

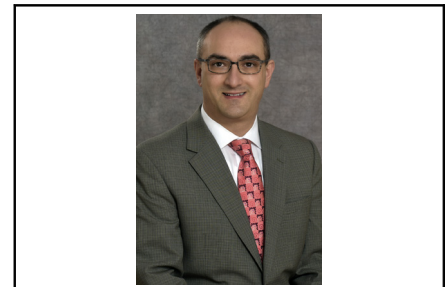
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Commentary: Acute kidney injury after intrapleural cisplatin: Minimizing collateral damage

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CENTRAL MESSAGE

Hyperthermic intraoperative cisplatin has significant renal toxicity and a fragile survival benefit. Its use should be avoided in patients at elevated risk of even mild acute kidney injury.

Malignant pleural mesothelioma (MPM) is perhaps one of the most vexing problems facing thoracic surgeons. Hyperthermic intraoperative cisplatin chemotherapy (HIOC) is an adjunctive option for patients undergoing cytoreductive surgery. The feasibility and safety of HIOC has been established, although a clear benefit has never been definitively proven.¹ Cisplatin administered within the pleura has significant systemic absorption, which is known to injure the renal tubules and cause direct cytotoxicity.

In this issue of the *Journal*, Hod and colleagues² report a retrospective observational study of their institutional prospectively maintained database for patients undergoing surgical therapy for MPM, hypothesizing that HIOC contributes to the incidence of acute kidney injury (AKI). A total of 503 patients underwent either extrapleural pneumonectomy (n = 241) or pleurectomy/decortication (n = 262) over a 9-year period. HIOC was administered to 312 patients.

Remarkably, more than 50% of the patients who received HIOC developed AKI. Ostensibly, this seems to represent

an unacceptably high risk for a therapy with unproven benefit. Approximately 25% of the patients who did not receive HIOC also developed AKI.

AKI was described using the Kidney Disease Improving Global Outcomes (KDIGO) definition, composed of 3 stages. KDIGO stage I is met when serum creatinine (SCr) rises by 0.3 mg/dL (or 50%-99%) over baseline. Stage II is moderate AKI, and stage III is severe AKI and includes all patients who require renal replacement therapy. Of the patients developing AKI, 78% were classified as the seemingly benign KDIGO stage I. Risk factors for AKI included male sex, HIOC, previous cisplatin exposure, hypertension, and longer operative time.

It should be mentioned that KDIGO stage I might not even be recognized as AKI during routine postoperative care, given that the SCr level may fall within the normal laboratory reference range. Stage I is generally not alarming to surgeons or nephrologists. So why do we care? Might this study, which proclaims a surprisingly high

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rate of acute tubular necrosis after HIOC, be much ado about nothing?

At the other extreme, 22 patients developed KDIGO stage III. Sixteen of these patients required dialysis, each of whom had received HIOC. It is clearly demonstrated that HIOC is associated with renal injury; however, it is known that even small increases in SCr are important and associated with a higher mortality rate.³

Although not a primary endpoint of the study, survival was also evaluated. Patients who received HIOC had a lower risk of death but a higher risk of AKI. So do we consider the kidneys to be collateral damage while waging a difficult battle? The benefit of HIOC was nullified in the patients who developed AKI—including those with KDIGO stage I. Conversely, improved survival was enjoyed by those who received HIOC but avoided AKI.

HIOC is an adjunctive therapy with significant toxicity given to patients who are concurrently sustaining the risk of a relatively morbid operation. We must be very selective in its use. The authors stress the importance of prevention and early recognition of AKI. It may be more impactful and strategic to avoid HIOC altogether in patients at elevated risk for even mild AKI.

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