Oral Communications 4
Chronic Kidney Disease (CKD)

December 6, 2025 (Saturday) 09:30~11:00 **Venue：Room 7 (703)**

Chair(s)	Soo Kun Lim, Pringgodigdo Nugroho	
09:30-09:39	PEMP: A Highly Automated Super-Resolution Platform for Quantitative Analysis of Podocyte Foot Process Morphology Across Research and Clinical Applications APCN20250402	**Nicole Endlich** Institute of Anatomy and Cell Biology, University Medicine Greifswald, Greifswald
09:39-09:48	Enhancing Caveolin-1 Expression with DIC: A Novel Strategy for Promoting TGFβR1 Degradation in Chronic Kidney Disease APCN20250703	**Zhenghaoyi** The State Key Laboratory of Mechanism and Quality of Chinese Medicine, University of Macau
09:48-09:57	PRIP Deficiency Promotes YAP Nuclear Translocation, Thereby Enhancing Renal Fibrosi APCN20250250	**Meiqun Yuan** Department of Cell Biology, Aging Science and Pharmacology, Faculty of Dental Science, Kyushu University
09:57-10:06	Tubular Extracellular Vesicles Mediate Vascular Calcification in Chronic Kidney Disease via Complement C3 APCN20250156	**Zhang Yuxia** Southeast University School of Medicine
10:06-10:15	CONFIDENCE Asia: Effect of Simultaneous Initiation of Finerenone and Empagliflozin on Urinary Albumin-To-Creatinine Ratio in Asian Participants From The CONFIDENCE Trial APCN20250623	**Masaomi Nangaku** The University of Tokyo Hospital
10:15-10:24	Development of a Modified Renal Function Assessment Using Calf Circumference as a Proxy for Muscle Mass in the Elderly APCN20250341	**Shigemi Morishita** Department of Surgery, Oida Hospital

10:24-10:33	Maternal Insulin Therapy and Its Impact on Immune Regulation in Infants of Mothers with Kidney Disease and Gestational Diabetes APCN20251139	**Pardeep Kumar** Department of Biochemistry, FH Medical college and hospital
10:33-10:42	Proteomics Integrated with Bidirectional Mendelian Randomization Prioritizes Plasma Proteins for Influencing and Predicting Kidney Function APCN20251104	**Ya-Chi Lin** China Medical University Hospital, China Medical University
10:42-10:51	Oral Semaglutide Use in The Real World, Multi-Centre Experience on Renal Outcomes Of Diabetic Kidney Disease in Malaysia (Sword Trial) - An Interim Analysis APCN20250432	**Jun Min Em** Division of Nephrology, Medical Department, University Malaya Medical Centre
10:51-11:00	Dapagliflozin Efficacy and Safety in Chronic Kidney Disease Stage 4–5: An Investigator-Led, Randomized, Open-Label Trial APCN20250930	**Chi-Chih Hung** Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250402

PEMP: A Highly Automated Super-Resolution Platform for Quantitative Analysis of Podocyte Foot Process Morphology Across Research and Clinical Applications

Bjoern Tampe[1]; Christos E Chadjichristos[2,3]; Christos Chatziantoniou[2,3]; Ingmar Alexander Kluge[1]; Vedran Drenic[6]; Tim Endlich[6]; Samy Hakroush[4]; Nicole Endlich[5,6]

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Abstract

Podocyte foot process (FP) morphology is a critical determinant of glomerular filtration barrier integrity. Due to their nanoscale dimensions, FPs have historically been analyzed via electron microscopy (EM), a time-consuming and manual approach with limited throughput. To address these challenges, we developed the Podocyte Exact Morphology Measurement Procedure (PEMP), a super-resolution microscopy (SIM)-based method enabling precise and largely automated quantification of foot process morphology, particularly filtration slit density (FSD), in standard paraffin-embedded kidney tissue.

PEMP combines multichannel immunofluorescence (e.g., nephrin/podocin, synaptopodin/integrin α3) with structured illumination microscopy to acquire high-resolution images. A software—and AI-assisted pipeline developed at NIPOKA GmbH performs fully automated FSD quantification, reducing human bias and enabling robust comparison across samples. The only manual steps are IF staining and physical slide loading, making PEMP well-suited for research and diagnostic laboratories.

We applied PEMP in a wide range of settings. In experimental nephrotoxic serum (NTS) models, PEMP detected a significant reduction in FSD as early as 24 hours post-injury, well before the onset of measurable proteinuria. In a real-world feasibility study involving over 80 human kidney biopsies across various kidney diseases, FSD values correlated with functional parameters and provided added morphometric insights compared to EM. Importantly, PEMP also captured physiological changes: in a murine aging cohort, we observed a progressive, age-dependent decline in FSD and increased glomerular diameter, highlighting the method's sensitivity to structural changes beyond disease.

Thus, PEMP provides a robust, scalable, reproducible platform for assessing podocyte structure in preclinical and clinical settings. Its compatibility with routine histological sections, high throughput, and minimal user input establishes PEMP as a next-generation tool for glomerular pathology. The method's applicability in early disease detection, longitudinal monitoring, and aging research underscores its potential for widespread implementation in translational nephrology.

Keywords：Super-resolution microscopy, podocyte foot process, ultrastructure, glomerular filtration barrier, automated image analysis, kidney aging, proteinuria, digital pathology, glomerular disease

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250703

Enhancing Caveolin-1 Expression with DIC: A Novel Strategy for Promoting TGFβR1 Degradation in chronic kidney disease

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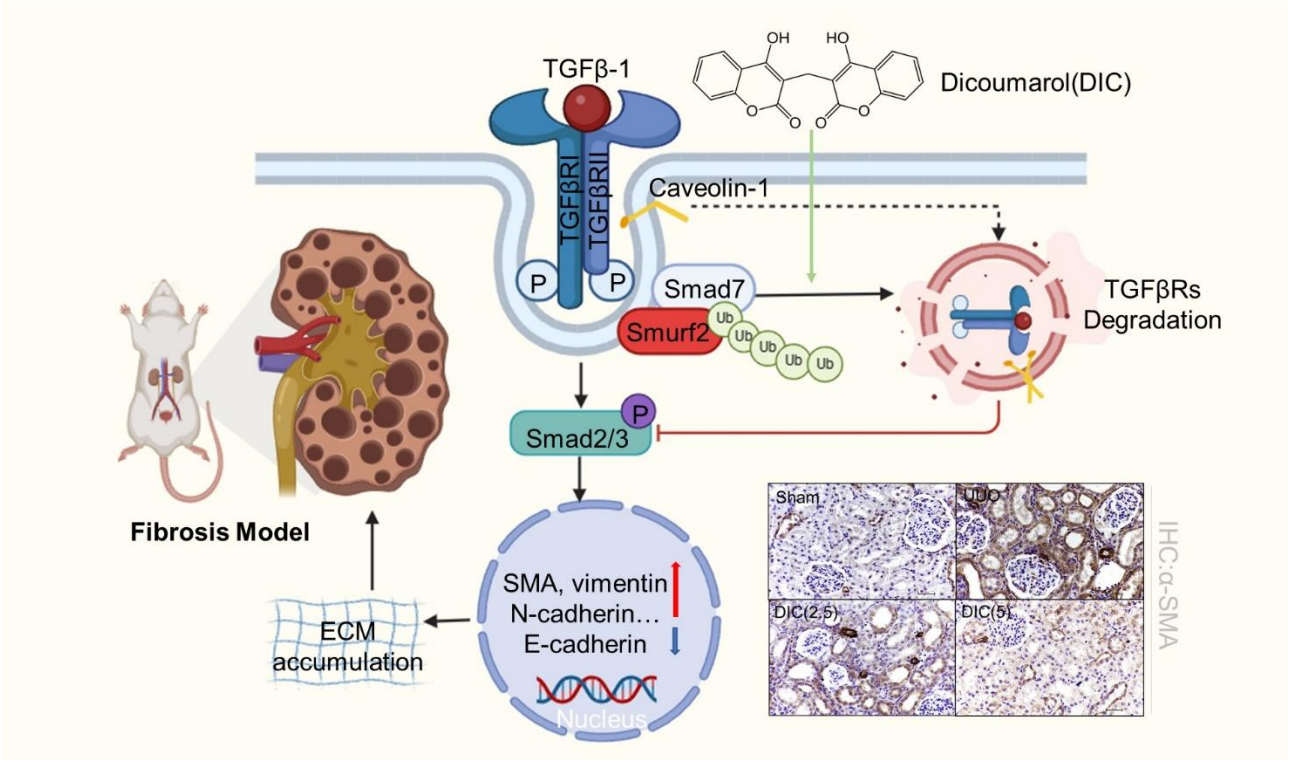
Abstract
Background: Kidney fibrosis, the inevitable terminal manifestation of chronic kidney disease (CKD), stems from profound cellular dysregulation and pathological extracellular matrix (ECM) deposition, driving irreversible organ failure. Despite its causal role in CKD progression, targeting fibrosis remains a critical unresolved challenge, with no clinically approved anti-fibrotic therapies currently available. Caveolin-1 (CAV1), a master regulator of membrane receptor trafficking including TGFβRs, emerges as a promising antifibrotic target by modulating epithelial-mesenchymal transition (EMT). We aimed to explore dicoumarol (DIC)'s attenuates kidney fibrosis via caveolin-1-dependent suppression of EMT, revealing its therapeutic mechanism.
Method: Unilateral ureteral obstruction (UUO) or 45-min ischemia-reperfusion (IR) injury was surgically induced in mice. Mice received daily intragastric DIC (1.25, 2.5, 5 mg/kg) while the sham groups received 0.5% CMC-Na. Tissues were analyzed on day 14. In vitro, TGF-β1-stimulated HK-2 and NRK-52E cells were assessed for fibrotic/EMT markers (fibronectin, α-SMA, vimentin, N-cadherin, E-cadherin) via WB and qPCR. TGFβR-CAV1 co-localization and interaction was examined by immunofluorescence (IF) and co-IP. Compound binding to CAV1 was evaluated by thermal shift assay (TSA), with binding domains mapped using CAV1 domain-deletion cell lines.
Result: DIC administration ameliorated renal fibrosis in UUO and IR models, attenuating tubular damage and collagen deposition. In vitro, DIC counteracted TGFFβ-1-induced morphological alterations and reversed EMT marker dysregulation (SMA↑, E-cadherin↓). Mechanistically, DIC enhanced TGFβR-CAV1 co-localization without inhibiting kinase activity. TSA confirmed direct DIC-CAV1 binding, which was abolished upon specific domain deletion, definitively mapping the interaction site. These findings nominate CAV1 targeting as DIC's novel antifibrotic mechanism.
Conclusion: We identify CAV1 targeting as a novel therapeutic axis against chronic kidney disease progression. DIC directly binds CAV1, promotes TGFβ receptor endocytosis, and constrains TGF-β signaling, thereby attenuating EMT. These findings nominate DIC as a promising antifibrotic candidate.

Keywords：Kidney fibrosis; Caveolin-1; Transforming growth factor β receptor I; Dicoumarol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Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250250

PRIP Deficiency Promotes YAP Nuclear Translocation, Thereby Enhancing Renal Fibrosi

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Abstract

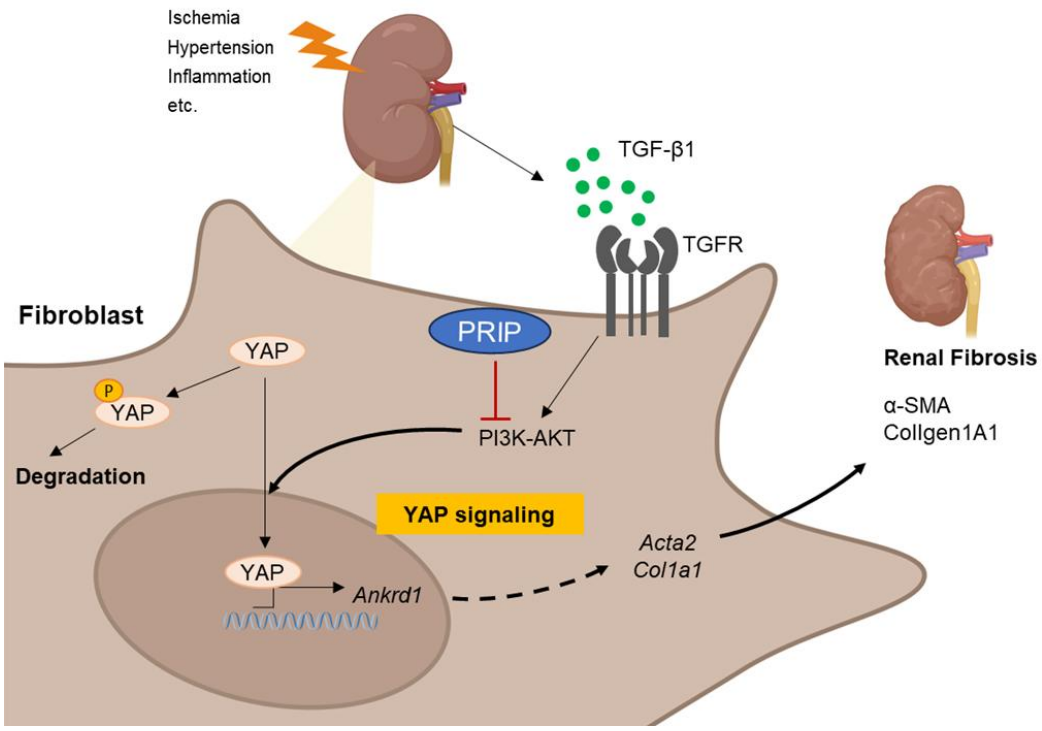
Introduction: Chronic kidney disease (CKD) is a significant global public health concern. Renal fibrosis is a prevalent pathological feature of CKD and a primary cause of end-stage renal failure. Mitigating renal fibrosis can effectively slow CKD progression. Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ), which are downstream effectors regulated by upstream kinases of the Hippo pathway, have emerged as critical modulators of transforming growth factor-beta (TGF-β) signaling in renal fibrosis. Phospholipase C-related catalytically inactive protein (PRIP) inhibits PI3K/AKT signaling, which is involved in numerous cellular processes. Given that the PI3K/AKT signaling pathway serves as a downstream effector of TGF-β, contributing to the progression of renal fibrosis, we hypothesized that PRIP may play a role in TGF-β-mediated, YAP/TAZ-regulated renal fibrosis development. Therefore, in this study, we aimed to investigate the role of PRIP in renal fibrogenesis.

Methods: To elucidate the role of PRIP in CKD progression, we conducted a comparative study between wild-type (WT) and Prip-knockout (KO) mice. The mice were treated with a 1.4 mg/kg/d peritoneal injection of angiotensin II to induce renal fibrosis in vivo. Additionally, we treated mouse embryonic fibroblasts (MEFs) derived from WT and Prip-KO mice with TGF-β1 to investigate the role of PRIP in fibroblast activation in vitro.

Results: Compared to WT mice, angiotensin II-injected Prip-KO mice exhibited increased collagen deposition in kidney tissue and higher alpha-smooth muscle actin (α-SMA) expression. In vitro experiments revealed that treating MEFs with TGF-β1 significantly suppressed PRIP1 expression. PRIP deficiency resulted in the upregulation of fibrosis-related markers, such as collagen 1A1 and α-SMA, in response to TGF-β1 stimulation. A scratch assay showed that the width of the scratch closed more quickly in Prip-KO MEFs than in WT MEFs, suggesting that PRIP deficiency promotes cell migration. Furthermore, enhanced activation of the PI3K/AKT signaling pathway was observed in Prip-KO MEFs. This facilitated MST2 phosphorylation at threonine 117, leading to Hippo pathway suppression. Consequently, YAP phosphorylation at serine 127 was inhibited, enabling YAP to translocate into the nucleus and promote transcription of the target gene Ankrd1. This resulted in more severe tissue fibrosis in Prip-KO MEFs.

Conclusion: PRIP deficiency exacerbates renal fibrosis by inducing nuclear translocation of YAP via PI3K/AKT activation. Therefore, a drug that enhances PRIP expression could be an effective new therapeutic approach for CKD.

Keywords： Chronic kidney disease (CKD), Renal fibrosis, YAP, PI3K/AKT signaling,Phospholipase C-related catalytically inactive protein (PRIP)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Col1a1
Renal Fibrosis
α-SMA
Collgen1A1

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250156

Tubular Extracellular Vesicles Mediate Vascular Calcification in Chronic Kidney Disease via Complement C3

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Abstract

Introduction

Chronic kidney disease (CKD) often leads to vascular calcification (VC), a severe complication recognized as a major cardiovascular risk factor. The molecular mechanisms underlying CKD-associated VC remain unclear. This study investigates the role of kidney-derived extracellular vesicles (EVs) in mediating CKD-related VC through the transport of complement component C3.

Methods

A CKD-VC mouse model was established using adenine combined with a high-phosphate diet. VC was assessed via VonKossa staining in CKD-VC mice treated with GW4869 (an exosome inhibitor), renal EVs, or C3aR inhibitor. Tubular EV trafficking was visualized in vascular walls using immunofluorescence in Tubular EV-tracing mice(Slc34a1 Cre/+;CD63-PAGFP fl/+ mice). Complement activation and localization in renal tubules were evaluated in CKD-VC mice via Western blot (WB), PCR, and immunofluorescence. EVs isolated from renal tissues and plasma were analyzed for C3 and tubular markers by WB. Plasma C3 levels in EVs, EV-depleted plasma, and total plasma were quantified via ELISA. Single-molecule imaging(ONI) and nanoflow cytometry determined the C3 distribution in renal and plasma EVs. Tubular-specific C3 knockdown mice was achieved using adeno-associated virus (AAV) to assess VC. In vitro, vascular smooth muscle cells (VSMCs) treated with high-phosphate were treated with tubular EVs or the C3aR inhibitor SB290157, and then osteogenic differentiation markers, C3aR, and pathway proteins were analyzed by PCR and WB, with calcification visualized via Alizarin Red staining. Plasma EVs from 30 CKD patients with VC and healthy controls were assayed for C3.

Results

Renal EVs exacerbated VC in CKD mice, while GW4869 attenuated calcification. Proteomics revealed high C3 expression in renal EVs. CKD-VC mice exhibited tubular complement activation and EV-mediated C3 secretion into circulation. Plasma EVs from CKD patients showed significantly elevated C3 levels compared to controls. Immunofluorescence confirmed uptake of tubular EVs by calcified vascular walls. In vitro, tubular EVs enhanced VSMC osteogenic differentiation and upregulated C3aR, mimicking C3a effects, while C3aR inhibition reversed these outcomes. Tubular C3 knockdown in vivo reduced VC severity. Clinically, plasma EV C3 levels correlated positively with abdominal aortic calcification scores in CKD-VC patients.

Conclusion

This study demonstrates that tubule-derived EVs mediate vascular smooth muscle osteogenic transdifferentiation and CKD-related VC via C3 transport. Targeting EV-C3 signaling may represent a novel therapeutic strategy for CKD-associated vascular calcification.

Keywords：CKD; Vascular calcification; Complement C3

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250623

CONFIDENCE Asia: Effect of simultaneous initiation of finerenone and empagliflozin on urinary albumin-to-creatinine ratio in Asian participants from the CONFIDENCE trial

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Abstract

Background and aims: Treatment benefits of simultaneous initiation and combination therapy with the nonsteroidal mineralocorticoid receptor antagonist finerenone and a sodium-glucose cotransporter 2 inhibitor (SGLT2i) in reducing urinary albumin-to-creatinine ratio (UACR) have been reported in the CONFIDENCE trial. We evaluated the benefits and safety profile of combination therapy with finerenone and an SGLT2i in participants enrolled in Asia.

Materials and methods: The CONFIDENCE trial enrolled adults with chronic kidney disease and type 2 diabetes with a UACR of ≥100 to <5000 mg/g and on a renin-angiotensin system inhibitor. Participants were randomized 1:1:1 to once-daily finerenone (10 or 20 mg) plus empagliflozin (10 mg), finerenone (10 or 20 mg) plus placebo, or empagliflozin (10 mg) plus placebo. In a subgroup analysis, treatment effects on the primary endpoint of relative change in UACR from baseline at day 180 were assessed for Asian participants.

Results: In CONFIDENCE, among 360 participants (45%) enrolled from Asia, change in UACR from baseline (95% CI) at day 180 with combination therapy was −30% (−44%, −11%) vs finerenone alone and −34% (−47%, −16%) vs empagliflozin alone; Table). The proportion of Asian participants with any treatment-emergent hyperkalaemia adverse events (AEs) was 10.7% for those receiving combination therapy, 13.8% for finerenone alone, and 4.8% for empagliflozin alone. No treatment-emergent hyperkalaemia AEs led to hospitalization, permanent discontinuation of study drug, or death. These findings are consistent with those for the overall study population.

Conclusion: Simultaneous initiation of finerenone and an SGLT2i was effective and well-tolerated among the nearly half of participants in CONFIDENCE who were enrolled from Asia.

This abstract was also submitted for the European Association for the Study of Diabetes (EASD) congress 2025. By submitting the abstract to APCN x TSN 2025, abstract authors declare that re-submitting the abstract is permitted by the organizers of the previous meeting.

Keywords：Finerenone, CONFIDENCE trial

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250341

Development of a Modified Renal Function Assessment Using Calf Circumference as a Proxy for Muscle Mass in the Elderly

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Abstract

Introduction:

Serum creatinine (sCr)-based estimated glomerular filtration rate (eGFRcr) often overestimates renal function in elderly patients with reduced muscle mass. We aimed to develop a modified eGFRcr equation incorporating calf circumference measurement to reduce overestimation.

Methods:

This multicenter study was conducted at four hospitals in Japan between November 2023 and May 2025. Hospitalized patients aged ≥60 years who were capable of 24-hour urine collection and had a sCr level <2.0 mg/dl were enrolled. Calf circumference was measured at the widest part of the non-dominant leg. In addition, the maximum circumference of the non-dominant calf was assessed using the finger-ring test, which compares the calf size to the ring formed by the patient's own thumb and index finger. Based on this comparison, patients were categorized into three groups: smaller, just fit, and larger. Twenty-four-hour creatinine clearance (24hrCCr) was used as the reference standard for renal function. Three predictive models for 24hrCCr were developed using linear regression analysis: (1) Model 1, which included eGFRcr and calf circumference as a continuous variable; (2) Model 2, which included eGFRcr and calf circumference categorized by sex-specific cutoff values; and (3) Model 3, which incorporated eGFRcr and finger-ring test results. The predictive performance of these models for 24hrCCr was comparatively evaluated.

Results:

The mean age of 80 eligible patients (30 males, 50 females) was 79. Mean sCr level was 0.94 mg/dl, mean eGFRcr was 56.3 ml/min/1.73 m², and mean 24hrCCr was 45.74 ml/min/1.73 m². Mean calf circumference was 30.8cm, with 53 patients classified as "smaller" and 27 as "just fit" or "larger" on the finger-ring test. In 24hrCCr prediction, the area under the receiver operating characteristic curve (AUC) of Model 3 was 0.906, that of Model 1 was AUC 0.900, and that of Model 2 was AUC 0.899. Additionally, we evaluated the ability to identify cases with a 24hrCCr of less than 45 ml/min/1.73 m². Among 38 cases with 24hrCCr of ≤ 45 ml/min/1.73 m², only 24 patients were identified using eGFRcr. In contrast, Model 1, Model 2, and Model 3 identified 32, 31, and 32 cases, respectively.

Conclusion:

Incorporating calf circumference into the GFR estimation may help improve its accuracy and reduce the risk of underestimating kidney impairment in elderly patients.

Keywords：eGFRcr, 24hrCCr, muscle mass, calf circumference, finger-ring test

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20251139

Maternal Insulin Therapy and Its Impact on Immune Regulation in Infants of Mothers with Kidney Disease and Gestational Diabetes

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Abstract

Background

Gestational diabetes mellitus (GDM) is a metabolic disorder that can influence fetal immune development, particularly in infants born to mothers with pre-existing kidney disease. Given the intricate relationship between metabolic dysfunction, inflammation, and renal health, this study explores how maternal insulin therapy modulates immune responses in utero. Specifically, we investigated the effect of insulin on regulatory T cell development, proinflammatory cytokine production, and immune gene expression in the cord blood of infants born to mothers with kidney disease and GDM.

Methods

Cord blood mononuclear cells (CBMCs) were isolated from 124 infants born to mothers with kidney disease and GDM and 48 infants born to obese mothers without GDM. Flow cytometry was used to quantify CD4+CD25+FOXP3+ regulatory T cells, both ex vivo and after in vitro insulin stimulation. Reverse transcription polymerase chain reaction (RT-PCR) was performed to analyze mRNA expression of immune-related genes, including FOXP3, NFATc2, STIM1, IL-10, IFN-γ, TNF-α, and TGF-β. Immune markers were correlated with levels of anti-GAD65 autoantibodies, a key indicator of autoimmune risk.

Results

Infants of mothers with kidney disease and GDM exhibited a significantly higher percentage of FOXP3+ regulatory T cells within the CD4+CD25(high) population compared to those born to obese mothers without GDM. In vitro insulin stimulation further enhanced FOXP3+ cell proportions and upregulated FOXP3, NFATc2, STIM1, IL-10, and TGF-β expression, a response exclusive to infants of mothers with kidney disease and GDM. Additionally, infants carrying the PTPN22 allele demonstrated reduced activation of STIM1 and NFATc2 post-insulin stimulation. TNF-α and IL-10 levels were elevated, correlating with an increased frequency of CD4+CD25+ T cells and higher anti-GAD65 autoantibody levels.

Conclusion

Maternal insulin therapy enhances regulatory T cells and modulates inflammation in infants of mothers with kidney disease and GDM, potentially improving renal resilience and reducing autoimmune risk.

Keywords：Maternal insulin therapy, kidney disease, Gestational diabetes mellitus, Cord blood mononuclear cells

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20251104

Proteomics Integrated with Bidirectional Mendelian Randomization Prioritizes Plasma Proteins for Influencing and Predicting Kidney Function

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Abstract

Introduction:

Early identification of causal factors for kidney function decline is crucial for prevention and intervention, as chronic kidney disease (CKD) affects millions worldwide. However, the underlying molecular mechanisms of CKD are not fully understood. This study utilized bidirectional Mendelian randomization (MR) to investigate potential causal links between circulating plasma proteins and kidney function.

Methods:

We analyzed data on 2,920 plasma proteins from 46,451 UK Biobank participants with complete phenotypes, including demographic data and measurements of creatinine and cystatin C. Kidney function was assessed using estimated glomerular filtration rate (eGFR), calculated with the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation based on both serum creatinine and cystatin C. CKD was defined as eGFR < 60 mL/min/1.73 m². Association analyses were conducted to identify proteins associated with eGFR levels and CKD status. Bidirectional two-sample MR and colocalization analyses were then applied to determine causal relationships. The ability to predict 5-year incident CKD by incorporating age and sex with forwardly causal proteins or with reversely causal proteins, was evaluated using Harrell's C-index and net reclassification index (NRI).

Results:

The median age of the study population at baseline was 58.0 years (interquartile range [IQR] 50.0–64.0). Of these, 3% had CKD, with a median age of 65.0 years (IQR 61.0–68.0). We identified 855 plasma proteins significantly associated with both eGFR and CKD. Bidirectional MR and colocalization provided evidence of potential causal effects between proteins and eGFR. The bidirectional interactions between 52 proteins and eGFR demonstrated the complex interplay between plasma proteins and kidney function. We found 7 forwardly causal proteins with effects on eGFR, and another 265 biomarker proteins where eGFR exerted a unidirectional reverse effect. The clinical relevance of the top unidirectional proteins was assessed (Table 1). Compared with demographic varia-

bles (Harrell's C-index 0.692), incorporating 7 forwardly causal proteins (0.723) or 10 biomarkers influenced unidirectionally by eGFR (0.798) significantly improved the 5-year prediction of incident CKD. Additionally, both models demonstrated notable improvements in risk reclassification (NRI 0.183 and 0.385, respectively).

Conclusions:

This study links plasma proteins to kidney function, identifying potential mediators and prioritizing biomarkers for kidney health prediction. Integrating proteomics with MR analyses enhances our understanding of CKD pathophysiology. Further investigation is warranted to assess the prognostic value of these proteins.

Keywords：proteomics, estimated glomerular filtration rate, Mendelian randomization

Table 1. Prediction performance of kidney function-related plasma proteins for 5-year incident CKD.

Feature in Model[a]	Harrell's C-index (95% CI)	NRI (95% CI)[b]
Demographics	0.692 (0.674–0.710)	Reference
Demographics+7 Proteins	0.723 (0.703–0.742)	0.183 (0.139–0.221)**
Demographics+10 Biomarkers	0.798 (0.783–0.814)	0.385 (0.336–0.413)**

[a] Demographics: Age, Sex; 7 Proteins: forwardly causal proteins affecting eGFR; 10 Biomarkers: reversely causal proteins influenced unidirectionally by eGFR.

[b] Compared to the Demographics model.**: $p < 0.001$

Abbreviations: C-index, concordance index; CI, confidence interval; NRI, net reclassification improvement.

Oral Communications：Chronic Kidney Disease (CKD)
Abstract Submission No.：APCN20250432

Oral Semaglutide Use In The Real World, Multi-Centre Experience On Renal Outcomes Of Diabetic Kidney Disease In Malaysia (Sword Trial) - An Interim Analysis

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Abstract

INTRODUCTION

Diabetic kidney disease (DKD) is a common leading cause to end-stage kidney disease (ESKD). Semaglutide has been shown to improve glycaemic control and reduce cardiovascular events in type 2 diabetes (T2DM) patients. This study aims to evaluate its real-world renal outcomes, safety and effectiveness in DKD patients.

METHODOLOGY

This was a prospective, observational study involving 11 hospitals in Malaysia. Adults (≥18 years) with T2DM and DKD, prescribed oral Semaglutide for at least 6 months were recruited. Those who were non-diabetic, known ESKD, had history of GLP-1Ra intolerance or hypersensitivity, or significant co-morbidities that may confound renal outcomes were excluded. Patient clinical status and biochemical results were collected until 30/04/2025 and analysed using SPSS v29.0.2.

RESULTS

Total 366 patients were analysed, with 48.1% male, 57.4% Malay, mean age 57.5±12.4 years old and mean T2DM duration of 14.8±10.0 years. They had pre-existing ASCVD (23.5%) and heart failure (3.6%). At baseline, the median urine albumin-creatinine ratio (UACR) was 9.40 (interquartile range, 1.95 to 54.65) mg/mmol and mean eGFR was 80.1±37.4 ml/min/1.72m2. About 37.5% of patients fulfilled the eGFR and UACR inclusion criteria of FLOW trial. For anti-proteinuric therapy, 74.0% on RAAS blockade (81.6% on optimal dose), 80.6% on SGLT-2 inhibitors and 4.4% on Finerenone. The mean Semaglutide use was 396.8±166.2 days, with 78.7% of patients on 14mg

once-daily dosing. Discontinuation of Semaglutide occurred in 14.8% of patients during the follow-up, due to gastrointestinal side effects (72.2%), switched to subcutaneous GLP-1a formulation (18.5%) or defaulted follow-up (9.3%).

For primary outcomes, oral Semaglutide had significant median UACR reduction by 45.2% (P=0.003) and stabilised eGFR trend up to 12 months (P=0.457) from initiation. For secondary outcomes at 12 months, it significantly reduced mean weight by 5.2±2.5kg (P<0.001), BMI by 5.7% (P<0.001), reduced systolic blood pressure (SBP) by 3.4mmHg (P=0.018), improved serum triglyceride by 12.5% (P=0.008), and reduced HbA1c by 5.0% (P=0.003), despite no significant change in daily insulin requirement (P=0.124). For safety profile, it was well tolerated with minimal side effects, including nausea or vomiting (18.3%), hypoglycaemia (2.2%), diarrhoea (1.9%), constipation (1.9%), abdominal pain (1.4%) and heartburn (0.5%).

CONCLUSIONS
In this interim analysis, oral Semaglutide demonstrated significant albuminuria reduction and eGFR stabilisation at 12 months. It also showed improvements in weight and metabolic, with a favourable safety profile in the real-world settings.

Keywords：Semaglutide, SWORD, Chronic Kidney Disease, Diabetic Kidney Disease, Albuminuria reduction

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Dapagliflozin Efficacy and Safety in Chronic Kidney Disease Stage 4–5: an Investigator-Led, Randomized, Open-Label Trial

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Abstract

Background:

While dapagliflozin improves renal and cardiovascular outcomes in patients with chronic kidney disease (CKD), data are lacking for those with estimated glomerular filtration rate (eGFR) <20 ml/min/1.73 m2.

Methods:

This investigator-led, randomized, open-label trial in Taiwan aimed to assess dapagliflozin efficacy and safety in patients with CKD stage 4–5. 180 patients with eGFR 10–30 ml/min/1.73 m2 and eGFR decline >2.5 ml/min/1.73 m2/yr were randomized 2:1 to dapagliflozin (n=120) plus integrated CKD care, or integrated CKD care alone (control; n=60). The primary endpoint was the difference in total eGFR slope. Hierarchical secondary composite outcomes included a renal outcome, a renal and heart failure outcome, and a renal and cardiovascular outcome.

Results:

The primary and all secondary endpoints were met. Over a median 1.62 years (84 weeks) follow-up, total eGFR slopes (ml/min/1.73 m2/yr) were −2.37 (95% CI −2.96, −1.79) and −3.58 (95% CI −4.58, −2.58) in the dapagliflozin and control groups, respectively; the primary outcome of eGFR slope difference was 1.21 (95% CI 0.07, 2.35; p=0.019). For hierarchical secondary outcomes, significantly smaller proportions of patients in the dapagliflozin versus control group had a renal composite outcome (HR 0.42 [95% CI 0.23, 0.77]; p=0.006], renal and heart failure outcome (HR 0.46 [95% CI 0.25, 0.82; p=0.008], or renal and cardiovascular outcome (HR 0.53 [95% CI 0.30, 0.94]; p=0.030). Adverse event and CKD complication rates were similar in both groups.

Conclusion:

Overall, Dapagliflozin treatment led to a significantly slower eGFR decline, as assessed by the total eGFR slopes, and better renal and cardiovascular outcomes compared with control in patients with CKD stage 4–5. The safety profile of dapagliflozin was consistent with the control group.

Keywords：chronic kidney disease, sodium-glucose co-transporter 2 inhibitor