

Urinary Tract Resections in Advanced-stage Cervical Cancer – A Series of Eight Cases

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Abstract. *Background/Aim:* Cervical cancer is one of the most frequent malignancies in women worldwide and is unfortunately diagnosed in advanced stages of the disease. Whenever local invasion is present, neoadjuvant therapy might be needed in order to limit the degree of local invasion. However, in certain cases local invasion persists even after completing the neoadjuvant radiochemotherapy; in these patients more extensive resections might be needed in order to achieve a radical resection. *Patients and Methods:* We present a case series of eight patients in whom segmental ureteral or uretero-vesical resections were performed as part of the radical resections for locally advanced cervical tumors. *Results:* The continuity of the urinary tract was re-established by performing ureteral reimplantation via uretero-neocystostomy, augmentation cystoplasties with ureteral reimplantations. In a single case ureteral reimplantation was not feasible, a definitive cutaneous ureterostomy being performed. The postoperative course was uneventful in seven cases while in a single case urinary leak occurred, necessitating the exteriorization of the ureter in terminal cutaneous ureterostomy. *Conclusion:* Ureteral resections can be safely performed in patients with locally advanced cervical cancer.

Advanced cervical cancer is defined by the presence of a maximum tumoral diameter of at least 4 cm, FIGO (The International Federation of Gynecology and Obstetrics) stage >IIA or relapsed tumors and has been advocated to represent up to 50% of cases, especially in developing countries (1, 2). When it comes to the standard therapeutic options in cervical cancer, cases diagnosed in FIGO stages I and II can be submitted to radical hysterectomy with pelvic and eventually

para-aortic lymph node dissection as the first therapeutic option; in the meantime, patients diagnosed in advanced stages of the disease (FIGO stage III and IVA) are treated with chemoradiation excepting the cases in which radiation therapy is hampered (by the presence of vesicovaginal or rectovaginal fistulas). However, in certain cases, although neoadjuvant chemotherapy is performed local invasion of the surrounding viscera persists; in all these cases multiple visceral resections might be needed in order to achieve a good local control of the disease. Due to the close proximity of the urinary bladder and of the rectum with the uterine cervix, these segments are most often affected by the neoplastic process. Depending on the degree of invasion, different variants of resections have been proposed; while cases presenting a high grade of local invasion are usually treated by performing a pelvic exenteration, cases with a lower degree of invasion are suitable to a more conservative type of surgery consisting of segmental digestive or urinary resections followed by anastomosis of the remnant partners (3).

Materials and methods

Between 2015 and 2016 eight patients with advanced-stage cervical cancer and persistent invasion of the urinary tract were submitted to radical surgery followed by urinary tract reconstruction. In all cases ureteral reimplantations were protected by placing ureteral stents which were removed 21 days postoperatively. Postoperative complications were classified according to Dindo-Clavien scale (4).

Results

All eight cases were initially diagnosed with locally advanced cervical cancer with urinary tract involvement, so they were initially submitted to neo-adjuvant chemo-irradiation. Seven of the eight cases successfully performed the entire neoadjuvant protocol while in the eight case the radiation therapy was interrupted due to the apparition of a severe hemorrhagic episode, so the patient was submitted to surgery in emergency. The main characteristics of the

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Table I. The main intraoperative characteristics of the group of eight patients.

	Age (years)	Localization of the invaded segment	Type of resection	Urinary tract reconstruction
Case 1	57	Left ureteral ostium	Distal ureterectomy	Ureteral reimplantation through neo-cystostomy
Case 2	53	Bilateral ureteral ostium	Partial cystectomy, bilateral ureteral resection	Bilateral reimplantation through neo-cystostomy
Case 3	48	Bilateral ureteral ostium, bladder trigone	Partial cystectomy, bilateral ureteral resection	Bilateral reimplantation through neo-cystostomy
Case 4	42	Left ureteral ostium	Distal ureterectomy	Ureteral reimplantation through neo-cystostomy
Case 5	44	Right ureteral ostium	Distal ureterectomy	Ureteral reimplantation through neo-cystostomy
Case 6	59	Bilateral ureteral ostium, bladder trigone	Partial cystectomy <i>en bloc</i> with distal ureterectomy	Augmentation cystoplasty, ureteral reimplantation through neo-cystostomy
Case 7	62	Left ureteral ostium	Distal ureterectomy	Cutaneous ureterostomy
Case 8	51	Right ureteral ostium	Distal ureterectomy	Ureteral reimplantation through neo-cystostomy

patients are presented in Table I. The main intraoperative aspects are shown in Figures 1-10.

In all cases ureteral reimplantation through neo-cystostomy was attempted; however, in a case due to the presence of a high grade of retroperitoneal fibrosis affecting more than a half of the ureter, we decided to create a cutaneous ureterostomy. All the reimplantation procedures were protected by placing Cook ureteral catheters which were removed through cystoscopy at the end of the first month postoperatively (days 21-30). The postoperative course was uneventful in seven cases, while in a single case a 4 grade Dindo-Clavien complication occurred; the patient developed a postoperative febrile episode and a urinary leak was diagnosed in the seventh postoperative day. The patient had been submitted to surgery for locally advanced cervical cancer with invasion into the bladder trigon; although initially both ureters were reinserted in the remnant urinary bladder, the apparition of the urinary leak imposed re-operation and exteriorization of the both ureters in terminal cutaneous ureterostomy. The mean length of stay in hospital was 7 days (range 6-38 days).

Discussion

Cervical cancer is part of the solid types of tumors which are characterized by progressive tissue destruction, a process known under the generic name of morpholysis. Throughout this process the malignant disease provides an isotopic invasion of the tumor cells into the peritumoral tissues (5). Although initially this process is limited by the compartmental natural borders, defined by the embryological development of the pelvic viscera, these borders seem to be destroyed by the evolution of the malignant process. It has been postulated that in the early stages of the disease the malignant solid tumors spread on the paths of the least

mechanical resistance, defined by the anatomical landmarks of the morphogenetic unit of the viscera from which the tumor originates (6). It has been demonstrated that in women the genital ducts (consisting of fallopian tubes, corpus and cervix uteri as well as the vagina) originate from the Mullerian ducts except from the distal part of the vagina which originates in the Wolffian ducts (6). During the embryogenetic process three distinct morphogenetic units rise: the proximal, intermediate and distal units. The proximal units consist of the fallopian tubes and the mesosalpinx, the intermediate unit consists of the uterine corpus and the broad ligaments while the distal unit consists of the uterine cervix, vagina, the neurovascular structures and the connective tissue, has a subperitoneal disposition and is the most complex segment (7). Studies have shown that in cases presenting with low stages of disease (FIGO stage IB-IIB), the malignant process is confined to the Mullerian morphogenetic unit; due to this aspect, according to Hockel's study, in these cases total mesometrial resection provides an R0 resection and minimizes the rates of local failure even in the absence of adjuvant radiotherapy (6). In this way, in cases in which the compartmental borders are not destroyed, the resection of the tumor *en bloc* with the tumor-permissive domain allows the preservation of the other structures situated in the close proximity to the malignant process and minimizes the surgery related morbidity (8). This type of surgical approach was defined by Michael Hockel as radical compartmentalized surgery and refers to the removal of a morphogenetic unit or a part of it.

During a slowly developing tumor, when the natural borders are destroyed, malignant cells can invade the surrounding viscera and compartments; in all these cases more aggressive surgical procedures might be needed in order to achieve a good control of the disease. In this way the concept of ultra-radical compartmentalized surgery developed; this concept refers to the *en bloc* removal of the

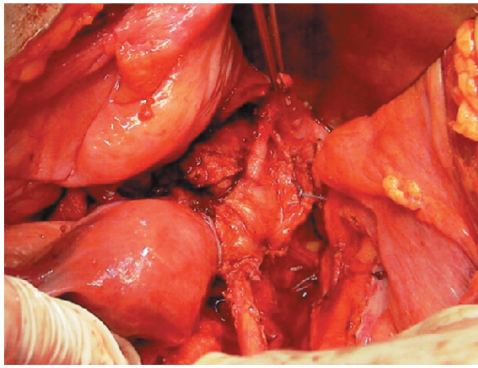


Figure 1. Locally advanced cervical cancer invading the right ureter.

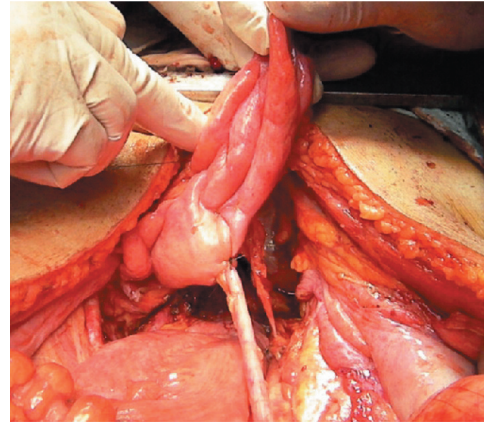


Figure 4. The final aspect after ureteral reimplantation and mobilization of the urinary bladder.

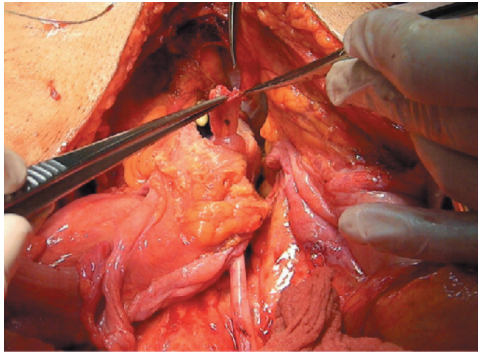


Figure 2. Right ureter reimplantation through uretero-neocystostomy.

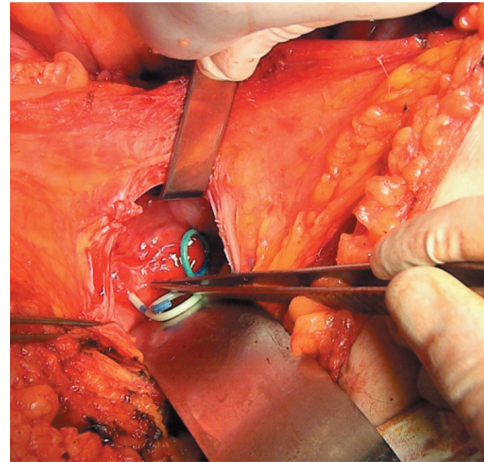


Figure 5. Cervical tumor with bladder trigon invasion. The two ureters were stented preoperatively with double J catheters.

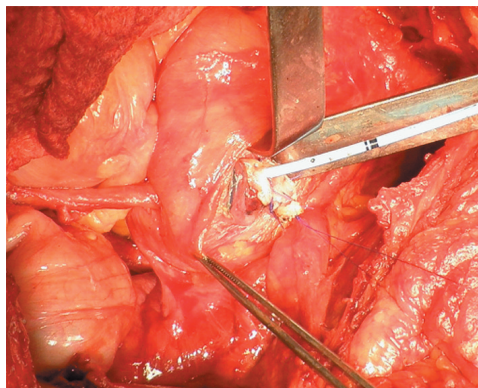


Figure 3. Placing the ureteral stent.

tumor *en bloc* with the invaded pelvic viscera, the cornerstone procedure being pelvic exenteration (9, 10). However, in gynecologic oncology patients, in certain cases in which the

local invasion is not so important, more conservative procedures might be taken in consideration (11-13).

In the study conducted by Mitchel Hoffmanin 2006 regarding the necessity of performing ureteral surgery in university gynecologic oncology service, the authors included 4,844 patients that were submitted to surgery between 1997 and 2004 for gynecologic malignancies. Among these cases ureteral surgery was performed in 46 cases, 16 patients being submitted to ureteral resection due to the extent of the malignant process. The indication for ureteral resection consisted of locally advanced or relapsed ovarian cancer (in nine cases), vaginal cancer (in two cases), recurrent cervical cancer (in two cases), class V radical hysterectomy (consisting in *en bloc* removal of the distal ureter and partial cystectomy

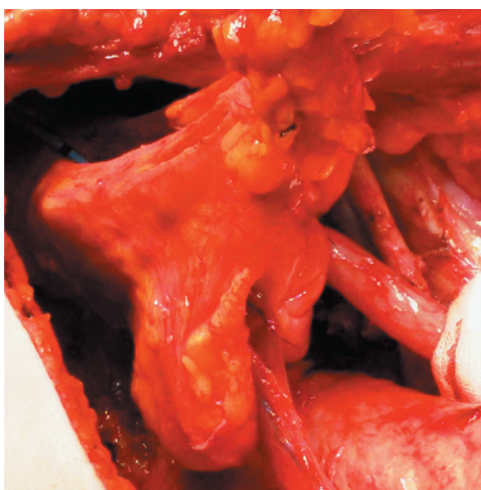


Figure 6. The two ureters are reimplanted through bilateral uretero-neocystostomy.

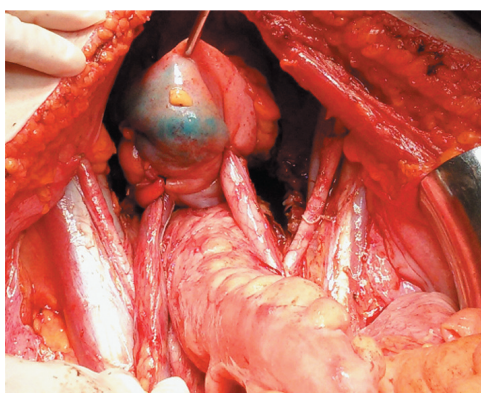


Figure 7. The final aspect after bilateral ureteral reimplantation.

for locally advanced tumors – in two cases) and bilateral intrinsic ureteral endometriosis in one case. The authors also reported that partial cystectomies were associated in three cases while the mean upper level of ureteral transection was estimated to be 5.7 cm (range 2-10 cm). In all cases the continuity of the urinary tract was re-established through uretero-neocystostomy. Moreover, in one case presenting bilateral ureteral invasion both ureters were re-inserted in the remnant urinary bladder through uretero-neocystostomy. Regarding the postoperative outcome, a single patient developed a major complication requiring re-operation (a vesicovaginal fistula which required reoperation at two weeks postoperatively); this complication was treated by performing an ileal conduit. Other less severe complications consisted of

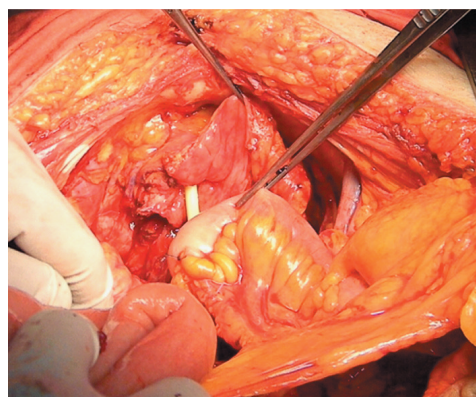


Figure 8. Augmentation cystoplasty using an ileal loop – preparing the anastomosis.

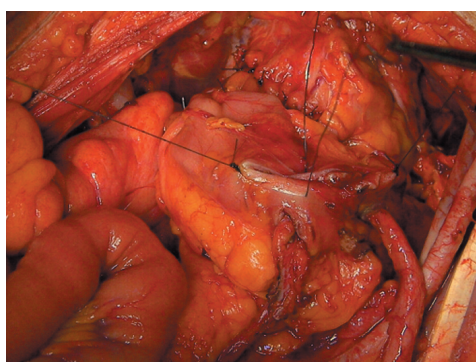


Figure 9. Insertion of the two ureters in the neo-bladder.



Figure 10. The final aspect after augmentation cystoplasty and bilateral ureteral reimplantation.

the persistence of the aspect of a hydroureter after removing the ureteral stent or the apparition of urinary incontinence due to the small capacity of the urinary bladder (12).

Regarding the surgical technique of the ureteral neocystostomy, two options have been reported so far: with or without tunnel anastomosis. When performed in children (as an anti-reflux procedure) or in young women (who are submitted to conservative fertility sparing procedures and who plan to obtain a pregnancy), a tunneled anastomosis should be the option of choice (14, 15). In all the other cases, the surgeon can choose between the two options in function of the anatomical particularity of each case. In our study all cases were submitted to a non-tunneled anastomosis. In order to achieve a tension-free anastomosis, various technical tips such as renal or bladder mobilization were used.

However, when it comes to urinary tract reconstruction after ureteral resection for locally invasive cervical tumors, other surgical techniques such as ileal ureter, transureteroureterostomy or cutaneous ureterostomy might be taken into consideration according to the anatomical particularities of each patient (12, 16).

When it comes to the role of augmentation cystoplasty in re-establishing the continuity of the urinary tract in patients with a more extended area of tumoral invasion at the level of the urinary bladder, this method was performed in the current study in a single patient who presented a cervical tumor invading both ureteral ostia as well as the bladder trigon. After resection the remnant urinary bladder volume was insufficient, so we decided to perform an augmentation cystoplasty using an ileal loop, followed by bilateral ureteral reinsertion. The method was initially used in children with vesico-ureteral reflux as well as in cases with neurogenic bladder. This technique has multiple advantages: it increases the urinary bladder volume, it decreases intravesical pressure and, in the meantime improves the compliance (17-19). Other digestive segments which have been used for augmentation cystoplasty include jejunal loops or colonic segments. Although most authors consider that small bowel segments are even more appropriate in order to enlarge the remnant urinary bladder (due to the rich blood supply and due to the capacity of providing an extremely low pressure system) (20), attention should be given to certain aspects: ileal segments might induce severe metabolic dysfunctions such as hyperchloremic metabolic acidosis and might also have an increased risk of malignant transformation of the epithelium (21, 22).

Conclusion

Ureteral resections can be safely performed as part of the ultra-radical surgical procedures for locally advanced cervical cancer in order to achieve negative resection margins and a good control of the disease, with acceptable rates of postoperative complications. As for the most appropriate technique, different procedures have been proposed, depending on the extent of the resected area.

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