

Survival Outcome of Urinary Diversion in Advanced Cervical Cancer Patients with Hydronephrosis

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Abstract

Objective: Urinary diversion is the treatment of choice for cervical cancer patients with urinary tract obstruction. The aim of this study is to determine the survival rate among advanced cervical cancer patients with hydronephrosis who undergo urinary diversion and factors that affect patient survival. **Methods:** Clinical data of cervical cancer patients with International Federation of Gynecology and Obstetrics (FIGO) Stage-IIIB or advanced cervical cancer were not surgical candidates admitted to Saiful Anwar Hospital, Malang from May 2016 to August 2022 were retrospectively analyzed. The parameters including age, cancer stage, comorbidity, cancer treatment at diagnosis, hydronephrosis treatment, grade, site, and survival, were analyzed using the IBM SPSS Statistics version 21. The significance level was set up to 0.05. **Result:** One hundred eighteen patients were included in this study. Most patients were under 60 (84.75%) and presented with stage IIIB (79.66%). Diabetes mellitus type 2 (8.47%), hypertension (7.63%), acute kidney injury (16.10%), and chronic kidney disease (36.78%) were comorbidities discovered in patients. More than half of patients received chemotherapy (54.24%). Ureteral stents were inserted in 85.59% of patients. Patients with moderate hydronephrosis were the most common, accounting for 67.80% of all cases. Patients with bilateral hydronephrosis outnumber those with unilateral by 91.53% to 8.47%. The survival rate did not differ significantly between ureteral stents (median survival was 11.00 months) and percutaneous nephrostomies (median survival was 15.00 months), $p=0.749$. In univariate analysis, age, cancer stage, and hydronephrosis stage were associated with worse 1-year survival. In multivariate analysis, age, DM type 2, cancer staging and hydronephrosis staging were associated with worse 1-year survival. **Conclusion:** In advanced cervical cancer patients, urinary diversion techniques such as ureteral stents and percutaneous nephrostomy offer similar survival rates. In addition, age, cancer stage, DM type 2, and hydronephrosis site are strong predictors of a worsening survival rate in patients.

Keywords: Cervical cancer- hydronephrosis- percutaneous nephrostomy- survival rate- ureteral stent

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Introduction

The 4th most common cancer-related cause of death in women worldwide is cervical cancer (Mattiuzzi and Lippi, 2020). In the last 30 years, the incidence of cervical cancer in women worldwide has increased from 10% to 40% (Song et al., 2015). This increasing trend occurs more significantly in lower-middle-income countries. Indonesia ranks third with 21,003 deaths, or 9%, and the incidence rate is 68.43 per 100,000 population (WHO, 2018).

Numerous potentially fatal complications, such as renal failure, thrombosis, and serious hemorrhages, are frequently seen in advanced cervical cancer patients (Mukesh et al., 2010; Tsai et al., 2011; Eleje et al., 2015). Urinary tract obstruction caused by a cervical cancer mass accounts for 11-44% of cervical cancer complications (Perri et al., 2019). Patients with hydronephrosis have a lower 3-year survival rate of 37% and 74% compared to those who did not develop hydronephrosis, respectively

(Patel et al., 2015).

In cervical cancer patients with hydronephrosis, urinary diversion is an appropriate therapeutic option. Obstruction recovery is often an important consideration before starting systemic treatment (Thornton and Covey, 2016). Ureteral stents have been widely recommended as the preferred method to reduce obstructive symptoms and improve renal function (Goldfarb et al., 2017). On the other hand, percutaneous nephrostomy is a minimally invasive, efficient, and secure surgical method that can directly drain urine and enhance renal function, regardless of the state of the ureter (Hsu et al., 2016). However, there are currently no recommendations for the best outcome of management urinary tract obstruction by cervical cancer. It is often difficult for clinicians to decide whether a ureteral stent or a percutaneous nephrostomy is the best option.

This study aims to determine the survival rate among advanced cervical cancer patients with hydronephrosis who undergo ureteral stents or percutaneous nephrostomy

and factors that affect patient survival.

Materials and Methods

This study is a retrospective cross-sectional study carried out at a referral hospital in one of Java's largest provinces, Indonesia. Data were obtained from the medical records of cervical cancer patients with hydronephrosis at Saiful Anwar General Hospital, Malang. Data collection involved patients admitted from May 1, 2016, to August 30, 2022. This study includes all the patients had stage IIIB or more advanced disease with histologically confirmed cervical cancer, and none of them had surgical treatment. However, this study excludes patients who did not attend regular follow-up visits and patients who failed a ureteral stent then refused a percutaneous nephrostomy or refused all hydronephrosis treatments. All staging was reviewed and classified according to FIGO 2018 staging for cervical cancer. Hydronephrosis was diagnosed with an abdominal ultrasound (US).

Descriptive data obtained, including age, cancer stage, comorbidity, cancer treatment at diagnosis, hydronephrosis treatment, hydronephrosis grade, hydronephrosis site, and survival, were analyzed. For nonparametric data, the Kaplan-Meier (log-rank) approach was used to analyze the survival rate of cervical cancer patients. Clinical variables and the 1-year survival rate were examined in relation to one another using univariate and multivariate logistic regression models. Statistics were considered significant for P-values under 0.05. The statistical analyses were performed using SPSS 22.0 (Statistical Package for Social Sciences, Chigaco, IL, USA).

Results

One hundred eighty-nine cervical cancer patients were referred from hospitals in East Java between 2016 and 2022. However, 71 patients were excluded because 15 were lost to follow-up, and 56 patients failed to insert a ureteral stent and then refused percutaneous nephrostomy or all hydronephrosis treatments. One hundred and eighteen cervical cancer patients were included in this study (Table 1). The median age at cancer diagnosis was 51 years (range 27–75). There 84.75% of those under 60, and 15.25% were over 60. Most of the patients presented with stage IIIB, 79.66% (94 patients). Diabetes mellitus (DM) type 2 (8.47%), hypertension (7.63%), AKI (all stages), 16.10% (19 patients), and CKD (all stages) 36.78% (64 patients) were among the comorbidities discovered in patients. Most of the patients received chemotherapy, 54.24% (64 patients). The hydronephrosis treatments for all the patients were ureteral stent 85.59% (101 patients) and percutaneous nephrostomy 9.77% (17 patients). Patients with moderate hydronephrosis were the most common, with 67.80% (80 patients), followed by 8.47% (10 patients) with unilateral hydronephrosis and 91.53% (108 patients) with bilateral hydronephrosis.

The patients were compared in terms of survival after being grouped according to the study's criteria (Table 2). The median survival rate did not differ significantly between ureteral stent [11.0 months, 95% CI (8.45-13.56)]

Table 1. Characteristics of Cervical Cancer Patients

Characteristic	N	%
Age		
<60	100	84.75
>60	18	15.25
Cancer Stage		
IIIB	94	79.66
IVA	20	16.95
IVB	4	3.39
Comorbid		
DM Type 2	10	8.47
Hypertension	9	7.63
AKI (All Stage)	19	16.10
CKD (All Stage)	64	54.24
Cancer Treatment at Diagnosis		
Radiation	24	20.34
Chemotherapy	94	79.66
Hydronephrosis Treatment		
Ureteral Stent	101	85.59
Percutaneous Nephrostomy	17	14.41
Hydronephrosis Grade		
Mild	12	10.17
Moderate	80	67.80
Severe	26	22.03
Hydronephrosis Site		
Unilateral	10	8.47
Bilateral	108	91.53

and percutaneous nephrostomy [15.00 months, 95% CI (13.01-16.98)] ($p=0.749$). There was no statistically significant difference in median survival rates at stage 3B between stent [11.00 months, 95% CI (8.47-13.53)] and percutaneous nephrostomy [16.00 months, 95% CI (13.07-18.92)] ($p=0.589$). When we compared stages 4A and 4B, there was no significant difference in median survival rates between patients undergoing ureteral stent placement [13.00 months 95% CI (4.27-21.75)] and percutaneous nephrostomy [13.00 months 95% CI (10.22-

Table 2. Survival Analysis Based on Cervical Cancer Staging

Treatment	Median (Month)	CI-95%		P Value*
		Lower	Upper	
All Stage				
Ureteral Stent	11.00	8.45	13.56	0.749
Percutaneous Nephrostomy	15.00	13.01	16.98	
3B				
Ureteral Stent	11.00	8.47	13.53	0.589
Percutaneous Nephrostomy	16.00	13.07	18.92	
4A-4B				
Ureteral Stent	13.00	4.27	21.75	0.938
Percutaneous Nephrostomy	13.00	10.22	15.77	

*, Kaplan-Meier (Log-rank); CI, Confidence Interval; **, Statistically Significant

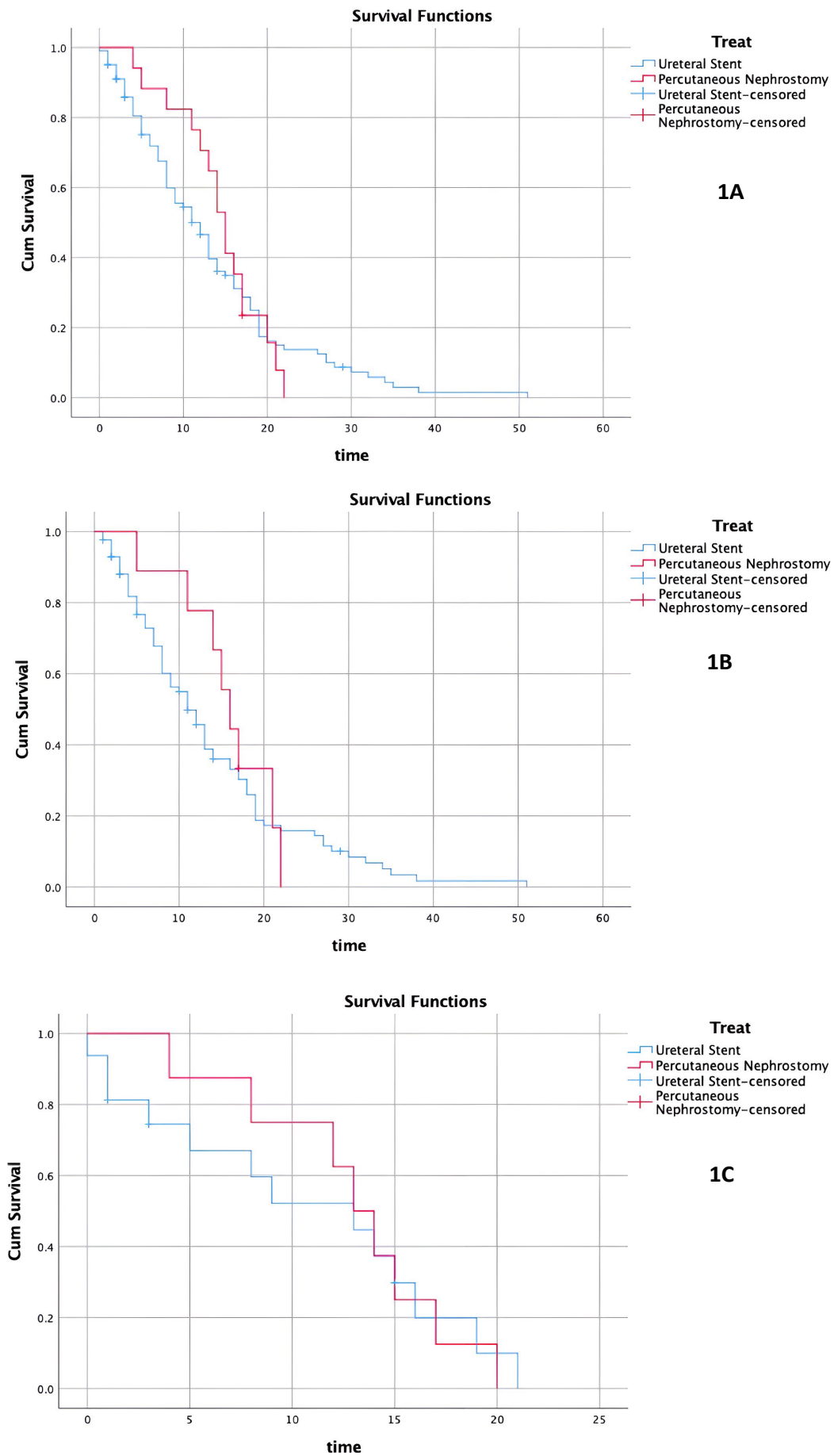


Figure 1. Kaplan Meier Curve of Study Group. A, Survival based on All Stage Cervical Cancer; B, Survival based on stage 3B; C, Survival based on stage 4A-4B

Table 3. Univariate and Multivariate 1-Year Survival Analysis of Cervical Cancer Patients

	Odds ratio(95 % CI)	p Value*	Odds ratio (95 % CI)	p Value*
Age				
<60 versus ≥ 60	8.617 (1.873-39.649)	0.001*	6.452 (1.286-32.382)	0.024*
Stadium				
IIIB versus IVA-IVB	7.806 (2.165-28.143)	0.000*	5.972 (1.425-25.026)	0.015*
Comorbid				
DM Type 2	4.000 (0.812-19.708)	0.069	7.324 (1.085-49.446)	0.041*
Hypertension	1.893 (0.450-7.956)	0.377		
AKI (All Stage)	2.211 (0.778-6.283)	0.13	1.857 (0.502-6.869)	0.354
CKD (All Stage)	0.607 (0.292-1.261)	0.18	0.616 (0.238-1.593)	0.317
Cancer Treatment at Diagnosis				
Radiation versus Chemotherapy	1.402 (0.570-3.446)	0.461		
Hydronephrosis Grade				
Mild - Moderate versus Moderate	0.878 (0.367-2.097)	0.769		
Hydronephrosis Site				
Unilateral versus Bilateral	11.681 (1.429-95.456)	0.005*	11.782 (1.242-111.767)	0.032*

CI, confidence interval; *, Likelihood ratio p value; **, Statistically Significant

15.77)] (p=0.938).

Among the two groups, the 6-month survival rates were 71% for ureteral stents and 82% for percutaneous nephrostomy. Whereas at one year, the survival rate was ureteral stent 46% and percutaneous nephrostomy 70% and the survival rate at 18 months in the two groups, ureteral stent and percutaneous nephrostomy, was 25% and 23%, respectively (Figure 1).

The median follow-up was 12.1 months (range, 0-51 months), and 15 of the 118 patients for whose survival data were available were still alive at the time of this publication. In univariate survival analyses, patients who were older than 60 at any stage during their cancer course displayed a worse prognosis compared to those who were younger than 60 in univariate survival analyses, which were measured from the date of cancer diagnosis [Odd Ratio (OR) 8.617 95% CI (1.873-39.649)] (p=0.000) (Table 3). On the other hand, stage IIIB [OR 7.806 95% CI (2.165-28.143)] (p = 0.005) and patients with bilateral hydronephrosis [OR 11.681 95% CI (1.429-95.456) (p = 0.005) remained statistically significant prognostic factors associated with poor one-year survival (Table 3). However, some of these prognostic effects, such as hypertension, cancer treatment at diagnosis, and hydronephrosis grade, were no longer observed in the multivariate analysis. In landmark multivariate analyses, patients aged over 60 compared to those under 60 [OR 6.452 95% CI (1.286-32.382)] (p=0.024), cancer stage IVA-IVB compare to stage IIIB [OR 5.972 95% CI (1.425-25.026)] (p=0.015), patients with DM type 2 compared to the patient without DM type 2 [OR 7.324 95% CI (1.085-49.446)] (p=0.041), and bilateral hydronephrosis site compared to unilateral [OR 11.782 95% CI (1.242-111.767)] (p=0.032) were statistically significant prognostic factor of worse one-year survival (Table 3).

Discussion

Hydronephrosis is more common in advanced cervical

cancer patients, and it is a significant predictor of poor prognosis in these patients (Atuhairwe et al., 2011; Rose et al., 2010). Nobrega et al., (2022) reported that moderate degrees of hydronephrosis were common and unilateral. However, different things were found in this study. Despite moderate hydronephrosis being the most common finding, almost all patients had bilateral hydronephrosis. The cervix and the ureters are closely related anatomically, and both the tumor itself and any enlarged lymph nodes that may be present can impact the ureters and cause hydronephrosis (Tan et al., 2019). Patients are usually referred when clinical or radiological evaluation resulting from urinary stasis, often with worsening kidney function, is observed as a consequence of ureteral obstruction (Gauhar et al., 2022). Similarly, this study was carried out at a referral hospital, where many of the patients who were referred already had advanced cervical cancer and either unilateral or bilateral hydronephrosis. Therefore, it is crucial to monitor the urinary system of individuals with cervical cancer. According to recent studies, active treatment for hydronephrosis can increase patients' quality of life and increase their survival time (Budaya et al., 2015).

In order to reduce obstructive symptoms and enhance renal function, ureteral stenting has been proposed as a viable treatment. Percutaneous nephrostomy has been recommended as an alternative to help with the palliative treatment of malignant ureteral obstruction when stenting is not possible (Song et al., 2015). In contrast, percutaneous nephrostomy may be preferable to ureteral stent in patients whose preprocedural mean serum cystatin C is higher than 2.5 mg/L and whose ureteral stenosis segment is longer than 3 cm (Song et al., 2012). According to the current study, the median survival rates for patients who underwent percutaneous nephrostomy or ureteral stents were 11 months and 15 months, respectively, and there was no statistically significant difference in the rates of survival between the two groups of patients. The survival rate between stages IIIB and IVA-IVB is not significantly different when we explicitly compare each

stage group. Therefore, advanced cervical cancer patients with hydronephrosis are treated with ureteral stents or percutaneous nephrostomies.

The one-year survival rate of patients with cervical cancer complicated with hydronephrosis varies between 12% to 36% (Patel et al., 2015; Damian et al., 2022). This evidence was also found in a study by Noegroho et al., (2021) that patients with advanced cervical cancer have a one-year survival rate of only 4%. However, this is different from this present study in that patient who had stents and percutaneous nephrostomy placed had a one-year survival rate of 46% and 70%, respectively. However, our study did not compare unilateral and bilateral hydronephrosis, as reported by Pradhan et al., (2011) bilateral hydronephrosis manifested a shorter survival compared to unilateral hydronephrosis patients with advanced cervical cancer. Furthermore, it was discovered that hydronephrosis had a negative impact on survival regardless of laterality.

From a prognostic standpoint, this study demonstrates that cervical cancer patients who are over 60 years old at cancer diagnosis manifest a trend toward poor survival compared to younger age. This observation has not been previously investigated and reported that older patients with end-stage cervical cancer have a worse survival outcome, and in general, the elderly population often receives incomplete or substandard medical treatment (Quinn et al., 2019). For another prognostic factor, this study showed IVA and IVB cervical cancer stage and DM type 2 also significantly predicted a worse survival rate. Diabetes is a cancer risk factor because previous studies have shown that it promotes carcinogenesis and tumor growth (Li et al., 2019). Diabetes is a significant prognostic factor in cervical cancer patients and is associated with a poor prognosis, according to a meta-analysis by Chen et al., (2017). The fact that the hydronephrosis group had a high all-cause mortality rate may be due to the coexistence of many comorbidities (Yang et al., 2021).

The strength of this study is that it is the first to focus on the survival rate evaluation of management hydronephrosis in advanced cervical cancer stages. The data of this study included uniform clinical staging: all patients were assessed and treated under the same department of gynecologic oncology and urology at one large referral hospital. Although FIGO staging strives to create a consistent global clinical staging system, some variations can lead to upstaging. For example, percutaneous nephrostomy was used during cystoscopy evaluation for ureteral stent placement if the operator could not differentiate the ureteral orifice. This cystoscopy finding would upstage the patient from IIIB to IVA. As a result, in the future, the importance of measurable radiologic examination for the cancer stage will determine the treatment of choice for these patients.

The limited sample size, retrospective methodology, and use of data from a single center are some of the limitations of this study. Future research should involve a multi-center prospective study to include more participants and do an in-depth analysis. In advanced cervical cancer patients with hydronephrosis, the only treatment options are ureteral stents or percutaneous nephrostomy (Gauhar

et al., 2022). Tan et al., (2019) reported that ureteral stent placement is minimally traumatic but has a low success rate compared to percutaneous nephrostomy. However, it is easier to maintain, resulting in a relatively small impact on quality of life and high patient compliance (Hsu et al., 2016). To make the decision that best serves the patient's genuine needs, the physician must thoroughly evaluate the patient's ureters, bladder, and hydronephrosis. In addition, the physician must explain in detail the advantages and disadvantages of each therapeutic option that can be given to the patient. In the end, the decision about which action to take is the patient's prerogative.

Based on the results of the study, it can be concluded that in advanced cervical cancer patients, urinary diversion techniques such as ureteral stents and percutaneous nephrostomy offer similar survival rates. In addition, age, cancer stage, DM type 2, and hydronephrosis site are strong predictors of a worsening survival rate in patients.

Author Contribution Statement

BD, KPS, and FKD gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. BD, KPS, and FKD had a part in article preparing for drafting or revising it critically for important intellectual content BD, KPS, and FKD gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Approval

This study is not for a student thesis.

Ethical Declaration

The authors state that they have obtained appropriate institutional review board of Health Research Ethic Commission General Hospital dr. Saiful Anwar approval (Ethical Number: 400/277/K.3/102.7/2022)

Data Availability

The corresponding author can obtain the study's data on reasonable written request.

Conflict of Interest

There are no conflicts of interest.

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