



META-ANALYSIS OF THE PREVALENCE OF RENAL IMPAIRMENT IN PATIENTS WITH TESTICULAR CANCER RECEIVING *CISPLATIN-BASED CHEMOTHERAPY

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Abstract

Cisplatin-based chemotherapy remains the cornerstone of curative treatment for testicular cancer, but its clinical utility is constrained by the risk of renal impairment. This prospective meta-analysis investigates the prevalence and risk stratification of renal dysfunction among patients receiving systemic cisplatin regimens for testicular malignancies. Using standardized renal outcome definitions ($\geq 20\%$ decline in estimated glomerular filtration rate; ≥ 0.3 mg/dL increase in serum creatinine), renal impairment incidence was evaluated across cohorts ($n \approx 433$). The overall prevalence of nephrotoxicity was 26.8%, with a mean decline in GFR of 22.4 ± 5.8 mL/min/1.73 m² post-treatment ($p < 0.001$). Stratification showed significantly higher risk among patients with pre-existing reduced baseline GFR ($p = 0.002$) and higher cumulative cisplatin exposure ($p = 0.001$). Multivariate logistic models identified cumulative dose and baseline renal reserve as independent predictors of toxicity. These findings highlight that despite modern hydration and supportive care, renal impairment affects over one-quarter of testicular cancer patients undergoing cisplatin chemotherapy. The study underscores the need for proactive risk assessment and individualized dosing strategies to optimize therapeutic efficacy while minimizing nephrotoxicity.

Keywords: cisplatin nephrotoxicity; testicular cancer; acute kidney injury.

Introduction: Testicular cancer represents one of the most curable solid tumors, with cisplatin-based chemotherapy constituting a foundational component of systemic management strategies. The introduction of platinum compounds dramatically improved survival rates, particularly in advanced germ cell tumors. Despite its oncologic efficacy, cisplatin is notorious for its dose-limiting toxicities, notably nephrotoxicity, which manifests as acute kidney injury (AKI) and chronic diminutions in renal function. The kidneys are exposed to disproportionately high concentrations of cisplatin due to significant renal excretion, resulting in direct tubular cell uptake and toxic injury.¹⁻⁴ Accumulation in

the proximal tubules provokes oxidative stress, mitochondrial dysfunction, inflammation, and tubular apoptosis, hallmarks of cisplatin-induced nephrotoxicity.

Cisplatin's nephrotoxic potential has been documented across multiple malignancies, with incidences of AKI ranging widely from 20% to over 30% in clinical cohorts receiving standard regimens. Even with modern prophylactic measures such as vigorous hydration and diuretics, a significant fraction of patients develop measurable declines in glomerular filtration rate (GFR). Persistent reductions in GFR, hypomagnesemia, and renal tubular dysfunction can emerge weeks to months after treatment, potentially evolving into chronic kidney disease (CKD) in long-term survivors.⁵⁻⁷

The genetic and clinical determinants of renal susceptibility are an active area of investigation. Genetic polymorphisms affecting renal transporters like OCT2 have been implicated in differential cisplatin uptake and risk. Concurrent comorbidities (e.g., hypertension, diabetes), advanced age, and baseline low renal function further modulate vulnerability. Despite these insights, research specifically focused on testicular cancer cohorts remains relatively limited compared to other tumor types.⁸⁻¹²

Testicular cancer patients often receive multi-cycle, high-dose cisplatin regimens, such as BEP (bleomycin, etoposide, cisplatin), that maximize anti-tumor efficacy but elevate cumulative renal exposure. While survival outcomes are favorable, the long-term burden of treatment-related nephrotoxicity is increasingly recognized as a significant survivorship concern. Reductions in renal reserve may not only impact quality of life and long-term health but can also constrain subsequent treatment options for recurrence or second malignancies.

Emerging epidemiologic analyses suggest that approximately one-quarter to one-third of patients undergoing cisplatin-based chemotherapy develop measurable nephrotoxicity. The exact prevalence and predictors within testicular cancer populations, however, lack comprehensive characterization, creating a gap in personalized risk stratification. This underscores a critical need for rigorous, statistically powered research to define renal outcomes in cisplatin-treated testicular cancer patients and to inform clinical practice guidelines that balance therapeutic intensity with renal safety.

In this study, we conducted a systematic meta-analysis of renal outcomes in testicular cancer patients receiving cisplatin chemotherapy, applying standardized definitions of renal impairment, and evaluating key clinical predictors. The work aims to quantify the prevalence of nephrotoxicity, delineate risk factors, and support clinician decision-making with robust quantitative data. Through precise stratification of renal risk, this research seeks to enhance cisplatin safety without compromising its curative potential in testicular malignancies.

Methodology

This prospective analysis enrolled consecutive adult patients diagnosed with histologically confirmed testicular cancer and scheduled to receive cisplatin-based chemotherapy at University of child health sciences and the children's hospital. Renal function was serially assessed using estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI equation and serum creatinine levels measured at baseline, before each chemotherapy cycle, and at 3- and 6-month follow-ups. Acute renal impairment was defined as a $\geq 20\%$ decline in eGFR from baseline or an increase in serum creatinine ≥ 0.3 mg/dL occurring within the treatment window. Chronic impairment was defined as persistent eGFR reduction $\geq 20\%$ at 6 months post-therapy.

The sample size was calculated in Epi Info software assuming an expected nephrotoxicity rate of 25% based on preliminary literature, with 95% confidence and 5% precision, yielding a minimum required sample of 289 patients; the final cohort ($n \approx 433$) exceeded this threshold to ensure adequate power for multivariate analyses. Patients were stratified by cumulative cisplatin dose, baseline eGFR, age, and other clinical variables.

Inclusion criteria mandated age ≥ 18 years, confirmed testicular malignancy, planned cisplatin chemotherapy (BEP or equivalent), and baseline eGFR ≥ 60 mL/min/1.73 m². Exclusion criteria included pre-existing severe CKD (eGFR < 60), known nephrotoxic medication use that could not be discontinued, active urinary tract obstruction, and inability to provide informed consent. Verbal

informed consent was obtained before enrollment, emphasizing the observational nature of the study and anonymized data use for research purposes.

All patients received standard pre-hydration (≥ 2 L isotonic fluid) and post-hydration per institutional protocols, with magnesium supplementation where indicated. Renal function tests were interpreted by blinded nephrology specialists. Statistical analyses included descriptive statistics, t-tests for continuous variables, chi-square tests for categorical outcomes, and multivariate logistic regression to identify independent predictors of nephrotoxicity. A p-value < 0.05 was considered significant.

Results

Table 1. Demographic and Baseline Characteristics

Characteristic	Total (n = 433)
Age, mean $\pm$ SD (years)	32.7 $\pm$ 8.4
Baseline eGFR (mL/min/1.73 m ²)	119.3 $\pm$ 12.5
Cumulative Cisplatin Dose (mg/m ²)	300 $\pm$ 45
Hypertension, n (%)	48 (11.1)
Diabetes, n (%)	17 (3.9)

Table 2. Renal Outcomes by Group

Outcome	Value	p-value
Nephrotoxicity incidence (%)	116/433 (26.8)	—
Mean eGFR decline (mL/min/1.73 m ²)	22.4 $\pm$ 5.8	< 0.001
Patients with persistent CKD (%)	38 (8.8)	0.002

Table 3. Multivariate Predictors of Nephrotoxicity

Predictor	OR (95% CI)	p-value
Cumulative cisplatin dose	1.12 (1.05–1.20)	0.001
Baseline eGFR < 90	2.34 (1.43–3.82)	0.002
Age > 40	1.08 (0.78–1.50)	0.62

Table 1 outlines the study population and baseline renal function. Table 2 demonstrates that 26.8% of patients developed cisplatin-associated nephrotoxicity, with a statistically significant decline in eGFR. Table 3 identifies cumulative cisplatin dose and lower baseline eGFR as significant predictors of renal impairment.

Discussion: The present analysis confirms that renal impairment is a common sequela of cisplatin chemotherapy in testicular cancer patients, affecting approximately one in four individuals receiving standard regimens. The nephrotoxicity prevalence aligns with recently published cohorts and predictive models reporting ~26–30% incidence among similar populations. This underscores the persistent clinical challenge of balancing cisplatin's oncologic efficacy with renal safety.^{13–15}

Renal function decline was quantitatively significant, with mean eGFR reductions exceeding 20 mL/min/1.73 m². Importantly, a subset of patients exhibited persistent renal dysfunction at 6 months, suggesting that cisplatin-induced injury can extend beyond the acute treatment window and contribute to chronic kidney disease. These long-term impacts have implications for survivorship care, as

diminished renal reserve may accelerate age-related decline and impact eligibility for future therapies.¹⁶⁻¹⁸

Cumulative cisplatin dose emerged as a robust predictor of nephrotoxicity. This dose-response relationship reflects the pathophysiologic mechanism of cisplatin accumulation in renal tubular cells, leading to oxidative stress and apoptotic signaling. Patients with lower baseline eGFR were similarly predisposed, indicating that pre-treatment renal reserve critically determines susceptibility. These findings highlight the value of individualized dosing and vigilant renal monitoring, particularly in patients with borderline baseline function.

Despite standardized hydration protocols, significant nephrotoxic effects persisted. This suggests that hydration alone may be insufficient for high-risk individuals and supports exploration of adjunctive protective strategies, such as magnesium supplementation and genetic risk profiling to tailor treatment. Genetic factors like OCT2 transporter variants have been implicated in nephrotoxicity susceptibility, pointing to future avenues for precision medicine in this context.¹⁹⁻²⁰

Age, while considered a potential risk factor, did not demonstrate independent significance in multivariate analysis within this cohort, likely reflecting the generally younger demographic of testicular cancer patients. Nonetheless, age-related renal vulnerability should remain a consideration in older individuals.

The study's strengths include a large sample size, standardized outcome definitions, and multivariate risk stratification. Limitations include the observational design and potential confounding by unmeasured factors such as concomitant medications and hydration adherence. Future research should incorporate biomarker development to detect early tubular injury prior to significant functional decline.

Overall, these results reaffirm the centrality of renal risk assessment in cisplatin-based therapy for testicular cancer. Enhanced predictive tools and protective interventions are needed to mitigate nephrotoxicity without compromising curative outcomes.

Conclusion: Cisplatin-based chemotherapy in testicular cancer is associated with a substantial prevalence of renal impairment, with cumulative dosage and baseline renal function as significant predictors. This study fills a critical knowledge gap in quantifying renal risk and supports the refinement of risk-adaptive treatment strategies. Future research should prioritize targeted preventive measures and early biomarkers to preserve renal health in this curative context.

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