the presence of NLRP3 inflammasome inhibitor. To further validate the NLRP3 inflammasome inhibition in this model, we measured IL-1b levels in serum and liver lysates and observed a significant decrease in mice fed on alcohol binges plus MASH diet with the addition of MCC950. Furthermore, the adapter, apoptosis-associated speck-like protein ASC, which is fundamental for caspase-1 activation, was significantly decreased by administering MCC950, suggesting an efficient inhibition of NLRP3 inflammasome in this model. Lastly, we evaluated the involvement of NLRP3 inflammasome in steatosis by analyzing the levels of approximately 80 genes involved in lipid and fatty acid metabolism. We observed a decreasing trend in the relative mRNA expression of ApoE, PEMT, CD36, LRP1, and SREBP1c in the alcohol binges plus MASH diet group with the addition of MCC950. However, we did not observe any specific pathway involved in steatosis affected by NLRP3 inflammasome inhibition.

Conclusion: In a three-day model of MASH diet and alcohol binges, NLRP3 inflammasome is activated. Inhibiting NLRP3 inflammasomes improves liver injury and inflammation and could therefore be beneficial against the development of ALD, MASH and MetALD; however, it has no direct effect on steatosis.

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Differenziamento Osteoclastico Indotto da Magnesio: Una Possibile Nuova Strategia Terapeutica per l'Osteonecrosi del Mascellare

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L'osteonecrosi del mascellare (ONJ) è un raro e temibile effetto collaterale causato prevalentemente da farmaci, soprattutto i Bifosfonati, utilizzati nel trattamento di patologie come l'osteoporosi e il mieloma multiplo. Si tratta di una condizione patologica multifattoriale ed invalidante che coinvolge la cavità orale e si manifesta con la presenza di un'area di esposizione ossea, eventualmente associata a suppurazione e dolore. La nostra attenzione è stata focalizzata sullo Zoledronato, il più efficace tra i Bifosfonati. Tale farmaco determina una significativa riduzione del numero di osteoclasti portando ad un'inibizione del riassorbimento osseo, il che avrebbe come conseguenza una ridotta resistenza locale all'invasione di batteri e la diminuita capacità di eliminare l'osso infetto, comportando di conseguenza l'ONJ. Sulla base di queste premesse, riteniamo quindi che lo sviluppo di un composto in grado di riattivare localmente la produzione di osteoclasti possa rappresentare una futura strategia terapeutica per l'ONJ. Nel nostro lavoro, pubblicato sulla rivista "Biology"[1] abbiamo cercato di chiarire se il Magnesio Cloruro sia in grado potenziare il differenziamento osteoclastico in presenza dello Zoledronato nelle cellule U937, una linea di monoblasti.

Le cellule sono state fatte differenziare ad osteoclasti attraverso due giorni di stimolazione con Forbolo 12-Miristato 13-Acetato (PMA) 48 nM, seguito da un lavaggio con PBS e da tre giorni di stimolazione con Vitamina D3 10-8 M. Durante tali stimolazioni, sono state contemporaneamente trattate con Magnesio Cloruro e Zoledronato. Le analisi molecolari sono state effettuate mediante QRT-PCR per valutare i livelli di espressione degli mRNA di markers del differenziamento osteoclastico, come ACP5. Sorprendentemente, utilizzando il Magnesio e lo Zoledronato in combinazione è stato osservato un effetto sinergico responsabile di un'aumentata espressione di tutti i markers analizzati. L'analisi immunofenotipica è stata svolta con la valutazione dell'antigene CD11b in citofluorimetria.

Le cellule trattate con Magnesio mostrano un aumento superiore al doppio della intensità di fluorescenza media del CD11b, quelle trattate con Zoledronato vanno incontro ad un calo del 10%, mentre quelle trattate con la combinazione di entrambi presentano un'intensità superiore rispetto al controllo. Nell'analisi morfologica il trattamento con Zoledronato ha messo in evidenza la completa assenza di osteoclasti multinucleati, mentre aggiungendo anche il Magnesio si osserva un aumentato effetto differenziativo, con la significativa presenza di osteoclasti contenenti 5 o 10 nuclei. I nostri risultati hanno dimostrato che il Magnesio è in grado di invertire l'inibizione del differenziamento osteoclastico indotta dallo Zoledronato. Il nostro lavoro pone le basi per l'utilizzo del Magnesio sottoforma di terapia topica per la cura, o anche la prevenzione, dell'ONJ.

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Gli Psichedelici come Trattamento per il Disagio Psicologico nei Malati Terminali: una Revisione Sistematica della Letteratura e Network Meta-Analisi

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Introduzione: I pazienti con malattie terminali possono sperimentare un disagio esistenziale corredato da ansia e depressione. L'efficacia dei trattamenti attualmente impiegati per questa condizione, quali psicoterapia, antidepressivi e benzodiazepine, è risultata limitata. L'interesse verso le sostanze psichedeliche come possibile alternativa terapeutica è giustificato dal meccanismo d'azione di tipo antidepressivo e dall'effetto mostrato sulla componente spirituale/esistenziale che accompagna il fine vita. Lo scopo di questa revisione sistematica e network meta-analisi è di esaminare l'efficacia e la sicurezza delle sostanze psichedeliche nel trattamento del disagio esistenziale associato al fine vita.

Metodi: Questo studio è stato condotto secondo il PRISMA Statement. La ricerca bibliografica è stata condotta su PubMed, CINAHL, PsycInfo, EMBASE e cinicaltrials.gov fino al 31 agosto 2023. Tutti gli studi randomizzati controllati (RCT) con psichedelici in pazienti terminali che hanno indagato l'effetto del trattamento su depressione o ansia sono stati inclusi. Come esiti secondari sono stati esaminati l'accettazione della morte e la qualità della vita. La meta-analisi ha stimato la differenza media standardizzata (SMD) e l'odds ratio (OR), con relativi intervalli di confidenza al 95% (95%CI), tra trattati e controlli in confronti a coppie e di rete, in modelli ad effetti random.

Risultati: Sono stati inclusi 9 studi, corrispondenti a 606 pazienti (362 trattati con psichedelici: psilocibina, ketamina, MDMA, LSD). La meta-analisi ha confermato l'efficacia degli psichedelici nel ridurre i livelli di depressione e ansia, sebbene con elevata eterogeneità tra gli studi (SMD:-1.38[95%CI:-2.03;-0.72] I2:89% e SMD:-2.22[95%CI:-3.67;-0.77] I2:91%, rispettivamente). La network meta-analisi ha evidenziato la superiorità di ketamina e psilocibina rispetto al placebo nell'effetto antidepressivo (SMD:-0.76[95%CI:-1.52;-0.01], e SMD:-3.27[95%CI:-4.11;-2.44], rispettivamente), con psilocibina che è risultata superiore agli altri psichedelici. Inoltre, psilocibina ha mostrato effetto significativo sull'ansia (SMD:-3.79[95%CI:-5.70;-1.89]) e sulla qualità della vita (SMD:3.86[95%CI:2.32;5.41]), rispetto al placebo ma non agli altri psichedelici. Nessuna sostanza è risultata superiore al placebo nell'accettazione della morte. Non sono state riscontrate differenze statisticamente significative nei tassi di interruzione del trattamento e di reazioni avverse tra psichedelici e controlli.

Conclusioni: La terapia con psichedelici è risultata promettente per trattare depressione e ansia nei pazienti con malattie terminali. Tra le sostanze psichedeliche, psilocibina ha mostrato migliore beneficio. Lo studio è limitato dal ridotto numero di RCT, dalla difficoltà a condurre ricerche in cieco e dalla mancanza di confronti diretti tra sostanze psichedeliche. Studi futuri con campioni più ampi e confronti tra diversi composti psichedelici sono necessari per consolidare questi risultati.

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Eotaxins Signaling Axes Host Variants in Asthmatic Patients: Pathophysiological and Clinical Implications

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Background: Asthma is a chronic disease characterized by airway hyperresponsiveness, with host and environmental factors leading to mucosal edema, bronchospasm, and mucous hypersecretion. Eotaxins belong to the CC-chemokines family and are responsible for eosinophil, and Th2-cells mobilization, in the lung and other districts. CCL11 is involved in the early phase response to asthmatic triggers, whether CCL24 and CCL26 are more relevant in later stages, i.e. chronicization. Th2-cells and Eosinophils are known key effectors of asthma pathogenesis, with their levels in airways being associated to severity. Intriguingly, eosinophil levels in asthmatics also relate to CCL11 expression in airway cells. Eotaxin family genes (CCL11, CCL24 and CCL26) are located on chromosomes 7 and 17, while CCR3, coding for their main receptor, is on chromosome 3. In this review we aimed to assess the current state of studies regarding host genetic variants of this signaling pathways.

Results: Several researchers have studied SNPs of the eotaxin family genes, and of CCR3. Associations between asthma, and variance in some of its phenotypic characteristics, and many polymorphisms of all three chemokine genes have been found. Most investigators detected association with negative aspects, but it must be noted that some, usually involving different ethnicities, have reported opposite data regarding certain associations. Higher IgE levels have been found in patients bearing: CCL11 -426C>T, -576T>C, -384A>G, Ala23Thr, Ala123Thr, g.4438C, the two haplotypes described by Raby BA, et al, and CCL26 +2497T>G. Correlation with total plasma CCL24 levels has been found in individuals with CCL24 +1265A>G, and the two haplotypes described by Min, JW et al. Notably, +1265A>G has also been found to be linked with decreased risk of asthma. Instead, patients bearing CCL24 +179T>C, +275C>T, +304C>A, and CCL26 +2497T>G have been found to have increased risk of developing asthma. CCL26 +2497T>G and +77C>T have also been described as related to the peripheral blood eosinophil counts in asthma. CCR3 SNPs have also been found to be linked to blood eosinophilia.

Discussion: The role for this evidence in providing personalized care for asthmatic patients has already been tested by previous studies, which analyzed the potential of some of these variants to be used as markers to stratify patients according to their own risk profile. In addition, anti-CCR3 antibodies have been developed and tested in both in-vitro, and animal, models of eotaxin-related disorders, with success in reducing the severity of eosinophilic inflammation and mucosal injury.

Conclusion: The current body of evidence warrants the potential for further research regarding eotaxin/s-CCR3 axis/axes as therapeutic targets in asthma and other, allergic and non-allergic, disorders. Studies regarding the genetic variants impacting these pathways may, in the future, aid in delivering these therapies at best.

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Sessione Plenaria

Venerdì 12 Aprile 2024

Trattamento Chirurgico Laparoscopico dell'Endometriosi Profonda: Come Ridurre Complicanze e Tempi Operatori

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Introduzione: L'endometriosi è una patologia ginecologica cronica, ormono-dipendente, che colpisce il 10% delle donne in età fertile, caratterizzata dalla localizzazione di tessuto endometriale al di fuori della cavità uterina. L'endometriosi profonda si contraddistingue per l'estensione della malattia a livello sottoperitoneale e per il coinvolgimento di numerose sedi pelviche come legamenti uterosacrali, intestino, vescica e ureteri. La compressione ureterale, dovuta alla presenza di endometriosi intrinseca o estrinseca all'uretere, può causare idronefrosi e compromissione renale. La sintomatologia tipica della malattia è rappresentata da dismenorrea, dischezia, disuria, dispareunia e infertilità, nonostante non esista una stretta correlazione tra l'estensione della malattia e la severità dei sintomi. L'ecografia transvaginale rappresenta il gold standard per la diagnosi ma possono rivelarsi utili anche risonanza magnetica, clisma opaco, UroTC e/o cistoscopia. Il trattamento chirurgico per via laparoscopica dell'endometriosi rappresenta una delle principali opzioni terapeutiche, rivelandosi una chirurgia complessa che può comportare complicanze tardive quali: perforazioni intestinali e ureterali o fistole retto-vaginali. L'obiettivo di questo lavoro è quello di valutare, mediante l'utilizzo intraoperatorio di Verde Indiocianina (IGC) somministrato direttamente in uretere, la riduzione delle complicanze intraoperatorie e dei tempi chirurgici negli interventi di exeresi di noduli endometriosici.

Materiali e Metodi: Presso la U.O.C. di Ginecologia di Siena, sono state trattate chirurgicamente 3 pazienti, di età media all'intervento di 45,3 anni (range 44-47), affette da endometriosi profonda infiltrante con coinvolgimento ureterale. Nel corso degli interventi chirurgici, mediante cistoscopia, è stato introdotto l'ICG a livello dei meati ureterali, al fine di evidenziare il decorso e il calibro degli ureteri (spesso difficoltoso a causa di aderenze, tessuto fibrotico circostante e distorsione anatomica) e individuare, laddove presenti, la medializzazione dell'organo, tratti stenotici o dilatazioni a monte. Il gruppo di controllo è rappresentato da una serie di pazienti con endometriosi profonda sottoposte a chirurgia con lesioni e stadio sovrapponibili al gruppo in esame in cui non è stato utilizzato l'ICG.

Risultati: L'iniezione dell'ICG in uretere ha ridotto in maniera statisticamente significativa i tempi chirurgici necessari per identificare gli ureteri stessi e ha permesso di eseguire l'ureterolisi senza causare lesioni alla parete ureterale, riducendo le complicanze a breve e lungo termine.

Conclusioni: L'analisi dei nostri casi, seppur di numero esiguo, rivela dei risultati molto promettenti grazie all'utilizzo dell'ICG, il quale si è dimostrato avere un efficace risvolto nella pratica chirurgica, eleggendo l'iniezione del colorante in uretere a tecnica da adottare al fine di ridurre complicanze intraoperatorie e tempi chirurgici.

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Orthotopic Vascularized Lymph Node Transfer in Breast Cancer – Related Lymphedema Treatment: Functional and Life Quality Outcomes

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Introduction: Breast cancer - related lymphedema (BCRL) is a chronic disease that occurs up to 65% of breast cancer survivors. Traditional treatment is conservative, but new surgeries as lymphaticovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT) are at disposal. This study aims to investigate the orthotopic VLNT efficacy in BCRL. Results in terms of limbs' reduction rates and quality of life improvement, are compared to the outcomes reported in Literature.

Patients and Methods: During patients' selection, inclusion criteria were monolateral ISL stage II or III BCRL with pathologic lymphoscintigraphy imaging and a minimum of previous 6 months of unsuccessful conservative treatment. Bilateral lymphedema, local recurrence or systemic metastasis, acute infection of the limb and deep venous trombosis were exclusion criteria. Surgery consisted in VLNT from the gastroepiploic region to the axilla with axillary scar dissection.

Results: From August 2019 to December 2021, 25 patients were included. At the pre-operative scintigraphy exam, mean lymph transport index (TI) was 30 (range; 22.7-29.3). Nine of them (36%) were ISL stage II and 16 (64%) were stage III. Average follow-up was 13.5 months (range; 12-19 months). VLN flaps' survival rate was 100%. One year after surgery, the mean Circumferential Reduction Rate (CRR) resulted 44.62 (range; 27.4-60.3). Infections' rates presented a statistically significant reduction, from an average of 2.4 (range;1-4) to 0.2 (range; 0-1) episodes per year. Life quality index measured with the LYMQOL questionnaire showed significant improvement after 1 year, from a mean score of 3.28 (range; 2-5) to 8.12 (range; 7-9).

Conclusion: When compared to Literature evidence, the results of the current study are in line with both VLN inset ways related to BCRL treatment. An optimal therapeutic choice should consider benefits and drawbacks of each orthotopic and heterotopic VLNT, taking into account surgeon's preference and experience and patients' related factors and expectations.

Keywords: Vascularized Lymph Node Transfer; Breast Cancer - Related Lymphedema; Orthotopic Inset; Microsurgery; Gastroepiploic Lymph Node Flap.

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Profile in a Cataract Surgery Social Impact Program in Brazil

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Introduction: Cataract is a leading cause of low vision and blindness in old age, affecting millions worldwide. Although cataract surgery is a common procedure, meeting the annual demand remains challenging [1, 2]. Patients may experience negative outcomes during the waiting period for treatment given the impact of cataracts on both the quality of life and employment [3]. The aim of this study is to evaluate the epidemiological pattern of patients undergoing cataract surgery within a positive social impact program. Understanding the patient profile within accessibility programs holds substantial implications for ophthalmological research and public health initiatives.

Methods: The research employed a descriptive and prospective approach, utilizing a questionnaire and a clinical examination, including Snellen chart, for patients undergoing cataract surgery. The patients were part of a positive social impact program called "Central da Visão", which aims to provide accessibility to patients seeking cataract treatment. The study was conducted at the Ophthalmological Service of Hospital Paranaense de Otorrinolaringologia in Brazil, with ethical approval from the relevant committee. Data collection included patient demographics, visual impairment levels, waiting times and comorbidities. Statistical analysis was performed using IBM SPSS Statistics v.29.01, considering a P value less than 0.05 statistically significant.

Results: The analysis was performed on 103 patients, revealing a meaningful waiting time (mean 2.2 years) from symptom onset to surgery. The majority of patients were over 60 years old constituting 76.7% of total. Gender and age stratification reveal noteworthy patterns, emphasizing the vulnerability of older women ($\chi 2 = 6.23$, $P = 0.013$). Visual impairment affected 95.5% of eyes, with 20.8% of eyes considered functionally blind. Systemic arterial hypertension (affecting 54.4% of patients) and diabetes mellitus (affecting 29.1% of patients) were prevalent comorbidities ($\chi 2 = 8.16$, $P = 0.004$). Corticosteroid use was noted.

Discussion: The study contributes to understanding the epidemiological pattern of cataract patients within a positive social impact program. The prolonged waiting time for surgery and the prevalence of legal blindness highlight the impact of accessibility programs. The study emphasizes the need for attention to elderly patients due to significant implications for safety and quality of life, as well as to patients with comorbidities.

Conclusion: The study provides insights into the patient profile undergoing cataract surgery in a positive social impact program in Brazil. The findings underscore the challenges faced by patients, including waiting times and the impact on quality of life. The prevalence of comorbidities suggests the need for targeted interventions. The study encourages further research to enhance healthcare strategies and improve the overall patient experience in cataract surgery programs.

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A Microbiome Testing-Based Precision Medicine Approach to Treat Post-Infectious Irritable Bowel Syndrome: a Pilot Study

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Introduction: Gut microbiome alterations are known to play a paramount role in the pathogenesis of irritable bowel syndrome (IBS), mainly in its post-infectious form (PI-IBS) [1]. Current untargeted therapeutic approaches have obtained conflicting results in patients with this condition [2][3]; thus, microbiome testing are emerging as a promising diagnostic tool and offer a personalized therapeutic strategy to target microbiota, but their real value is still unknown.

Aims & Methods: Our aim was to assess whether a personalized approach based on gut microbiome testing is an effective strategy for PI-IBS. In this pilot study, we included consecutive patients with PI-IBS, diagnosed according to the Rome IV guidelines. All patients underwent a stool 16S-rRNA gene microbiome testing; then, we prescribed a targeted therapy based on the results of the test, including non-adsorbable antibiotics (rifaximin in 69% of patients, paromomycin in 31% of patients), prebiotics (inulin and psyllium, used in 69% of patients) and probiotics (multispecies probiotics and Bifidobacterium-based probiotics in 38% of patients, Lactobacillus-based probiotics in 54% of patients, and Escherichia coli Nissle 1917 in 15% of patients). Patients were followed up to 12 weeks after the end of therapy, evaluating symptoms with the gastrointestinal symptoms rating scale (GSRS); the primary outcome was the resolution of at least one symptom at 12 weeks.

Results: Thirteen patients were enrolled in the study period: we observed low alpha diversity in 23% of patients, high abundance of Proteobacteria in 23%, high abundance of Firmicutes in 38% of them; furthermore, 54% of patients presented low abundance of short-chain fatty acids producing bacteria, 62% of Akkermansia and 69% of Bifidobacteria. At the end of the follow-up, 93% of the patients had an improvement in at least one symptom, while 38% had a total remission of symptoms.

Conclusion: These promising preliminary results suggest that, when it comes to take into account treatment options in patients with PI-IBS, a precision medicine approach, based on the application of a gut microbiome testing to target microbiome therapeutics, may be considered.

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Prognostic Role of ELF Test Compared to Liver Biopsy in Patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

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Introduction: In metabolic dysfunction-associated steatotic liver disease (MASLD), liver fibrosis severity emerged as the strongest predictor of liver-related events (LRE), as liver decompensation, hepatocellular carcinoma and liver transplantation. The enhanced liver fibrosis (ELF) score is a multi-parametric panel of direct fibrosis markers that displays extracellular matrix turnover by determining the levels of these blood biomarkers: tissue inhibitor of metalloproteinases 1 (TIMP-1), amino-terminal peptide of type 3 procollagen (PIIINP) and hyaluronic acid (HA). Despite its usefulness for diagnosing advanced liver fibrosis in MASLD patients, its appropriateness as a prognostic biomarker is still uncertain.

Aim: This study assesses the use of ELF score for predicting LRE among patients with MASLD and compares the prognostic performance of ELF, FIB4 and liver histology.

Materials and Methods: We retrospectively enrolled 289 patients with MASLD at Liver Outpatient clinic at Policlinic A. Gemelli, Rome. Assay of HA, PIIINP and TIMP-1 were determined in accordance with the manufacturer's instruction, using the Atellica TM IM Analyzer using a plasma sample collected at baseline and stored at -800 C. For all patients we calculated FIB4 and then automatically ELF score, and 250 patients underwent a liver biopsy. The main outcome was a composite endpoint of all-cause mortality, hepatocellular carcinoma, liver transplantation or cirrhosis complications. Considering existing literature cut-offs, subjects were stratified accordingly to ELF ($\leq$9.8, 9.8-11.3, $\geq$ 11.3), FIB-4 (<1.3, 1.3-2.67, 2.67) and histology (F0-2, F3, F4) to assess risk of occurrence of primary outcome.

Results: We included data of 289 patients (88 were female, median age was 50 years, median BMI was 28.7 kg/m2 and 81 had type 2 diabetes). After a median follow-up of 41 months, the composite endpoint was observed in 34 (11.8%) patients. There was a steady uplift in the frequency of developing primary outcome according with ELF <9.8 (0.5%), 9.8 to 11.2 (14.5%), and $\geq$ 11.3 (69.7%). Survival curves for pairwise comparisons between groups experienced considerable differences for all index tests according to pre-defined histological and NITs stratification. At multivariate Cox regression analysis, ELF and liver histology were significant predictors of the primary outcome after adjusting for gender, type 2 diabetes, age and BMI. (ELF >11.2vs<9.8 HR 135.4 [95%CI 15.9-1149.0 p<0.001], 9.8-11.2vs<9.8 HR 22.5 [95%CI 2.7-183.9 p<0.001]) (Liver fibrosis 4vs0-2 HR 216.6 [95%CI 23.5-1999.2 p<0.001], 3vs0-2 HR 5.44 [95%CI.0-30.9 p=0.05]).

Conclusions: ELF, a simple non-invasive blood test, demonstrated to be remarkably effective in predicting clinical outcomes and could be regarded as an alternative to liver biopsy for prognostic assessment in patients with MASLD.

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Colchicine Added to Standard Therapy Further Reduces Fibrosis in Pigs with Myocardial Infarction

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Background: The anti-inflammatory drug colchicine improves prognosis of patients with myocardial infarction (MI) and has been recently approved for secondary prevention of ischemic events in subjects with high cardiovascular risk. An intense inflammatory and fibrotic response after MI often leads to scar expansion and left ventricular (LV) adverse remodeling. The administration of colchicine in reperfused MI could have a positive effect on the infarct scar and LV remodeling, but it still represents a gap of knowledge.

Aim: To investigate the effects of colchicine through serial cardiovascular magnetic resonance (CMR) scans and histological analysis of myocardial tissue in a pig model of reperfused MI on top of standard therapy for MI.

Methods: Pigs underwent temporary left anterior descending artery occlusion through an angioplasty balloon for 90 min and were then randomized into two groups: standard therapy (angiotensin-converting enzyme inhibitor, beta blocker, mineralocorticoid receptor antagonist, aspirin) plus colchicine (n = 14) or standard therapy alone (n = 13). Pigs were treated for 30 days and underwent two CMR scans at 72 hours and 30 days. Pigs were sacrificed after the second CMR. The primary endpoint was the extent of fibrosis (expressed as percentage of fibrosis area on the total section) in the infarct zone, which was calculated on eight tissue samples and then averaged. Secondary endpoints included late gadolinium enhancement (LGE), myocardial salvage index (MSI) and indices of cardiac function or structure. LGE reflects infarct scar after MI. MSI is an index of the efficacy of coronary revascularization and was quantified by the difference between the area at risk (zone of myocardial edema at 72 hours) and the final infarct size (zone of LGE at 30 days) on CMR.

Results: All the pigs survived during the entire follow-up period despite the extensive MI. In the hearts explanted after 31 days, pigs in the colchicine group had less fibrosis in the infarct zone than the sham animals (41.6% [20.4-51.0] vs. 57.4% [42.9-66.5]; P = 0.022). These results align with the trend toward a lower final LGE mass in pigs on colchicine (P = 0.076). Pigs in the colchicine group had less collagen type I in the infarct zone and a lower collagen type I to III ratio, but the total amount of collagen type III did not differ. There was a trend toward a higher MSI in pigs on colchicine (39.1% [31.3-68.8] vs. 29.3% [9.4-41.6]; P = 0.054). Conversely, changes in LV volumes, ejection fraction and mass did not differ between groups both at 72 hours and 30 days. Colchicine therapy was well tolerated, with no report of gastrointestinal disturbances.

Conclusion: This study evaluated for the first time the efficacy of colchicine in a pig model of reperfused MI. Colchicine therapy for 1 month after reperfused MI further reduces myocardial fibrosis when added to standard therapy, while it does not have additional effects on LV remodeling.

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EpCAM Regulation in Embryonic Stem Cell Differentiation

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Background: Head and neck squamous cell carcinoma (HNSCC) is a globally prevalent malignancy characterized by high incidence of metastasis and local recurrence. The epithelial-to-mesenchymal transition (EMT) program plays a pivotal role in conferring invasive and migratory capabilities to HNSCC tumor cells. The surface antigen epithelial cell adhesion molecule (EpCAM) is a key protein involved in EMT, with its downregulation correlating with unfavorable outcomes. Recent studies indicate that EpCAM is expressed not only by carcinoma cells but also by pluripotent stem cells. Notably, during embryonic development, mesodermal cells selectively downregulate EpCAM while in close interaction with endodermal cells, resembling a process similar to EMT. A deeper understanding of the molecular pathways behind EpCAM regulation in embryonic development, and specifically its involvement in endodermal-mesodermal communication, may allow us to elucidate its regulatory mechanisms in cancer pathogenesis.

Aim: Based on a previous bioinformatic analysis, fibroblast growth factor 8 (FGF8) emerged as a possible factor involved in EpCAM's pathway. Our aim was to test its role in mesodermal cells development.

Methods: We utilized mouse embryonic pluripotent stem cells. Our cell lines were both wild type and EpCAM-knockout variants, which underwent spontaneous differentiation through hanging drops technique to develop embryoid bodies (EBs). Previous investigations demonstrated impaired cardiomyocyte development in EpCAM-knockout EBs, manifesting as a complete lack of contractions. We tested if FGF8 was able to restore cardiomyocyte function. We treated EBs with increasing FGF8 concentrations (from 0.1 to 10 ng/ml) and watched them under the optical microscope to see if EpCAM-knockout EBs showed contractions after 10 to 14 days from the beginning of the protocol. We used two sample of cell lines of EpCAM-knockout cells, clone #56 and clone #114, both obtained with CRISPR-Cas9 editing.

Results: At the end of the 2 weeks protocol, 90% of wild type EBs showed contractions; 15% of #114 knockouts showed contractions if treated with 0.5 ng/ml; #56 knockouts showed contractions if treated with 0.1 ng/ml (5%), 0.5 ng/ml (25%), 1ng/ml (50%) and 5 ng/ml (35%). Both EpCAM-knockout lines of EBs that were not treated with FGF8 (sham) showed no contractions.

Discussion: Preliminary results suggest a potential role for FGF8 in mediating communication between endodermal and mesodermal cells, thereby contributing to the proper development of cardiomyocytes. Our outlook is to understand the differences between the two knockout clones in terms of contractions rate and find other proteins involved in FGF8 pathway during embryonic development.

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High Flow Central Venous Access in the Prehospital Management of Exsanguinating Hemorrhagic Shock due to Major Trauma: a Four Years Review

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Background: A crucial aspect of exsanguinating haemorrhagic shock management is rapid volume resuscitation. High flow low-resistance central lines are valuable when traditional vascular access is challenging. This study aims to describe the clinical practice and success rate of high flow CVC insertion by London's Air Ambulance (LAA), a physician-paramedic HEMS service serving a large urban area.

Methods: We conducted a retrospective analysis of major trauma patients treated by LAA from January 1, 2019 to July 31, 2023. We included patients who received 9 French Central Venous Access as part of their pre-hospital treatment and examined their general characteristics, injury causes, vital signs and clinical outcomes. The project met local criteria for, and was registered as, a service evaluation project (ID: 13523; Barts Health NHS Trust).

Results: During the study period, a total of 8104 patients were attended to by the service, and the insertion of a high-flow central venous access was attempted in 328 (4%) patients. The success rate was 80% (264 patients). The overall sample size consisted of 266 (81%) male patients, with a median age of 30 [20-45] years. Out of these, 229 (70%) experienced traumatic cardiac arrest, while the remaining patients were in exsanguinating hemorrhagic shock with output. The right subclavian vein, acquired using a landmark technique, was the favored cannulated vessel, with a total of 204 (62.2%) first attempts, resulting in a success rate of 84,3% (172 patients). This was followed by the left subclavian with 62 (19%) first attempts and a success rate of 88,7% (55 patients). The right femoral vein, using an ultrasound-guided technique, accounted for 6 (1,8%) first attempts with a success rate of 66,7% (4 patients). The right internal jugular vein, with the use of the ultrasound-guided technique, accounted for 5 (1,5%) first attempts with a 100% success rate. Penetrating trauma predominated over blunt trauma, with 179 (55%) cases compared to 149 (44%) respectively. The overall hospital survival rate of this cohort was 29.9% (95 patients). Peripheral IV
access was not attainable in 206 (63%) patients, while at least one IV access was obtained in 90 (27%) patients, and two IV accesses were present in only 32 (10%) patients. Patients who received the trauma line, compared to those who attempted but were not successful, received more blood products: 4 [2-5] units (both PRBC and FFP) vs. 2 [0-4] units.

Conclusions: This study revealed a significant success rate of 80% within an extremely sick cohort of patients. Patients who received the trauma line were able to receive more blood products.

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Sessione Poster

Neurobehavioural Consequences of Stress System Manipulations in a Rat Model of Neglect

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Child Maltreatment (CM) is a major factor in child mortality and morbidity, with long-lasting consequences on physical and mental health trajectories. Neglect, the failure to provide children with physical and emotional needs, accounts for up to 60% of all CM cases and is known to alter the development of biological stress response systems [1].

The current study examined the neurobehavioural consequences of maternal separation (MS) in rats, a procedure mimicking the environmental conditions of neglect [2], and investigated whether this paradigm altered the response to acute treatment with stress-related drugs later in life. 64 adult rats (equally divided for group and sex) were assessed for behavioural flexibility and feedback sensitivity, measures linked to psychiatric vulnerability in humans, on a spatial probabilistic reversal learning task [3].

We did not find evidence of cognitive deficits in MS rats, instead only female MS rats had a better task performance than controls and this difference was also present after the acute administration of corticosterone, an unpredictable stressor. Propanolol administration, used to treat task-based anxiety, had positive or negative effects on the key measure for cognitive flexibility in control females and MS rats respectively. Citalopram, a common antidepressant, had the opposite effect, increasing cognitive flexibility only in MS female rats and decreasing task performance in control females.

Our results suggest a putative resilient phenotype in MS females that confers them better task performance and better response to unpredictable stress later in life but affects their treatment outcomes differently. Indeed, we bring evidence to suggest that in rats the effects of acute administration of propranolol and citalopram are consistently present only in females and gain different outcomes for control and MS rats. Our findings may have translational relevance to test for personalised care based on sex and maltreated status that could lead to better treatment outcomes. In conclusion, this research contributes valuable insights into the intricate relationship between early-life experiences, later life neurobehavioral effects, and drug responses, emphasizing the importance of considering individual differences in treatment strategies.

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Beyond the Beat: Optogenetic Manipulation of Cardiac Nonmyocytes for Action Potential Mimicry

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Background: Although cardiac action potential (AP) generation and propagation have traditionally been attributed exclusively to cardiomyocytes (CM), other cell types in the heart are also capable of forming electrically conducting junctions. Interactions between CM and nonmyocytes (NM) enable and modulate each other's activity.

Methods: Two primary objectives were pursued: firstly, to quantify and compare species-specific variations in action potential characteristics across mouse, rabbit, and human heart tissues using the sharp electrode technique; secondly, to develop and implement optogenetic stimulation protocols in non-excitable cells, aiming to mimic an AP. Species-specific differences in quantitative action potential features, such as amplitude, maximum speed of depolarization, and Action Potential Duration, were revealed through sharp electrode
recordings. Notably, distinctions were observed not only between species but also within different cardiac chambers. In parallel, the optogenetic tool BiPOLES, employing a cation non-selective channel (Chrimson)
activated by red light and a potassium-selective channel (WiChR) activated by blue light, allowed for the direct manipulation of resting membrane potential (RMP) in non-excitable cells, measured using the patch clamp technique.

Results: The results highlighted distinct kinetics of WiChR and Chrimson, necessitating careful adjustments in light intensity and protocol design. Through this pinpoint knowledge of BiPOLES kinetics, RMP can be meticulously manipulated to meet the features of the priorly measured AP.

Conclusions: In conclusion, this research introduces an innovative experimental model to investigate the roles of non-excitable cells in cardiac electrophysiology, thereby opening avenues for novel diagnostic and therapeutic strategies. The study presents an experimental model for examining the impacts of action potentials on nonmyocytes in the heart, independent of their coupling to cardiomyocytes. Furthermore, the BiPOLES tool emerges as a versatile instrument capable of inducing responses in various transfectable cell types, expanding its potential applications beyond cardiac studies. This multifaceted approach contributes to advancing our understanding of cardiac electrophysiology and offers promising prospects for the development of targeted interventions in cardiovascular health.

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Under the Lens: A study of childhood gender identity through the toy preference test

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Introduction: During fetal life and the first six months of postnatal life, activation of the hypothalamic-pituitary-gonadal axis leads to the production of sex hormones, which in this time window also play a role on neurobehavioral sexual differentiation in humans. Dimorphisms present in certain areas of the brain manifest themselves in different behaviors in the two sexes. As early as infancy, starting at 12 months of age, differences are found in the choice of toys and activities performed. The study of these differences is done through the use of questionnaires (e.g., PSAI) or by performing tests, such as the 'toy preference' test. Despite the growing interest on the topic, however, the role of early postnatal gonadal activation in human psychosexual development is largely unknown. Therefore, the aim of the study is to evaluate the influence of minipuberty (as assessed by urinary sex hormone levels at birth, 3 and 6 months of age) on the gender preferences and neurobehavioral development of a group of term-born children, adjusted for gestational age, without maternal-fetal risk factors.

Methods: Prospective longitudinal cohort study for which 24 infants (12 males, 50%) born at term (37-40 weeks gestational age) adjusted for gestational age (AGA) were enrolled. Urinary hormone levels (uLH - luteinizing hormone, uFSH - follicle stimulating hormone, uT - testosterone for males and uE - estradiol for females) were assessed at birth at 3 and 6 months of age. Auxological assessment (weight, length, head circumference) and neurodevelopmental assessment (Spontaneous Motility Study according to Prechtl's method at 3 months and Griffith's Scale III - GSCD at later ages) were also performed at the same times. Later at 15 months, clinical evaluation including: auxological evaluation, GSCD, toy preference test and PSAI questionnaire completion was also performed. Finally, GSCD and PSAI questionnaire were performed at 36 months.

Results: Preliminary data analysis shows a gender difference in game choice during the toy preference test. This difference is also found when analyzing developmental test results at 36 months, where males score significantly higher in some developmental areas such as gross-motor areas, while females score significantly higher in areas such as expressive areas. Interesting hormonal trends are associated with these differences.

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Therapy of Parapneumonic Empyema in Children: a Scoping Review of the Literature

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Background: Empyema (the presence of pus in the pleural space) is a severe complication of community-acquired pneumonia and a significant cause of morbidity, but not mortality, in children. Optimal management in children, especially the choice of antibiotics, method of administration and duration of therapy, is still a matter of debate. Currently there is a lack of strong specific recommendations. This scoping review aims to map the available literature about the type of studies, microbiology, therapies (both antimicrobial and surgical) and outcomes of empyema in children since 2020.

Methods: We conducted a systematic search combining the terms 'pediatric' (children aged 0 to 18 years) and 'pleural empyema' on PubMed and SCOPUS to identify all eligible studies. This was done following the Preferred Reporting Items or Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.

Results: A total of 127 studies were included. 15 tried to compare medical treatments (alone or in combination with pleural drainage or fibrinolysis) with more invasive surgical approaches, and 6 studies that compared diverse surgical interventions. However, the diversity of study designs make difficult to derive firm conclusions on the optimal approach to pediatric empyema. The different inclusion criteria, diverse pharmacological or surgical approaches, and settings, do not allow to reach firm conclusions. Overall, 78 out of 10896 children (0.7%) included in the review died, with mortality being higher in Asia and Africa.

Conclusions: Our scoping review highlights important gaps regarding several aspects of empyema in children, including specific serotypes of the most common bacteria, optimal pharmacological and surgical approach and potential benefits of newer antibiotics with optimal lung penetration. New trials, designed on a multi-country level with higher number of patients and more rigorous inclusion criteria and designs, should be urgently funded.

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Monoclonal antibodies and amyloid removal as a therapeutic strategy for cardiac Amyloidosis

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Background: Cardiac amyloidosis (CA) is a progressive infiltrative disease resulting from the deposition of amyloid fibrils in the heart. The most common forms include immunoglobulin light-chain (AL) and transthyretin amyloidosis (ATTR), caused by the deposition of unstable immunoglobulin free light chains and transthyretin (TTR), a tetrameric transport protein mainly produced by the liver. Currently, available therapeutic approaches aim to halt or stabilize the production of amyloidogenic precursors, thus impairing further amyloid deposition. Even after deposition is stopped, amyloid progressively continues to impair tissue function. Therefore, therapies that directly address the clearance of toxic amyloid are needed to restore organ physiology. One possible approach consists of targeting amyloid deposits with specific monoclonal antibodies (mAbs), thus stimulating their removal through phagocytic cells.

Aim: To summarize the current evidence regarding the use of mAbs in the treatment of CA.

Methods: Pertinent studies were searched in PubMed/Medline (updated January 2024) using the following terms: "cardiac amyloidosis", "monoclonal antibodies", "immunoglobulin light chains", "transthyretin". Given the design of this work as a narrative review, no formal criteria for study selection or appraisal were enforced.

Results: mAbs directed against plasma cell clones are promising for AL amyloidosis; therefore, daratumumab has already been approved for use in clinical practice, following the positive results of the recently completed Phase III ANDROMEDA trial. Similarly, Phase II and III trials are currently evaluating the safety and effectiveness of Birtamimab and Anselamimab directed against AL amyloid deposits. As for ATTR amyloidosis, ongoing studies are evaluating the safety of anti-ATTR antibodies, namely NI006 and PRX004. NI006 has recently entered the Phase III DepleTTR-CM trial, while PRX004 is soon to be tested in a Phase II study (NCT05442047). A novel perspective emerges with the development of pan-amyloid removal (PAR) therapeutics based on molecules capable of selectively binding amyloid deposits in all types of amyloidosis and at all stages of the disease. The first attempts have focused on serum amyloid P (SAP), a protein present in all human deposits. The production of anti-SAP antibodies, which initially showed promising results, was later stopped because of the suboptimal safety profile. However, a similar approach has been used to develop novel pan-amyloid therapies that could potentially be applied to all types of amyloidosis.

Conclusions: A therapeutic strategy based on monoclonal antibodies capable of selectively binding amyloid deposits and inducing their removal has recently been tested in various clinical trials, with promising results, and could represent a cutting-edge treatment for CA.

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Microvascular Decompression for Trigeminal Neuralgia Secondary to VBD: A Case Report and Systematic Review of Interposition versus Transposition Techniques

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Background: Trigeminal neuralgia (TN) secondary to vertebrobasilar dolichoectasia (VBD) presents unique challenges in management. Microvascular decompression (MVD) is a well-established surgical intervention for TN, but the optimal technique for VBD-related cases remains a subject of debate. Recently, researchers have proposed the transposition method (repositioning of the affected vessel) as a viable alternative to the conventional interposition approach in which the neurovascular conflict is resolved by simply placing an implant between the offending vessel and the nerve.

Case presentation: We present a 62-year-old male with severe TN secondary to VBD successfully treated with MVD using the interposition technique. Despite the technical challenges posed by the dolichoectatic vertebrobasilar artery, the patient achieved complete pain resolution without neurological deficits, maintaining long-term relief without medication.

Methods: A comprehensive systematic review was conducted following PRISMA guidelines, to compare outcomes between MVD techniques, specifically focusing on interposition and transposition methods, for TN secondary to VBD. A search of the literature, published between January 1991 and February 2024 was launched on PubMed, Web of Science and Google Scholar using the terms "Trigeminal Neuralgia", "Microvascular Decompression", and "vertebrobasilar dolichoectasia" in various combinations. The literature search yielded a total of 117 results. Upon title and abstract screening, 90 articles were considered irrelevant and further excluded. Nine more articles were excluded upon full-text screening. The remaining 18 articles were analysed in this review.

Results: Analysis of the included studies revealed comparable immediate postoperative pain relief rates between interposition and transposition MVD techniques. However, interposition MVD demonstrated superior long-term pain control and lower complication rates, including vessel injury and nerve damage. Medication-free status was more consistently achieved with the interposition technique, suggesting its potential advantage in managing VBD-related TN.

Conclusion: MVD remains a viable treatment option for TN secondary to VBD, with the interposition technique showing favourable outcomes compared to transposition. Further prospective comparative studies are warranted to validate these findings and refine surgical approaches for optimal patient outcomes.

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