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Urachal Cancer: Experience of a High-Volume Bladder Cancer Center

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Abstract

Introduction: Primary urachal cancer (UrCa) is rare, with an estimated incidence of 0.2% - 0.5% of all bladder tumors. Although the preferred treatment is surgical, there is no consensus on the best approach. We present our experience managing 14 cases of primary UrCa. **Methods:** A retrospective analysis was conducted on the clinical records of a high-volume bladder cancer center in the UK to identify patients diagnosed with UrCa between May 2013 and June 2022. **Results:** 9 males and 6 females, aged between 30 and 85 years, were included. The diagnosis was most commonly made via flexible cystoscopy and CT for haematuria. 3 patients had metastasis at presentation, and while radiologically no patients showed positive lymph nodes, 2 patients were found to have positive lymph nodes on histopathology. 13 patients underwent partial cystectomy, with 1 undergoing radical cystoprostatectomy. 8 patients underwent concurrent umbilectomy and/or lymphadenectomy. The most common histological subtype was mucinous adenocarcinoma. 2 patients experienced local recurrence and underwent transurethral resection, while 6 patients experienced metastasis. Metastasis-free survival rate was 74.1% and 55.6% at 12 and 24 months, respectively. Umbilectomy and lymphadenectomy did not decrease rates of positive surgical margin, local recurrence, metastasis, or mortality. **Conclusions:** UrCa is a rare and aggressive malignancy that can occur at any age and may be advanced upon presentation. Bladder-sparing surgery is becoming more prevalent, with chemotherapy being reserved for recurrence or metastasis. In our series, routine umbilectomy and lymphadenectomy did not improve oncologic outcomes. However, lymphadenectomy may have a role in cancer staging.

Keywords

Urachal Cancer, Urachus, Bladder Cancer

1. Introduction

Urachal cancer (UrCa) is a rare malignancy, with an estimated incidence of 0.01% of all adult neoplasms and 0.2% - 0.5% of all bladder tumors [1]. During embryonic development, the bladder apex is connected to the allantois through the urachus, a structure comprised of a muscular layer, connective tissue, and a transitional or cuboidal epithelium that lines the lumen [2]. As the bladder descends, it stretches the urachus, eventually causing the loss of its lumen and the formation of the median umbilical ligament [3]. Urachal remnants have been documented in approximately one-third of the general population [2].

The histology of the urachus is more similar to the intestinal epithelium than the bladder urothelium. The origin of UrCa pathology is believed to stem from urachal epithelial metaplasia and the persistence of cloacal remnants within the urachus, resulting in distinct histological differences between UrCa and other bladder tumors [2]. Mucinous adenocarcinoma is the predominant histopathological subtype of UrCa, but others such as non-specified, enteric, or villous adenocarcinoma and signet ring cells have also been reported [4].

Due to the scarcity of UrCa cases, there is a lack of agreement on the most effective management. Currently, there has been an increasing trend towards using surgical techniques that preserve the bladder, while reserving chemotherapy for cases of cancer recurrence or spread [2] [4]. For localized or locally advanced UrCa, the standard surgical approach that has been recommended is partial cystectomy (PC) with en-bloc urachus excision. Previous studies have shown that this approach yields comparable survival rates to radical cystectomy, indicating that it is a viable alternative with no significant difference in outcomes [4] [5] [6].

The question of whether concurrent umbilectomy and lymph node dissection (LND) enhance oncological outcomes remains a subject of ongoing debate. While some studies have suggested that umbilectomy may lead to improved survival rates [3] [5] [6] [7]. Other research, such as the study conducted by Ashley and colleagues, did not find a significant improvement in prognosis [8]. Similarly, there have been numerous studies investigating the role of lymphadenectomy, with the majority indicating that it does not provide a survival benefit. However, the literature has raised questions about the value of lymphadenectomy in the staging of UrCa [3] [4] [5] [6] [7] [9].

Prompt identification and early diagnosis of diseases are crucial for timely intervention. Additionally, there is a need for enhanced comprehension regarding the management of primary UrCa. In this context, we would like to share our experience in managing 14 cases of primary UrCa, aiming to contribute to the existing knowledge in this area.

2. Materials and Methods

2.1. Patient Selection

A retrospective analysis was conducted on the operative, clinical, and histopa-

thology records of a high-volume bladder cancer center in the UK at the Charing Cross Hospital to identify patients diagnosed with primary UrCa between May 2013 and June 2022.

Patients with a histopathologically confirmed diagnosis of primary UrCa who underwent surgery were included in the study, while those with benign urachus such as inflammation or metastatic UrCa who were not eligible for surgery were excluded. Furthermore, we excluded cases of primary adenocarcinoma originating from any other organ such as patients with a previous history of gastrointestinal malignancy. Moreover, no cases of urothelial carcinoma in situ were identified within the bladder.

2.2. Procedure

The surgical approaches employed in this study included either PC or open radical cystoprostatectomy with en-bloc urachal excision. Concurrent umbilectomy and/or lymphadenectomy were performed in select cases based on patient presentation and surgeon discretion. Umbilectomy consisted of the excision of the umbilicus along with the median and medial umbilical ligaments, while lymphadenectomy involved the dissection of the bilateral iliac and obturator lymph nodes (LN). PC was performed using either robotic, laparoscopic, or open techniques. In all PC cases, the urachal lesion was cystoscopically demarcated using either Collin's knife or a roller ball, followed by en-bloc excision. Postoperative drain placement was performed in some patients at the discretion of the surgeon. Prior to the trial without a catheter (TWOC), all PC patients underwent cystograms.

2.3. Variables

We retrospectively gathered data from our electronic bladder cancer database at Charing Cross Hospital. Data were extracted on pre-operative factors (baseline demographics, mode of presentation, cystoscopy findings and imaging modalities, and findings) and peri-operative factors (surgical method, early complications < 30 days, and histopathology results). The diagnostic modalities used included flexible cystoscope, contrast-enhanced CT, ultrasound, or MRI. The TNM classification system was used for the staging of UrCa. To categorize post-operative complications, the Clavien-Dindo classification system was used.

2.4. Follow-Up and Outcomes

The study collected data on post-operative oncological outcomes, including local recurrence, metastasis, metastasis-free survival (MFS), and mortality. Furthermore, sub-analyses were conducted to compare outcomes between patients who underwent concurrent umbilectomy and those who did not, as well as patients who underwent concurrent lymphadenectomy and those who did not. It is important to note that not all patients who underwent umbilectomy also received lymphadenectomy, and vice versa.

Local recurrence was defined as a recurrence within the bladder, while metastasis was considered as any recurrence or metastasis outside the bladder, including the pelvis, peritoneum, anterior abdominal, and prostatic urethra or any other distant metastasis site. MFS was calculated along with the duration of follow-up, which was limited by either death or the most recent available clinic visit.

2.5. Statistical Analysis

Descriptive statistics were employed to summarize the data, with continuous variables presented as mean, range, or median, and categorical variables reported as numbers. MFS was calculated using the Kaplan-Meier test. IBM® SPSS® Statistics version 29 was utilized for statistical analyses.

2.6. Ethics Approval

All local governance protocols were strictly followed throughout the study.

3. Results

3.1. Patient Demographics and Clinical Features

A total of 14 cases of UrCa were retrospectively reviewed. The mean age of diagnosis was 60 years (range: 30 - 85 years). The most common presenting symptom was visible haematuria. The bladder dome was the most common site of UrCa (n = 8), with 3 and 2 cases located on the anterior and posterior walls, respectively (Table 1).

3.2. Treatment Approaches and Peri-Operative Results

PC was performed on 13 patients, with one patient undergoing open radical cystoprostatectomy. 8 patients received additional procedures, including concurrent umbilectomy and/or lymphadenectomy. No patient received neoadjuvant treatment.

The mean intraoperative blood loss was 47.5 mL (range: 20 - 100 mL), and 7 patients had a drain for a mean of 4.5 days (range: 1 - 15 days). The average hospital stay was 3.6 days (range: 1 - 8 days), and all patients successfully passed the TWOC after a mean of 16.8 days (range: 9 - 27 days).

Three patients experienced complications, including bladder overactivity post-robotic PC (Clavien-Dindo 1), subcutaneous abdominal hematoma 1-month post open PC (Clavien-Dindo 3a), and myocardial infarction one-week post-radical cystoprostatectomy (Clavien-Dindo 4a).

3.3. Tumor Pathology

Histopathology results revealed that mucinous adenocarcinoma was the most commonly observed subtype (n = 8). The majority of the cases (n = 8) were diagnosed with pathological stage pT3. Additionally, 8 cases displayed differentiation grade (G) 3 (Table 2). 5 specimens exhibited focal signet ring cells, and 2 cases had positive surgical margins (PSM).

Table 1. Socio-demographic characteristics and clinical features.

	Number
Sex	
Male	9
Female	5
Smoking	
Smoker	4
Ex-smoker	1
Non-smoker	9
Presentation	
Visible haematuria	9
Asymptomatic	3
Storage LUTS	1
Suprapubic pain	1
Metastasis to the anterior abdominal	3
Metastasis to the pelvis	2
Metastasis to the umbilicus	1
Investigations	
Flexible cystoscope	8
Contrast-enhanced CT	8
Ultrasound	5
MRI	3
Surgery method	
Open radical cystoprostatectomy	1
Total PC	13
Open PC	8
Robotic PC	3
Laparoscopic PC	2

LUTS: lower urinary tract symptoms. CT: computed tomography. MRI: magnetic resonance imaging. PC: partial cystectomy.

Table 2. Histopathological results of the specimens.

	Number
UrCa subtype	
Mucinous adenocarcinoma	8
Non-specified adenocarcinoma	2

Continued

Enteric adenocarcinoma	1
Villous adenocarcinoma	1
Sarcomatoid urothelial carcinoma	1
No residual cancer	1
Pathological pT stage according to the TNM system	
pT0	1
pT1	1
pT2	1
pT3	8
pT4	1
Differentiation grade	
G1	1
G2	1
G3	8
Positive lymph nodes	2

UrCa: urachal cancer. pT: pathological stage. TNM: Tumour, node, and metastases staging classification. G: differentiation grade.

One unexpected finding was observed in a 30-year-old non-smoker female patient who presented with a 3 cm solid-appearing tumor on the bladder dome, initially managed with transurethral resection (TURBT). Pathological examination of the TURBT specimen revealed pT1 urachal mucinous adenocarcinoma. Following a multidisciplinary team review, the patient underwent open PC, umbilectomy, and LND. The pathological examination of the cystectomy specimen was benign, with no evidence of residual disease. The patient had a clear 10-month follow-up, with the final stage pT1N0M0.

3.4. Clinical Follow-Up and Oncological Outcomes

Among the patients, the mean duration of follow-up was 41.5 months, ranging from 10 to 120 months. All patients had a 1-year follow-up, with 8 and 5 patients having 3-year and 5-year follow-ups, respectively. The follow-up was limited either by death or the last available clinic visit.

6 patients exhibited metastasis post-surgery, with a mean interval of 26.3 months (range: 2 - 102 months). The most frequently observed locations of metastasis were the lungs and bones, with 2 cases in each site. Metastasis also occurred in the liver, pelvis, peritoneum, brain, prostatic urethra, bone marrow, and rectus muscle, with 1 case in each group. MFS rates were 83.3%, 74.1%, and 55.6% at 3, 12, and 24 months, respectively (Table 3 and Figure 1). And the estimated median MFS was found to be 102 months.

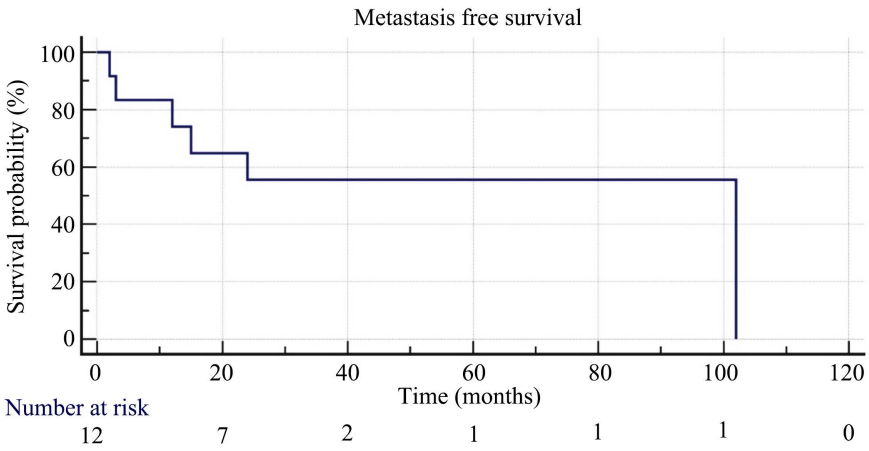

Figure 1. Metastasis-free survival curve.

Table 3. Survival probability.

Survival time (months)	Survival Probability	Standard Error
2	91.7%	0.0798
3	83.3%	0.108
10	-	-
12	74.1%	0.129
15	64.8%	0.143
24	55.6%	0.149
30	-	-
60	-	-
102	0.000	0.000

2 local recurrences were reported in the series, for which TURBT was performed. Pathological examination of both cases was mucinous adenocarcinoma with focal signet ring cells. One patient underwent open PC and umbilectomy for pT2bG2N0M0 and received adjuvant chemotherapy 6 months post-surgery, but experienced local recurrence after 24 months. No further follow-up data is available after the TURBT. The other patient underwent robotic PC and LND for pT3G3N0M0 and experienced local recurrence 19 months post-surgery. After undergoing TURBT, the patient remained cancer-free during the 5-month follow-up period for which data was available.

Postoperative chemotherapy was administered in three cases. One patient received palliative treatment with six cycles of gemcitabine and cisplatin, along with palliative radiotherapy, for metastasis to bone and bone marrow that occurred two months after surgery. However, the patient died 13 months later. The second patient received 12 cycles of FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin), along with cytoreductive surgery, for metastasis to the pelvis and peritoneum that occurred three months after surgery. This patient survived for

another 16 months, according to the last available follow-up data. The third patient received an unknown regimen of adjuvant chemotherapy six months after surgery. Despite this treatment, the patient experienced local recurrence 24 months post-treatment and underwent TURBT as a result.

At the time of the study, two patients had died. One patient was a 53-year-old male who underwent open PC and umbilectomy for mucinous adenocarcinoma and pT1N0M0. He had distant metastasis to the lung and brain 8.5 years later. He received supportive palliative care and died 6 months later. The other patient was a 78-year-old female who underwent open PC, umbilectomy, and LND for non-specified urachal adenocarcinoma and pT3G3N1M0, but experienced metastasis to bone and bone marrow 2 months after the surgery for which she received palliative 6 cycles of gemcitabine and cisplatin along with palliative radiotherapy, but she died 13 months later. None of the patients had PSM or focal signet ring cells in their surgical specimens.

Subgroup analysis of concurrent umbilectomy and lymphadenectomy: The study compared the outcomes of patients who underwent concurrent umbilectomy versus those who did not and concurrent LND versus those who did not.

In the comparison of patients who underwent concurrent umbilectomy (n = 8) versus those who did not (n = 6), 2 and 1 patients had metastasis at presentation, respectively. All patients underwent PC surgery, with the exception of one patient in the non-umbilectomy group who underwent radical cystoprostatectomy. LND was performed in 4 patients in both groups.

The histopathology results showed that 3 and 1 patients had pT3 and pT4 stages, respectively, in the umbilectomy group, while 5 patients had pT3 stages in the non-umbilectomy group. 3 and 5 cases had G3 in the umbilectomy and non-umbilectomy groups, respectively. PSM was reported in one patient in each group. One patient in each group experienced local recurrence after 30 and 19 months, respectively. 4 patients in the umbilectomy group and 2 patients in the non-umbilectomy group developed metastasis after a mean of 35.7 (range: 2 - 102) and 7.5 (range: 3 - 12) months, respectively. The two deaths occurred in patients who had undergone umbilectomy.

In the comparison of patients who underwent concurrent LND (n = 8) versus those who did not (n = 6), 2 and 1 patients had metastasis at presentation in the LND and non-LND arms, respectively. All the patients in both arms underwent PC surgery, except for one patient in the LND arm who underwent radical cystoprostatectomy. 4 patients in both arms underwent umbilectomy. The histopathology results showed that 6 patients had pT3 stage in the LND arm, while 2 and 1 patients had pT3 and pT4 stages, respectively, in the non-LND arm. 6 and 2 cases had G3 in the LND and non-LND arms, respectively. PSM was found in one patient in each arm. One patient in each arm experienced local recurrence after 19 and 30 months for the LND and non-LND arms, respectively. 4 cases in the LND arm and 2 cases in the non-LND arm had metastasis, with a mean du-

ration of 8 and 63 months (range: 2 - 15 and 24 - 102) for the LND and non-LND arms, respectively. One patient died in each arm.

4. Discussion

UrCa is a rare and aggressive type of cancer that often presents at an advanced stage and has a high risk of metastases, with MFS rates of 83.3%, 74.1%, and 55.6% at 3, 12, and 24 months, respectively, according to our study. The majority of our cases exhibited pathological stage 3 and differentiation grade 3 along with three instances of local metastasis upon presentation. Our analysis revealed a greater incidence of UrCa among male patients. Nonetheless, no disparities were observed in the clinical or pathological characteristics, nor the prognosis, between males and females [3].

After a 5-year period, the overall survival rate was demonstrated to be between 45% and 51% [6] [10]. The median overall survival time for all stages of UrCa was determined to be 4.8 years. Prognostic assessment using the TNM staging system revealed that when the tumor is limited to the urachus alone, the median overall survival time extends to 6.2 years. However, a considerable decline in life expectancy was observed when patients exhibited regional lymph node involvement or distant metastasis [3].

The recurrence-free rates at 1 year, 2 years, and 5 years were estimated to be 63.4%, 50.7%, and 44.3%, respectively [11]. Patients diagnosed with metastatic disease experienced a bleak overall survival outcome, with a 5-year survival rate of 14% [4]. Among patients with metastatic disease who underwent chemotherapy, the estimated median overall survival time from the initial detection of metastasis was 23.5 months [11].

There is a variance in the presenting characteristics, diagnostic methods, and treatment options available for UrCa. Haematuria was a common presenting symptom in most of our cases. The diagnosis of UrCa was established using CT, ultrasound, or MRI, in combination with flexible cystoscopy, which served as a valuable diagnostic modality for evaluating haematuria. On cystoscopic examination, UrCa appeared as a solid or partly cystic and partly solid lesion with well-circumscribed margins and occasional ulcerated areas (**Figure 2**). Radiologically, the lesions were depicted as solid or partly cystic heterogeneous masses arising from the bladder wall or urachus, with enhancement on contrast and the presence of calcifications (**Figure 3** and **Figure 4**).

Despite the availability of several radiological staging systems, including TNM, Sheldon, and Mayo, there is still controversy surrounding the best protocol for predicting oncological outcomes [1] [2] [3] [6]. However, Ding and colleagues conducted a study where they developed and validated nomograms, along with creating online calculators, to enhance the prediction of overall survival and cancer-specific survival. They compared the three staging systems in clinical practice. They recommended the utilization of nomograms based on the TNM staging system due to their superior predictive efficacy [1].

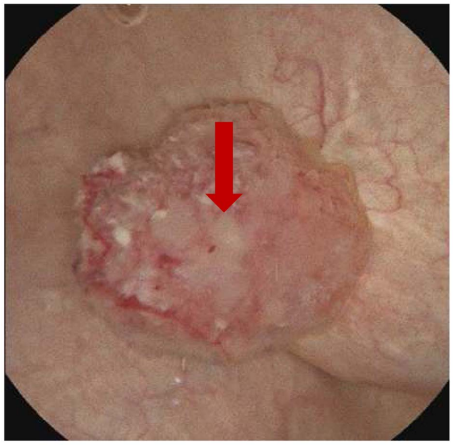

Figure 2. A flexible cystoscope revealed a solid, 3 cm, well-demarcated tumor on the bladder dome. (The arrow)

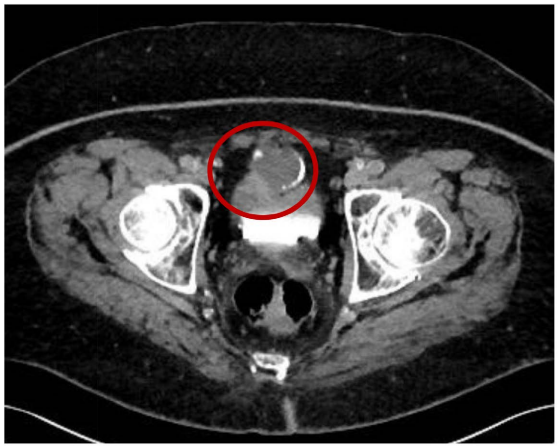

Figure 3. Contrast-enhanced CT (axial view) showed a cystic structure adjacent to the anterior bladder wall in the midline. It showed some scattered areas of mural calcification. There was possibly a minor soft tissue thickening with enhancement within the lesion. Moreover, there was also perhaps some associated urothelial thickening within the bladder in this region. (The circle)

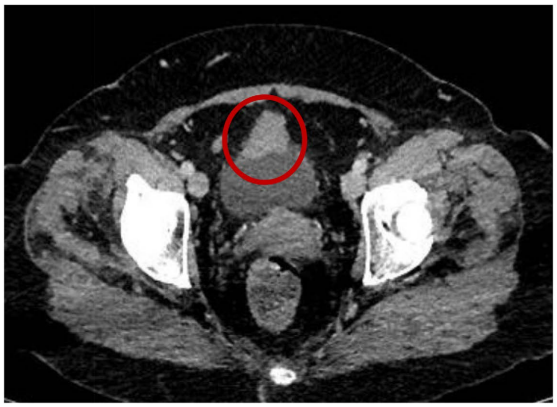

Figure 4. Contrast-enhanced CT (axial view) revealed a urachal remnant measuring 3 cm. A mass of soft tissue was seen at the base of the urachus. This did appear to involve the bladder wall. (The circle)

The histopathological subtypes of UrCa vary, with mucinous adenocarcinoma being the most common, but others such as non-specified, enteric or villous adenocarcinoma, sarcomatoid urothelial carcinoma, and signet ring cells have also been reported. The presence of these different subtypes can affect oncological outcomes [1] [4]. A significant improvement in survival was observed in patients with glandular histology when compared to those with non-glandular histology [4].

As UrCa is a rare malignancy, there is currently no established treatment protocol. However, based on our experience and in accordance with most studies, the majority of our cases underwent PC with en-bloc urachus excision. This has been recommended as the standard surgical approach for localized or locally advanced UrCa, with no significant difference in survival rates compared to radical cystectomy [4] [5] [6].

The value of performing concurrent umbilical resection and LND remains a topic of discussion. Our study results indicated that these procedures did not result in a reduction in the rates of PSM, local recurrence, metastasis, or mortality. It is important to acknowledge that several factors, including the presence of metastasis at presentation, pathological stage, and differentiation grade may have influenced our results.

In contrast to our results, most studies have recommended umbilectomy due to improved survival [3] [5] [6] [7]. Ashley and colleagues found that umbilectomy improved prognosis in univariate analysis without affecting it in multivariate models. However, they recommended umbilectomy, which resulted in a lower PSM rate [8].

Lymphadenectomy has been the subject of numerous studies, with the majority reporting that it offers no survival benefit, which is consistent with our results. However, our findings align with prior research that suggested that imaging modalities such as CT and MRI may not be reliable in detecting all LN metastases. Our study identified instances where radiologically negative patients were found to have positive pathological LN postoperatively, leading to questions about the value of lymphadenectomy in the staging of UrCa. Moreover, the survival outcome for LN metastasis was found to be worse as that of distant metastases, which may support the argument for undergoing lymphadenectomy [4] [5] [6] [7] [9].

Chen *et al.*, on the other hand, recommended lymphadenectomy only if a positive radiological LN was present. They observed that positive pathological LN postoperatively was correlated with preoperative imaging. The study found that patients who underwent LND without a positive radiological LN resulted in a pathologically negative LN postoperatively [3].

According to existing literature, adjuvant radiotherapy and chemotherapy have not yet demonstrated clear effectiveness in treating UrCa. However, Chemotherapy may be considered in metastatic disease, positive lymph node involvement, or as adjuvant therapy. Nonetheless, the specific characteristics of chemotherapy regimens, including the type and number of cycles, and their im-

pact on survival, have not been definitively established. In our series and other studies cisplatin-based chemotherapy, fluorouracil, and gemcitabine have been utilized [1] [2] [4] [12] [13].

It was demonstrated that systemic chemotherapy did not result in improved overall survival for the management of localized or advanced UrCa [4] [5] [11]. However, Flammia *et al.* demonstrated a significant survival benefit in patients with metastatic UrCa who received chemotherapy, with a median overall survival of 16 months compared to 3 months for those who did not receive chemotherapy [14]. Similarly, Szarvas and colleagues found that the combination of cisplatin-based chemotherapy with fluorouracil led to improved radiographic progression-free survival in UrCa patients [5]. Hayashi *et al.* reported estimated 1-year, 2-year, and 5-year overall survival rates of 79.8%, 49.7%, and 12.4%, respectively, in patients who received chemotherapy for metastatic UrCa [11]. However, further research is needed to investigate the comprehensive treatment of UrCa patients after surgery and for advanced disease.

Our study has several limitations, including its retrospective, single-center design, small sample size, missing data, and incomplete follow-up for some patients. Additionally, detailed information regarding anatomic dissection limits was not always available, and there are no available data to measure overall and cancer-specific survival. However, it is important to note that some of these limitations are common in studies of rare diseases. Despite these limitations, our findings can provide valuable insights for future systematic reviews and meta-analyses, which are important tools for studying rare diseases.

5. Conclusion

UrCa is a rare and aggressive form of cancer that can occur at any age and may be advanced upon presentation. Early recognition and diagnosis are crucial for prompt intervention. Bladder-sparing surgical management is becoming more prevalent, with chemotherapy reserved for recurrence or metastasis. Our series demonstrates that bladder-sparing surgery is a feasible option that reduces the morbidity associated with cystectomy. In our study, routine umbilectomy and lymphadenectomy did not lead to improved oncologic outcomes. However, LND may have a role in cancer staging. Endoscopic management may be an option for selected patients with small, non-muscle invasive UrCa to achieve oncologic clearance. Further research is needed through multi-center studies, systematic reviews, and meta-analyses to confirm our findings and provide more insights into the management of UrCa and its survival rates.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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