

# Are voiding symptoms associated with the survival outcome of primary female urethral cancer?

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## Abstract

Primary female urethral cancer (PFUC) is a rare urologic malignancy. Some patients who primarily presented with voiding symptoms experienced delayed investigation due to a lack of awareness. Therefore, this retrospective study aimed to compare the clinical information, treatment, and survival outcomes of PFUC between patients who initially presented with voiding symptoms and those with other symptoms. We retrospectively

reviewed 13 PFUC patients who were treated at our hospital between January 2010 and December 2023. The overall 2-year survival rate was 55.4%. Factors including high-risk tumor, R1 resection, adenocarcinoma pathology, and nodal metastasis showed statistically significant differences between survival curves. The 2-year survival rates for patients with voiding symptoms and other symptoms were 34.3% and 80%, respectively. Although the overall survival rates between the two groups were not significantly different, PFUC patients with voiding symptoms demonstrated characteristics of advanced disease, including larger tumor size and nodal metastasis.

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## Introduction

Primary female urethral cancer (PFUC) is a rare urologic malignancy. Overall annual incidence from national cancer databases ranged from 0.7 to 1.5 per million women and increased with age.<sup>1,2</sup> Previous studies reported that the 5-year cancer-specific survival rate was 53-58.9%.<sup>3,4</sup> Prognostic factors affecting survival rate included advanced age,<sup>3</sup> stage,<sup>2,5</sup> involvement of the entire urethra,<sup>6</sup> disease site,<sup>5</sup> tumor size,<sup>7</sup> nodal status,<sup>3,5,8</sup> and histologic features,<sup>2,7</sup> especially non-squamous cell carcinoma (SCC).<sup>3</sup> If PFUC was resectable, surgery was the primary treatment and/or combined with other modalities, including radiotherapy (RT) and chemotherapy.<sup>2,4,8</sup> There was a study that demonstrated 46% of patients were at an advanced stage at the time of diagnosis.<sup>2</sup> Because clinical presentations varied among bleeding, voiding symptoms, other lower urinary tract symptoms, or no symptoms,<sup>4,8</sup> we noticed that the majority of PFUC patients who presented with bleeding were promptly investigated. On the other hand, some patients who primarily presented with voiding symptoms were often delayed in investigation due to a lack of awareness. Therefore, this study aims to compare clinical information, treatment, and survival outcomes of PFUC between those initially presenting with voiding symptoms and those presenting with other symptoms, and to facilitate early diagnosis.

## Materials and Methods

This retrospective cohort study of PFUC diagnosed at our institute was conducted between January 2010 and December 2023. All patients were aged over 18 years old, pathologically confirmed, and primarily treated by surgery. Data on demographic characteristics, clinical presentations, tumor characteristics, surgical procedures, and pathological findings were extracted from medical records. Clinical presentations included bleeding, hematuria, voiding symptoms, vaginal discharge, and others. Tumor characteristics included size, location, and staging according to the relevant staging system. Surgical procedures were categorized as pelvic exenteration, distal urethrectomy, or transurethral resection.

Neoadjuvant and adjuvant treatment data, including radiation or chemotherapy, were also collected for analysis.

### Statistical analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Continuous variables were presented as means with standard deviations (SD), and categorical variables were expressed as frequencies and percentages. The Kaplan-Meier method was used to calculate overall survival (OS) after surgery, and log-rank tests were used to determine statistically significant differences between survival curves. All statistical analyses were conducted using the SPSS software.

## Results

A total of 13 cases of PFUC were diagnosed during the study period, with a mean age of 65.6 years (SD ±12.8). The average follow-up time was 40.4 months (SD ±35.7) after surgery. Overall, the 2-year survival rate was 55.4%. The majority of cases initially presented with voiding symptoms (53.9%), while other symptoms, including urinary frequency, bleeding, vaginal discharge, and incidental findings from cystoscopy, were observed in 23.1%, 7.7%, 7.7%, and 7.7%, respectively, as shown in Table 1. Preoperative imaging studies, including computed tomography and/or magnetic resonance imaging (MRI) of the lower abdomen, were performed in 6 and 10 cases, respectively. Moreover, tumors were distributed throughout the urethra, with 53.9% affecting the entire urethra, 23.1% in the proximal urethra, and 23.1% in the distal urethra. Tumor size varied, with an average dimension of 3.7 cm (SD ±2.1). The majority of tumors were staged T4 (61.5%), with smaller proportions categorized as Ta, T1, and T2 stages, as detailed in Table 2.

Pelvic exenteration emerged as the predominant surgical intervention, performed in 69.2% of cases, followed by distal urethrectomy (23.1%) and transurethral resection (7.7%). Pathological analysis revealed adenocarcinoma (ACC) as the most common pathology (46.2%), with urothelial carcinoma, SCC, and clear cell

carcinoma accounting for 30.8%, 15.4%, and 7.7% of cases, respectively. Resection status indicated complete tumor removal (R0) in 61.5% of cases, while microscopic residual tumor (R1) was observed in 38.5% of cases. Nodal staging revealed that 53.9% (n=7) of patients were classified as N0, indicating no regional lymph node involvement. N1 staging was observed in 15.4% (n=2) of cases, while N2 staging was present in 30.8% (n=4) of cases.

Regarding other treatment modalities, neoadjuvant therapy was administered in 23.1% of cases. Adjuvant therapy was administered in 46.2% of cases, with adjuvant concurrent chemoradiotherapy, adjuvant chemotherapy alone, and adjuvant RT alone being utilized in 23.1%, 7.7%, and 15.4% of cases, respectively. A notable proportion (53.9%) of patients did not receive adjuvant therapy.

Survival outcomes demonstrated that 38.5% of patients had passed away during our observation period. The 2-year survival rate stood at 55.4% as shown in Figure 1A. Factors including high-risk tumor, R1 resection, ACC pathology, and nodal metastasis exhibited statistically significant differences between survival curves, with p-values of 0.037, 0.001, 0.001, and 0.007, respectively, as illustrated in Figure 1C-F. The 2-year survival rates of voiding symptoms and other symptoms were 34.3% and 80%, respectively. However, the survival rate between voiding symptoms and other symptoms showed no statistically significant differences with p-values of 0.088, as depicted in Figure 1B. A patient who initially presented with voiding symptoms had a significantly palpable mass on vaginal examination, a larger tumor size, and the presence of nodal metastasis, as detailed in Table 3.

## Discussion

The incidence of PFUC in national cancer databases was 0.7-1.5 per million women and increased with age.<sup>1,2</sup> PFUC is usually presented at an average age of more than 60 years.<sup>1-3,8</sup> The mean age in our study was also 65.6 years.

**Table 1.** Clinical and treatment data.

Clinical data	Total (n=13)	%
<b>Initial presentation</b>		
Obstructive symptoms	7	53.9
Urinary frequency	3	23.1
Bleeding	1	7.7
Vaginal discharge	1	7.7
Asymptomatic	1	7.7
<b>Therapeutic management</b>		
<b>Surgical treatment</b>		
Anterior pelvic exenteration	9	69.2
Distal urethrectomy	3	23.1
Transurethral resection	1	7.7
<b>Neoadjuvant treatment</b>		
Neoadjuvant chemotherapy and radiotherapy	2	15.4
Neoadjuvant chemotherapy alone	1	7.7
None	10	76.9
<b>Adjuvant treatment</b>		
Adjuvant chemotherapy and radiotherapy	3	23.1
Adjuvant chemotherapy alone	1	7.7
Adjuvant radiotherapy alone	2	15.4
None	7	53.9

## Survival rate

Previous studies reported a 5-year cancer-specific survival rate of 53-58.9%.<sup>3,4</sup> Studies from Korea demonstrated that the 5-year OS rate ranged from 58.9% to 65%.<sup>4,8</sup> Due to the short follow-up time in our population, a 2-year survival rate was used instead of the 5-year one. The 2-year survival rate in our study is 55.4%, consistent with trends observed in previous studies.

## Factors related to the survival rate

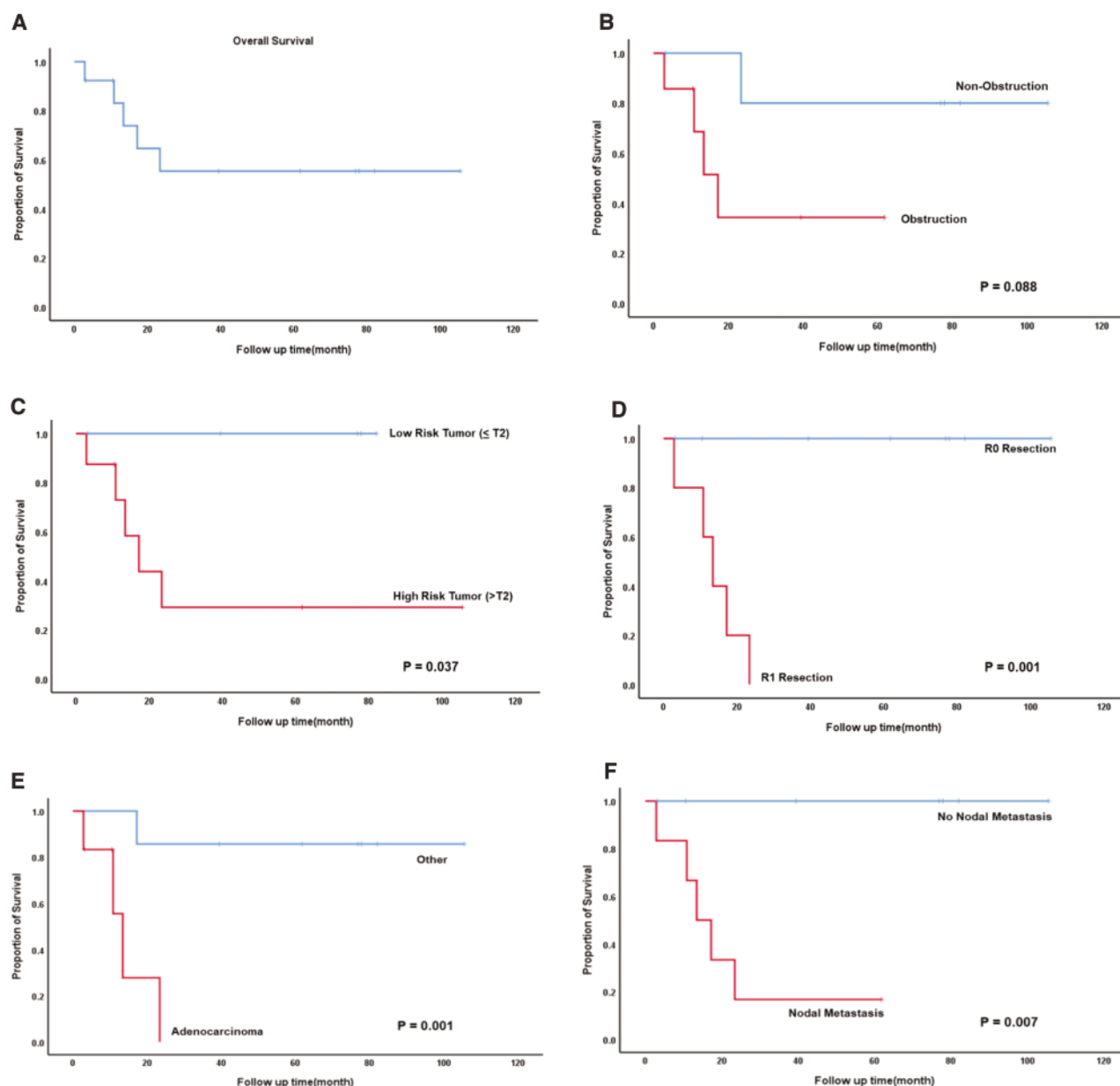
### Tumor size and location

Tumor site, involvement of the entire urethra, and tumor size are associated with survival rates.<sup>4-7</sup> However, there was no significant difference in survival rates between patients with tumors

larger than 3.7 cm and those with tumors smaller than 3.7 cm, with  $p=0.088$ . The study by Kang showed that tumor involvement of the entire urethra is related to survival rates with a hazard ratio (HR) of 4.63.<sup>4</sup> However, in our study, tumor involvement of the entire urethra showed no significant difference in survival rates. This discrepancy is suspected to be due to the small sample size in our study.

### Staging

Tumor staging and nodal metastasis were identified as prognostic factors related to survival.<sup>2-5,8,9</sup> The study by Champ *et al.* reported a HR of 1.89 for nodal metastasis, 2.64 for T3 stage, and 3.11 for T4 stage,<sup>3</sup> while the study by Gakis *et al.* reported a HR of 3.5 for nodal metastasis and 2.8 for advanced T stage (defined as



**Figure 1.** A) Overall survival; B) overall survival comparison based on clinical presentation; C) overall survival comparison based on tumor risk; D) overall survival comparison based on resection status; E) overall survival comparison based on pathology; F) overall survival comparison based on nodal metastasis.

stages beyond T2).<sup>9</sup> Our univariate results align with prior research, highlighting advanced T stage and nodal metastasis as negative prognostic factors.

### Cell type

Derksen *et al.* reported 5-year survival rates of 64%, 61%, and 31% for SCC, urothelial cell carcinoma (UCC), and ACC, respectively.<sup>2</sup> Sui *et al.* identified ACC as a risk factor for worse OS with a HR of 1.57.<sup>10</sup> In our study, ACC also emerged as the most fatal histological subtype, with a 1-year survival rate of 55.6% and a 2-year survival rate of 0%. Importantly, our findings indicate a poorer prognosis compared to previous studies, potentially due to a higher prevalence of T4 staging (61.5%) in our cohort, highlighting an increased burden of advanced disease at diagnosis.

### Treatment and management

In terms of treatment, pelvic exenteration was the primary surgical approach, emphasizing radical excision to ensure complete

tumor removal. Notably, all patients with R1 resection status in our study experienced unfavorable outcomes, with a 2-year survival rate of 0%, highlighting the critical importance of achieving surgical completeness for improved survival.

In advanced disease, multimodal treatment is recommended to enhance OS and recurrence-free survival.<sup>11</sup> According to prior research by Gakis (2015), neoadjuvant chemotherapy or chemoradiotherapy has shown superiority over adjuvant chemotherapy or surgery alone for patients with cT3 or nodal metastasis, with HR of 0.14 and 0.1, respectively.<sup>12</sup> In our study, 3 patients underwent neoadjuvant treatment, resulting in survival outcomes for 2 patients.

Regarding radiation, findings from Son *et al.* indicated that the combination of surgery and adjuvant RT provided the highest OS probabilities. Adjuvant RT was found to be superior to surgery alone, with HRs of 0.27 for ACC and 0.45 for UCC. However, no significant difference in OS was observed in patients with SCC.<sup>13</sup> In our study, 5 patients received adjuvant RT: 3 with ACC histolo-

**Table 2.** Pathological data.

Pathological data	Total (n=13)	%
<b>Tumor location</b>		
Entire urethra	7	53.9
Proximal urethra	3	23.1
Distal urethra	3	23.1
<b>Tumor staging</b>		
Ta	1	7.7
T1	3	23.1
T2	1	7.7
T4	8	61.5
<b>Nodal staging</b>		
N0	7	53.9
N1	2	15.4
N2	4	30.8
<b>Resection status</b>		
R0	8	61.5
R1	5	38.5
<b>Pathological subtype</b>		
Adenocarcinoma	6	46.2
Urothelial cell carcinoma	4	30.8
Squamous cell carcinoma	2	15.4
Clear cell carcinoma	1	7.7

**Table 3.** Comparison between primary female urethral cancer with voiding symptoms and other symptoms.

Parameters	Voiding symptoms (n=7)	Other symptoms (n=6)	p
Age (year)	63.9	69.2	0.494
Symptom onset (months)	5.6	7.2	0.466
Follow-up time (months)	22.3	61.4	0.042
Palpable mass on vaginal examination	7/7	3/6	0.033
Groin node enlargement on examination	1/7	1/6	0.906
<b>Tumor</b>			
Location: distal urethra	7/7	3/6	0.033
Tumor size (cm)	5.0	2.2	0.008
Nodal metastasis	5/7	1/6	0.048
Advanced T stage (T>2)	6/7	2/6	0.053
<b>Surgical treatment</b>			
Anterior pelvic exenteration	7/7	2/6	0.009
Positive resection margin (exclude TUR)	4/7	1/5	0.198
<b>Treatment</b>			
Neoadjuvant	2/7	1/6	0.612
Adjuvant	4/7	2/6	0.391

TUR, transurethral resection.

gy, all of whom passed away, 1 with UCC histology who survived, and 1 with SCC histology who also survived. This inconsistency in outcomes may potentially be attributed to the small sample size of our study.

Diagnosis of PFUC was usually delayed due to a non-specific initial presentation, including bleeding, voiding symptoms, urinary frequency, and asymptomatic. From the previous studies, the most common presentation was bleeding, accounting for 40.6–42.1%, and voiding symptoms were presented in about 21.8–31.6%.<sup>4,8</sup> On the other hand, our study demonstrated that the most common presentation was voiding symptoms, accounting for 53.9% while bleeding was 7.7%. The discrepancy in presenting symptoms might be attributed to variations in patient populations and health-care-seeking behaviors. It was possible that patients presenting with obstruction might have been overlooked, leading to a delay in diagnosis and subsequently underreporting. In contrast, patients presenting with bleeding might have been more likely to undergo further investigations, such as cystoscopy or imaging, resulting in higher detection rates. However, voiding symptoms may not directly affect the survival rate; the symptoms were significantly associated with characteristics of the advanced stage, including large tumor size and nodal metastasis.

A study suggested vaginal examination needed to be performed in every female patient with lower urinary tract symptoms. In cases of palpable mass, MRI was recommended.<sup>2</sup> Moreover, recommendations from the French Urology Association stated that MRI was the imaging of choice to diagnose and assess disease extension.<sup>14</sup> In our study, all patients who initially presented with voiding symptoms had a significantly palpable mass on vaginal examination, so they underwent imaging studies.

## Conclusions

To conclude, the OS rate of both initial presentations was not different. However, PFUC patients with voiding symptoms demonstrated characteristics of the advanced stage, including large tumor size and nodal metastasis. Factors indicated poor prognosis included histological subtype of ACC, microscopic residual tumor, nodal metastasis, and tumor stage more than 2.

Limitations of our study were its retrospective nature, small population, and single-center database, which may not perfectly represent the general population, and did not demonstrate a significant factor. Moreover, long-term follow-up data and a larger population were required to validate our findings and elucidate optimal management strategies for PFUC.

## References

- Swartz MA, Porter MP, Lin DW, Weiss NS. Incidence of primary urethral carcinoma in the United States. *Urology* 2006;68:1164-8.
- Derksen JW, Visser O, de la Riviere GB, et al. Primary urethral carcinoma in females: an epidemiologic study on demographical factors, histological types, tumour stage and survival. *World J Urol* 2013;31:147-53.
- Champ CE, Hegarty SE, Shen X, et al. Prognostic factors and outcomes after definitive treatment of female urethral cancer: a population-based analysis. *Urology* 2012;80:374-81.
- Kang M, Jeong CW, Kwak C, et al. Survival outcomes and predictive factors for female urethral cancer: long-term experience with Korean patients. *J Korean Med Sci* 2015;30:1143-9.
- Dalbagni G, Zhang ZF, Lacombe L, Herr HW. Female urethral carcinoma: an analysis of treatment outcome and a plea for a standardized management strategy. *Br J Urol* 1998;82:835-41.
- Garden AS, Zagars GK, Delclos L. Primary carcinoma of the female urethra. Results of radiation therapy. *Cancer* 1993;71:3102-8.
- Grigsby PW. Carcinoma of the urethra in women. *Int J Radiat Oncol Biol Phys* 1998;41:535-41.
- Lee W, Yu J, Lee JL, et al. Clinical features and oncological outcomes of primary female urethral cancer. *J Surg Oncol* 2022;125:907-15.
- Gakis G, Morgan TM, Efstathiou JA, et al. Prognostic factors and outcomes in primary urethral cancer: results from the international collaboration on primary urethral carcinoma. *World J Urol* 2016;34:97-103.
- Sui W, RoyChoudhury A, Wenske S, et al. Outcomes and prognostic factors of primary urethral cancer. *Urology* 2017;100:180-6.
- Janisch F, Abufaraj M, Fajkovic H, et al. Current disease management of primary urethral carcinoma. *Eur Urol Focus* 2019;5:722-34.
- Gakis G, Morgan TM, Daneshmand S, et al. Impact of perioperative chemotherapy on survival in patients with advanced primary urethral cancer: results of the international collaboration on primary urethral carcinoma. *Ann Oncol* 2015;26:1754-9.
- Son CH, Liauw SL, Hasan Y, Solanki AA. Optimizing the role of surgery and radiation therapy in urethral cancer based on histology and disease extent. *Int J Radiat Oncol Biol Phys* 2018;102:304-13.
- Neuville P, Murez T, Savoie PH, et al. Primary urethral carcinoma: Recommendations of the oncology committee of the French Urology Association. *Fr J Urol* 2024;34:102606.