

Ureteral Stenting in Cytoreductive Surgery plus Hyperthermic Intraperitoneal Chemotherapy as a Routine Procedure: Evidence and Necessity

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Key Words

Hyperthermic intraperitoneal chemotherapy · Chemotherapy · Ureteral stent · Cytoreduction surgery · Cancer

Abstract

Introduction: There is a need for more exhaustive data concerning the use of prophylactic ureteral stenting for extended debulking and cytoreductive procedures in the literature.

Material and Methods: A retrospective analysis of the CARPEPACEM study protocol database was performed. The trial protocol schedules the positioning of bilateral ureteral stents before cytoreductive surgery + hyperthermic intraperitoneal chemotherapy (HIPEC). **Results:** Fifty-one operated patients: 31 (59.6%) with peritoneal dissemination from ovarian cancer, 8 (15.3%) from colorectal cancer, 4 (7.9%) from pseudomyxoma peritonei, 3 (5.7%) from gastric cancer, 2 (3.8%) from peritoneal mesothelioma, 1 (1.9%) from appendiceal cancer, 1 (1.9%) from endometrial cancer, and 1 (1.9%) from leiomyosarcoma. Mean and median peritoneal cancer index: 11 and 10 (range: 0–28). CC-score: CC-0 in 45 (86.5%) patients, CC-1 in 5 (9.6%) and CC-2 in 1 (1.9%). HIPEC was performed with platinum + taxol in 22 patients (42.3%), plati-

num + adriablastin in 10 (19.2%), mitomycin in 9 (17.3%), platinum + mitomycin in 7 (13.4%), platinum + doxorubicin in 2 (3.8%), and taxol + adriablastin in 1 (1.9%). Two major ureteral complications were observed (3.9%). **Discussion:** Prophylactic ureteral stenting could reduce the risk of postoperative ureteral complications without an increase in stent placement-related complications; however, a randomized clinical trial is needed.

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Introduction

Ureter identification during major debulking and cytoreductive surgery (CRS) is rarely reported as a simple procedure. Many factors can influence the difficulty of the procedure, including patient size, tumor dimension and extension, patient medical and surgical history, and surgeon experience and skill. Lower urinary tract injury is always a risk during major debulking surgery, especially for pelvic procedures performed for gynecological or colorectal malignant pathologies. This high risk is due to the anatomic proximity and embryologic relationship between the reproductive, intestinal, and lower urinary

tract [1, 2]. Moreover, the anatomic distortion and the extensive surgery required in patients with gynecological, gastric, and colorectal malignancies extended to the peritoneum may result in a higher rate of injury. Lastly, during complex procedures like CRS + hyperthermic intraperitoneal chemotherapy (HIPEC), extended resections and lymphadenectomies have to be performed before to expose the internal organs and structures to the hyperthermic perfusion. In such procedures, the risk that ureters suffer for partial devascularization and/or direct mechanical, chemical, or thermic damage is high. Neither Sugarbaker [3] in his first description of his surgical technique, total peritonectomy with intraperitoneal hyperthermic chemotherapy, nor the review of his case study mentions the use of ureteral prophylactic stenting [3, 4].

Few studies discussing the efficacy and the necessity of routine ureteral stent placement before these kinds of major surgical procedures have been reported. The majority derives from the experience of colorectal surgeons [2, 5–11]. The incidence of ureter injury during abdominal and pelvic surgery has been reported to range from 1 to 8% [9, 10, 12–18]. The most frequent place where ureters are injured is at the level of the infundibulopelvic ligament, the uterine artery, and the angles of the vagina [2]. One of the prophylactic and therapeutic options of the ureteral complications is the ureteral stent placement [19–21].

In 2009, the General and Transplant Surgery Department of Sant'Orsola-Malpighi University Hospital (Bologna, Italy) started a trial to evaluate the effectiveness of CRS with HIPEC for disseminated intraperitoneal cancer (ovarian, colorectal, pseudomyxoma peritonei, gastric, appendiceal, endometrial, and mesothelioma). The study protocol (Carcinosi Peritoneale Trattata con Peritonectomia Associata a Chemioipertermia Intra Peritoneale, CARPEPACEM) was approved by the Sant'Orsola-Malpighi Hospital's Ethical Review Board and the trial was registered with the EUDRACT No. 2007-001185-32.

One year ago, the General and Emergency Surgery Department of Ospedali Riuniti (Bergamo, Italy) started the same study, which was also approved by the Ospedali Riuniti Hospital's Ethical Review Board.

The present study analyzes the rate of major urinary tract complication in patients enrolled in the two centers.

Material and Methods

A retrospective analysis of the CARPEPACEM study protocol data base of the two centers was performed. The trial protocol schedules the positioning of bilateral ureteral stents (JJ silastic stent) before the surgical procedure. Stents are positioned by the

urologists of both centers cystoscopically with one-shot antibiotic prophylaxis. Moreover, a broad-spectrum antibiotic prophylaxis was administered immediately before the intervention and continued for 10 days after the operation.

In patients with gynecological cancer, aortic and caval lymph nodes until the origin of the gonadic vessels were removed. In all patients, the intervention consisted of a complete pelvic peritonectomy and bilateral lymphadenectomy of internal and external iliac and obturator lymph nodes and in the removing of the interested peritoneum on abdominal wall, on diaphragms, and on the visceral and mesenteric surfaces. In patients with gastric cancer, a complete D2 lymphadenectomy was performed. Appendectomy and cholecystectomy were always performed in order to prevent HIPEC-induced ischemia. When indicated by the primitive disease or by the tumor infiltration, gastric or intestinal resections, splenectomy, partial hepatectomy, or distal pancreatectomy were required. Ureters were completely mobilized in all procedures. At the end of the CRS phase, HIPEC was performed for 90 min at a temperature between 41° and 43°C.

Results

From 2009 to today, 52 patients in the two centers have been enrolled: 45 women (86.5%) and 7 men (13.4%), with a mean and median age of 51.3 and 51 years, respectively (range: 33–70). All patients presented disseminated intraperitoneal cancer, 31 (59.6%) with ovarian cancer, 8 (15.3%) with colorectal cancer, 4 (7.9%) with pseudomyxoma peritonei, 3 (5.7%) with gastric cancer, 2 (3.8%) with peritoneal mesothelioma, 1 (1.9%) with appendiceal cancer, 1 (1.9%) with endometrial cancer, and 1 (1.9%) with leiomyosarcoma. In all patients, ureteral stents were placed preoperatively and removed 21 days after the procedure. Fifty-one of 52 patients (98%) have been definitively referred to CRS + HIPEC.

The mean and median peritoneal cancer index were 11 and 10, respectively (range 0–28), and the completeness of cytoreduction score (CC-score) was: CC-0 in 45 patients (86.5%), CC-1 in 5 (9.6%), and CC-2 in 1 (1.9%).

HIPEC was performed with: platinum + taxol in 22 patients (42.3%), platinum + adriablastin in 10 (19.2%), mitomycin in 9 (17.3%), platinum + mitomycin in 7 (13.4%), platinum + doxorubicin in 2 (3.8%), and taxol + adriablastin in 1 (1.9%).

At histopathologic examination 34 patients (65.4%) demonstrated positivity either in internal iliac, external iliac, obturator, or para-aortic/paracaval lymph nodes. Of patients with gastric cancer, 1 patient (33.3%) also presented positivity in excised D2 lymphadenectomy nodes.

In 4 patients (7.9%), due to the extremely compromised pelvic condition, a pelvic exenteration was necessary and a cutaneous ureterostomy was made. In one

patient, it was necessary to stitch one ureter due to a traumatic lesion during the pelvic lymphadenectomy procedure. However, this patient experienced no urinary complications. The only minor complication observed in the majority of the patients was self-limiting hematuria. Two patients (3.9%) had a postoperative major ureteral complication. In one case a urinary bladder resection was necessary and ureterovesical anastomosis (Lich-Gregoir) was done. During the procedure the ureteral stent was removed. In the postoperative period, the patient experienced a urinary fistula. The other patient experienced a postoperative urinary fistula. Both patients were treated with a percutaneous nephrostomy. Before the closure of the percutaneous nephrostomies, an urethrocytography through the nephrostomy was performed with no pathological signs. None of the patients incurred urinary tract infections.

Discussion

Operative injury to the ureters is an uncommon but potentially serious complication of pelvic surgery. The risk of injury to a ureter is increased when difficult pelvic dissections are undertaken for either malignant or benign pathologies. Some authors suggest that careful surgical technique with exploration of the retroperitoneum and direct visualization of the ureter is probably the optimal method to avoid ureteral injury. Some pelvic surgeons suggest that preoperative placement of a ureteral stent may aid in the identification of the ureters. Some surgeons place directly the ureteral stents in the operating room, others are helped by urologists. The benefit of prophylactic ureteral catheters in major debulking and pelvic surgery is controversial. Some authors suggest that the presence of a catheter increases the likelihood of injury to the ureter by reducing their pliability. Others suggest that the catheter may situate the ureter in an ectopic location and thus increase the risk of an inadvertent injury [2, 22]. Some studies have investigated the cost-effectiveness of the ureteral catheterization before surgical procedures and demonstrated that the catheterization should be considered where the ureteral injury risk exceeds 3%. They suggested that each surgeon should revise his/her ureteral injury rate to plan the stent positioning [10]. Other authors affirmed that prophylactic ureteral catheterization does not affect the ureteral injury rate, but only the meticulous surgical technique [23]. However, different studies from general and gynecologic surgeons demonstrated the usefulness and the necessity

to protect the ureters during major debulking colorectal and pelvic, either laparoscopic or open, surgical procedures [24–28].

The absolute heterogeneity of data about this topic does not allow obtaining definitive teachings. The complexity of some patients, who underwent very difficult surgical procedures like CRS + HIPEC with pelvic and aortocaval extended lymphadenectomy, are objectively exposed to a higher risk of ureteral injury. The violent mechanical stress of the aggressive surgery, the chemical and thermic insult of HIPEC, and the high risk of ureteral circulation impairment determine the high possibility of nonvisible or microscopic ureteral damages. Ureters, in fact, are exposed to the same or higher risk of HIPEC-induced ischemia of the appendix and gallbladder. The postoperative ureteral complications in such delicate patients could potentially increase the mortality rate. The possible increased risk of urinary tract infection as a result of cystoscopy and ureteral catheterization was not confirmed by different studies [23, 29, 30].

In the present study, the demonstration of a very low incidence of urological complications suggests that routine prophylactic ureteral catheterization in patients who undergo major debulking and CRS, especially if associated to HIPEC, should be indicated. Moreover, the fact that 1 of the 2 patients who experienced a urological major complication had it when the catheter must have been removed intraoperatively from the urinary bladder enforces the necessity for routine stent placement. The absence of urinary tract infections or stent placement-related complications suggests that the procedure is safe and has a very low complication rate, with a risk-benefit balance favorable to the stent use.

Prophylactic ureteral stenting before CRS + HIPEC procedures seems to reduce the risk of postoperative ureteral complications without evidence of an increase in stent placement-related complications. A randomized controlled trial, however, is needed to definitively clarify the usefulness of prophylactic ureteral stenting.

Disclosure Statement

All authors declare no conflict of interest.

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