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Routine prophylactic ureteral stenting before cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: Safety and usefulness from a single-center experience

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ABSTRACT

Objective: There are very few evidences about safety and usefulness of routine prophylactic ureteral stenting (PUS) before cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).

Material and methods: An analysis of prospectively collected data about patients who underwent CRS and HIPEC for different sites of primary disease was carried out focusing on ureteral complications.

Results: A total of 138 patients who underwent CRS and HIPEC between December 2010 and June 2017 were considered. All patients underwent PUS before CRS and HIPEC. Of them, 91 (66.4%) patients received pelvic peritonectomy, 49 (35.8%) pelvic lymphadenectomy, 31 (22.6%) left hemicolectomy, 44 (32.4%) right hemicolectomy, 46 (33.6%) rectal resection, 56 (40.9%) hysteroannessiectomy, and 39 (28.5%) appendectomy. There was one (0.7%) postoperative ureteral fistula. The cumulative risk of ureteral stent-related major complications was 4.3% (two patients (1.4%) had protracted gross hematuria, two patients (1.4%) had urinary sepsis, and three patients (2.9%) developed hydronephrosis after a period from removing ureteral stents and required restenting. Morbidity due to ureteral stenting was associated with a longer length of stay (LOS) (p=0.053). A total of 52 patients (44.1%) developed renal dysfunction according to the RIFLE (Risk, Injury, Failure, Loss of kidney function, End-stage kidney-disease) criteria: 19.5% were in risk class, 10.2% in acute renal injury class, and 14.4% in acute renal failure class.

Conclusion: PUS could be a useful tool for reducing iatrogenic ureteral injury, but it is associated with a non-negligible morbidity, which implies longer LOS. A more accurate patient selection for PUS is necessary.

Keywords: Cytoreductive surgery; HIPEC; hydronephrosis; peritoneal carcinomatosis; prophylactic ureteral stenting.

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Introduction

Prophylactic ureteral stenting (PUS) is routinely used before cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in many centers in order to prevent iatrogenic ureteral injury (IUI), but its safety and usefulness is still a matter of debate. IUIs always represent a risk during pelvic and abdominal debulking surgery, occurring during gynecological and urological procedures (IUI rate 0.2%-3%), and also in colorectal and vascular surgery (IUI rate 0.05%-5.7%).[1-8] Then, PUS is often used in gynecological oncological surgery[1,9] and, in recent years, minimally invasive surgery has expanded PUS indications to colorectal procedures.[10] However, many authors question the effectiveness of PUS in avoiding ureteral injuries[9,11-15] and recently some authors have shown that PUS could increase the risk of postoperative acute kidney injury (AKI).[16] Therefore, no definitive conclusion can be made regarding the real benefit of ureteral stenting. Furthermore, very few studies[17-19] focused on PUS applied to CRS and HIPEC.

In this kind of procedure, the risk of ureteral injury is particularly high due to different factors. The aggressive surgery to obtain a complete cytoreduction often leads to a complete ureteral dissection. Furthermore, there is the risk of ureteral suffering due to partial devascularization or chemical or thermal damage due to HIPEC. Finally, the presence of metastatic disease, weight loss, and malnutrition, which affect patients with advanced cancer, are recognized as risk factors for IUIs.[3,4] The aim of this study was to analyze patients undergoing CRS and HIPEC for different sites of primary disease focusing on IUIs and ureteral stenting-related morbidity.

Material and methods

An analysis of prospectively collected data was conducted regarding patients who underwent CRS and HIPEC for gastric, colorectal, appendiceal, ovarian, and other organs cancers, both in a prophylactic setting and for a therapeutic purpose. Patients characteristics, procedures performed during surgery, peritoneal cancer index (PCI), and clinical outcomes were analyzed, focusing on ureteral injuries, ureteral stent-related major (CTCAE>3) complications, and renal function analysis. Only patients for whom all these data were available were considered. All patients underwent prophylactic bilateral ureteral stenting with double J stents, according to the protocol of our center. An experienced urologist placed ureteral stents the day before HIPEC with spinal anesthesia or in the same day of HIPEC, before the surgery and after general anesthesia induction. All patients received broad-spectrum antimicrobial prophylaxis before the urological procedure.

Hyperthermic intraperitoneal chemotherapy was performed with the coliseum technique for 90 minutes at a temperature of 39°C-42°C. One inflow and four outflow catheters were placed with the open abdomen that was partially closed with a surgical adhesive drape while performing a "closed-HIPEC with open abdomen technique." Chemotherapy regimens were different depending on the primary site of disease (e.g., cisplatin and taxol for gastric and ovarian cancer, cisplatin and mitomycin for colorectal and appendiceal cancer). Afterward, the perfusate was drained and the reconstructive time was determined.

The study was approved by provincial ethics board of Bergamo (protocol number of ethics committee approval: Ch1BG.01) and informed consent was obtained from all the patients.

Statistical analysis

Statistical analysis was performed with T-test for continuous quantitative variables. A *p* value lower than 0.05 was considered significant. IBM Statistical Package for the Social Sciences (IBM SPSS Corp.; Armonk, NY, USA) version 20.0 was used for statistical analysis.

Results

A total of 150 patients underwent CRS and HIPEC between December 2010 and June 2017 at Papa Giovanni XXIII Hospital in Bergamo (Italy). The primary site of disease was stomach for 40 patients, colon or rectum for 31 patients, appendix for 18 patients, ovary for 49 patients, and other organs for 12 patients. Twelve patients were excluded for incompleteness of data about ureteral stenting. A total of 138 patients were included in the study. All patients underwent PUS. The characteristics of patients are listed in Table 1. All patients had a CC0 or CC1 cytoreduction. Stent removal was about 7 days after HIPEC for patients undergoing peritonectomy with ureters dissection and 2 or 3 days after HIPEC for patients undergoing prophylactic HIPEC or for those with PCI 0. In patients undergoing ureteral dissection, we leave the stents in place for 7 days to be sure to exclude undetected ureteral lesions during surgery or ureteral suffering due to partial devascularization or chemical or thermal damage due to HIPEC. One patient (0.7%) had an IUI that required intervention. All patients had hematuria (self-limited in most cases) and back pain, in a few cases hardly controllable by drugs. The rate of major complications attributable to ureteral stenting was 4.3% (Table 1). Two patients (1.4%) had urinary sepsis, two patients (1.4%) had protracted gross hematuria requiring blood transfusion, and three patients (2.9%) had hydroureteronephrosis requiring ureteral restenting. One patient had hydronephrosis 25 days after stent removal due to mucosal edema. One patient with protracted gross hematuria had ureteral occlusion and acute renal failure requiring dialysis, 5 days after stent removal, due to clots formation. Finally, one patient had hydronephrosis 4 months after stent removal for ureteral stenosis without recurrence of disease, probably due to retracting scar.

Patients with ureteral stents-related complications had longer length of stay (LOS) (p=0.053) (Table 2).

Complete data about renal function were available only for 118 patients (Table 1). A total of 52 patients (44.1%) developed renal dysfunction. Patients were classified with RIFLE (Risk, Injury, Failure, Loss of kidney function, End-stage kidney-disease) criteria: 23 patients (19.5%) were in risk (R) class, 12 patients (10.2%) were in acute renal injury (ARI) class, and 17 patients (14.4%) were in acute renal failure (ARF) class.

Discussion

The incidence of ureteral injuries associated with advanced oncological abdominal and pelvic surgery reaches 6%.[1-8,20-22] According to the present data of patients undergoing CRS and HIPEC, thanks to routinely applied PUS, the cumulative risk of IUIs was 0.7%, despite the high numbers of pelvic and colorec-

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Table 1. Patient characteristics, ureteral complications, and postoperative renal dysfunction rates

Patients Characteristics (%)	
n=138	
M/F	47(34.1)/91(65.9)
Age mean±SD [median (range)]	54.9±10.1 [56.0 (29–74)
Site of primary disease:	
Stomach	40 (29.0)
Colon	31 (22.5)
Appendix	18 (13.0)
Ovary	49 (35.5)
Pelvic peritonectomy	91 (66.4)
Pelvic LAD	49 (35.8)
Left hemicolectomy	31 (22.6)
Right hemicolectomy	44 (32.4)
Rectal resection	46 (33.6)
Hysteroannessiectomy	56 (40.9)
Appendectomy	39 (28.5)
Patients with PCI 0	38 (27.9)
Previous surgery	57 (49.6)
PCI mean±DS [median (range)]	9.2±9.9 [5.0 (0–39)]
ICU stay	4.4±9.8 [2.0 (1–70)]
LOS	26.6±19.7 [20.0 (8–124)]
Ureteral complications (%)	
n=138	
Ureteral injury	1 (0.7)
Ureteral stent major complications (CTCAE>3)*:	6 (4.3)
Protracted hematuria	2 (1.4)
Sepsis from urinary tract	2 (1.4)
Hydroureteronephrosis	3 (2.9)
Ureteral restenting	3 (2.9)
*One patient had both protracted hematuria and hydroureteronephrosis	
Postoperative renal dysfunction (%) according to the RIFLE criteria	
n=118	
Renal dysfunction	52 (44.1)
Risk class	23 (19.5)
Acute renal injury class	12 (10.2)
Acute renal failure class	17 (14.4)

M: male; F: female; LAD: lymphadenectomy; PCI: Peritoneal Cancer Index; ICU: intensive care unit; LOS: length of stay; CTCAE: Common Terminology Criteria for Adverse Events

Table 2. Intensive care unit stay and length of stay of patients with ureteral stent-related complications

	ICU stay	LOS
Ureteral stent complications	2.25±0.5 [2.0 (2–3)]	34.0±9.2 [33.0 (25–45)]
No ureteral stent complications	4.5±9.9 [2.0 (1–70)]	26.3±20.0 [19.0 (8–124)]
p	n.s.	0.053

ICU: intensive care unit; LOS: length of stay; n.s: nonsignificant

tal procedures, of peritonectomies and of patients with previous surgical interventions. This data is consistent with literature.[17-19] Furthermore, PUS allowed the achievement of C0/C1 cytoreduction in all patients of the present study.

However, ureteral stenting was associated with a non-negligible morbidity (major morbidity: 4.3%) that implied longer LOS. Ureteral stent-related complications such as back pain, urologic sepsis, hydronephrosis, and gross hematuria are described by many authors.[10,13,15,23,24]

Focusing on hydronephrosis due to ureteral stenosis (caused by edema or scar retraction), it is difficult to say if it is stent-related or due to surgery or to the thermal or chemical insult of HIPEC. Hydronephrosis is described, with an incidence of about 2%, by other authors after CRS + HIPEC,[25] but it is also reported, with the same incidence, after PUS before laparoscopic colorectal surgery.[10] Probably, during CRS and HIPEC, different factors could have a role in ureteral inflammation and stenosis: the PUS, the aggressive ureteral dissection during CRS, and the extended ureteral exposure to the thermal and chemical insult during HIPEC. Then, for patients at high risk for ureteral stenosis, like those with extended ureteral dissection during surgery, probably stents could be kept for a longer period.

Furthermore, in order to try to decrease the stent-related back pain, it could be desirable to place ureteral stents on the same day of HIPEC after general anesthesia induction, because in our patients, the peak of pain was in the first 24 h, and patients could have a better pain control in ICU.

According to a recent work[16] on colorectal surgery, AKI was three times more common in patients who underwent PUS, and the multivariable logistic regression model identified PUS as a risk factor for postoperative AKI following colon or rectal resection. Some authors found a significant association between PUS and AKI also after CRS and HIPEC.[26,27] The present study included only patients undergoing PUS and showed a renal dysfunction rate of 44.1% (R + ARI + ARF classes), which is similar to those of the stented patients undergoing HIPEC,

according to the literature. Probably, ureteral stenting has a role in development of post-HIPEC renal dysfunction, even if AKI in these patients has a multifactorial origin. Although the exact pathophysiology of the association between PUS and AKI is unclear, it is probably related to two processes: the reflex anuria (a bilateral ureteral or arteriolar constriction reflex as a result of a traumatic stimulus to only one kidney or ureter) and the mucosal edema due to the direct ureteral trauma related to stent removal (which could prompt bilateral ureteral constriction leading to a mild postrenal process).[16] Combined with the physiologic insult of a major cytoreductive surgery and HIPEC, the two processes may synergistically interact and result in the clinical appearance of AKI in these patients.

The limit of the study is that this is an observational study, even if it is prospective and lacks a control group without ureteral stenting. A randomized study should be necessary in order to find if PUS really decreases ureteral iatrogenic complications during CRS and HIPEC and if it has a role in postoperative hydronephrosis and AKI development. However, given the low incidence of ureteral complications, a very large sample size could be necessary.

Probably, instead of a routine PUS, a more accurate selection of patients who really could benefit from PUS before CRS + HIPEC could be done. It is known that the preoperative radiological investigations are not reliable enough in defining the site of the nodules of carcinosis, and therefore it is difficult to preoperatively select patients who really need PUS. Maybe PUS could be avoided in prophylactic HIPEC, when IUIs are less likely.

In conclusion, PUS could be a useful tool for reducing IUIs during a high risk procedure like CRS and HIPEC and in allowing a complete cytoreduction, but it is associated with a non-negligible morbidity. A more accurate selection of patients who really could benefit from PUS before CRS and HIPEC could be done.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of ASST Papa Giovanni XXIII.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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