

Platinum-based chemotherapy and nephrotoxicity: frequency, clinical characteristics and outcomes in a mexican tertiary-centre cohort

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Abstract

Background Platinum-based agents (cisplatin, carboplatin, and oxaliplatin) are essential in the treatment of solid tumors, but they are associated with nephrotoxicity. Acute kidney injury (AKI) occurs most frequently with cisplatin and can lead to treatment delays, dose reduction, or discontinuation, as well as increasing the risk of renal adverse events and mortality. In Latin America, evidence on incidence, associated factors, and outcomes is limited.

Aims To estimate the frequency of platinum-based chemotherapy-induced nephrotoxicity, describe the clinical characteristics, and determine the renal and clinical outcomes in adults with solid tumors.

Methods A retrospective, analytical cohort study was conducted on patients aged 18 years or older diagnosed with any solid tumor who had received at least one cycle of platinum-based chemotherapy over a 5-year period. AKI was defined and classified according to the KDIGO 2012 criteria. Demographic variables, comorbidities, electrolyte disturbance, tumor type, treatment regimen, and cumulative dose were collected. The frequency of nephrotoxicity by drug was estimated, and outcomes such as development of electrolyte disturbance, chronic kidney disease, need for renal replacement therapy, regimen modifications/discontinuation, and mortality at 120 days from the initiation of the platinum agent were examined.

Results A total of 114 patients were included in the study. Testicular cancer was the most frequent neoplasm (29.8%). AKI occurred in 31.6%, while electrolyte imbalances were documented in 35.1% of patients. Renal replacement therapy was required in 7.9%, and 7.0% developed chronic kidney disease. Treatment discontinuation occurred in 7.0% of the study population, while dose modification was necessary in 11.4%. Overall 120 days mortality was 1.8% and did not differ between groups, whereas chronic kidney disease, dose modification and treatment discontinuation were significantly more frequent among patients who developed AKI.

Conclusions AKI was frequent even in a young population with preserved baseline renal function and a low prevalence of traditional renal risk factors. Although short-term mortality did not differ, acute kidney injury was

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associated with chronic kidney disease, renal replacement therapy, dose modification and treatment discontinuation, indicating that the clinical burden of platinum nephrotoxicity extends beyond short-term increases in serum creatinine and affects the delivery of cancer treatment.

Keywords Nephrotoxicity · Platinum chemotherapy · Acute kidney injury · Cisplatin · Carboplatin · Oxaliplatin · Solid tumors.

Background

Platinum-derived compounds, primarily cisplatin, carboplatin, and oxaliplatin, constitute a fundamental part of the systemic treatment of many solid tumors. These drugs are used in gynecological, genitourinary, gastrointestinal, pulmonary, and head and neck tumors, among others. However, their clinical utility can be limited by systemic toxicity, among which nephrotoxicity represents one of the most relevant complications due to its impact on patient safety and continuity of cancer treatment [1, 2].

Platinum-induced nephrotoxicity can manifest as AKI, acute kidney disease, electrolyte imbalances, tubulopathies or persistent decline in renal function. Cisplatin is the agent with the greatest nephrotoxic potential, with a reported incidence of AKI of approximately 20–30% in different clinical series, although the frequency varies depending on the population studied, the definition used, the administered dose, the type of tumor, the chemotherapy regimen, comorbidities, and the preventive strategies employed [1–4]. Carboplatin and oxaliplatin are considered less nephrotoxic than cisplatin; however, they are not without renal toxicity [2, 4, 5].

AKI is defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, which consider any of the following parameters: an increase in serum creatinine ≥ 0.3 mg/dL in 48 h, an increase ≥ 1.5 times from baseline in the previous seven days, or a decrease in urine output < 0.5 mL/kg/h for at least six hours [6]. This classification allows for stratification of severity into three stages and has facilitated comparisons between studies.

From a pathophysiological standpoint, cisplatin accumulates primarily in the epithelial cells of the proximal tubule. Intracellular accumulation promotes mitochondrial dysfunction, oxidative stress, activation of inflammatory pathways, renal vascular injury, apoptosis, and acute tubular necrosis [1, 2, 7–10]. These mechanisms explain the decline in glomerular filtration rate and the development of tubular abnormalities such as hypomagnesemia, hypokalemia, renal solute loss, tubular acidosis, and, in some cases, phenotypes consistent with proximal tubulopathy or Fanconi-like syndrome.

Cisplatin nephrotoxicity is dose-dependent and cumulative, and the factors associated with platinum-induced nephrotoxicity include advanced age, hypertension, diabetes, cardiovascular disease, hypoalbuminemia, impaired baseline renal function, high cisplatin doses, higher cumulative doses, dehydration, nausea or vomiting, concomitant exposure to nephrotoxic agents, and electrolyte imbalances before or during treatment [2–4, 8, 11–13]. Some of these factors are potentially modifiable, highlighting the importance of identifying them before and during platinum exposure. Commonly used preventive strategies include intravenous hydration, magnesium and potassium supplementation, adequate management of emesis, monitoring of creatinine and electrolytes, dose adjustment, and reduction of concomitant nephrotoxic agents [1, 2, 4, 11]. In addition, recent observational data suggest that sodium-glucose cotransporter 2 inhibitors (SGLT2i) may be associated with a lower risk of cisplatin-associated acute kidney injury and hypomagnesemia in patients with diabetes [14], although this finding has not been reproduced in all series [15] and requires confirmation in prospective studies.

The clinical consequences of platinum-induced nephrotoxicity extend beyond a transient increase in creatinine. Kidney injury can lead to incomplete renal recovery, persistent acute kidney disease, progression to chronic kidney disease, the need for renal replacement therapy, longer hospital stays, interruption or modification of cancer treatment, and increased mortality [5, 7–9, 13, 16].

Despite international evidence, in Mexico and Latin America there is limited information on the frequency, clinical characteristics, associated factors, and outcomes of platinum-induced nephrotoxicity in adults with solid tumors. This gap is significant because the conditions of care, comorbidities, hydration regimens, availability of monitoring, and clinical characteristics of patients may differ from those reported in other countries.

Methods

Aims

To estimate the frequency of platinum-based chemotherapy-induced nephrotoxicity, describe the clinical characteristics, and determine the renal and clinical outcomes in adults with solid tumors.

Study design and period

Observational, retrospective, analytical cohort study of cancer patients with solid tumors exposed to platinum-based chemotherapy (cisplatin, carboplatin or oxaliplatin) treated in the Department of Medical Oncology in a tertiary referral hospital in Mexico (Hospital General de México “Dr. Eduardo Liceaga”) over a period of 5 years (January 1, 2021 to March 31, 2026). For analyses by platinum agent, patients were classified by the platinum compound initially administered, resulting in three mutually exclusive groups.

Sample size

To determine the sample size, the statistical software G*Power (v.3.1.9.7) [17] was used, assuming a design comparing two independent proportions via a one-tailed Fisher’s exact test. Configuration parameters included a significance level (α) of 0.05 and a power of 80% ($1-\beta$). Baseline nephrotoxicity rates for the comparison were estimated based on findings reported in previous literature [1–4].

Inclusion criteria

1. Aged ≥ 18 years.
2. ≥ 1 cycle of platinum-based chemotherapy.
3. At least two serum creatinine measurements: pre-treatment and follow-up during the cycle, as well as serum electrolyte measurements.

Exclusion criteria

1. Chronic kidney disease prior to treatment initiation, estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m².
2. Prior renal replacement therapy or history of kidney transplantation.
3. Presence of acute kidney injury prior to exposure to the first cycle of platinum-based chemotherapy.
4. Undefined primary tumor.

Patient identification: review of physical medical records from the Department of Medical Oncology (Fig. 1). This study complies with STROBE guidelines.

Median (IQR) follow-up from the first dose of the platinum agent: 4 (2.2–5.8) months.

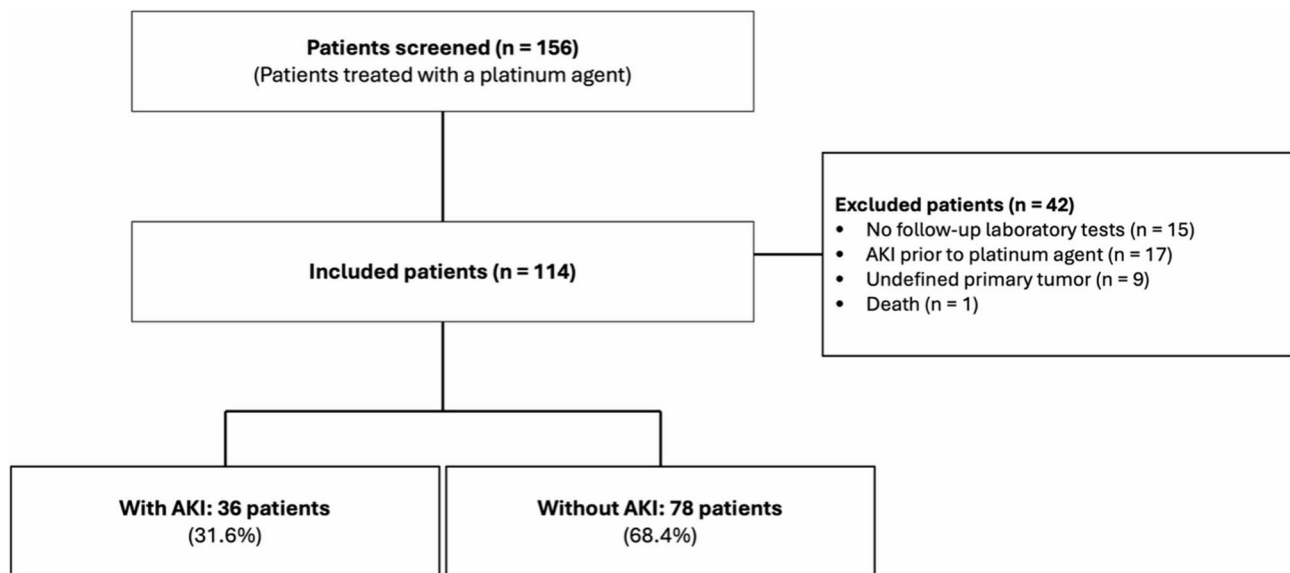


Fig. 1 STROBE participant flow diagram. Abbreviations: AKI, acute kidney injury; n, number

Outcome definitions

Acute kidney injury

- Defined according to the KDIGO 2012 [6] acute kidney injury, based solely on blood creatinine levels. Base-line serum creatinine was defined as the serum creatinine level prior to the first cycle of the platinum agent.
- **Measurement timing:** 48–72 h prior to the start of each platinum-agent cycle and at the end of treatment.
- **Follow-up visits:** 2–4 weeks after the platinum agent infusion.

Electrolyte disturbance

- **Measured electrolytes and thresholds:** Sodium (135–145 mEq/L), Potassium (3.5–5.5 mEq/L), Chloride (99–110 mEq/L), Calcium (8.5–10 mg/dL), Phosphorus (2.5–4.5 mg/dL), and Magnesium (1.8–2.2 mg/dL).
- **Measurement timing:** 48–72 h prior to the start of each platinum-agent cycle and at the end of treatment.
- **Classification:** Hyponatremia: <135 mEq/L; hypokalemia: <3.5 mEq/L; hypochloremia: <99 mEq/L; XXXuspensiónXXXa: <8.5 mg/dL; hypophosphatemia: <2.5 mg/dL; and hypomagnesemia: <1.8 mg/dL.

Chronic kidney disease

- **Measurement timing:** Serum creatinine was measured 48–72 h prior to the start of each cycle of platinum agent and at the end of treatment.
- **KDIGO 2024 [18] definition:** eGFR < 60 ml/min/1.73 m² for ≥ 90 days.

Dose modification

- **Definition:** reduction of the platinum agent dose below the full dose calculated based on the patient's body surface area.

This measure was determined by the oncologist during follow-up consultations if one or more of the following factors were present: decreased renal function ($\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$) or signs of non-severe hematologic, neurologic, auditory, or gastrointestinal toxicity.

Treatment discontinuation

- **Definition:** suspension of the platinum agent. This measure was determined by the oncologist during follow-up consultations if one or more of the following factors were present: decreased renal function ($\text{eGFR} < 30 \text{ ml/min/1.73 m}^2$) or signs of severe hematologic, neurologic, auditory, or gastrointestinal toxicity

Renal replacement therapy

- **Modality:** Intermittent hemodialysis
- **Indications:** Severe metabolic acidosis refractory to pharmacological treatment, hyperkalemia refractory to pharmacological treatment, fluid overload refractory to diuretics, and severe symptomatic uremia
- **Timing of initiation:** $< 24 \text{ h}$ after the indication

Institutional standard for supportive care prevention strategies and hydration protocols

6 to 12 h before and after platinum agent administration:

- Hydration with 0.9% saline solution: Continuous infusion at 100–200 mL/hour.
- Magnesium and potassium supplementation: 4 g magnesium sulfate + 40 mEq potassium chloride.
- Prophylactic antiemetic therapy: Ondansetron 8 mg intravenously.
- Monitoring of creatinine and serum electrolytes: 48–72 h prior to platinum agent administration.

Statistical analysis

The distribution of quantitative variables was assessed using the Shapiro-Wilk normality test. Normally distributed variables were described using the mean and standard deviation, while non-normally distributed variables were expressed as the median and interquartile range. Categorical variables were presented using absolute frequencies and percentages. For comparative analysis, patients were classified according to the presence or absence of acute kidney injury as defined by KDIGO 2012 criteria. Accordingly, all comparisons were made between platinum-treated patients who developed acute kidney injury and those who did not; the study did not include a control group of cancer patients not exposed to platinum. Quantitative variables were compared using the Student's t-test for independent samples and the Mann-Whitney U test, as appropriate. Categorical variables were analyzed using the chi-square test or Fisher's exact test when expected frequencies were less than five.

Given the limited number of AKI events ($n = 36$), no multivariable regression model was performed. A $p < 0.05$ value was considered statistically significant.

Due the exploratory nature of the study, no adjustment for multiple comparisons was applied, and all analyses should be regarded as exploratory and hypothesis-generating.

Statistical analysis was performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 114 patients with solid tumors treated with platinum-based chemotherapy were included in the study. The mean age was 46.6 ± 15.5 years, and the majority of patients were women (64.9%). Hypertension and type 2 diabetes were each present in 23.7% of the cohort. Concomitant use of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers was reported in 22.8% of patients, while sodium-glucose cotransporter-2 inhibitors (SGLT2i) were used by 13.2%. A history of smoking and alcohol consumption was reported in 43.9% and 44.7% of patients, respectively. Statin therapy was documented in 12.3% of patients, while diuretic use was infrequent (0.9%). Pre-treatment renal function was generally preserved. Serum creatinine before the start of platinum therapy was 0.70 mg/dL (0.60–0.90), corresponding to an eGFR by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) of 109.6 mL/min/1.73 m² (99.4–122.5) (Table 1).

In the overall cohort testicular cancer was the most common neoplasm (29.8%), followed by colon cancer (14.0%), head and neck cancer (13.2%), ovarian cancer (13.2%), rectal cancer (9.6%), bone cancer (7.0%), cholangiocarcinoma (5.3%), bladder cancer (5.3%), lung cancer (1.8%), and endometrial cancer (0.9%) (Table 2).

In the overall cohort at the last dose of chemotherapy, serum creatinine increased to 0.90 mg/dL (0.70–1.10), while the eGFR decreased to 98.2 mL/min/1.73 m² (76.4–115.7). Serum magnesium decreased from 2.0 mg/dL (1.9–2.1) before treatment to 1.8 mg/dL (1.7–2.0) after platinum exposure (Table 3).

Cisplatin was the most frequently administered platinum agent (48.2%), followed by carboplatin (26.3%) and oxaliplatin (25.4%). Patients received a median of 5 [4–6] platinum cycles. Among patients treated with carboplatin, the median number of cycles was 3 (IQR 2–6), with 4 [2–6] cycles among patients without AKI and 2

Table 1 Baseline patient characteristics

Variable	Without AKI (<i>n</i> = 78)	AKI (<i>n</i> = 36)	<i>p</i> -value
Age, years (mean ± SD)	45.8 ± 15.7	48.2 ± 15.3	0.442
Female, <i>n</i> (%)	49 (62.8)	25 (69.4)	0.533
Systemic arterial hypertension, <i>n</i> (%)	17 (21.8)	10 (27.8)	0.487
Type 2 diabetes, <i>n</i> (%)	16 (20.5)	11 (30.6)	0.247
ACE inhibitors/ARBs, <i>n</i> (%)	16 (20.5)	10 (27.8)	0.472
Diuretics, <i>n</i> (%)	0 (0.0)	1 (2.8)	0.316
SGLT2 inhibitors, <i>n</i> (%)	9 (11.5)	6 (16.7)	0.553
History of smoking, <i>n</i> (%)	33 (42.3)	17 (47.2)	0.687
Alcohol consumption, <i>n</i> (%)	35 (44.9)	16 (44.4)	0.999
Statins, <i>n</i> (%)	9 (11.5)	5 (13.9)	0.763
Consumption of toxic substances*, <i>n</i> (%)	11 (14.1)	2 (5.6)	0.222
Serum creatinine (mg/dL), median (IQR)	0.80 (0.60–0.90)	0.70 (0.60–0.90)	0.466
eGFR (mL/min/1.73 m ²), median (IQR)	110.4 (98.9–120.0)	108.5 (100.3–125.0)	0.833
Urea (mg/dL), median (IQR)	28.2 (22.3–36.1)	33.5 (21.7–39.7)	0.359
Sodium (mEq/L), median (IQR)	138.5 (136.0–140.0)	138.5 (135.5–140.0)	0.854
Potassium (mEq/L), median (IQR)	4.1 (3.9–4.4)	4.1 (3.8–4.3)	0.449
Chloride (mEq/L), median (IQR)	102.5 (100.0–105.0)	102.0 (101.0–105.0)	0.741
Calcium (mg/dL), median (IQR)	9.1 (8.8–9.4)	9.0 (8.8–9.2)	0.371
Phosphorus (mg/dL), median (IQR)	3.75 (3.30–4.00)	3.50 (3.15–3.90)	0.170
Magnesium (mg/dL), median (IQR)	2.0 (1.9–2.1)	2.0 (1.9–2.1)	0.259
Albumin (g/dL), median (IQR)	3.9 (3.5–4.2)	3.8 (3.4–4.1)	0.537

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; SGLT2, sodium-glucose cotransporter-2; SD, standard deviation; *n*, number. IQR, interquartile range.*Alcoholism, illicit drugs and/or solvents

Table 2 Types of solid tumors

Solid tumor	Without AKI (<i>n</i> = 78) <i>n</i> (%)	AKI (<i>n</i> = 36) <i>n</i> (%)	<i>p</i> -value*
Head and neck cancer	9 (11.5)	6 (16.7)	0.279
Cholangiocarcinoma	2 (2.6)	4 (11.1)	
Colon cancer	11 (14.1)	5 (13.9)	
Endometrial cancer	1 (1.3)	0 (0.0)	
Bone cancer	5 (6.4)	3 (8.3)	
Ovarian cancer	12 (15.4)	3 (8.3)	
Lung cancer	2 (2.6)	0 (0.0)	
Rectal cancer	5 (6.4)	6 (16.7)	
Testicular cancer	27 (34.6)	7 (19.4)	
Bladder cancer	4 (5.1)	2 (5.6)	

Abbreviations: AKI, acute kidney injury; *n*, number. *The variables were analyzed using the chi-square test or Fisher's exact test when expected frequencies were less than five

Table 3 Laboratory characteristics after the use of platinum chemotherapy

Variable	Without AKI (<i>n</i> = 78) median (IQR)	AKI (<i>n</i> = 36) median (IQR)	<i>p</i> -value
Serum creatinine (mg/dL)	0.80 (0.60–0.90)	1.10 (1.00–1.30)	-
eGFR (mL/min/1.73 m ²)	105.9 (90.6–117.6)	74.4 (61.5–88.6)	-
Urea (mg/dL)	30.8 (25.1–40.2)	47.1 (35.2–56.1)	-
Sodium (mEq/L)	137.0 (136.0–139.0)	138.0 (136.0–139.0)	0.922
Potassium (mEq/L)	4.1 (3.9–4.3)	4.0 (3.6–4.4)	0.531
Chloride (mEq/L)	102.0 (101.0–105.0)	102.0 (100.0–103.0)	0.225
Calcium (mg/dL)	9.0 (8.8–9.2)	9.0 (8.7–9.3)	0.510
Phosphorus (mg/dL)	3.6 (3.3–3.9)	3.4 (3.2–4.0)	0.475
Magnesium (mg/dL)	1.9 (1.7–2.0)	1.7 (1.6–1.9)	0.006

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; *n*, number; IQR, interquartile range

Table 4 Platinum chemotherapy exposure according to acute kidney injury status

Platinum chemotherapy exposure	Without AKI (<i>n</i> = 78) median (IQR) <i>n</i>	AKI (<i>n</i> = 36) median (IQR) <i>n</i>	<i>p</i> -value
Cisplatin cumulative dose (mg/m ²)	407.6 (348.2–504.7) <i>n</i> = 34	356.5 (222.0–517.4) <i>n</i> = 21	0.249
Carboplatin* (number of cycles)	4 (2–6) <i>n</i> = 25	2 (2–5) <i>n</i> = 5	—
Oxaliplatin cumulative dose (mg/m ²)	720.2 (632.0–906.9) <i>n</i> = 19	699.1 (625.1–877.1) <i>n</i> = 10	0.909

*Carboplatin target AUC was not available; therefore, carboplatin exposure is presented as the number of treatment cycles rather than cumulative dose in milligrams

Abbreviations: AKI, acute kidney injury; *n*, number; IQR, interquartile range

[2–5] among those with AKI. Target carboplatin AUC was not available. The cumulative doses (Cisplatin and Oxaliplatin), which varied by agent, did not differ significantly between patients with and without AKI (Table 4).

AKI occurred in 36 patients (31.6%) and its frequency varied across the initially administered platinum agents: 21 of 55 patients receiving cisplatin (38.2%), 5 of 30 receiving carboplatin (16.7%), and 10 of 29 receiving oxaliplatin (34.5%). Among patients initially treated with cisplatin who developed AKI, 13 had KDIGO stage 1 and 8 had stage 3 AKI. Among those initially treated with carboplatin, 4 had stage 1 and 1 had stage 3 AKI, while among those initially treated with oxaliplatin, 8 had stage 1, 1 had stage 2, and 1 had stage 3 AKI (Fig. 2). Overall, among the 36 patients with AKI, 25 (69.4%) were classified as KDIGO stage 1, 1 (2.8%) as stage 2, and 10 (27.8%) as stage 3 (Fig. 2).

Electrolyte disturbances were documented in 40 patients (35.1%). They were more frequent among patients with AKI (19/36, 52.8%) than among those without AKI (21/78, 26.9%; *p* = 0.007). Notably, 21 patients had electrolyte disturbances without meeting creatinine-based criteria for AKI. Among patients with AKI, 9 (25.0%) received renal replacement therapy. In all nine patients, the documented indication for hemodialysis was clinically

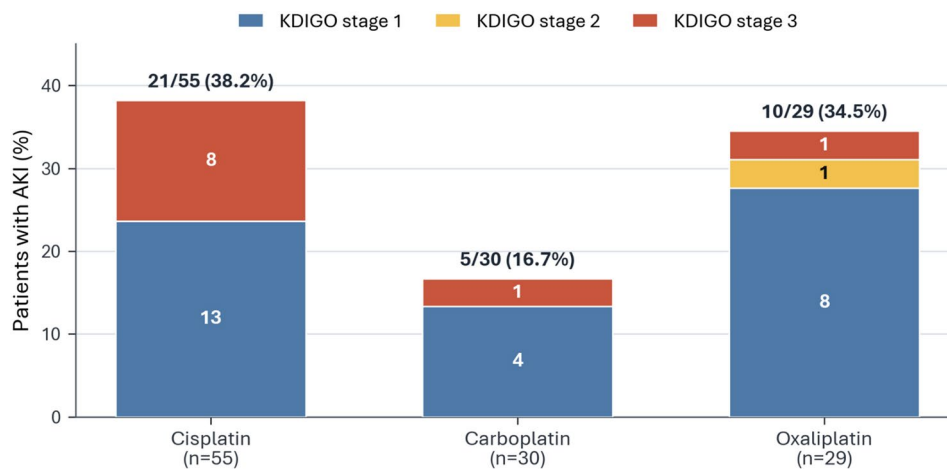


Fig. 2 AKI frequency and KDIGO stage according to platinum agent. Stacked bars represent the proportion of patients classified according to the initially administered platinum agent. Numbers within each segment indicate the number of patients in each KDIGO stage, while values above the bars indicate the overall frequency of AKI for each agent. Among the 36 patients who developed AKI, 25 (69.4%) were classified as KDIGO stage 1, 1 (2.8%) as stage 2, and 10 (27.8%) as stage 3. AKI staging was based on available serum creatinine and kidney replacement therapy criteria, as urine output was not systematically recorded. Abbreviations: AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes

Table 5 Outcomes after the use of platinum chemotherapy

Abbreviations: AKI, acute kidney injury; n, number

Outcome	AKI (n = 36), n (%)
Renal replacement therapy	9 (25.0)
Chronic kidney disease	6 (16.7)
Treatment discontinuation	8 (22.2)
Dose modification	10 (27.8)
Mortality	1 (2.8)

significant fluid overload with respiratory compromise. Renal replacement therapy was temporary in all cases; all patients subsequently became independent of kidney replacement therapy during the available follow-up, and none remained on maintenance dialysis. CKD was documented in 6 patients (16.7%), treatment was discontinued in 8 (22.2%), dose modification was required in 10 (27.8%), and 1 patient (2.8%) died during the available follow-up, median (IQR) 4 months (2.2-5-8).(Table 5).

Discussion

In this retrospective cohort of 114 patients with solid tumors who received platinum-based chemotherapy, nearly one-third of the patients developed acute kidney injury despite having preserved pre-treatment renal function and a relatively young age. Among patients who developed AKI, clinically relevant kidney and oncologic outcomes were frequently observed, including kidney replacement therapy, chronic kidney disease, chemotherapy dose modification, and treatment discontinuation. These findings suggest that platinum nephrotoxicity remains a significant clinical challenge and emphasize the need to assess kidney injury the broader context of cancer treatment and kidney-related outcomes [2, 3, 8, 19].

The incidence of AKI observed in our study (31.6%) is consistent with contemporary reports describing nephrotoxicity rates ranging from 20% to 35% among patients receiving platinum-based chemotherapy [3, 8, 12, 13, 19]. However, the clinical significance of our findings lies not only in the frequency of AKI but also in the characteristics of the affected population. Pre-treatment renal function was largely preserved, with a median estimated

glomerular filtration rate greater than 100 mL/min/1.73 m², and the mean age was less than 50 years. In this cohort, “low renal risk” refers to the absence of the classical risk factors for platinum nephrotoxicity: by design, patients with an eGFR below 60 mL/min/1.73 m², prior renal replacement therapy or AKI before the first cycle were excluded; the prevalence of hypertension and diabetes was low (23.7% each); diuretic use was exceptional; and no patient was receiving nonsteroidal anti-inflammatory drugs or proton pump inhibitors at baseline. Thus, the substantial burden of kidney injury observed in our cohort indicates that platinum-associated acute kidney injury is common even in patients without traditional renal risk factors. This low-risk profile is, however, partly a consequence of the eligibility criteria rather than a natural characteristic of the platinum-treated population, since the patients at highest a priori renal risk were excluded by design. It should be emphasized that our study did not include a control group of cancer patients not exposed to platinum: all comparisons were made between platinum-treated patients who did and did not develop AKI. Consequently, our data describe the frequency and consequences of AKI in this setting and do not allow the independent effect of platinum exposure on renal or clinical outcomes to be isolated from that of the underlying malignancy or its treatment.

The clinical course of patients who developed AKI deserves particular attention. In particular, one-quarter of patients with AKI required renal replacement therapy (with fluid overload refractory to diuretics being the primary cause), approximately one in six developed chronic kidney disease, and more than one in five discontinued chemotherapy. These observations suggest that the clinical burden of platinum nephrotoxicity extends beyond short-term increases in serum creatinine and affects both renal outcomes and the delivery of cancer treatment [20–23].

Another clinically relevant observation was the frequency of cancer treatment modification among patients with AKI. Maintaining treatment intensity and cumulative dose exposure are recognized determinants of therapeutic efficacy, particularly in potentially curable neoplasms such as testicular cancer, which represented the largest subgroup in our cohort [8, 20–22]. However, our study did not collect data on tumor response or disease progression, and therefore it cannot establish whether these treatment modifications translated into poorer tumor control. Whether platinum-associated AKI affects oncological outcomes through reduced treatment intensity should be addressed in studies with prospective assessment of tumor response and survival.

Another notable finding was the high frequency of electrolyte abnormalities, which were documented in 40 patients (35.1%). Electrolyte disturbances were more frequent among patients with AKI than among those without AKI (52.8% vs. 26.9%, $p=0.007$). However, 21 patients without creatinine-defined AKI also had electrolyte abnormalities. Only serum magnesium after platinum exposure was significantly lower in patients who developed AKI (median 1.7 vs. 1.9 mg/dL), whereas post-treatment sodium, potassium, chloride, calcium and phosphorus did not differ between groups and their median values remained within the normal range. These findings are therefore consistent with the tubular component of platinum nephrotoxicity, with magnesium wasting as its most sensitive biochemical expression, but they do not indicate widespread or clinically severe electrolyte disturbances in this population. Furthermore, although electrolyte abnormalities occurring without creatinine-defined AKI may reflect platinum-associated tubular effects, our data cannot establish that these abnormalities represent subclinical kidney injury. Furthermore, given the large number of comparisons performed without adjustment for multiplicity, the isolated association between lower post-treatment magnesium and AKI ($p=0.006$) should be interpreted as exploratory and hypothesis-generating.

Experimental studies have demonstrated preferential accumulation of platinum compounds within proximal tubular epithelial cells via OCT2, leading to mitochondrial dysfunction, oxidative stress, inflammatory signaling, and tubular cell death [2, 19, 24, 25]. From a practical point of view, these findings support monitoring serum electrolytes, particularly magnesium, during platinum-based chemotherapy [26, 27].

In our cohort, none of the evaluated baseline clinical characteristics showed a statistically significant association with AKI in the univariate comparisons. Previous studies have identified age, hypertension, diabetes, hypoalbuminemia, reduced renal function and cumulative cisplatin exposure [3, 12, 28, 29]. Our population, however, was relatively homogeneous, with preserved baseline renal function and a low prevalence of comorbidities, which limits the between-group variability needed to detect such associations, and the sample size was

not designed for the identification of risk factors. Only 36 AKI events occurred, and therefore a multivariable model was not performed. The absence of significant associations in our cohort should therefore be interpreted in this context and does not contradict the established role of these risk factors in other populations. Validation of existing risk prediction models [28, 29] in Latin American patients will require larger, multicenter studies.

Similarly, the cumulative platinum dose did not differ between patients with and without AKI. Several factors may explain this observation. First, cisplatin-associated AKI frequently develops after the first cycles of treatment, when the cumulative dose is still low, so that the dose administered per cycle may be more relevant than the total dose received [28, 29]. Second, the occurrence of AKI itself led to dose reduction or treatment discontinuation in a substantial proportion of patients, which lowers the cumulative dose ultimately received by the AKI group and attenuates, or even reverses, any dose–response relationship in a retrospective analysis. Third, cumulative doses were relatively homogeneous within each agent, reflecting the use of standardized regimens, and the number of patients per agent limited the power to detect differences. The dose-dependent nature of cisplatin nephrotoxicity is well established [1, 2], and our results should not be interpreted as questioning it, but rather as indicating that, within the dose ranges used in standard regimens, cumulative dose alone did not discriminate between patients who did or did not develop AKI. Of note, SGLT2 inhibitors, which have recently been associated with a lower risk of cisplatin-associated AKI and hypomagnesemia in patients with diabetes [14, 15], were used by 13.2% of our patients, with no difference in their use between patients with and without AKI (16.7% vs. 11.5%, $p = 0.553$); the small number of exposed patients, however, precludes any conclusion regarding a potential protective effect.

Mortality was low (1.8%) and did not differ between groups, which likely reflects the relatively young population, the predominance of curative-intent treatment strategies, and the limited duration of follow-up, median (IQR) 4 months (2.2–5–8). Given the small number of events, our study was not powered to detect differences in mortality, and no conclusion regarding the effect of AKI on survival can be drawn from these data. In this setting, the measurable burden of platinum nephrotoxicity was related to treatment modification and to renal sequelae (chronic kidney disease and renal replacement therapy); whether these outcomes translate into differences in long-term survival, as reported in other cohorts [20–23], would require longer follow-up.

Strengths of this study include the evaluation of a real-world Latin American population, a region considerably underrepresented in the onconephrology literature; the inclusion of all major platinum compounds in different solid tumor types; and the assessment of clinically relevant outcomes beyond the incidence of AKI. Furthermore, the simultaneous assessment of electrolyte disturbances provides a more comprehensive characterization of the renal abnormalities observed during platinum-based chemotherapy.

Several limitations should be noted. First, the retrospective, single-center design, limits the generalizability of results and causal inference, and introduces the possibility of residual confounding. Furthermore, complete specific information was not available in some of the medical records, making it impossible to fully determine the factors leading to dose modification or discontinuation of the platinum agent, or whether there was exposure to other nephrotoxic agents. Second, the modest sample size and the 36 observed AKI events limited the ability to perform a reliable multivariable analysis. A conventional model including several candidate predictors would have resulted in a low number of events per variable and a substantial risk of overfitting; therefore, no adjusted model was performed. Third, while all patients had serum creatinine and electrolyte measurements taken before and at the end of treatment, not all had these measurements taken prior to the start of each platinum-agent cycle; furthermore, reliance on serum creatinine likely underestimated subclinical tubular injury, especially given the delayed rise in creatinine following platinum exposure [2, 19, 30]. Urine output was not systematically recorded, and therefore AKI staging was based on serum creatinine and kidney replacement therapy criteria. The exact date and treatment cycle at AKI onset were not consistently available, which precluded reliable reporting of the cycle at first AKI and time from the first platinum dose to AKI. In addition, serum creatinine was not measured at standardized time points after AKI, preventing a formal assessment of complete or partial kidney recovery. Fourth, treatment regimens, supportive-care strategies, hydration protocols, and other potential contributors to kidney injury were not systematically collected in this retrospective study; therefore, their potential influence on the observed incidence of AKI could not be adequately assessed, and residual confounding cannot be excluded.

In particular, data on prophylactic or reactive magnesium supplementation were not systematically recorded and could not be analyzed; since magnesium repletion is part of standard supportive care during cisplatin administration and may modify both the risk of hypomagnesemia and of acute kidney injury, this represents a relevant source of unmeasured confounding. In addition, AKI episodes were not adjudicated for competing causes that are frequent in cancer patients, such as volume depletion, sepsis, urinary tract obstruction or iodinated contrast exposure, so a proportion of the events attributed to platinum may be multifactorial. Moreover, the inclusion criteria required at least two serum creatinine measurements and serum electrolyte determinations, which conditions the cohort on the intensity of laboratory monitoring and may have selected patients with closer follow-up, while the exclusion of patients with an eGFR below 60 mL/min/1.73 m² removed the group at highest a priori risk of nephrotoxicity; the reported frequencies therefore apply to monitored patients with preserved baseline renal function and cannot be extrapolated to unselected populations. In addition, target AUC data for carboplatin were not available, limiting the assessment of the relationship between carboplatin exposure and nephrotoxicity. Fifth, the study lacked a control group of cancer patients not exposed to platinum, and data on tumor response or disease progression were not collected; therefore, our findings describe the consequences of AKI among platinum-treated patients and cannot quantify the oncological impact of treatment modifications. Finally, the relatively short follow-up period limited the assessment of long-term renal outcomes and survival.

In summary, these findings support a proactive onconeurological approach that incorporates structured monitoring of renal function and electrolytes, correction of hypomagnesemia, and early intervention by a nephrologist when nephrotoxicity develops. Future prospective, multicenter studies including biomarkers of tubular injury and longer follow-up are needed to refine risk stratification and optimize renal-protective strategies in patients receiving platinum-based chemotherapy.

Conclusion

In this Latin American cohort, acute kidney injury occurred in nearly one-third of patients receiving platinum-based chemotherapy, despite preserved baseline renal function and a low prevalence of traditional renal risk factors. Acute kidney injury was associated with hypomagnesemia, chronic kidney disease, the need for renal replacement therapy and, notably, with chemotherapy dose modification and treatment discontinuation, whereas short-term mortality did not differ. These findings support systematic monitoring of renal function and serum magnesium during platinum therapy and early nephrological involvement, with the aim of preserving both kidney function and the delivery of cancer treatment.

Abbreviations

AKI	Acute kidney injury
DNA	Deoxyribonucleic acid
KDIGO	Kidney Disease: Improving Global Outcomes
AKD	Acute kidney disease
OCT2	Organic cation transporter 2
CTR1	Copper transporter 1
MATE1	Multidrug and toxin extrusion protein 1
eGFR	Estimated glomerular filtration rate
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
ACEI	Angiotensin-converting enzyme inhibitor
ARB	Angiotensin II receptor antagonist
SGLT2	Sodium-glucose cotransporter-2
SD	Standard deviation

N Number
IQR Interquartile range

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Declarations

Ethics approval and consent to participate The study was approved by the institutional ethics committee of Hospital General de México “Dr. Eduardo Liceaga”, and was conducted in accordance with the Declaration of Helsinki. The institutional ethics committee granted a waiver of informed consent, as the study was observational and retrospective, based exclusively on a review of medical records, without direct clinical interventions involving the patients.

Consent for publication Not applicable.

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Competing interests The authors declare no competing interests.

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References

1. Zhang J, Ye ZW, Tew KD, Townsend DM. Cisplatin chemotherapy and renal function. *Adv Cancer Res.* 2021;152:305–27. <https://doi.org/10.1016/bs.acr.2021.03.008>.
2. Lyrio RMC, Rocha BRA, Corrêa ALRM, Mascarenhas MGS, Santos FL, Maia RH, et al. Chemotherapy-induced acute kidney injury: epidemiology, pathophysiology, and therapeutic approaches. *Front Nephrol.* 2024;4:1436896. <https://doi.org/10.3389/fneph.2024.1436896>.
3. Burns CV, Edwin SB, Szpunar S, Forman J. Cisplatin-induced nephrotoxicity in an outpatient setting. *Pharmacotherapy.* 2021;41(2):184–90. <https://doi.org/10.1002/phar.2500>.
4. Shahrahmani F, Badamchizadeh S, Kaihani F, Alavi-Moghadam S, Keshtkari S, Rezaei-Tavirani M, et al. Platinum-based chemotherapies-induced nephrotoxicity: mechanisms, potential treatments, and management. *Int Urol Nephrol.* 2025;57(6):1563–83. <https://doi.org/10.1007/s11255-024-04303-2>.
5. Fernandes ARDS, de Brito GA, Baptista AL, Andrade LAS, Imanishe MH, Pereira BJ. The influence of acute kidney disease on the clinical outcomes of patients who received cisplatin, carboplatin, and oxaliplatin. *Health Sci Rep.* 2022;5(1):e479. <https://doi.org/10.1002/hsr.2.479>.

6. Kidney Disease. Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012;2(1):1–138.
7. Chawla LS, Bellomo R, Bihorac A, Goldstein SL, Siew ED, Bagshaw SM, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. *Nat Rev Nephrol.* 2017;13(4):241–57. <https://doi.org/10.1038/nrneph.2017.2>.
8. Trevisani F, Di Marco F, Quattrini G, Lepori N, Floris M, Valsecchi D, et al. Acute kidney injury and acute kidney disease in high-dose cisplatin-treated head and neck cancer. *Front Oncol.* 2023;13:1173578. <https://doi.org/10.3389/fonc.2023.1173578>.
9. Renaghan AD, Ostermann M, Ronco C, Ballen K, Cosmai L, Fenoglio R, et al. The nephrotoxic effects of anti-cancer therapies: consensus report of the 34th Acute Disease Quality Initiative workgroup. *Nat Rev Nephrol.* 2026;22(4):283–300. <https://doi.org/10.1038/s41581-025-01031-3>.
10. Volarevic V, Djokovic B, Gazdic Jankovic M, Harrell CR, Fellabaum C, Djonov V, et al. Molecular mechanisms of cisplatin-induced nephrotoxicity: a balance on the knife edge between renoprotection and tumor toxicity. *J Biomed Sci.* 2019;26(1):25. <https://doi.org/10.1186/s12929-019-0518-9>.
11. n der Vorst MJDL, Neefjes ECW, Toffoli EC, Oosterling-Jansen JEW, Vergeer MR, Leemans CR, et al. Incidence and risk factors for acute kidney injury in head and neck cancer patients treated with concurrent chemoradiation with high-dose cisplatin. *BMC Cancer.* 2019;19(1):1066. <https://doi.org/10.1186/s12885-019-6233-9>.
12. Liu JQ, Cai GY, Wang SY, Song YH, Xia YY, Liang S, et al. The characteristics and risk factors for cisplatin-induced acute kidney injury in the elderly. *Ther Clin Risk Manag.* 2018;14:1279–85. <https://doi.org/10.2147/TCRM.S165531>.
13. Wondm SA, Dagnew SB, Dagnew FN, Tarekegn GY, Moges TA, Abebe RB, et al. Cisplatin-based chemotherapy-induced nephrotoxicity and its impact on the survival status of patients with gynecological cancer in Ethiopia: a multicenter retrospective cohort study. *Sci Afr.* 2025;28:e02666. <https://doi.org/10.1016/j.sciaf.2025.e02666>.
14. Cintrón-García JJ, Patel M, Andersen CR, Page V, Workeneh B, Mandayam S, et al. Potential benefit of sodium-glucose cotransporter 2-inhibitors in cisplatin-associated nephrotoxicity among patients with cancer having diabetes mellitus. *Kidney Int Rep.* 2026;11(6):106538. <https://doi.org/10.1016/j.ekir.2026.106538>.
15. Ishigami Y, Takahashi M, Nakatsukasa H, Nishiura H, Kohara Y, Nakamura Y. Efficacy of SGLT-2 inhibitors in preventing cisplatin-induced kidney injury in patients with diabetes. *Anticancer Res.* 2025;45(11):5185–90. <https://doi.org/10.21873/anticancer.17858>.
16. Latcha S, Jaimes EA, Patil S, Glezerman IG, Mehta S, Flombaum CD. Long-term renal outcomes after cisplatin treatment. *Clin J Am Soc Nephrol.* 2016;11(7):1173–9. <https://doi.org/10.2215/CJN.08070715>.
17. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods.* 2009;41(4):1149–60. <https://doi.org/10.3758/BRM.41.4.1149>.
18. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024;105(4S):S117–314. <https://doi.org/10.1016/j.kint.2023.10.018>.
19. Tang C, Livingston MJ, Safirstein R, Dong Z. Cisplatin nephrotoxicity: new insights and therapeutic implications. *Nat Rev Nephrol.* 2023;19(1):53–72. <https://doi.org/10.1038/s41581-022-00631-7>.
20. Rosner MH, Perazella MA. Acute Kidney Injury in Patients with Cancer. *N Engl J Med.* 2017;376(18):1770–81. <https://doi.org/10.1056/NEJMr1613984>.
21. Kitchlu A, McArthur E, Amir E, et al. Acute Kidney Injury in Patients Receiving Systemic Treatment for Cancer: A Population-Based Cohort Study. *J Natl Cancer Inst.* 2019;111(7):727–36. <https://doi.org/10.1093/jnci/djy167>.
22. Rosner MH, Jhaveri KD, McMahon BA, Perazella MA. Onconephrology: The intersections between the kidney and cancer. *CA Cancer J Clin.* 2021;71(1):47–77. <https://doi.org/10.3322/caac.21636>.
23. Christiansen CF, Johansen MB, Langeberg WJ, Fryzek JP, Sørensen HT. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. *Eur J Intern Med.* 2011;22(4):399–406. <https://doi.org/10.1016/j.ejim.2011.05.005>.
24. Miller RP, Tadagavadi RK, Ramesh G, Reeves WB. Mechanisms of Cisplatin nephrotoxicity. *Toxins (Basel).* 2010;2(11):2490–518. <https://doi.org/10.3390/toxins2112490>.
25. Ozkok A, Edelstein CL. Pathophysiology of cisplatin-induced acute kidney injury. *Biomed Res Int.* 2014;2014:967826. <https://doi.org/10.1155/2014/967826>.
26. Hamroun A, Lenain R, Bigna JJ, et al. Prevention of Cisplatin-Induced Acute Kidney Injury: A Systematic Review and Meta-Analysis. *Drugs.* 2019;79(14):1567–82. <https://doi.org/10.1007/s40265-019-01182-1>.
27. Crona DJ, Faso A, Nishijima TF, McGraw KA, Galsky MD, Milowsky MI. A Systematic Review of Strategies to Prevent Cisplatin-Induced Nephrotoxicity. *Oncologist.* 2017;22(5):609–19. <https://doi.org/10.1634/theoncologist.2016-0319>.
28. Motwani SS, McMahon GM, Humphreys BD, Partridge AH, Waikar SS, Curhan GC. Development and Validation of a Risk Prediction Model for Acute Kidney Injury After the First Course of Cisplatin. *J Clin Oncol.* 2018;36(7):682–8. <https://doi.org/10.1200/JCO.2017.75.7161>.

29. Gupta S, Glezerman IG, Hirsch JS, et al. Derivation and external validation of a simple risk score for predicting severe acute kidney injury after intravenous cisplatin: cohort study. *BMJ*. 2024;384:e077169. <https://doi.org/10.1136/bmj-2023-077169>. Published 2024 Mar 27.
30. Vaidya VS, Ozer JS, Dieterle F, et al. Kidney injury molecule-1 outperforms traditional biomarkers of kidney injury in preclinical biomarker qualification studies. *Nat Biotechnol*. 2010;28(5):478–85. <https://doi.org/10.1038/nbt.1623>.

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