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# THE SHORT AND LONG-TERM EFFECTS OF HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY ON RENAL FUNCTION IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER

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## **Background and Aims:**

Cytoreductive surgery (CRS) with platinum based Hyperthermic Intraperitoneal Chemotherapy (HIPEC) represents a valid therapeutic approach in the treatment of ovarian cancer patients with peritoneal spread (vanDriel NEJM). Nevertheless, cisplatin nephrotoxicity represents one limitation to the diffusion of HIPEC in clinical practice. To date, few studies evaluated the nephrotoxicity of hyperthermic intraperitoneal cisplatin and the risk of acute kidney injury (AKI) in patients treated with HIPEC. The aim of our study is to evaluate short- and long-term changes in serum creatinine (SCr) levels in a cohort of patients with a first relapse of platinum-sensitive ovarian cancer, receiving CRS plus or minus HIPEC.

## Method:

We compared a cohort of patients with a first relapse of platinum-sensitive ovarian cancer, receiving CRS plus/minus HIPEC in a period from January 2013 to October 2018. The HIPEC technique required the perfusion of the abdominal cavity with a 4 L/m2 of a heated saline solution containing cisplatin 75 mg/m2. We assessed the estimated glomerular filtration rate (eGFR), using the CKD-EPI formula, and SCr from the preoperative value, at 24, 48, 72 hours, 7 days and the last SCr value available on the electronic record, at least 3 months after the procedure. We analyzed the effect of HIPEC treatment on SCr values over time and we used logistic regression models to investigate the effect of HIPEC treatment on clinical outcomes. No patient in the HIPEC group had kidney protective treatment with thiosulphate.

#### Results

Our analyses included complete data of 110 patients treated in our Institution from January 2013 to October 2018. The two groups had significant differences in baseline SCr (p-value = 0.002), with lower average values in the CRS+HIPEC group (mean 0.68, standard deviation [SD] 0.14 mg/dL) compared to the CRS group (mean 0.76, SD 0.13 mg/dL). The baseline eGFR was significantly higher in the CRS+HIPEC group (mean 95, SD 16 mL/min/1.73 m2) than in the CRS group (mean 88, SD 14 mL/min/1.73 m2) (p-value = 0.014) and three patients in each group had chronic kidney disease (CKD) before surgery. SCr values in the HIPEC group were significantly higher at post-operative day #7 (1.22  $\pm$  1.10 mg/dL vs 0.69  $\pm$  0.16 mg/dL; p-value <0.001) and the differences remained during follow-up at least three months after randomization (0.96  $\pm$  0.55 vs  $0.69 \pm 0.19$  mg/dL; p-value < 0.001). Seventeen patients (31%) developed Acute Kidney Injury (AKI), according to the KDIGO Guidelines, in the first week after CRS+HIPEC versus seven patients (13%) after CRS alone. No patients who developed AKI post-HIPEC needed renal replacement treatment, although 5 (9%) had AKI stage III and 7 (13%) stage II. The CRS+HIPEC group had a significantly higher risk of developing AKI [OR: 3.48 (2.30-5.27)] compared with the CRS group (p-value <0.001).

There were no statistically significant differences between the two groups with regard to risk of complications other than AKI.

### Conclusion:

To our knowledge, our study represents the first investigation on short- and long-term changes in SCr and on the risk of AKI in patients with a first relapse of platinum-sensitive ovarian cancer, treated with CRS and HIPEC. There is a strong correlation between the intraperitoneal cisplatin at elevated temperatures and the rise of SCr over the time. However, this event was no reversible and influenced following treatments in only eight women.

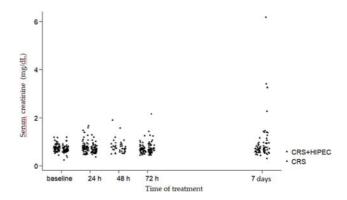


Figure 1. Scatter plot of serum creatinine values as function of the time of treatment

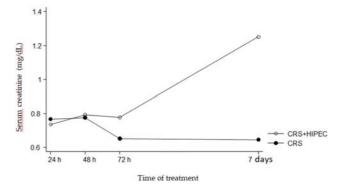


Figure 2. Linear prediction of serum creatinine as function of the time of treatment