



Nominees for APSN Young Nephrologist Awards

December 5, 2025 (Friday) 13:30~15:00

Venue : Room 8 (602)

Chair(s)

13:30-13:39	Endothelial Ferroptosis as a Causal Driver of Diabetic Nephropathy: Insights from Multi-omics and Mendelian Randomization APCN20250120	Lei Chen Department of Nephrology, West China Hospital, Sichuan University
13:39-13:48	The Organelle Tethering Protein PDZD8 Regulates Endolysosomal Maturation and TLR9–NF-κB Signaling in Cisplatin-Induced Acute Kidney Injury APCN20250331	Yuto Takenaka Division of Chronic Kidney Disease Pathophysiology, Graduate School of Medicine, The University of Tokyo
13:48-13:57	AI-Based Spatial Transcriptomic Modeling Identifies Key Immune-Fibrotic Interactions Underlying Glomerular Crescent Formation in Autoimmune Nephritis APCN20250937	Rini Winarti Department of Biology, Yogyakarta State University
13:57-14:06	Predicting IgA Nephropathy Progression Through CD8+ T-Cell Chromatin Accessibility Analysis APCN20250280	Soojin Lee Department of Internal Medicine, Uijeongbu Eulji University Medical Center, Uijeongbu
14:06-14:15	Activation of Discoidin Domain-containing Receptor 2 in Pericytes Plays A Crucial Role in The AKI-to-CKD Continuum APCN20250083	Hui-Chiun Tseng Graduate Institute of Physiology, College of Medicine, National Taiwan University
14:15-14:24	The Clinical Utility of Point-of-Care Ultrasound Measurements of Thigh Muscle and Adipose Tissue Thickness for Assessing Body Composition, Frailty, and Predicting Clinical Outcomes in Patients Undergoing Peritoneal Dialysis APCN20250874	Chan Chun Kau Gordon Division of Nephrology, Department of Medicine & Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong





14:24-14:33	Survival Advantage of Peritoneal Dialysis Over Hemodialysis During the Coronavirus Disease 2019 Pandemic: A Prospective Cohort Study APCN20250188	Tz-Heng Chen Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital
14:33-14:42	Early Dynamic Identification of Glomerular Hyperfiltration is Associated with Chronic Kidney Disease in Type 2 Diabetes APCN20250198	Qinbo Yang Department of Nephrology, West China Hospital, Sichuan University
14:42-14:51	Deep Learning Integration of Cell-Free DNA Methylation and Clinical Trajectories to Predict Acute Rejection in Pediatric Kidney Transplantation APCN20250906	Rifaldy Fajar AI-BioMedicine Research Group, IMCDS-BioMed Research Foundation
14:51-15:00	The Involvement of Interstitial Palladin Expression in Patients with Chronic Kidney Diseases APCN20250411	Naoki Yamamoto Department of Nephrology and Rheumatology, Kanazawa University



Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250120

Endothelial Ferroptosis as a Causal Driver of Diabetic Nephropathy: Insights from Multi-omics and Mendelian Randomization

Lei Chen¹; Wanxin Tang¹

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Abstract

Diabetic nephropathy (DN) has emerged as a predominant contributor to end-stage renal disease globally, representing a substantial and escalating public health challenge. Recent studies have highlighted ferroptosis as a potentially critical factor in DN pathogenesis. Despite growing evidence linking ferroptosis to DN progression, the causal mechanisms remain poorly understood. Moreover, the precise involvement of ferroptosis-related genes in glomerular cell dysfunction during DN development warrants further investigation.

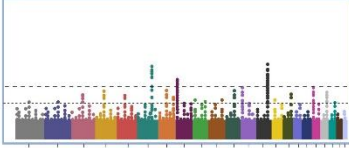
We first retrieved 933 ferroptosis-related genes from the FerrDb database. Using cis-expression quantitative trait loci data from the eQTLGen consortium, we performed Mendelian randomization to assess the causal effects of these genes on type 2 diabetes. Genes demonstrating significant associations were further evaluated for their causal roles in DN. To ensure robustness, we validated key candidate genes using independent datasets from multiple sources. Finally, we integrated single-cell RNA sequencing (scRNA-seq) and single-cell ATAC sequencing (scATAC-seq) data from DN kidney tissues to explore cell-type-specific expression patterns, differential expression across glomerular cell subtypes, and potential transcriptional regulators of these genes.

Our analysis revealed significant causal associations of CDKN1A, CEBPG, and EPAS1 with DN. Notably, CDKN1A was identified as a potential risk factor for DN, whereas CEBPG and EPAS1 exhibited protective effects. Multi-omics integration demonstrated pronounced activation of ferroptosis signaling in endothelial cells, which was closely linked to inflammatory cell infiltration. CDKN1A, CEBPG, and EPAS1 were predominantly enriched in endothelial cells and displayed elevated chromatin accessibility, implicating their pivotal roles in endothelial ferroptosis and DN progression. Furthermore, transcription factor binding analysis suggested that FOS, FOSL2, and BHLHE40 may serve as upstream regulators of CDKN1A, potentially governing its expression and downstream pathological effects.

Our study highlights endothelial ferroptosis as a potential causal driver in DN pathogenesis. Through integrative Mendelian randomization and multi-omics approaches, we identified CDKN1A as a putative risk factor for DN, while CEBPG and EPAS1 emerged as protective genes. These candidate genes demonstrate endothelial-specific enrichment with heightened chromatin accessibility, implicating their roles in transcriptional regulation and ferroptosis signaling pathways. These findings provide mechanistic insights into endothelial dysfunction in DN and highlight promising molecular targets for therapeutic intervention.

Keywords : Diabetic nephropathy; endothelial cell; Ferroptosis; Mendelian randomization; Multi-omics

Genome-wide Association Study



Ferropotosis

933 genes

◦ eQTLGen



Type 2 diabetes

Precondition



Diabetic nephropathy

Discovery

◦ FinnGen R11

Validation

◦ ukb-a-75
 ◦ ukb-b-13806
 ◦ GCST90038634
 ◦ GCST90029024
 ◦ GCST90018926
 ◦ GCST90013892
 ◦ GCST010118
 ◦ GCST006867

Discovery

◦ FinnGen R11

Validation

◦ GCST90435706
 ◦ GCST90018832
 ◦ UKB

Instrumental variable selection

- $P < 5 \times 10^{-8}$
- Clumping: kb = 10,000, $r^2 = 0.001$
- ± 1 Mb of the transcription start sites
- F statistics > 10

Methods

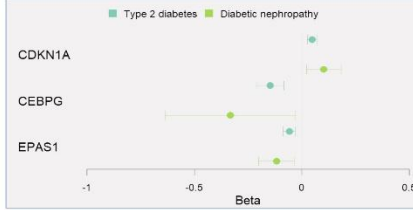
- Inverse variance weighted
- Wald ratio
- MR Egger
- Weighted median
- Simple mode
- Weighted mode

Quality control

- Not associated with cofounders
- Horizontal pleiotropy test
- Heterogeneity test
- Leave-one-out test

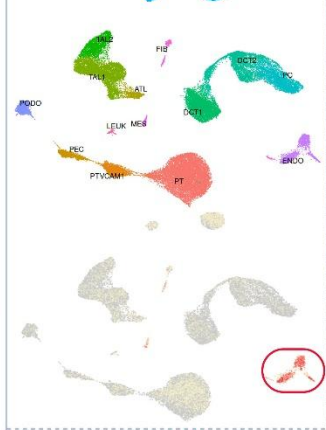
Mendelian randomization (MR)

- Drug target MR
- Tissue-specific MR
- Mediation MR
- Phenome-wide MR



Transcriptomic Validation

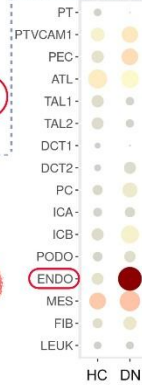
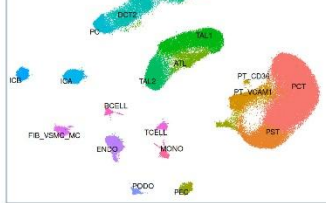
scRNA



10 samples
(5 vs 5)

- GSE131882
- GSE151302
- GSE195460

scATAC



Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250331

The Organelle Tethering Protein PDZD8 Regulates Endolysosomal Maturation and TLR9–NF- κ B Signaling in Cisplatin-Induced Acute Kidney Injury

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Abstract

Introduction:

Membrane contact sites (MCSs) between the endoplasmic reticulum (ER) and endolysosomes have emerged as key regulators of organelle communication and intracellular signaling. PDZD8 is an ER-resident tethering protein that facilitates endolysosomal maturation. While endolysosomes serve as critical platforms for Toll-like receptor 9 (TLR9)-mediated NF- κ B activation in innate immunity, the role of ER–endolysosome interactions in kidney inflammation remains largely unknown. In cisplatin-induced acute kidney injury (AKI), inflammation is a major contributor to tissue damage, yet how organelle crosstalk influences this process is poorly understood.

Methods:

We investigated the role of PDZD8 in cisplatin-induced AKI using *Pdzd8* knockout (KO) mice. Kidney injury was evaluated 48 hours after cisplatin injection by histological scoring and serum creatinine levels. Kidney inflammation was assessed by examining NF- κ B activation and the expression of downstream cytokines using immunoblotting and quantitative PCR. Based on the in vivo findings, we focused on proximal tubular cells and used human HK-2 cells, in which PDZD8 was silenced by siRNA transfection and subsequently treated with cisplatin. Endolysosomal function was evaluated by measuring acidification and cathepsin B activity. TLR9 trafficking was assessed through immunofluorescence microscopy and immunoblotting of isolated endolysosomal fractions.

Results:

Compared to wild-type mice, *Pdzd8* KO mice exhibited reduced tubular injury and lower serum creatinine levels following cisplatin treatment. Proximal tubular NF- κ B activation and proinflammatory cytokine expression were also significantly attenuated. In HK-2 cells, PDZD8 knockdown suppressed NF- κ B phosphorylation and cytokine secretion while improving cell viability. Importantly, mitochondrial integrity and cytosolic mitochondrial DNA release were unchanged by PDZD8 knockdown, indicating that the extent of cisplatin-induced cellular damage was comparable regardless of PDZD8 status. These findings suggest that the anti-inflammatory effects observed with PDZD8 loss are not due to reduced injury severity but rather to disruption of ER–endolysosome signaling. Mechanistically, PDZD8 deficiency impaired endolysosomal acidification and cathepsin B activity, reduced TLR9 colocalization with LAMP1-positive compartments (mature endolysosomes), and suppressed downstream signaling through MyD88, a key adaptor protein in the TLR9 pathway. Pharmacological inhibition of endolysosomal acidification mimicked the effects of PDZD8 knockdown, further supporting the role of endolysosomal maturation in TLR9–NF- κ B

pathway activation.

Conclusion:

This study identifies PDZD8 as a critical regulator of TLR9-dependent inflammatory signaling through ER–endolysosome interactions in cisplatin-induced AKI. By maintaining endolysosomal maturation and TLR9 trafficking, PDZD8 facilitates NF- κ B activation and inflammatory responses. These findings highlight ER–endolysosome contact sites as potential therapeutic targets in inflammatory kidney diseases.

Keywords : PDZD8, TLR9, endolysosome, organelle contact sites, cisplatin, acute kidney injury, innate immune system

Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250937

AI-Based Spatial Transcriptomic Modeling Identifies Key Immune-Fibrotic Interactions Underlying Glomerular Crescent Formation in Autoimmune Nephritis

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Abstract

Introduction: Crescentic glomerulonephritis (GN) is a rapidly progressive form of autoimmune kidney disease characterized by severe glomerular injury, often leading to irreversible fibrosis and kidney failure. Although histological crescents are well recognized, the spatial relationships between immune cell infiltration and fibrotic signaling within crescents remain poorly defined. This study aimed to build an artificial intelligence (AI)-based model using spatial transcriptomic data to identify immune-epithelial interactions associated with fibrotic progression in crescentic GN.

Methods: We analyzed spatial transcriptomics data from the Gene Expression Omnibus (GEO), dataset GSE294965, which includes eight Xenium ST slides (32 biopsies from patients with crescentic GN and 6 healthy controls). Each spatial transcriptomic spot was represented as a node in a graph, with edges defined by physical distance and co-expression of ligand-receptor pairs. We applied a graph neural network (GNN) to classify each spot as “fibrotic-prone” or “non-fibrotic” based on expression of key fibrosis-related genes such as COL1A1, ACTA2, and FN1. Cell types (macrophages, PECs, mesangial cells) were annotated using a kidney-specific Bayesian deconvolution model. Transcriptomic fibrosis scores were normalized across slides, and graph input features included spatial coordinates, scaled gene expression vectors, and inferred ligand-receptor activation scores. Model interpretability was achieved using SHAP (SHapley Additive exPlanations) analysis to identify spatial signaling features most associated with fibrosis prediction. Cross-validation was performed using spatially stratified 5-fold evaluation.

Results: The GNN model achieved an area under the ROC curve (AUROC) of 0.79 [95% CI: 0.74–0.84], with a precision of 81.2% and F1-score of 0.77. The most influential ligand-receptor pairs in predicting fibrotic zones were CCL2-CCR2 (mean SHAP = 0.21), TGFB1-TGFBR2 (0.18), and JAG1-NOTCH2 (0.16). CD163-positive macrophages were found adjacent to PECs in 73.5% of fibrosis-prone crescent zones. MMP9 and IL1B were upregulated 2.6-fold in fibrotic areas ($p < 0.001$). The model correctly identified fibrosis-prone regions in 26 of 32 GN biopsies (81.3%), with consistent performance across ANCA-associated GN, lupus nephritis, and anti-GBM disease. Spatial distribution maps showed fibrosis-predictive zones clustered near the Bowman’s capsule interface, particularly in regions with disrupted endothelial gene signatures and elevated CXCL10 expression in adjacent leukocyte nodes. In high-scoring fibrotic clusters, SPP1, SERPINE1, and TNFRSF12A expression was increased, corresponding to areas of early PEC activation and glomerular tuft adhesion.

Conclusion: This study presents an AI-based spatial modeling approach that combines transcriptomic data and graph analysis to characterize fibrotic risk within glomerular crescents. The findings support spatial ligand-receptor interactions as potential targets in autoimmune glomerulonephritis.

Keywords : Spatial Transcriptomics, Crescentic Glomerulonephritis, Fibrosis Prediction, Graph Neural Network, Ligand-Receptor Interaction

Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250280

Predicting IgA Nephropathy Progression Through CD8⁺ T-Cell Chromatin Accessibility Analysis

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Abstract

Background: IgA nephropathy (IgAN) is a prevalent primary glomerulonephritis with progressive potential. Early identification of high-risk patients is critical, but current clinical and pathological markers are limited. This study aimed to identify epigenetic biomarkers in circulating CD8⁺ T cells that distinguish early-stage IgAN patients at risk of progression.

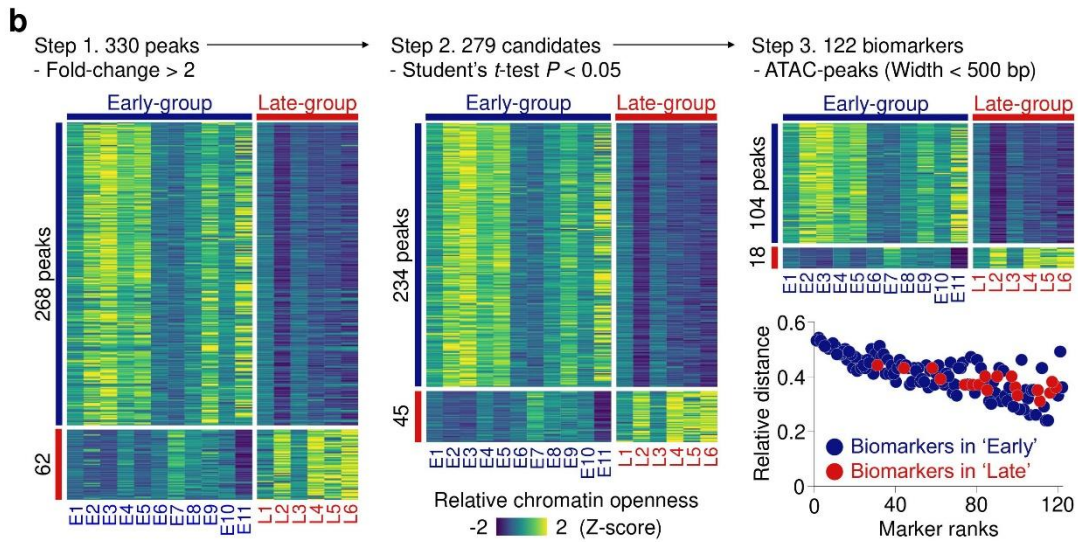
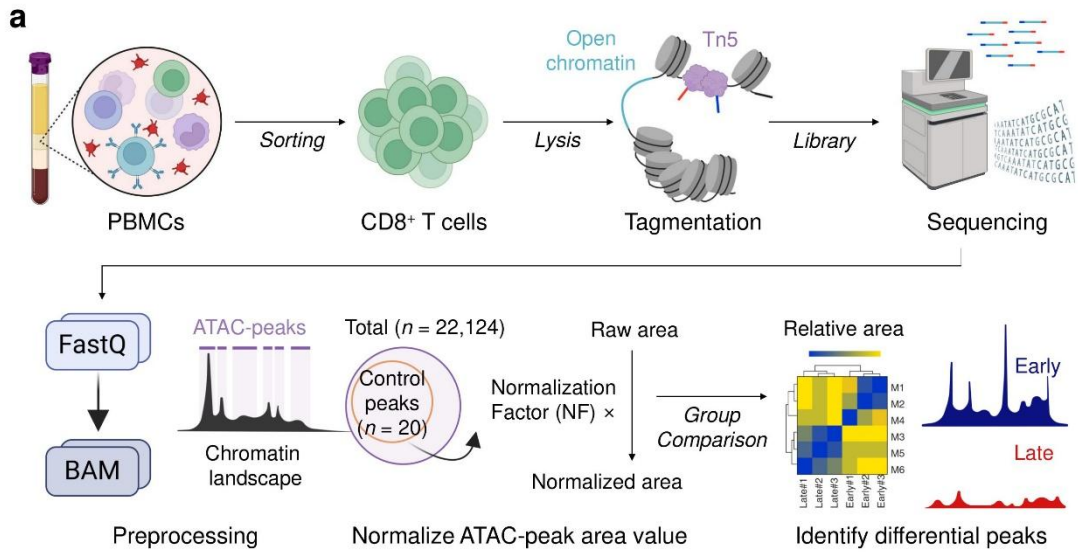
Methods: Seventeen biopsy-proven IgAN patients were stratified into early- and late-stage groups based on kidney function. CD8⁺ T cells were isolated and analyzed using assay for transposase-accessible chromatin sequencing (ATAC-Seq) to assess chromatin accessibility (Figure 1a). Differentially accessible regions (DARs) were identified, and selected biomarkers were validated using ATAC-qPCR.

Results: A total of 279 DARs were identified, with 122 peaks selected as stage-specific biomarkers. CD8⁺ T cells from early-stage group exhibited higher chromatin accessibility, and t-SNE showed clear separation between stages (Figure 1b). Deconvolution analysis revealed enrichment of naïve CD8⁺ T cells in early-stage and terminally differentiated effector memory CD8⁺ T cells in late-stage groups. Motif analysis uncovered distinct regulatory signatures: ETS1, LEF1, and RUNX2 in early-stage; EOMES, TBX21, and IRF4 in late-stage. Receiver operating characteristic (ROC) analysis showed strong discriminatory power of top biomarkers, enhanced by a composite weighted score. ATAC-qPCR confirmed the chromatin accessibility patterns observed in ATAC-Seq.

Conclusion: This study defines stage-specific chromatin landscapes in circulating CD8⁺ T cells of IgAN patients and identifies non-invasive epigenetic biomarkers for early risk stratification and personalized management.

Keywords : IgA Nephropathy, CD8⁺ T cells, chromatin accessibility, biomarkers, chronic kidney disease

Figure 1



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Abstract Submission No. : APCN20250083

Activation of Discoidin Domain-containing Receptor 2 in Pericytes Plays A Crucial Role in The AKI-to-CKD Continuum

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Abstract

Background and Aims

Acute kidney injury (AKI) is a critical risk factor for the development of chronic kidney disease (CKD), yet the underlying molecular mechanisms driving this transition remain poorly understood. Discoidin domain receptors (DDR2), particularly DDR2, are receptor tyrosine kinases that are activated by collagen within the extracellular matrix (ECM). Although DDR2 has been implicated in various fibrotic processes, its specific functional role in kidney pathology, especially within the context of AKI-to-CKD progression, remains insufficiently characterized. In this study, we aim to investigate the role of DDR2 in pericytes and its contribution to the AKI-to-CKD continuum.

Methods

This study assessed DDR2 expression in whole kidney tissues and isolated pericytes across the AKI-to-CKD continuum. In vivo, we employed a kidney pericyte-specific Ddr2 knockout mouse model to quantify DDR2 levels and the expression of fibrosis-associated genes and proteins following AKI. In vitro, NIH/3T3 cells were treated with collagen 1 to stimulate DDR2, and treated with WRG-28 to inhibit DDR2 activity, allowing measurement of subsequent changes in fibrosis-related gene and protein expression.

Results

Our findings indicate that DDR2 is predominantly expressed in pericytes, with its expression levels increasing in both whole kidney tissues and isolated pericytes during the AKI-to-CKD progression. In vitro experiments demonstrated that treatment with 200 µg/ml of collagen 1 activated fibrosis-related genes and proteins. Furthermore, the application of the DDR2 inhibitor WRG-28 effectively suppressed collagen 1-induced DDR2 activation and the expression of fibrosis-associated genes. In addition, WRG-28 also inhibited collagen 1-induced cell migration and proliferation.

Conclusion

DDR2 is expressed in pericytes and its expression is upregulated during the AKI-to-CKD continuum. In vivo, AKI induces DDR2 activation, leading to increased expression of pro-fibrotic genes in the kidney. In vitro, collagen 1 activates DDR2, promoting pro-fibrotic gene expression in pericytes. Inhibition of DDR2 ameliorates pericyte activity and collagen production. Therefore, regulating DDR2 activity may represent a crucial therapeutic strategy for preventing the progression from AKI to CKD.

Keywords : AKI-CKD continuum, DDR2, pericyte

Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250874

The clinical utility of point-of-care ultrasound measurements of thigh muscle and adipose tissue thickness for assessing body composition, frailty, and predicting clinical outcomes in patients undergoing peritoneal dialysis.

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Abstract

Method:

This single-center prospective study enrolled consecutive adult patients undergoing peritoneal dialysis (PD). Muscle thickness (MT) (combined rectus femoris and vastus intermedius thickness) and adipose thickness (AT) were measured using a handheld ultrasound device (Vscan Extend™, GE Healthcare), at the mid-point of anterior thigh. Body composition and nutritional status were assessed using bioimpedance spectroscopy (lean tissue index, adipose tissue index) and normalized protein nitrogen appearance (nPNA). Sarcopenia was defined by the Asian Working Group for Sarcopenia (AWGS) 2019 criteria. Frailty was evaluated by the Fried Phenotype (FP) and Clinical Frailty Scale (CFS). Low MT and AT were defined by values below first quartile. All patients were followed for one year. The primary outcomes were PD technique failure rate.

Result:

A total of 174 consecutive patients were recruited, including 98 men (56.3%), with a mean age of 65.0 ± 11.2 years.

MT showed a significant correlation with the bioimpedance-derived lean tissue index ($r = 0.23$, $p < 0.004$), and was also significantly associated with physical status measures (walking speed: $r = -0.31$, $p < 0.001$; CFS: $r = -0.31$, $p < 0.001$; FP: $r = -0.22$, $p = 0.006$). AT was similarly correlated with the adipose tissue index ($r = 0.40$, $p < 0.001$) and nutrition (nPNA: $r = -0.37$, $p < 0.001$). MT demonstrated good diagnostic accuracy for sarcopenia, with an area under the receiver operating characteristic curve of 0.79 (Figure 1A, $p < 0.001$). Using a height-adjusted cutoff of 24.79 cm, MT yielded a sensitivity of 72.5% and a specificity of 85.4%.

Over time, 14 patients died and 8 patients were converted to haemodialysis. The technique failure rate was highest among individuals with concomitant low adiposity and muscle wasting (Figure 1B; log-rank test, $p = 0.005$). After adjusting for confounding factors, concomitant low adiposity and muscle wasting were associated with a significantly increased risk of technique failure (adjusted hazard ratio [AHR] 11.7; 95% confidence interval [CI]: 1.51–90.76; $p = 0.01$). Other significant predictors in the model included: Serum albumin (AHR 0.79; 95% CI: 0.67–0.93; $p = 0.004$) and FP (AHR 2.12; 95% CI: 1.21–3.72; $p = 0.009$)

Conclusion:

Point-of-care thigh ultrasound yields essential measurements of muscle and fat thickness, reflecting body composition, physical condition, and nutritional status. It enables timely sarcopenia detection with reasonable sensitivity and specificity. Combined muscle and fat assessments also provide valuable prognostic insights. Further study is needed to clarify its role in universal screening.

Keywords : Sarcopenia, malnutrition, ultrasound, peritoneal dialysis

Figure 1A

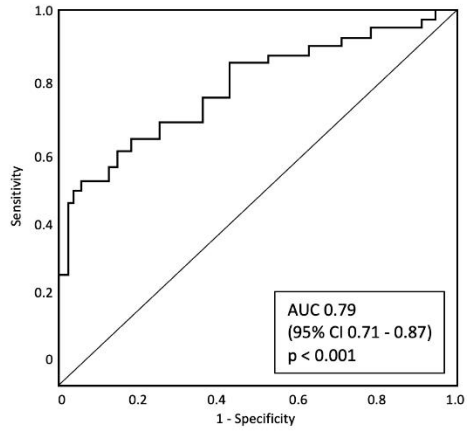
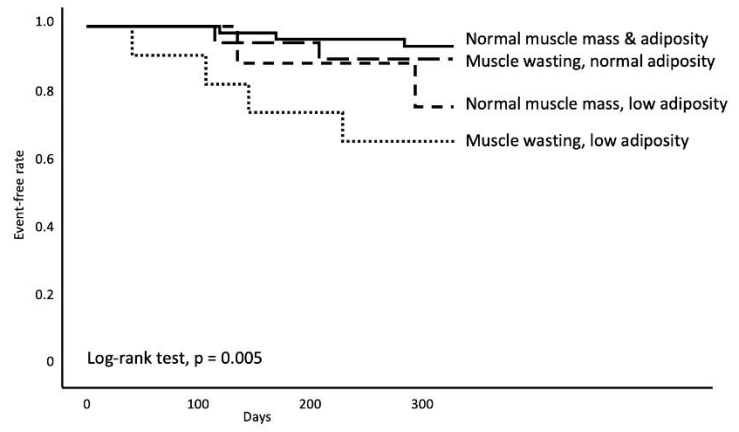


Figure 1B



Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250188

Survival Advantage of Peritoneal Dialysis Over Hemodialysis During the Coronavirus Disease 2019 Pandemic: A Prospective Cohort Study

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Abstract

Background

Patients with end-stage renal disease (ESRD) are at particularly high risk of mortality during the coronavirus disease 2019 (COVID-19) pandemic due to their immunocompromised status and multiple comorbidities. Although both hemodialysis (HD) and peritoneal dialysis (PD) are widely used renal replacement therapies, their comparative outcomes during the pandemic remain uncertain.

Methods

We conducted a prospective, hospital-based cohort study at Taipei Veterans General Hospital, enrolling patients undergoing HD or PD between July 2021 and April 2022. Patients with prior SARS-CoV-2 infection were excluded. Baseline demographic, clinical data, as well as vaccination status, were collected, and serum anti-SARS-CoV-2 spike protein receptor-binding domain (S protein RBD) antibody levels were measured. Patients were followed to compare the risks of SARS-CoV-2 infection and all-cause mortality between the HD and PD groups.

Results

A total of 595 ESRD patients were enrolled, comprising 440 HD patients and 155 PD patients. During the follow-up period, PD patients exhibited significantly lower risks of SARS-CoV-2 infection (adjusted hazard ratio [aHR], 0.33; 95% confidence interval [CI], 0.16–0.68) and all-cause mortality (aHR, 0.12; 95% CI, 0.05–0.34) compared to HD patients. Higher anti-S protein RBD antibody titers were significantly associated with reduced all-cause mortality (aHR, 0.31; 95% CI, 0.16–0.60), but not with SARS-CoV-2 infection risk. Similarly, COVID-19 vaccination was associated with a significant reduction in mortality, particularly among patients who received two or three doses, even after adjustment for antibody levels. Among all groups, PD patients who received three vaccine doses showed the most favorable survival rate.

Conclusion

PD was independently associated with lower risks of both SARS-CoV-2 infection and all-cause mortality compared to HD during the COVID-19 pandemic. Although higher serum anti-S protein RBD antibody titers and COVID-19 vaccination significantly reduced mortality, neither was associated with a lower risk of SARS-CoV-2 infection.

Keywords : Coronavirus disease 2019 (COVID-19); peritoneal dialysis (PD); hemodialysis (HD)

Oral Communications : Nominees for APSN Young Nephrologist Awards
Abstract Submission No. : APCN20250198

Early Dynamic Identification of Glomerular Hyperfiltration is Associated with Chronic Kidney Disease in Type 2 Diabetes

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Abstract

Background: Glomerular hyperfiltration (GHF), characterized by a supraphysiologic elevation in glomerular filtration rate (GFR), currently lacks a clear definition. The goal is to design an algorithm to identify GHF at early-stage diabetes and evaluate its association with chronic kidney disease (CKD).

Methods: This retrospective cohort study utilized data from the Genetics of Diabetes Audit and Research in Tayside Study (GoDARTS). We included participants with Type 2 Diabetes Mellitus (T2DM) who met the following criteria: (1) baseline estimated glomerular filtration rate (eGFR) > 60 mL/min/1.73 m², and (2) minimum diabetes duration of one year at study recruitment. To assess GHF, we developed a novel algorithm that analyzed longitudinal eGFR trajectories from the time of diabetes diagnosis through study enrollment. A Cox proportional hazards model was developed to investigate the association between GHF and the first onset of CKD stage 3b. Hierarchical linear mixed-effects (hlme) model was used to identify different patterns of eGFR trajectory during the first five years following the diagnosis of T2DM.

Results: Of the 9417 T2D participants in GoDARTS, 3246 met the criteria of this study. Among these, 1,825 participants were assigned to GHF Group 1, and 916 participants were assigned to GHF Group 2 (Table 1). At recruitment, participants in the GHF groups had slightly lower eGFR levels and a higher proportion had a history of congestive heart failure.

During the follow-up time, 18 events of CKD stage 3b occurred in the Non-GHF group, 194 in GHF Group 1, and 175 in GHF Group 2. In the unadjusted Cox regression analysis, GHF Group 1 showed a higher risk of CKD, though this risk was not statistically significant in the adjusted analysis. In contrast, GHF Group 2 was consistently associated with a higher risk of CKD compared with the Non-GHF group in both unadjusted (HR 6.90 [4.25–11.21]) and adjusted analyses (HR 1.92 [1.10–3.37]). In the Cox model with time-varying covariates, GHF Group 2 continued to show a higher risk of CKD (Table 2). The eGFR trajectory during the first 5 years after T2D diagnosis was categorized into four classes with the hlme model. As shown in Figure 1, two classes experienced early eGFR increases or decreases, followed by a more rapid decline in eGFR over the next 10 years.

Conclusion : GHF identified based on patients' dynamic eGFR may be more accurate. Among T2DM patients with preserved renal function, GHF independently predicted faster eGFR decline and CKD progression.

Keywords : Glomerular hyperfiltration, Diabetes Mellitus, Chronic kidney disease

Table 1 Baseline Characteristics of Participants

	Non-GHF group (n=505)	GHF group 1 (n=1825)	GHF group 2 (n=916)	P value
Age, mean (SD), years	59.7 (11.8)	64.8 (10.6)	67.5 (9.8)	<0.05
Male, No. (%)	310 (61.4)	1113 (61.0)	475 (51.9)	0.05
Body mass index, mean (SD)	32.0(7.0)	30.4 (6.0)	30.8 (6.1)	<0.05
Smoking history, No. (%)	242 (47.9)	946 (51.8)	487 (53.1)	0.55
eGFR, mean (SD), mL/min/1.73 m ²	91.7 (11.8)	85.2 (12.7)	88.1 (12.3)	<0.05
HbA1c, mean (SD)	7.5 (1.3)	7.5 (1.3)	7.7 (1.4)	<0.05
Duration of diabetes mellitus, median (IQR), y	3.7 (2.2-6.3)	5.3 (3.1-9.3)	6.3 (4.1-9.8)	<0.05
Total cholesterol, mean (SD), mmol/L	4.5 (1.0)	4.4 (0.9)	4.4 (1.0)	0.22
High-density lipoprotein cholesterol, mean (SD), mmol/L	1.3 (0.4)	1.4 (0.4)	1.4 (0.4)	<0.05
Systolic BP, mean (SD), mmHg	140.6 (17.1)	141.7 (18.1)	142.0 (18.5)	0.30
Diastolic BP, mean (SD), mmHg	80.2 (9.8)	77.7 (10.7)	76.2 (11.2)	<0.05
Hypertension, No. (%)	330 (65.3)	1399 (76.7)	734 (80.1)	0.06
Coronary Artery Disease, No. (%)	74 (14.6)	400 (21.9)	282 (30.8)	<0.05
Congestive Heart Failure, No. (%)	8 (1.6)	55 (3.0)	61 (6.7)	<0.05
Intake history of RAAS inhibitors, No. (%)	243 (48.1)	1132 (62.0)	599 (65.4)	<0.05

Table 2. Hazard Ratios for CKD in the Primary and Time-varying analysis.

Analysis	Unadjusted models		Adjusted models	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Primary analysis				
GHF group 1	3.19 (1.97, 5.16)	<0.05	1.34 (0.78, 2.32) *	0.28
GHF group 2	6.90 (4.25, 11.21)	<0.05	1.92 (1.10, 3.37) *	<0.05
Non-GHF group	—	—	—	—
Time-varying analysis				
GHF group 2	2.43 (1.77, 3.34)	<0.05	1.93 (1.40, 2.66) ▲	<0.05
Non-GHF group	—	—	—	—

* Adjusted models included age at recruitment, sex, eGFR at recruitment, BMI at recruitment, HbA1c at recruitment, duration of diabetes mellitus, history of hypertension, coronary artery disease, congestive heart failure and RAAS inhibitors intake, duration of RAAS inhibitors intake

▲ Adjusted models included age at diabetes diagnosis date, sex, eGFR at diabetes diagnosis date

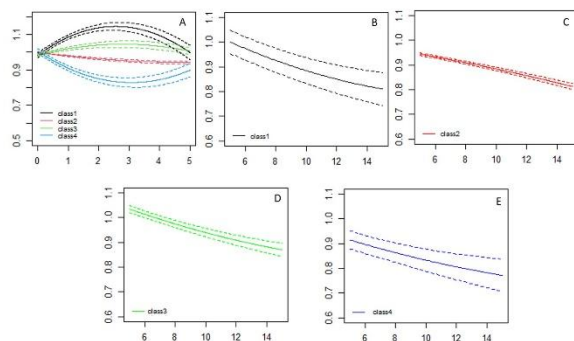


Figure 1. Predicted eGFR trajectory after T2D diagnosis

A is the eGFR trajectory during the first 5 years after T2D diagnosis; B is the eGFR trajectory for class 1 from 6th to 15th years after T2D diagnosis; C is the eGFR trajectory for class 2 from 6th to 15th years after T2D diagnosis; D is the eGFR trajectory for class 3 from 6th to 15th years after T2D diagnosis; E is the eGFR trajectory for class 4 from 6th to 15th years after T2D diagnosis

Oral Communications : Nominees for APSN Young Nephrologist Awards
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Deep Learning Integration of Cell-Free DNA Methylation and Clinical Trajectories to Predict Acute Rejection in Pediatric Kidney Transplantation

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Abstract

Introduction: Acute rejection is a significant cause of graft dysfunction in pediatric kidney transplant recipients, often occurring subclinically before histological evidence appears. Existing diagnostic approaches rely on delayed changes in serum creatinine or invasive biopsies, limiting early intervention. Cell-free DNA (cfDNA) methylation profiling offers a promising non-invasive biomarker of immune activation, but its predictive accuracy remains underutilized, particularly when decoupled from temporal clinical signals and pediatric immune maturation. This study aimed to develop and validate a transformer-based deep learning model that integrates cfDNA methylation with time-series clinical and immune data to predict acute rejection in an age-stratified pediatric population.

Methods: We analyzed cfDNA methylation data from the Gene Expression Omnibus (GEO), dataset GSE275017, which includes 20 pediatric kidney transplant recipients categorized into acute rejection (n=9), borderline rejection (n=5), and no rejection (n=6). Whole-genome bisulfite sequencing identified 34,356 differentially methylated cytosines. Longitudinal clinical data including serum creatinine and estimated glomerular filtration rate (eGFR) were manually extracted for a 3-month window before and after biopsy. Immune indices such as white blood cell count and C-reactive protein were included when available. A multi-modal architecture was developed comprising: (1) a transformer-based encoder for renal function trajectories, (2) a convolutional module for methylation features, and (3) a dense network for immune markers. These were fused via an attention-based DeepSurv++ layer to predict individualized rejection risk. Patients were stratified into <10 years, 10–15 years, and >15 years to capture age-dependent immune modulation. Model interpretability was assessed using SHAP value analysis.

Results: The model achieved an AUROC of 0.82 (95% CI: 0.77–0.88) for predicting biopsy-confirmed acute rejection and 0.79 (95% CI: 0.72–0.85) for borderline rejection. Stratified AUROC values were 0.88 for patients <10 years, 0.79 for those aged 10–15 years, and 0.76 for >15 years. Key predictive features included methylation at cg13754931 (IFNGR1 promoter) and cg09812044 (IL10RA intron), as well as creatinine slope >0.25 mg/dL/week and eGFR decline >25% over 14 days. The model successfully distinguished borderline rejection cases that were misclassified by conventional clinical thresholds. Additional SHAP-based analysis revealed combined effects between immune-related methylation changes and rapid renal function decline, particularly in younger patients experiencing early rejection, with enhanced pro-inflammatory signaling patterns.

Conclusion: This study presents a novel, explainable deep learning framework that integrates cfDNA methylation and clinical dynamics to non-invasively predict acute rejection in pediatric kidney transplant recipients. The model enables age-sensitive, individualized risk stratification with strong clinical relevance and potential for integration into post-transplant care pathways.

Keywords : acute rejection, pediatric kidney transplantation, cell-free DNA methylation, deep learning, risk prediction

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The Involvement of Interstitial Palladin Expression in Patients with Chronic Kidney Diseases

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Abstract

Introduction

Kidney fibrosis is a common mechanism underlying progressive kidney diseases. We have previously demonstrated that actin-associated protein palladin promotes kidney fibrosis through actin cytoskeleton-dependent myocardin-related transcription factors (MRTF)-serum response factor (SRF) signaling. However, it has not been elucidated whether palladin is related to the pathogenesis of human chronic kidney disease (CKD). In this study, we investigated the distribution of palladin in human kidney tissue and its relationship with kidney dysfunction and fibrosis.

Methods

We retrospectively analyzed Japanese patients who underwent kidney biopsy for CKD at Kanazawa University Hospital between March 2022 and December 2023. CKD was defined by either persistent urinary abnormalities or estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² for at least three months. Palladin expression was quantified as the percentage of positive area on immunohistochemistry. Co-localization of palladin and α -smooth muscle actin (α SMA) was assessed by dual immunofluorescence staining. At the time of biopsy, we recorded baseline eGFR, urinary protein-to-creatinine ratio (U-P/Cr), urinary β_2 -microglobulin (β_2 MG), and urinary N-acetyl- β -D-glucosaminidase (NAG). We also calculated Pearson's correlation coefficients between each parameter and palladin-positive area. Fibrotic area was also quantified by Azan–Mallory staining and analyzed its correlation with palladin positivity.

Results

A total of 57 patients were enrolled with a mean age of 56.4±17.1 years (54.4% female) and a mean eGFR of 49.0±23.8 mL/min/1.73 m². Palladin localized predominantly to the kidney interstitial space and colocalized with α SMA on immunofluorescence. Palladin-positive area was negatively correlated with eGFR ($r = -0.52$) and showed no significant association with the U-P/Cr ($r = 0.009$). In contrast, it was positively associated with urinary β_2 -MG ($r = 0.33$), urinary NAG ($r = 0.23$), and the percentage of AZAN-positive area ($r = 0.54$).

Conclusion

Palladin in kidney myofibroblasts may be involved in the progression of human CKD.

Keywords : Palladin, Kidney fibrosis, Chronic kidney disease