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ARTICLE

Prognostic score predicts overall survival following complete urinary tract extirpation

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ABSTRACT

Purpose: To evaluate the oncological outcome and complications of patients treated with complete urinary tract extirpation (CUTE) in our department, and to identify prognostic factors for survival.

Methods: Clinico-pathological data of patients treated with one-step or stepwise CUTE between 1999 and 2017 were collected retrospectively. Complications were classified according to the modified Clavien–Dindo classification (CDC) in the early (≤30 days) and late (>30 days) follow-up. Log-rank test was used to assess independent predictors of overall survival (OS), cancer-specific survival (CSS) and recurrence-free survival (RFS).

Results: Twenty-five patients (20 male) underwent CUTE (16 one-step) for BC + unilateral/bilateral UTUC. Minor (CDC 1-2) and major (CDC3-5) complications were observed in 72% and 40% of patients, respectively, in the early postoperative period (≤30 days). Five (20%) patients died in the perioperative period (CDC 5) with a median OS of 52 days (range: 25–77). Median time to last follow-up or death was 30 months (range: 0–161). Median OS was 50 months (95% Confidence Interval [CI]: 22–118 months), while median CCS and RFS were not reached. The 5-year OS, CSS and RFS were 42.7%, 69.6% and 66.7%, respectively. A score for determining which patients would benefit from CUTE was arbitrarily developed, and showed that the patients with a score of 0–2 points (good prognosis) had a better OS than the patients with a poor prognosis (3–4 points) in the log-rank test.

Conclusions: Because of lower OS rates, patients with ESRD or with a CUTE score of 3–4 points are probably not ideal candidates for CUTE.

Abbreviations: ACCI: Age-adjusted Charlson comorbidity index; ASA: American Society of Anesthesiologists; BC: Bladder cancer; BMI: Body-mass index; CCI: Charlson comorbidity index; CDC: Clavien–Dindo classification; CIS: Carcinoma in situ; CSS: Cancer-specific survival; CUTE: Complete urinary tract extirpation; EBL: Estimated blood loss; ECOG: Neoadjuvant chemotherapy; ESRD: End-stage renal disease; LND: Lymph node dissection; OS: Overall survival; OSP: One-step procedure; PSM: Positive surgical margin; RC: Radical cystectomy; RFS: Recurrence-free survival; SWP: Stepwise procedure; TNM: Tumor-Node-Metastasis; UC: Urothelial carcinoma; UT: Upper urinary tract

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Introduction

Urothelial carcinoma (UC) is the fourth most common malignancy in the United States after prostate, lung and colorectal cancer in men [1]. Bladder cancer (BC) is the most common malignancy of the urinary tract (accounts for 90–95% of UCs) and the sixth most commonly diagnosed cancer in men worldwide [2]. Upper urinary tract (UT) UCs are uncommon and account for only 5–10% of UCs [1]. Pyelocalyceal tumors are about twice as common as ureteral tumors. In 17% of cases, concurrent BC is present [3]. Recurrence of disease in the bladder occurs in 22–47% of UTUC patients, whereas recurrence in the contralateral UT is observed in 2–6% [4–6]. The natural history of UTUC is different from that of BC, where 60% of UTUCs are invasive at diagnosis compared with only 15–25% of BCs [7].

Radical nephroureterectomy with excision of bladder cuff remains the gold standard treatment for UTUC, regardless of tumor location [7]. Radical cystectomy (RC) with urinary diversion (either an orthotopic bladder substitution or an ileal conduit) is the gold standard treatment method for muscle-invasive and recurrent high-risk non-muscle-invasive BC [8]. When a BC is diagnosed with a simultaneous UTUC, the combination of the above treatments is needed, also called 'complete urinary tract extirpation (CUTE)'. Other clinical conditions such as dialysis-dependent end-stage renal disease (ESRD) or nonfunctioning kidney(s) constitute relative indications for unilateral or bilateral nephroureterectomy and simultaneous lower tract extirpation. CUTE can be performed in a stepwise procedure (SWP) in case of metachronous UC recurrence or in a one-step procedure (OSP) in selected cases.

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Supplemental data for this article can be accessed here.

In their review of 30 patients with UC and receiving hemodialysis for ESRD, Wu et al. were the first to conclude that one-stage CUTE should be considered an acceptable treatment for these patients [9]. Various authors have since reported that this complex and invasive surgery can be performed through an open, laparoscopic or robotic approach with acceptable morbidity and mortality [10–12]. However, experience remains low with only few single-center series available to date. Herein, we report our single-center experience with CUTE, in which we aimed to evaluate the oncological outcome and complications of patients treated with CUTE, and to identify prognostic factors for survival.

Materials and methods

The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments, with a waiver of informed consent because of its retrospective fashion. The confidentiality of patient data was guaranteed. A computerized database of consecutive patients treated with CUTE between January 1999 and April 2017 was retrospectively analyzed.

All operations were performed in open fashion by two experienced surgeons (SJ and HVP). CUTE was defined as bilateral nephroureterectomy and cystectomy or cystoprostatectomy (Figure 1). Lymph node dissection (LND) was performed according to the oncological status of the patient, with selection among one of the templates: standard LND, extended LND and super-extended LND. For the patients with a functioning transplant kidney or who were scheduled for renal transplantation after CUTE, a Bricker ileal conduit was created with isolation of an ileal segment of approximately 10–15 cm, located 20 cm proximal to the ileocecal valve.

Collected data included preoperative parameters including age, gender, Charlson comorbidity index (CCI), age-adjusted CCI (ACCI), American Society of Anesthesiologists (ASA) score, Eastern Cooperative Oncology Group (ECOG) score, body-mass index (BMI), smoking status, previous abdominal/pelvic surgery, preoperative serum creatinine, hemoglobin and hematocrit levels, symptoms, preoperative dialysis dependency, transplantation before CUTE, UC location and synchronous presence of BC and UTUC, operative parameters such as surgery type, CUTE type (OSP vs. SWP), extent of LND, duration of surgery, estimated blood loss (EBL), duration of hospitalization and intraoperative complications, with postoperative parameters including postoperative complications according to modified Clavien–Dindo classification (CDC), transplantation after CUTE, pathological Tumor-Node-Metastasis (TNM) status of BC and UTUC, positive surgical margin (PSM) and presence of carcinoma *in situ* (CIS), lymphovascular invasion and variant histology, time to clinical recurrence, location of recurrence, time to last follow-up or death and cause of death.

Follow-up during the first 2 years consisted of 3-monthly visits, which included a medical history, physical examination, imaging and serum creatinine. Imaging was performed by alternating an abdominal ultrasound and chest x-ray with a yearly computerized tomography scan. A six-monthly visit was arranged between the third and fifth years. After the fifth year, patients were invited to attend on an annual basis.

Statistical analyses were done using R version 3.4.3. Descriptive statistics were given as median and range (min-max) for the continuous quantitative variables, and as numbers and percentages for non-numeric variables.

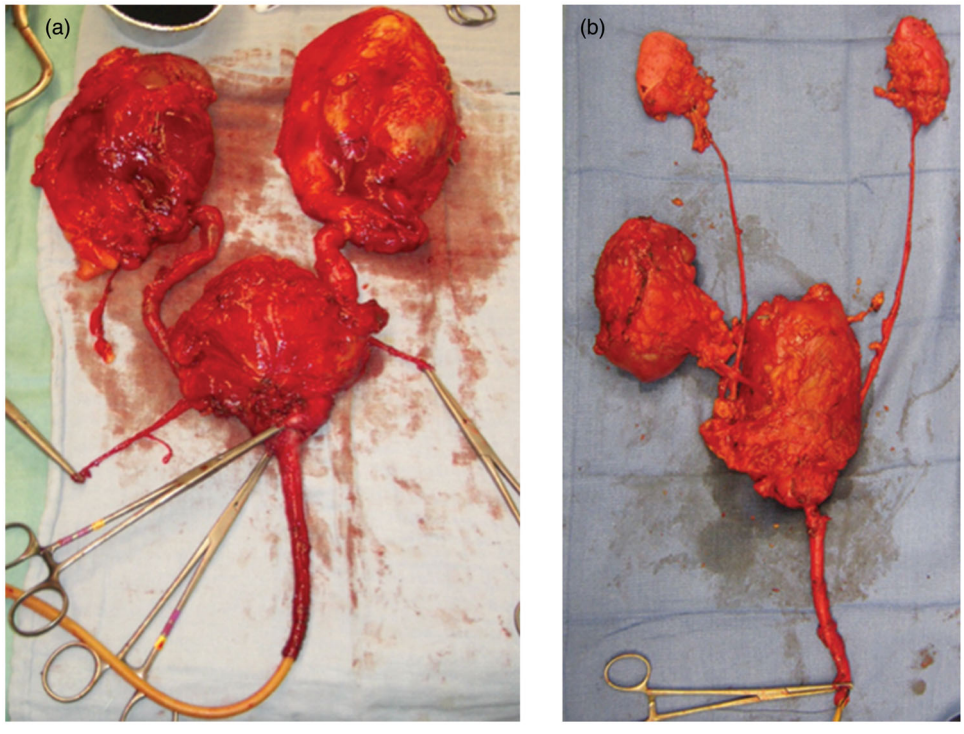

Figure 1. (a) Picture of a CUTE specimen. (b) Picture of a CUTE specimen with a transplantectomy.

Kaplan–Meier curves were used for overall survival (OS), cancer-specific survival (CSS) and recurrence-free survival (RFS) and log-rank test was used to compare survival between groups.

Results

Between January 1999 and November 2017, 25 CUTEs were performed, of which 16 were OSP while 9 were SWP. There were 20 male and 5 female patients. The median age was 66 years (range: 48–79 years). Of 25 patients, 13 were symptomatic at the time of diagnosis. Hematuria, dysuria and pain due to hydroureteronephrosis were the main symptoms. Preoperatively, 6 patients had dialysis-dependent ESRD, and 6 patients had a renal transplant, 1 patient had a renal + pancreas transplant and 2 patients had a heart transplant. Of the patients with renal transplants, 2 underwent transplantectomy during CUTE because of chronic rejection. A transplantectomy due to UC in the transplant ureter was performed in 1 patient 1 year after CUTE. He developed metastatic disease 20 months after CUTE and died after 22 months. A second tumor recurrence occurred in another

Table 1. Demographics, preoperative and intraoperative data of the patients.

	Median (Range) or *n* (%)		
	General ($n = 25$)	OSP ($n = 16$)	SWP ($n = 9$)
Age (years)	66 (48–79)	66 (48–78)	72 (58–79)
BMI (kg/m^2)	24.3 (17.3–34)	23.7 (17.3–31.2)	25.2 (19.8–34)
CCI	3 (0–9)	3.5 (1–9)	3 (0–6)
Age-adjusted CCI	6 (3–11)	5.5 (3–11)	6 (3–8)
ASA score	3 (1–4)	3 (1–4)	2 (2–3)
ECOG score	1 (0–3)	1 (0–3)	0 (0–2)
Smoking status			
Missing data	3 (12%)	2 (12.5%)	1 (11%)
Never smoked	12 (48%)	7 (43.75%)	5 (56%)
Ex-smoker	5 (20%)	4 (25%)	1 (11%)
Active smoker	5 (20%)	3 (18.75%)	2 (22%)
Previous abdominal/pelvic surgery	15 (60%)	10 (62.5%)	5 (55%)
Preoperative serum creatinine level (mg/dL)	3.08 (0.75–9.92)	3.11 (0.75–9.92)	1.82 (1.24–4.02)
Preoperative hemoglobin level (g/dL)	11.6 (8.5–15.7)	10.7 (8.5–15.7)	13.4 (9.6–15.1)
Preoperative hematocrit level (%)	36 (27.3–45.5)	35.8 (27.3–45.5)	41.5 (28.5–45)
Symptomatic patients	13 (52%)	10 (62.5%)	3 (33%)
Hematuria	6 (24%)	4 (25%)	2 (22%)
Dysuria	2 (8%)	2 (12.5%)	0 (0%)
Hematuria + Dysuria	1 (4%)	1 (6.25%)	0 (0%)
Urgency/UI	1 (4%)	1 (6.25%)	0 (0%)
Pain due to HUN	3 (12%)	2 (12.5%)	1 (11%)
UC location			
Bladder	8 (32%)	7 (43.75%)	1 (11%)
Bladder + Uni-UT	1 (4%)	0 (0%)	1 (11%)
Bladder + Bi-UT	4 (16%)	4 (25%)	0 (0%)
Bladder + renal Tx	2 (8%)	2 (12.5%)	0 (0%)
Uni-UT	5 (20%)	2 (12.5%)	3 (33%)
Bi-UT	3 (12%)	1 (6.25%)	2 (22%)
None	2 (8%)	0 (0%)	2 (22%)
End-stage renal disease	15 (60%)	12 (75%)	3 (33%)
Dialysis dependent	6 (24%)	5 (31.3%)	1 (11%)
Tx pre-CUTE	9 (36%)	9 (56.25%)	0 (0%)
Renal	6 (24%)	6 (37.5%)	
Renal + pancreas	1 (4%)	1 (6.25%)	
Heart	2 (8%)	2 (12.5%)	
Tx post-CUTE			
Renal	5 (20%)	3 (18.75%)	2 (22%)
Duration of surgery (minutes)	210 (120–480)	210 (146–480)	180 (120–300)
Estimated blood loss (mL)	1100 (150–4100)	1400 (350–4100)	825 (150–3500)
Extent of lymph node dissection			
No LND	11 (44%)	7 (44%)	4 (44%)
Standard LND	5 (20%)	2 (13%)	3 (33%)
Extended LND	4 (16%)	3 (19%)	1 (11%)
Super-extended LND	5 (20%)	4 (25%)	1 (11%)
Intra-operative complications			
Small bowel injury	1 (4%)	0 (0%)	1 (11%)
Rectal injury	1 (4%)	1 (6.25%)	0 (0%)
Major vascular injury	1 (4%)	1 (6.25%)	0 (0%)
Duration of hospitalization (days)	21 (12–77)	17 (12–77)	23 (15–60)
ICU admission	8 (32%)	5 (31.25%)	3 (33%)
Duration of ICU admission (days)	4 (1–34)	4 (1–12)	30 (1–34)
Time to oral intake (days)	6 (2–11)	7 (4–11)	6 (2–9)
Last serum creatinine level before discharge (mg/dL)	6.36 (0.41–11.81)	6.74 (0.41–11.81)	4.22 (1.11–9.14)

BMI: Body-mass index; CCI: Charlson comorbidity index; ASA: American Society of Anesthesiologists; ECOG: Eastern Cooperative Oncology Group; UI: Urge incontinence; HUN: Hydroureteronephrosis; UC: Urothelial carcinoma; Uni-UT: Unilateral upper urinary tract; Bi-UT: Bilateral upper urinary tract; CUTE: Complete urinary tract extirpation; Tx: Transplantation; LND: Lymph node dissection; ICU: Intensive care unit; OSP: One-step procedure; SWP: Step-wise procedure.

renal transplant 12 months after CUTE, but the disease stabilized with systemic therapy after a follow-up of 16 months. During follow-up, a de novo renal transplant was performed on an ileal conduit in five patients.

The median operative time was 210 min (range: 120–480 min), and the median EBL was 1100 mL (range: 150–4100 mL). Median hospitalization duration was 21 days (range: 12–77 days), where eight patients were transferred to the intensive care unit for a median duration of 4 days (range: 1–34 days). The major intraoperative complications were a small bowel injury, a rectal injury and a major vascular injury, each seen in one patient (total three patients). The median time to oral intake was 6 days (range: 2–11 days). For the patients who underwent a lymph node dissection, the median number of removed lymph nodes was 16 (range: 4–49). Demographic and perioperative parameters are listed in Table 1, while pathological data are given in Table 2.

In the early postoperative period (≤30 days), five (20%) patients did hot experience any complications (CDC 0), while 20 (80%) patients had one or more complications (CDC ≥1). Eighteen (72%) patients had a total of 29 minor complications (CDC 1–2), and 10 (40%) patients had a total of 18 major complications (CDC 3–5; Table 3). During the later period of follow-up (>30 days) of 24 evaluated patients, 17 (70.8%) did not have any complications (CDC 0) and 7 (29.2%) had one or more complications (CDC ≥1). Four (16.7%) patients had a total of five minor complications (CDC 1–2), and four (16.7%) patients had a total of six major complications (CDC 3–5; Table 4). Major complications were more common with the SWP than with the OSP and in the early

Table 2. Pathological data of the patients.

	Overall ($n = 25$)
BC pathologic T-stage	
pT0	6 (24%)
pTis	1 (4%)
pTa	3 (12%)
pT1	4 (16%)
pT2	5 (20%)
pT3	3 (12%)
pT4	2 (8%)
Unknown	1 (4%)
BC pathologic N-stage	
pN0	8 (32%)
pNx	7 (28%)
UTUC pT-stage	
pT0	11 (44%)
pTis	1 (4%)
pTa	6 (24%)
pT1	2 (8%)
pT2	1 (4%)
pT3	3 (12%)
pT4	1 (4%)
UTUC pN-stage	
pN0	4 (16%)
pNx	9 (36%)
Pathology details for BC and UTUC	
High grade	22 (88%)
Associated Tis	6 (24%)
Lymphovascular invasion	7 (28%)
Variant histology	2 (8%)
Tumor necrosis (>10%)	2 (8%)
Prostatic urethra involvement	3 (12%)
Positive surgical margin	1 (4%)

BC: Bladder carcinoma; Tis: Carcinoma *in situ*; UTUC: Upper urinary tract urothelial carcinoma.

Table 3. Complication data during the early follow-up (≤30 days).

Postoperative complications (CDC)	*n* (%)
Grade 0	5 (20%)
Grade 1	8 (32%)
Altered mental status	2 (8%)
Penile wound	1 (4%)
Scrotal hematoma	1 (4%)
Wound dehiscence	1 (4%)
Stoma stricture	1 (4%)
Transient blindness	1 (4%)
Double vision	1 (4%)
Grade 2	21 (84%)
Ileus	3 (12%)
Pneumonia	3 (12%)
Cholecystitis	2 (8%)
UTI	2 (8%)
Fever	2 (8%)
Altered mental status	2 (8%)
Gout	1 (4%)
Blood transfusion	1 (4%)
Adrenal insufficiency	1 (4%)
Deep vein thrombosis	1 (4%)
Wound infection	1 (4%)
Catheter infection	1 (4%)
Addison's crisis	1 (4%)
Grade 3a	3 (12%)
Esophagitis	1 (4%)
Melena	1 (4%)
Abscess drainage	1 (4%)
Grade 3b	8 (32%)
Peritonitis	2 (8%)
Hemothorax	2 (8%)
Carotis endarterectomy	1 (4%)
Wound dehiscence	1 (4%)
Cholecystitis	1 (4%)
Bowel injury	1 (4%)
Grade 4a	6 (24%)
Sepsis	3 (12%)
Over-dosage of morphine derivate	1 (4%)
Acute myocardial infarction	1 (4%)
Respiratory failure	1 (4%)
Grade 4b	0 (0%)
Grade 5	1 (4%)
Sepsis with MOF	1 (4%)

CDC: Clavien–Dindo classification; UTI: Urinary tract infection; MOF: Multiple organ failure.

Table 4. Complication data during the late follow-up (>30 days).

Postoperative complications (CDC)	*n* (%)
Grade 0	17 (68%)
Grade 1	0 (0%)
Grade 2	5 (20%)
Pneumonia	2 (8%)
Gastroenteritis	1 (4%)
Pulmonary edema	1 (4%)
Altered mental status	1 (4%)
Grade 3a	1 (4%)
Abscess drainage	1 (4%)
Grade 3b	2 (8%)
Penile wound	1 (4%)
Pressure skin ulcer + fecal incontinence	1 (4%)
Grade 4a	0 (0%)
Grade 4b	0 (0%)
Grade 5	3 (12%)
Aspiration + MOF	1 (4%)
Pneumonia	1 (4%)
Cardiac arrest	1 (4%)

CDC: Clavien–Dindo classification; MOF: Multiple organ failure.

Table 5. Follow-up data of the patients.

	Median (Range) or *n* (%)		
	Overall ($n = 25$)	OSP ($n = 16$)	SWP ($n = 9$)
Time to recurrence or last follow-up (months)	25 (0–161)	31 (0–161)	25 (1–119)
Recurrence			
None	19 (76%)	11 (68.75%)	8 (89%)
Local	4 (16%)	3 (18.75%)	1 (11%)
Systemic	2 (8%)	2 (12.5%)	0 (0%)
Time to last follow-up or death (months)	30 (0–161)	36.5 (0–161)	25 (1–119)
Number of alive patients	6 (24%)	4 (25%)	2 (22%)
Number of deaths	19 (76%)	12 (75%)	7 (77%)
UC-related	5 (20%)	4 (25%)	1 (11%)
Treatment-related	4 (16%)	2 (12.5%)	2 (22%)
Other malignancy-related	2 (8%)	1 (6.25%)	1 (11%)
Non-cancer-related	3 (12%)	2 (12.5%)	1 (11%)
Unknown causes	5 (20%)	3 (18.75%)	2 (22%)

UC: Urothelial carcinoma; OSP: One-step procedure; SWP: Step-wise procedure.

Table 6. Survival data of the patients.

	Median	5-year rate
Overall survival	50 months (95% CI: 26.3–69.3)	42.7% (95% CI: 26.3–69.3)
Cancer-specific survival	Not reached	69.6% (95% CI: 50.4–96.2)
Recurrence-free survival	Not reached	66.7% (95% CI: 47.9–93.0)

CI: Confidence interval.

postoperative period. Five (20%) patients died (CDC 5) in the perioperative period with a median OS of 52 days (range: 25–77 days) from CUTE (four because of a treatment-related factor; sepsis [$n = 1$], aspiration [$n = 1$], pneumonia [$n = 1$], cardiac arrest [$n = 1$] and one because of unknown reason).

The median time to the last follow-up or death was 30 months (range: 0–161 months). At the time of analysis, 6 (24%) patients were alive, 5 (20%) died UC-related, 2 (8%) died of other malignancies, 4 (16%) died of treatment-related causes, 3 (12%) died of non-cancer related causes and 5 (20%) died of unknown causes (Table 5). Median OS was 50 months (95% Confidence Interval [CI]: 22–118 months). The 5-year OS, CSS and RFS were 42.7%, 69.6% and 66.7%, respectively. The median OS, CSS and RFS times are listed in Table 6. Kaplan–Meier curves of OS, CSS and RFS are given in Figure 2(a–c).

We found significant difference for only OS ($p = .031$), but not for CSS and RFS ($p = .15$ for both) between the patients with and without ESRD (Supporting Information Figure 1(a)). Moreover, highest pT-stage of BC >3 was also a significant determinant of OS and CSS, but not of RFS (Supporting Information Figure 1(b,c)). No difference in all survival rates was observed when patients were subgrouped as $\leq$ pT1 and $>$ pT1 BC.

The following most clinically relevant parameters were picked with cut-off values determined arbitrarily or based on their median value (only age), and were found to be prognostic for OS in log-rank test: age ($\leq$66 vs. $>$66 years), ESRD (no vs. yes), CCI (0–2 vs. $>$2) and highest pT-stage of BC and UTUC (0–2 vs. 3–4). And then we arbitrarily gave a score of 0 or 1 for each of these parameters. The combined total score, which can be named as CUTE score, was used to stratify patients into two risk categories: good prognosis (0–2 points) and poor prognosis (3–4 points; Figure 3(a)). We performed OS, CSS and RFS analyses based on this CUTE score. Univariate analysis could stratify significantly between these risk groups for OS of patients ($p = .012$; Figure 3(b)), but not for CSS or RFS. Supporting Information Table 1 summarizes the main characteristics of all patients.

Discussion

Due to high recurrence rate and rapidly progressive behavior, a strict follow-up and an aggressive treatment strategy is recommended to prolong the survival and improve the quality of life of the patients with UC. CUTE has advantages of avoiding multistaged surgeries with repeated anesthesia, intraabdominal adhesions, delay in completion of treatment, intraoperative and postoperative complications and repeated use of analgesics [9,10]. Wu et al. reported that it is possible to avoid repeated surgeries and anesthesia with this procedure, as these patients had higher rates of multifocality and recurrence, increased anesthesia risk due to compromised immune system, poor cardiovascular system, susceptibility of fluid overload and coagulopathy diathesis, lack of suitability for conventional imaging studies with contrast agents and intolerance to chemotherapy or radiotherapy [9].

Traditionally, CUTE has been performed to treat a small subset of patients with BC and bilateral UTUC. Previous papers from experienced centers have reported the results of CUTE in ESRD patients, either undergoing dialysis or having a functioning renal transplant [9–17]. As expected, complication rates were high in uremic patients. Moreover, these patients had a higher incidence and recurrence of UC, more high-grade disease and higher rates of bilaterality and multifocality [18,19]. Because of a morbidity rate of 10% and a mortality rate of 5.5%, physicians remain reluctant to perform this complex surgery [9].

Recently, CUTE is being performed more often. Although, published series still have low numbers of patients and use different approaches (open, laparoscopic or robotic), most of the outcomes are comparable [10–17]. Mean operation times

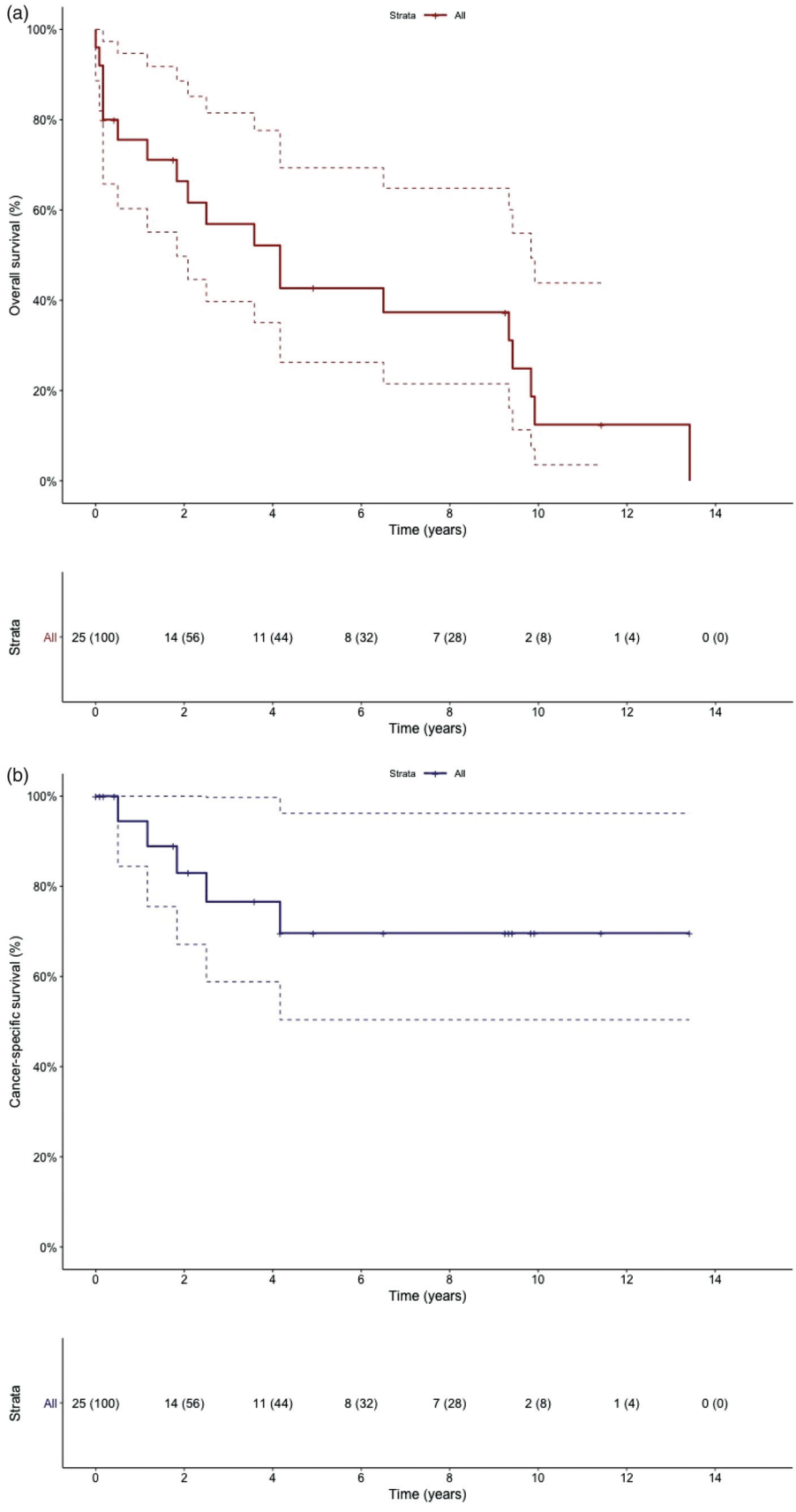

Figure 2. (a) Overall survival curve for all patients. (b) Cancer-specific survival curve for all patients. (c) Recurrence-free survival for all patients.

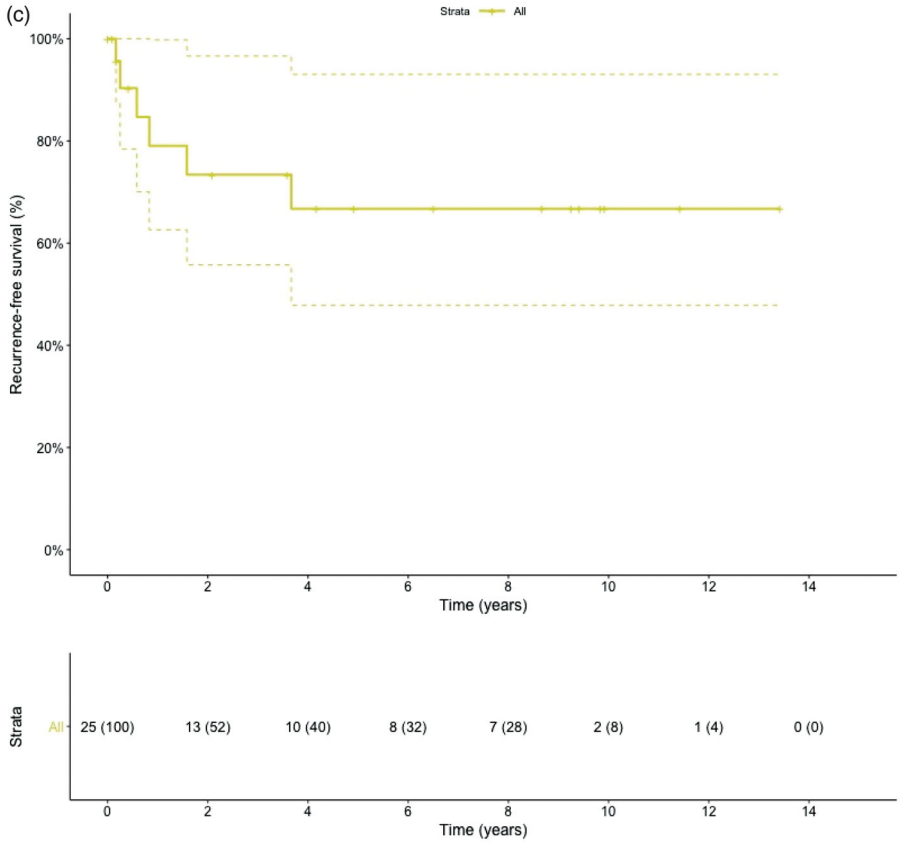

Figure 2. Continued.

differ between 237 and 540 min, while mean hospital stay and time to oral intake are reported to be between 7.5–14.7 days and 2–4 days, respectively. Reported complication rates range from 0% to 80% [10–17,20].

Although, our median operation time (210 min) seems to be similar with the other studies, the median EBL (1100 mL), duration of hospitalization (21 days) and time to oral intake (6 days) are higher than most of the previously reported results [10–16]. However, this difference can be a result of fewer patient numbers in the series, as we see that the results of large series are in accordance with ours [20,21]. Our (minor + major) complication rate of 84% is higher than all of the previous reports. These rather high results may arise from meticulously data gathering, combined with a moderately long follow-up (median >2 years) and using median values instead of mean values because of relatively small number of cases, which possibly has yielded more realistic rates than other series. Table 7 shows a comparison of the outcomes from different CUTE series.

It is well known that patients with ESRD have accelerated atherosclerosis and vascular calcification, compromised innate (inadequate monocyte and neutrophil function) and adaptive (reduced antigen-presenting function, T cell-mediated response and immune regulatory memory) immune system, increased all-cause and cardiovascular mortality, anemia, mineral-associated bone disorder and fractures, susceptibility of fluid overload and coagulopathy diathesis and frailty [22–25]. In our study, we observed that the OS of the patients with ESRD was significantly worse than non-ESRD ones. This can be attributed to the general increased risk of mortality in ESRD patients. Six patients died within 6 months after the operation, of which five died within 2 months. Interestingly, four of these five patients died due to treatment-related reasons, whereas the reason for the other patient is unknown. When those five patients died within 2 months are evaluated in detail, we see that four patients had an ASA score of 3 and the other has a score of 4, while their CCI scores were between 3 and 9. This data corroborates the finding of CCI $\geq$ 5 to be an independent predictor for major complications in a multicenter Taiwanese study performed by Huang et al. [21]. Moreover, 4 of the patients died within 6 months had a dialysis-dependent ESRD. Taking these data into account, we can conclude that the patients with ESRD had worse outcome after CUTE.

A pathological stage of higher than T3 for BC was a significant determinant for CSS. However, as the number of patients with a > pT3 disease was low to make a healthy comparison, we arbitrarily divided the patients into two groups as $\leq$ pT2 versus $\geq$ pT3 according to the highest pT-stage of BC and UTUC. And a significant difference in OS was found between these two groups.

(a)

	Points	
Parameters	0	1
Age (years)	≤66	>66
End-stage renal disease (ESRD)	No	Yes
Charlson comorbidity index (CCI)	0-2	>2
Highest pT-stage of BC and UTUC	0-2	3-4

BC: Bladder cancer, UTUC: Upper tract urothelial carcinoma.

Total score	0-2 points	Good prognosis
	3-4 points	Poor prognosis

(b)

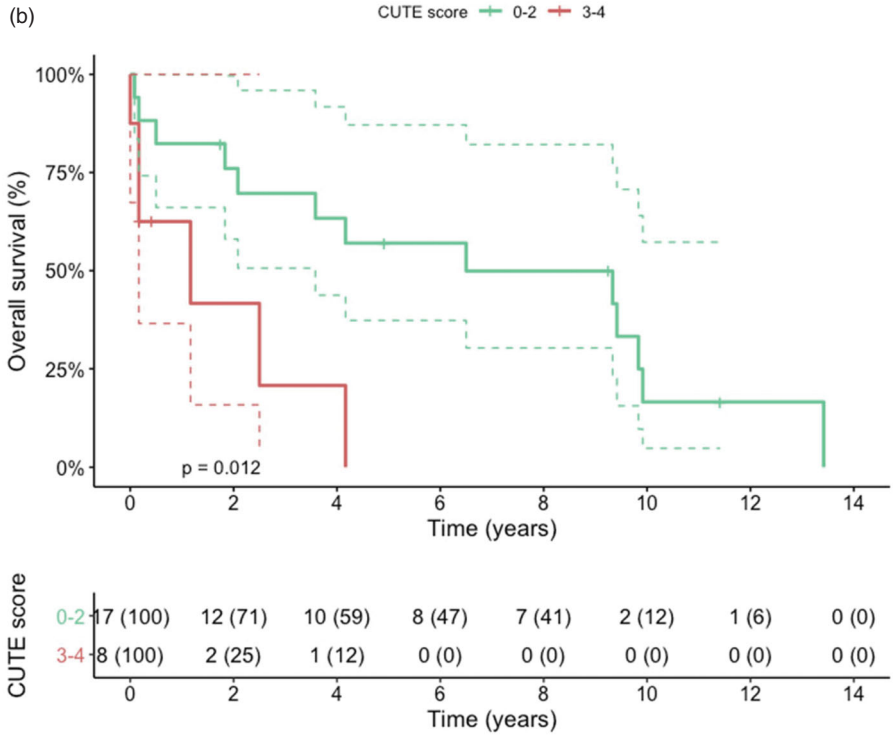

Figure 3. (a) CUTE score. (b) Overall survival curve according to the CUTE score.

With an attempt to define which patients would benefit from undergoing CUTE, we arbitrarily developed a scoring based on the most relevant clinico-pathological parameters found prognostic for OS in the univariate analysis, which could successfully and significantly stratify between patients with a good and poor prognosis. And we think that this tool can be helpful for clinicians to counsel their patients whether they are candidate for CUTE surgery based on the OS probability.

This study has some limitations. A retrospective study has an inevitable selection bias, and some of the complications treated outside our center might have been missed. However, this study also has some important strengths. All patients were treated in a single center, and the operations were performed by two experienced surgeons. Follow-up of all patients were performed at the same center according to a standard protocol.

In conclusion, the present study is the second largest single-center series of patients who underwent CUTE. Our results demonstrate that this complex procedure gives a reasonable expectation of cure with an acceptable amount of morbidity and mortality in non-ESRD patients. Moreover, we arbitrarily developed CUTE score and found that the patients with a score of 0–2 have a better OS. We think that this score can be used to define the patients who would benefit from this complex surgery.

Table 7. Comparison of outcomes from different CUTE series.

Publication details	Operation	Study design	Case no	No of ESRD patient No of RRT patients	Mean age (y)	Mean operation time (min)	Mean EBL (mL)	Mean hospital stay (d)	Mean time to oral intake (hr)	Complication
Holton et al. (2006) Urology [10]	Open	Single-center	9	All ESRD (all HD or FRA)	61.0	356	N/A	10.8	N/A	22.2% 44.4% ES-Tx
Barros et al. (2008) Int Braz J Urol [11]	Lap.	Single-center	8	2 ESRD Others not specified	76.5	540	755	7.5	96.0	25% minor 12.5% major
Li et al. (2009)	Lap.	Single-center	5	All ESRD	58.0	492	378	12.2	72.0	80.0%
BJU Int [13]	Open		3		58.0	268	1646	16.3	96.0	66.6%
Lin et al. (2011) Urology [14]	Lap.	Single-center	5	Not specified	66.6	397	532	10.8	91.2	20.0%
Ou and Yang (2011) Urology [15]	Open	Single-center	10	All ESRD (9 HD, 1 PD)	57.6	328	628	14.7	62.4	10.0%
Ou and Yang (2011) J Endourol [12]	Robotic	Single-center	8	All ESRD (all HD)	66.9	306	496	7.75	N/A	0% (37.5% ES-Tx not included in complications)
Chen et al. (2014) BioMed Res Int [16]	Open	Single-center	14	All ESRD (all HD)	61.0	237.5	560	12.1	48.0	21.4%
Ou and Yang (2017) Int Urol Nephrol [20]	N/A	Single-center	42	All ESRD (all HD)	58.2	N/A	1370	26.1	N/A	19% minor 28.5% major
Huang et al. (2018) Ann Surg Oncol [21][a]	Lap. + Open	Multicenter	81	80 ESRD (67 HD, 8 PD, 3 FRA)	62	380	500	9	N/A	48.2% minor 34.5% major
Present study[a]	Open	Single-center	25	15 ESRD (6 HD, 5 FRA)	66.5	210	1100	22	144	72% minor 40% major

ESRD: End-stage renal disease; RRT: Renal replacement therapy; HD: Hemodialysis; FRA: Functioning renal allograft; PD: Peritoneal dialysis; EBL: Estimated blood loss; ES-Tx: Erythrocyte transfusion; N/A: Not available.
[a]The median values are given for these studies.

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Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

For this type of study, formal consent is not required.

Disclosure statement

The authors declare that they have no conflict of interest related to this manuscript.

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