Original Research Report

URINE PERIOSTIN LEVELS AND RENAL FUNCTION IN MALIGNANCY PATIENTS TREATED WITH HIGH-DOSE CISPLATIN

Harry Yusuf[1], Andhika Rachman[2], M Bonar Marbun[3], Hamzah Shatri[4], Putri Aliya Ahadini[5]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia
[2]Division of Medical Hematology and Oncology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia
[3]Division of Nephrology/Hypertension, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia
[4]Division of Psychosomatic Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia
[5]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Cisplatin has been extensively used as a cancer treatment. The accumulation of cisplatin metabolites in the kidneys may cause nephrotoxicity, which can be assessed by blood urea levels, blood creatinine, and estimated glomerular filtration rate (eGFR). However, because these indicators have numerous flaws, optimal biological markers are required. Periostin is a key mediator of inflammatory processes, including kidney fibrosis and inflammation. This study aimed to ascertain the changes in urine periostin and its correlation with kidney function in 37 cancer patients undergoing high-dose cisplatin therapy. This cross-sectional study was conducted at Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia, starting in October 2019 and ending when the minimum sample was obtained through consecutive sampling. The urine periostin levels were examined using the Human Periostin (POSTN) enzyme-linked immunosorbent assay (ELISA) kits and reagents. The correlation between periostin urine levels and kidney function was determined using the Spearman test ($p<0.05$). Among the patients, 70.3% were male, 29.7% aged 41 to 50, 78.4% were married, 59.5% had completed high school, 37.8% were employed, 59.5% had nasopharyngeal carcinoma, and 64.9% had a Karnofsky score of 80. Between the period before and one week following the first chemotherapy, the patients exhibited elevated blood creatinine and urea levels, whereas the eGFR values decreased. The periostin levels indicated an inclination to rise one week following the third chemotherapy, with a prior reduction after the first and second therapies ($p>0.05$). Urine periostin levels and other kidney function indicators showed no significant correlation ($p>0.05$), with several domains displaying negative directions. The correlation coefficients were modest ($r=0.017–0.254$). In conclusion, malignancy patients receiving high-dose cisplatin therapy exhibit changes in urine periostin levels, which increase following the third chemotherapy. No significant correlation exists between urine periostin levels and kidney function in malignancy patients treated with high-dose cisplatin therapy.

Keywords: Cisplastin; malignancy; periostin; renal function; life expectancy

***Correspondence:** Harry Yusuf, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia; Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia. E-mail: harry30yusuf@gmail.com

Article history
●Submitted 28/10/2024 ● Revised 21/11/2024 ● Accepted 27/11/2024 ● Published 11/12/2024

How to cite: Yusuf H, Rachman A, Marbun MB, et al (2024). Urine Periostin Levels and Renal Function in Malignancy Patients Treated with High-Dose Cisplatin. Folia Medica Indonesiana 60(4), 310-316. doi:https://doi.org/10.20473/fmi.v60i4.63357

pISSN:2355-8393, eISSN: 2599-056x

Highlights:
1. As there has been a need for optimal biological markers of nephrotoxicity, this study used urine periostin to indicate kidney function in cancer patients undergoing high-dose cisplatin treatment.
2. This study can serve as a reference or comparison for future investigations on changes in urine periostin and its correlation with kidney function in cancer patients receiving high-dose cisplatin therapy.

INTRODUCTION

Cisplatin is widely used in the treatment of solid tumors and various cancers, such as sarcoma, as well as soft tissue, bone, testicular, ovarian, bladder, and head and neck cancers. The drug is mainly excreted via urine, leading to an accumulation of its metabolites in the kidneys. This unbalanced proportion contributes to nephrotoxicity, marked by a decrease in glomerular filtration rate (GFR), resulting in increased serum creatinine levels that manifest at six to seven days post-chemotherapy and may persist for the following three to four weeks (Dasari & Bernard Tchounwou 2014, Prasaja et al. 2015). Acute kidney injury (AKI) occurs in about 30% of cancer patients treated with a single high-dose cisplatin infusion. Therefore, low-dose cisplatin is more frequently used in current clinical practice to prevent adverse effects (Yu et al. 2024).

Serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin are commonly used as the markers of kidney disease. These markers exhibit significant alterations in response to systemic inflammation, metabolic changes, and medication (Muglia et al. 2024). However, serum creatinine levels are highly dependent on age, sex, muscle mass, and heavy physical exercise. This marker lacks specificity and sensitivity, as its appearance is slower than the decrease in GFR (Ostermann & Joannidis 2016). The weaknesses of these markers may hinder the timely diagnosis and treatment of kidney disease. For this reason, an ideal biological marker is required. Indicators of acute kidney injury include: (1) glomerular markers, e.g., glotransferrin, immunoglobulin G (IgG), transferrin, beta trace protein (BTP), β2-microglobulin (B2M), and nephrin; (2) tubular damage indicators, e.g., neutrophil gelatinase-associated lipocalin (NGAL), alpha-1-microglobulin (A1M), kidney injury molecule-1 (KIM-1), N-acetyl-beta-D-glucosaminidase, angiotensinogen, uromodulin, liver-type fatty acid-binding protein (L-FABP), and heart-type fatty acid-binding protein (H-FABP); and (3) inflammatory markers, e.g., tumor necrosis factor-α (TNF-α), interleukin 6 (IL-6), and monocyte chemotactic protein (MCP) (Żyłka et al. 2018, Muglia et al. 2024).

An extracellular matrix protein called periostin, also known as osteoblast-specific factor 2, is initially expressed in the bone. Periostin is also found in other organs, particularly distal tubular renal cells (Satirapoj et al. 2015, Satirapoj 2018). It has been recognized as a biomarker for cancer and fibrotic disorders. The level of periostin in the blood, urine, and sputum elevates in cases of various pathological conditions, indicating that this protein is easily produced from damage sites. The length and severity of kidney damage, as well as a decline in GFR, cause periostin concentrations in renal tissue and urine to rise (Turczyn & Pańczyk-Tomaszewska 2021). Aside from high levels of periostin in adults, other biomarkers of kidney injury include atrophic tubules, fibrotic vessels, glomerular sclerosis, Bowman's capsule, ischemic lesions, and tubular cytoplasm in diabetic individuals; cystic fluid, cyst extracellular matrix, and epithelial lining cells of the cysts in autosomal dominant polycystic kidney disease (ADPKD) patients; and renal tubular epithelial cells in lupus nephritis patients (Pană & Căpușă 2022). Satirapoj et al. (2015) demonstrated that periostin expression was elevated in the glomeruli and pathological tubules of diabetic nephropathy patients. The findings were further supported by changes in microalbuminuria levels (8.71, IQR 5.09-19.29, $p<0.001$) and macroalbuminuria levels (13.58, IQR 3.99-16.19, $p<0.001$). In a separate study, patients with chronic allograft nephropathy (CAN) exhibited an increased periostin expression after kidney transplantation, with remarkable sensitivity (95.8%) and specificity (77.8%) (Satirapoj et al. 2014).

Prakoura & Chatziantoniou (2017) used the quantitative enzyme-linked immunosorbent assay (ELISA) method to compare urine periostin levels between chronic kidney disease (CKD) patients and healthy individuals. The findings showed that CKD patients with proteinuric type (median 2473.58 pg/mg, $p<0.001$) and non-proteinuric type (median 3192.36 pg/mg, $p<0.001$) had higher levels of urine periostin compared to the healthy controls. Therefore, when compared to renal urea or creatinine evaluation, periostin is considered a predictor for detecting problems in kidney function and structure (Satirapoj et al. 2014). The purpose of this study was to determine the correlation between changes in urine periostin levels and renal function in cancer patients undergoing high-dose cisplatin treatment. This initial investigation of periostin should be able to demonstrate its potential as a precursor to kidney tissue inflammation in chemotherapy patients.

MATERIALS AND METHODS

This research was a prospective cohort study designed to examine the correlation between urine periostin levels and kidney function in malignancy patients undergoing high-dose cisplatin therapy. The study involved 37 malignancy patients who received high-dose cisplatin therapy and chemotherapy in the Medical Hematology and Oncology Ward located on the eighth floor of Building A at Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia. The recruitment of research subjects began in October 2019 and continued until the required number of samples was obtained. The

consecutive sampling method was employed to carry out the sampling procedure (Thewes et al. 2018). The inclusion criteria for the participants were individuals between the ages of 18 and 59 with a Karnofsky score of at least 80, scheduled for three cycles of cytostatic chemotherapy with a regimen containing high doses of cisplatin (≥75 mg/m^2 body surface area), displaying an eGFR of >60 mL/minute/1.73 m^2 at the start of chemotherapy, and having undergone a urine periostin examination and other tests required for the study. The exclusion criteria comprised individuals with acute infections, lung conditions (such as asthma and chronic obstructive pulmonary disease), autoimmune illnesses, kidney disease, heart disease, and type 2 diabetes mellitus, as well as those who were pregnant or consumed diuretics.

Prior to the first chemotherapy cycle and six to seven days following the first, second, and third cycles, the subjects had their blood urea, serum creatinine, urine periostin, and eGFR measured. The urine periostin levels were examined using the Human Periostin (POSTN) enzyme-linked immunosorbent assay (ELISA) kits and reagents. Standard laboratory reagents from Dr. Cipto Mangunkusumo National Central Public Hospital were used to analyze blood urea, serum creatinine, and eGFR. The collected data were coded for processing after being chosen according to the completeness of all necessary variables. The Spearman correlation test was employed to ascertain the correlation between urine periostin levels and kidney function, with $p<0.05$ considered statistically significant (Sedgwick 2014). All data processing and analysis were performed utilizing IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).

RESULTS

Among the 37 patients, the most common type of malignancy was nasopharyngeal carcinoma (NPC), affecting 22 individuals. The highest Karnofsky score recorded among the 37 patients was 80, which was demonstrated by 24 individuals. The cisplatin doses administered in this trial were 75, 100, and 150 mg/m^2, depending on the combination treatment. Table 1 displays the general and clinical characteristics of the research subjects.

In terms of pre-chemotherapy clinical features, it was discovered that all patients exhibited normal kidney function. The assessment of renal function markers included eGFR calculation, blood urea levels, and serum creatinine levels. The laboratory tests of the patients' kidney function conducted during pre-chemotherapy, one week following the first chemotherapy, one week following the second chemotherapy, and up to one week following the third chemotherapy revealed a decrease in eGFR and an increase in the median levels of blood urea and serum creatinine.

Table 1. Baseline characteristics of the study subjects.

Characteristics	%
Age (y.o.)	
18–30	18.9%
31–40	21.6%
41–50	29.8%
51–60	21.6%
>60	8.1%
Sex	
Male	70.3%
Female	29.7%
Marital status	
Single	13.5%
Married	78.4%
Widower	8.1%
Cancer diagnosis	
Cystic adenoid orbital cancer	2.7%
Gastric adenocarcinoma	2.7%
Lung adenocarcinoma	2.7%
Bladder carcinoma	2.7%
Cervical cancer	2.7%
Cholangiosarcoma	2.7%
NPC	59.5%
Esophageal SCC	2.7%
Laryngeal SCC	8.1%
Orbital SCC	2.7%
Sinonasal SCC	2.7%
Maxillaris sinus SCC	2.7%
Osteosarcoma	5.4%
Chemotherapy regimen	
Cisplatin-5FU	70.3%
Cisplatin-doxorubicin	5.4%
Cisplatin-docetaxel	13.5%
Cisplatin-gemcitabine	8.1%
Cisplatin-paclitaxel	2.7%
Karnofsky score	
80	64.9%
90	35.1%
100	0%

Legends: y.o.=years old; NPC=nasopharyngeal carcinoma; SCC=squamous cell carcinoma; 5FU=fluorouracil.

The periostin levels demonstrated a declining trend during the initial two cycles of chemotherapy, followed by a rise one week after the third chemotherapy, as shown in Table 2.

Table 2. Laboratory characteristics of the patients' renal function.

Markers	Pre-chemotherapy	One-week post-chemotherapy		
		Cycle I	Cycle II	Cycle III
Urine periostin (ng/mL)	0.44 (0.05–0.9)	0.34 (0.1–1.2)	0.32 (0.03–0.9)	0.37 (0.1–1.1)
Blood urea (mg/dL)	23.7 (8.5–364)	30 (11.1–81.2)	31.8 (14.8–59.4)	33.5 (14.4–75.8)
Serum creatinine (mg/dL)	0.7 (0.4–1.3)	0.9 (0.5–1.8)	1.1 (4–1.7)	1.1 (0.4–3)
eGFR (mL/min/1.73m^2)	108 (61.8–146.8)	95.1 (31.9–158.2)	76.9 (17–147.7)	75.5 (17.2–160.5)

Legends: eGFR= estimated glomerular filtration rate.

In order to assess the function of periostin as a marker of kidney disease development, it was necessary to find its correlation with a number of factors affecting renal function, including urea, creatinine, and eGFR.

Table 3. Correlation between urine periostin and renal function.

Urine periostin levels	Urea	Creatinin	eGFR	p
Pre-chemotherapy	-0.124	-0.027	-0.028	>0.05
One-week post-chemotherapy				
Cycle I	-0.017	-0.039	-0.125	>0.05
Cycle II	0.068	-0.07	0.021	>0.05
Cycle III	0.112	0.254	-0.182	>0.05

Legends: eGFR= estimated glomerular filtration rate.

The Spearman test results in this study showed poor correlation coefficient values and a negative correlation direction in some areas. The results indicated no significant correlation (p>0.05) between urine periostin levels and kidney function due to non-normal data distribution. Furthermore, the correlation coefficient between domains can be seen in Table 3.

DISCUSSION

According to Prasaja et al. (2015), cisplatin is one of the standard chemotherapy drugs for solid organ tumors, such as ovarian cancer, cervical cancer, breast cancer, nasopharyngeal cancer, and lung cancer. Cisplatin is also known by its chemical name, cis-diamminedichloroplatinum (II). It is a neutral anticancer agent that destroys deoxyribonucleic acid (DNA) by inducing cancer cells to form DNA adducts, which contain intrastrand, interstrand, and monostrand cisplatin DNA cross-links. This mechanism halts the cell cycle at the S, G1, or G2-M phases and causes apoptosis. However, cisplatin has severe adverse effects, including nephrotoxicity, ototoxicity, cardiotoxicity, neurotoxicity, gastrotoxicity, and hepatotoxicity (Aldossary 2019, Fang et al. 2021, Djordjević et al. 2023).

High doses of cisplatin have been associated with nephrotoxicity. Therefore, dose limiting is necessary for the administration of cisplatin (Aldossary 2019). Additionally, Zahedi et al. (2024) found the potential role of polyamine catabolism in repeated low-dose cisplatin (RLDC). This is correlated with renal parenchymal damage, the loss of renal function, and fibrosis. There are four main mechanisms of cisplatin nephrotoxicity (Ozkok & Edelstein 2014). First, cisplatin nephrotoxicity results from oxidative stress brought on by mitochondrial dysfunction and elevated reactive oxygen species (ROS). Second, cisplatin nephrotoxicity occurs due to inflammation brought on by the secretion of different cytokines. Third, cisplatin nephrotoxicity arises from proximal tubular injury, which involves apoptosis, autophagy, dysregulation of cell-cycle proteins, activation of the mitogen-activated protein kinase (MAPK) signaling pathways, direct toxicity to renal tubular epithelial cells, DNA damage, and mitochondrial dysfunction. Fourth, cisplatin nephrotoxicity develops because of vascular injury in the kidney, leading to acute ischemic damage with a decrease in medullary blood flow. Organic cation transporter 2 (OCT2) also induces histopathological alterations in renal tubular cells, which results in the loss of the brush-like morphology of renal tubular epithelial cells as cisplatin accumulation increases, as well as necrosis and the development of intratubular blockade (Fang et al. 2021).

Periostin has structural similarity to big-H3, a 68 kDa protein that is activated by transforming growth factor-ß1 and insect neural cell adhesion protein (fascilin). It possesses a characteristic signal sequence, four cysteine-rich repetition domains, and a C-terminal variable domain (Jia et al. 2020). Periostin is present in various tissues, such as periosteal tissue, periodontal ligaments, the heart, skin, and blood vessels. It is most abundant in the aorta, lower digestive tract, placenta, uterus, thyroid tissue, and breast. Its presence is significantly elevated in a number of renal pathological tissues and pathological processes, such as tumors, myocardial infarction, and wound repair (Jia et al.

2020). Periostin plays a main role in fibrosis and during the progression of acute kidney injury to chronic kidney disease. An in vitro study conducted by An et al. (2019) verified the dose-dependent effects of p38 MAPK inhibition. The study also discovered that elevated urine periostin levels during an acute kidney injury episode were linked to the progression of chronic kidney disease through alterations in fibrosis or apoptosis. Additionally, periostin contributes to the development of cysts and fibrosis in polycystic kidney disease by interacting with integrins and activating signaling pathways in aberrant tissue. In diabetic kidney damage, periostin reduces the release of pro-inflammatory cytokines and renal fibrosis (Watanabe et al. 2019, Duan et al. 2023).

This research focused on determining the correlation between periostin and renal function in acute kidney injury caused by cisplatin treatment. This study found no significant correlation between periostin levels and renal function, as assessed by the urea, creatinine, and eGFR measurements, according to the hypothesis testing. This might be due to the renal function markers (urea, creatinine, and eGFR) not exhibiting significant changes prior to or one week following the first, second, and third cycles of chemotherapy. The kidneys have a strong capacity for recovery, potentially affecting the expression of periostin, a protein implicated in the inflammatory process within the renal tubules. A study carried out by Sharp & Siskind (2017) demonstrated nephrotoxic effects due to an increase in caspase 3 cleavage in mice given large doses of cisplatin, which resulted in elevated creatinine levels. The resulting inflammation persisted in reparative actions that lead to either maladaptive or adaptive enhancements. While maladaptive repair can result in fibrosis and chronic kidney disease, adaptive repair persists during renal recovery. Ultrasmall ruthenium nanoparticles (URNPs) were used as switchable ROS generators in another study by stimulating multi-enzyme activities, such as superoxide dismutase and catalase, thereby reducing cisplatin-induced acute kidney injury and enhancing its therapeutic efficacy (Zhu et al. 2024).

Our investigation revealed a recovery process that probably prevented renal fibrosis. Periostin is known for mediating the onset of renal fibrosis, frequently observed in chronic kidney disease. In addition to contributing through the ROS signaling pathway, periostin is implicated in renal fibrosis and end-stage renal disease (ESRD) by promoting collagen cross-linking through the bone morphogenetic protein 1 (BMP-1)-mediated activation of matricellular lysyl oxidase (LOX), facilitating cell dedifferentiation, increasing TGF-β expression, and enhancing extracellular matrix deposition (Turczyn & Pańczyk-Tomaszewska 2021). Ashley et al. (2017) assert that periostin is produced in response to fibrosis, enhancing extracellular matrix deposition, mesenchymal cell proliferation, and wound closure by stimulating the phosphorylation of focal adhesion kinase (FAK), p38, and extracellular signal-regulated kinase (ERK). As previously indicated, recurrent high-dose cisplatin exposure will result in renal fibrosis, which is characterized by an increase in periostin, following repeated cycles of chemotherapy. This will lead to maladaptive improvement that may be followed by fibrosis.

According to our findings, patients taking high doses of cisplatin did not exhibit a discernible rise in periostin levels. Maladaptive repair, which may be followed by renal fibrosis, can occur after repeated cycles of chemotherapy. As a result, periostin might be deemed unsuitable for this investigation to evaluate acute renal impairment. The findings of this study differ from a previous study that measured periostin to assess chronic kidney dysfunction and various nephropathies (Turczyn & Pańczyk-Tomaszewska 2021). Future studies should involve a larger sample population, employ a prospective cohort study design, and incorporate more consecutive cycles of chemotherapy to validate urine periostin as a biomarker for kidney impairment caused by cisplatin therapy. It is also necessary to conduct research comparing the periostin levels of a control group and patients undergoing high-dose cisplatin therapy.

Strength and limitations

The strength of this study is that it is the first to investigate changes in urine periostin levels and how they correlate with kidney function in cancer patients receiving high doses of cisplatin. Therefore, it is anticipated that this study will serve as a reference or comparison for future research. The lack of a comparable study for reference became a restriction for this study. Additionally, the research participants in this study were only monitored for a maximum of three chemotherapy cycles.

CONCLUSION

This study finds that urine periostin levels in malignancy patients receiving high-dose cisplatin therapy are not significantly correlated with blood urea levels, serum creatinine levels, or glomerular filtration rate. It is imperative for future research to use a prospective cohort study design and incorporate comparisons with a control group, a bigger sample size, and consecutive cycles of chemotherapy.

Acknowledgment

The authors acknowledge everyone who provided help and support during the course of this research, mainly the Department of Internal Medicine of Universitas Indonesia and Dr. Cipto Mangunkusumo National Central Public Hospital, Jakarta, Indonesia.

Conflict of interest

None.

Ethical consideration

The ethical clearance of this study was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, under reference No. KET-778/UN2.F1/ETIK/PPM.00.02/2019 dated 8/7/2019.

Funding disclosure

None.

Author contribution

HY contributed to all of the steps for constructing the article, including the conception and design, the collection, analysis, and interpretation of the data, as well as the provision of funding and administrative, technical, and logistic support. AR and MRM contributed to the conception and design, the analysis and interpretation of the data, and the drafting and final approval of the article. HS provided statistical expertise for this study. PAA contributed to the drafting of the article.

REFERENCES

Aldossary SA (2019). Review on pharmacology of cisplatin: Clinical use, toxicity and mechanism of resistance of cisplatin. Biomedical and Pharmacology Journal 12**,** 07–15. doi: 10.13005/bpj/1608.

An JN, Yang SH, Kim YC, et al (2019). Periostin induces kidney fibrosis after acute kidney injury via the p38 MAPK pathway. American Journal of Physiology-Renal Physiology 316**,** F426–437. doi: 10.1152/ajprenal.00203.2018.

Ashley SL, Wilke CA, Kim KK, et al (2017). Periostin regulates fibrocyte function to promote myofibroblast differentiation and lung fibrosis. Mucosal Immunology 10**,** 341–351. doi: 10.1038/mi.2016.61.

Dasari S, Bernard Tchounwou P (2014). Cisplatin in cancer therapy: Molecular mechanisms of action. European Journal of Pharmacology 740**,** 364–378.

Djordjević M, Ilić J, Stojanovic NM (2023). Cisplatin - an overview of its efficiency and toxicity. Facta Universitatis, Series: Medicine and Biology. doi: 10.22190/FUMB230122002D.

Duan X, Chen C, Liu X, et al (2023). Interference of periostin attenuates pathological changes, proinflammatory markers and renal fibrosis in diabetic kidney injury. Genes & Genomics 45**,** 1389–1397. doi: 10.1007/s13258-023-01400-x.

Fang C, Lou D, Zhou L, et al (2021). Natural products: Potential treatments for cisplatin-induced nephrotoxicity. Acta Pharmacologica Sinica 42**,** 1951–1969. doi: 10.1038/s41401-021-00620-9.

IBM Corp. (2015). IBM SPSS statistics for Windows, version 23.0. Armonk, NY: IBM Corp. Available at: https://www-ibm-com.support/pages/downloading-ibm-spss-statistics-23?_x_tr_sl=en&_x_tr_tl=id&_x_tr_hl=id&_x_tr_pto=tc.

Jia Y, Yu Y, Li H (2020). The research status and prospect of Periostin in chronic kidney disease. Renal Failure 42**,** 1166–1172. doi: 10.1080/0886022X.2020.1846562.

Muglia L, Di Dio M, Filicetti E, et al (2024). Biomarkers of chronic kidney disease in older individuals: Navigating complexity in diagnosis. Frontiers in Medicine. doi: 10.3389/fmed.2024.1397160.

Ostermann M, Joannidis M (2016). Acute kidney injury 2016: Diagnosis and diagnostic workup. Critical Care 20**,** 299. doi: 10.1186/s13054-016-1478-z.

Ozkok A, Edelstein CL (2014). Pathophysiology of cisplatin-induced acute kidney injury. BioMed Research International 2014**,** 1–17. doi: 10.1155/2014/967826.

Pană N, Căpușă C (2022). Periostin as a biomarker in the setting of glomerular diseases—A review of the current literature. Biomedicines 10**,** 3211. doi: 10.3390/biomedicines10123211.

Prakoura N, Chatziantoniou C (2017). Periostin in kidney diseases. Cellular and Molecular Life Sciences 74**,** 4315–4320. doi: 10.1007/s00018-017-2650-6.

Prasaja Y, Sutandyo N, Andrajati R (2015). Incidence of cisplatin-induced nephrotoxicity and associated factors among cancer patients in Indonesia. Asian Pacific Journal of Cancer Prevention 16**,** 1117–1122. doi: 10.7314/APJCP.2015.16.3.1117.

Satirapoj B (2018). Tubulointerstitial biomarkers for diabetic nephropathy. Journal of Diabetes Research 2018**,** 1–6. doi: 10.1155/2018/2852398.

Satirapoj B, Tassanasorn S, Charoenpitakchai M, et al. (2015). Periostin as a tissue and urinary biomarker of renal injury in type 2 diabetes mellitus ed. Sen U. PLoS One 10**,** e0124055. doi: 10.1371/journal.pone.0124055.

Satirapoj B, Witoon R, Ruangkanchanasetr P, et al

(2014). Urine periostin as a biomarker of renal injury in chronic allograft nephropathy. Transplantation Proceedings 46**,** 135–40. doi: 10.1016/j.transproceed.2013.07.069.

Sedgwick P (2014). Spearman's rank correlation coefficient. BMJg7327. doi: 10.1136/bmj.g7327.

Sharp CN, Siskind LJ (2017). Developing better mouse models to study cisplatin-induced kidney injury. American Journal of Physiology-Renal Physiology 313**,** F835–841. doi: 10.1152/ajprenal.00285.2017.

Thewes B, Rietjens JAC, van den Berg SW, et al (2018). One way or another: The opportunities and pitfalls of self-referral and consecutive sampling as recruitment strategies for psycho-oncology intervention trials. Psychooncology 27**,** 2056–2059. doi: 10.1002/pon.4780.

Turczyn A, Pańczyk-Tomaszewska M (2021). The role of periostin in kidney diseases. Central European Journal of Immunology 46**,** 494–501. doi: 10.5114/ceji.2021.110317.

Watanabe EH, Amaral AG, Onuchic LF (2019). Periostin and polycystic kidney disease: More pieces in the puzzle. American Journal of Physiology-Renal Physiology 316**,** F159–161. doi: 10.1152/ajprenal.00518.2018.

Yu J-B, Padanilam BJ, Kim J (2024). Activation of yes-associated protein is indispensable for transformation of kidney fibroblasts into myofibroblasts during repeated administration of cisplatin. Cells 13**,** 1475. doi: 10.3390/cells13171475.

Zahedi K, Barone S, Brooks M, et al (2024). Polyamine catabolism and its role in renal injury and fibrosis in mice subjected to repeated low-dose cisplatin treatment. Biomedicines 12**,** 640. doi: 10.3390/biomedicines12030640.

Zhu S, Huo L, Zeng J, et al (2024). Differentiated management of ROS level in tumor and kidney to alleviate Cis-platinum induced acute kidney injury with improved efficacy. Journal of Nanobiotechnology 22**,** 436. doi: 10.1186/s12951-024-02710-2.

Żyłka A, Dumnicka P, Kuśnierz-Cabala B, et al (2018). Markers of glomerular and tubular damage in the early stage of kidney disease in type 2 diabetic patients. Mediators of Inflammation 2018**,** 1–12. doi: 10.1155/2018/7659243.