



Ureteral stenting in patients with locally advanced cervical cancer: Predictors of low success rate

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ABSTRACT

Objective: Cervical cancer is the leading gynecologic malignancy in Ethiopia. The diagnosis is often delayed and many patients present with locally advanced disease. Involvement of the ureters with or without the development of hydronephrosis is a common finding. Ureteral stent placement is a modality utilized to relieve an established obstruction (therapeutic) or to prevent its early occurrence (prophylactic). However, the procedure may not be successful in all patients. The objective of this study is to assess the factors associated with low success rate of ureteral stenting in these patients with locally advanced disease.

Methods: This is a hospital based cross-sectional study of patients diagnosed with locally advanced cervical cancer for whom a retrograde ureteral stent placement is attempted from January 2019 to March 2020. Data of 175 patients were retrieved by a retrospective chart review and analyzed for factors associated with low procedural success.

Results: Socio-demographic data were similar between patients regardless of procedural success. The overall success rate of stenting was 54.2 %. In the prophylactic group (with no hydronephrosis and normal creatinine) success rate was 94 % and in the therapeutic group 42.6 %. Logistic regression analysis showed that bilateral hydronephrosis and increased serum creatinine were indicators of significant ureteral obstruction and were predictors of stent placement failure.

Conclusion: Increased serum creatinine and presence of hydronephrosis are risk factors for failed ureteral stenting. For these patients, other options of urinary diversion such as percutaneous nephrostomy should be considered from the outset.

1. Introduction

Cervical cancer is the leading cause of gynecologic malignancy in the world with more than 500,000 women being newly diagnosed every year (Kantelhardt et al., 2014; Goldfarb et al., 2017). Evidences have shown that in, 111, 632 new cases of cervical cancer were diagnosed in Sub-Saharan Africa in 2018; of which, 80 % were diagnosed at a late (advanced) stage and present with involvement of adjacent structures such as ureters and bladder (Amado et al., 2022). In Ethiopia, close to 7000 new cases of cervical cancer are diagnosed annually and more than 70 % of them are detected at late stage (Kantelhardt et al., 2014; Disease prevention and control directorate, 2015).

Ureteral invasion and obstruction in cervical cancer is the result of disease progression and has an incidence of 10–30 % (Goldfarb et al.,

2017; Heo et al., 2023). The obstruction often leads to the development of hydronephrosis and mandates urgent consultation of a urologist for decompression so that renal failure, urosepsis and death can be avoided (Fields et al., 2015). In this regard, ureteral stenting and percutaneous placement of a nephrostomy tube are two main urologic procedures commonly performed to decompress an obstructed upper urinary tract.

Ureteral stenting is generally performed in a retrograde fashion using a cystoscope and is considered the first line modality to decompress a malignant ureteral obstruction (Heo et al., 2023). Ureteral stent can also be inserted in anticipation of an imminent ureteral obstruction without the development of overt hydronephrosis (Wang et al., 2016). Although it is a relatively straightforward and often successful procedure, a high procedural failure rate has been reported specifically in patients with locally advanced cervical cancer (Heo et al., 2023; Fields et al., 2015;

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Wang et al., 2016; Lapitan and Buckley, 2011). Once ureteral stenting is failed, the patients will have to undergo a salvage urologic procedure i. e., placement of percutaneous nephrostomy tube under conscious sedation.

There is no any clinical study in Ethiopia that explore factors associated with failure of ureteral stenting in these patients. The primary objective of our research is to characterize patients with locally advanced cervical cancer and explore the factors that predict low success rate of ureteral stenting. The findings of this study can guide physicians in stratifying patients that can benefit from trial of stenting from those that better undergo a salvage procedure from the outset due to low success rate of stenting.

2. Methods

2.1. Study setting

The study was conducted at Addis Ababa University, Tikur Anbessa Specialized Hospital (TASH) which has the largest urology training and treatment center in the country. The hospital receives referred urology patients from all over the country. It has a dedicated urology ward with 22 beds and an emergency procedure room where most of the emergency urologic procedures including ureteral stenting are performed. Patients with locally advanced cervical cancer are often followed jointly by clinical oncologist and onco-gynecologist. When the disease process involves the ureters and stenting is mandated, a urologist is consulted. The procedure is done in the urology minor procedure room. In failed procedures, a percutaneous nephrostomy (PCN) tube is often placed in one or both kidneys.

2.2. Study design and participants

Ethical clearance for this study was obtained from the Addis Ababa University, College of Health Sciences ethics and publication committee. We conducted a facility-based cross-sectional study by reviewing medical charts of 175 consecutive patients with locally advanced cervical cancer for whom ureteral stent placement was done from January 2019 to March 2020. The procedure was performed for an established or imminent ureteral obstruction by the disease process. All stenting procedures performed for reasons other than cervical cancer are excluded from the study. Moreover, patient charts with missing data on one or more of the evaluation criteria on the questionnaire are also excluded. Retrieved patient data was then analyzed for disease pattern, clinical characteristics and factors associated with low procedural success.

2.3. Operational definition

All of the patients included in this study had a biopsy confirmed cervical cancer and also had an abdomino-pelvic imaging (i.e. ultrasound, CT scan or MRI) suggesting locally advanced disease. We defined prophylactic stenting as stent placement performed for patients with imminent ureteral obstruction (i.e., a CT scan/MRI finding of ureteral involvement/encroachment by the tumor without a noticeable pelvicalyceal dilatation) whereas therapeutic one is stenting for cervical cancer patients with an established ureteral obstruction and hydronephrosis. Failure of procedure is defined as failure in identifying the orifice, failure in advancing the guidewire or failure to advance the stent itself over the guidewire into the ureter.

2.4. Data processing and analysis

Data were initially cleaned and then exported into and analyzed using Statistical Package for Social Sciences (SPSS) version 26. Continuous variables on patient demographics, clinical characteristics and outcomes of interest were expressed using descriptive statistics. Binary logistic regression was used to analyze the outcome variable. An odds

ratio (OR) with 95 % confidence interval (CI) was used to measure the strength of association. A cut-off value of $p < 0.05$ was used to determine the level of statistical significance.

3. Results

3.1. Socio-demographic and clinical characteristics

Of the evaluated 175 patients the mean age (\pm SD) was 50 ± 10.2 years, ranging from 26 to 85 years. The large majority of patients fall in the 40–45 yrs. range (Fig. 1). Regarding their socio-economic background, more than 80 % of the patients are from rural areas and did not have any kind of formal education. The most common presenting symptoms were vaginal bleeding/spotting (60 %), flank pain (58 %), and a decrease in urine output (23 %). There is a significant delay in the time to hospital visit after symptom onset. The large majority of our patients (88 %) visited the hospital three or more months after the onset of symptoms (Fig. 2). All patients were in a moderately limited functional performance status and fall under Eastern Cooperative Oncology Group (ECOG) categories 1 and 2. Majority of our patients (83 %) did not have a concomitant comorbid illness at the time of stenting. HIV infection was detected in 16 and hypertension was diagnosed in 14 patients. All patients present with advanced stage disease (stage 3 and above) according to the international federation of gynecology and obstetrics (FIGO) staging system. Data from cross-sectional imaging revealed that the urinary tract was involved by the locally advanced disease process and urinary bladder was the most commonly involved urologic organ (90 %) followed by ureters and urethra. Regarding laboratory data, mild anemia (Hgb 10–11.9 g/dL) was detected in 40 patients. Serum creatinine level was deranged (>1.2 mg/dl) in 51 % of patients.

3.2. Procedure-related findings

Ureteral stenting was performed under sterile setup with the patients put in a lithotomy position. It was done retrogradely in all patients using a Karl Storz rigid cystoscope with a 17 Fr sheath. A 2 % lidocaine jelly local anesthesia was used during advancing the cystoscope. The cystoscope is used to examine the entire urinary bladder systematically and to identify the ureteral orifice to be stented. Once the orifice is identified, a guide wire is passed through it and advanced up to the kidney. In all patients, a 6 Fr polyurethane double pigtail stent was passed over the guidewire after which the wire is removed and procedure is concluded. Proper stent placement was confirmed by plain abdominal radiography performed immediately after the procedure. All procedures were performed by senior urologists in training.

Regarding the indication for intervention (stenting), decompression of obstructive uropathy was the most common reason. About 135 patients had ureteral obstruction of variable degree and 49.7 % of them had bilateral obstruction with hydronephrosis while 27.4 % had unilateral hydronephrosis. On the other hand, 40 (22.9 %) patients underwent prophylactic stenting for imminent ureteral involvement on imaging without established hydronephrosis. Cystoscopy findings at the time of stenting revealed that 56.6 % of the patients had a disfiguring mass over the trigone area and ureteric orifices were not visualized in 28 % of them.

3.3. Failure of ureteral stenting and predictors

In our study, the overall failure rate of retrograde stenting in advanced cervical cancer patients is 46 % ($n = 80$). Failure rate is high in patients with established hydronephrosis (57.3 %) as compared to prophylactic stenting (5.1 %). Out of the failed cases, 87.5 % (70) of them had bilateral obstruction. All patients with failed ureteral stenting underwent an ultrasound guided percutaneous nephrostomy tube insertion. The results of the univariate and multivariate analyses of

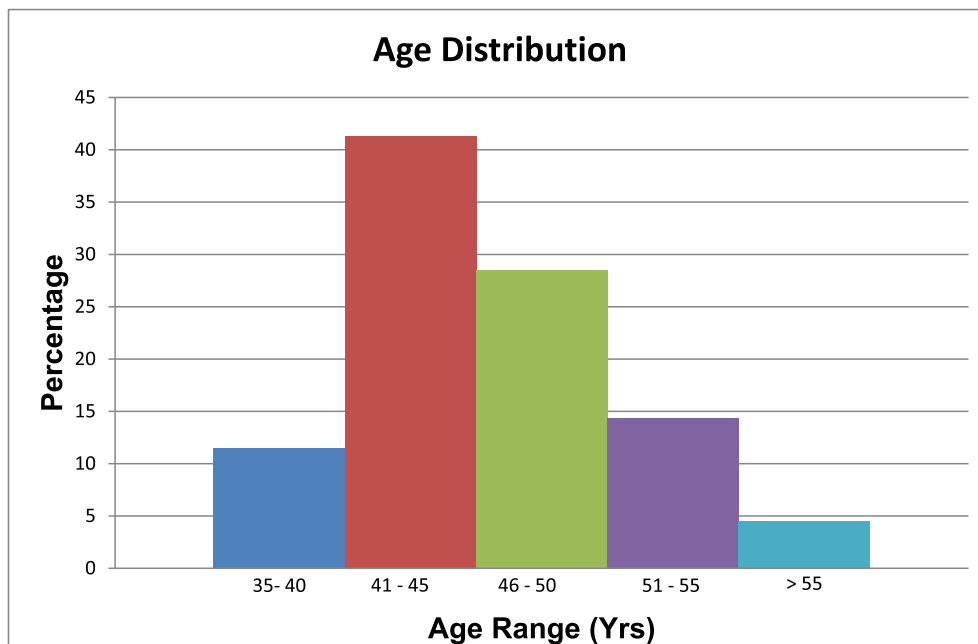


Fig. 1. Age distribution of patients with locally advanced cervical cancer who underwent stenting procedure.

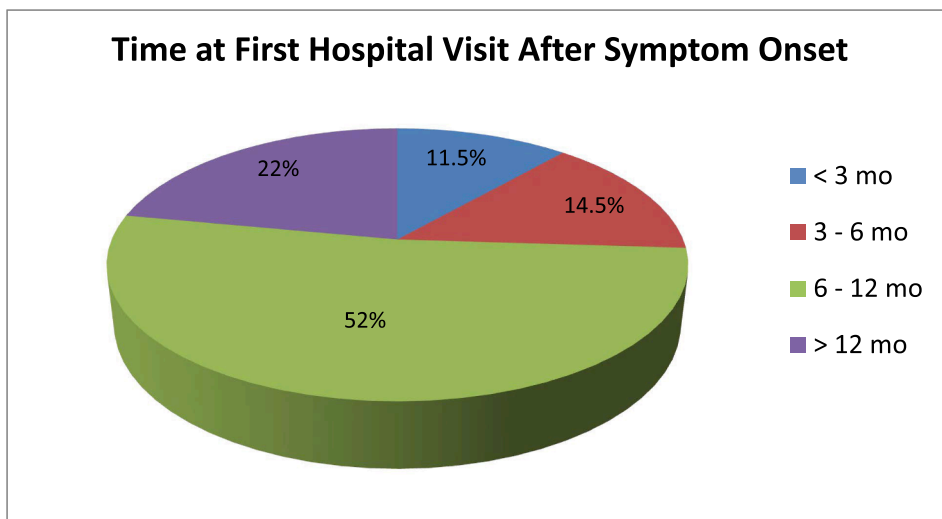


Fig. 2. Timing of initial hospital visit after onset symptom in patients with locally advanced cervical cancer.

association between patient factors and overall failure rate of ureteral stenting are shown in Table 1.

The results of our study indicate that the presence of any degree of hydronephrosis at presentation is associated with a five times increased risk of procedural failure [OR = 4.94 (2.26–13.60) at 95 % CI; p = 0.02]. Similarly, involvement of urinary bladder by the disease process also increases the risk of ureteral stenting failure three fold. Delayed presentation to the hospital after onset of symptoms is another factor associated with failure of ureteral stenting. Patients who visited the hospital more than three months after the onset of symptoms have a three to four times increased likelihood of procedural failure as compared to those who present themselves early within the first few months [OR = 3.52 (1.29–7.99) at 95 % CI; p = 0.04]. Increment in serum creatinine level above the upper limit of the normal range (i.e., 1.2 mg/dl) is also found to be a predictor of stenting failure [OR = 2.24 (1.21–3.08) at 95 % CI; p = 0.045].

4. Discussion

Ureteral obstruction in women with locally advanced cervical cancer is a worrisome urologic complication that, if not handled in time, will lead to renal failure, infection and pain. The optimal urologic procedure that should be employed to manage the obstruction has been controversial primarily floating between ureteral stenting and percutaneous nephrostomy. Both urologic procedures are safe and effective but there is still active debate among urologists regarding which procedure should be considered the first line (Heo et al., 2023; Noegroho and Mustafa, 2019). The American Urological Association (AUA) updated practice guideline recommends stenting as initial mode of treatment in patients with malignant ureteric obstruction including advanced pelvic malignancy. However, initial PCN may also be considered by a urologist based on a case-based approach (Derek and Matthew, 2023). Our literature review also indicated that many urologists perform initial ureteral stenting as it is technically easy, doable in short time with local

Table 1
Factors associated with low success rate of retrograde ureteral stenting among patients with locally advanced cervical cancer.

Patient Factors	Failed Ureteral Stenting		COR (95 % CI)	AOR (95 % CI)
	Yes (n = 80)	No (n = 95)		
Hydronephrosis Present	78	58	4.40 (1.88–11.02)*	4.94 (2.26–13.60)*
Absent	2	37	1	1
Urinary Bladder Involved	80	78	2.88 (1.01–6.56)	3.10 (1.78–7.22)*
Not involved	0	17	1	1
Presentation after onset				
> 3 months	80	36	3.25 (1.21–7.40)*	3.52 (1.29–7.99)*
< 3 months	0	59	1	1
Serum Creatinine level				
Cr. > 1.2 mg/dl	72	17	1.99 (0.74–2.63)	2.24 (1.21–3.08)*
Cr. < 1.2 mg/dl	8	78	1	1

Notes: *p-value < 0.05, COR – Crude Odds Ratio; AOR – Adjusted Odds Ratio.

analgesia and cost effective. From the patients' perspective, stenting is also considered well tolerable with minimal morbidity and little impact on routine activity (Noegroho and Mustafa, 2019; Dhani et al., 2023; Tan et al., 2019). However, procedural success is also an important consideration that should be made to optimize clinical outcome. In this regard, multiple hospital based studies globally reported a high procedural failure rate of ureteral stenting in patients with locally advanced cervical cancer ranging from 30 to 55 % (Noegroho and Mustafa, 2019; Tan et al., 2019; Wu et al., 2021). Our study, with a failure rate of 46 % also correlates well with these studies.

Despite the ease of the procedure and patient comfort, ureteral stenting has high failure rate in our study population. Many studies tried to analyze specific patient factors that can predict procedural failure. For instance, an elevated preoperative serum creatinine was found to predict failure of ureteral stenting in patients with locally advanced cervical cancer (Noegroho and Mustafa, 2019; Wu et al., 2021). We also observed a 2.24 fold increased risk of stenting failure among similar group of patients. Other studies also identified urinary bladder invasion by the tumor as a predictor of stenting failure (Dhani et al., 2023; Gu et al., 2022). The findings of our study also coincides with these results. We have identified a threefold increased risk of stent failure among cervical cancer patients with bladder invasion. The anatomic proximity between the cervix and the bladder trigone appears to be the main contributing factor for this strong association.

On the other hand, a couple of hospital based studies identified a predictive association between stenting failure and a higher degree of hydronephrosis (Wu et al., 2021; Salunkhe et al., 2020; Ho et al., 2020). Our findings do not indicate such association between severity of hydronephrosis and stent failure. Rather, the diagnosis of hydronephrosis itself, regardless of its severity is found to be significant predictor of stenting failure. Similarly, other studies indicated an association between preoperative performance status of patients and failure of stenting (Wu et al., 2021; Ganesarajah et al., 2022; Hafsari and Wardaya, 2021). Both univariate and multivariate analyses of our study did not reveal a similar finding. This can be probably related with the fact that the performance status of the patients in our study fall under

ECOG 1 or ECOG 2 which do not significantly vary from each other in terms of patient characteristics.

A relatively peculiar finding in our study is the presence of a predictive association between the timing of patient presentation and failure of stenting. There is a 3.5 fold increased risk of ureteral stenting failure in patients with delayed presentation to the hospital three or more months after the diagnosis of locally advanced cervical cancer is made. Based on the natural history of cervical cancer, there is a general consensus that a delayed presentation after diagnosis will lead to a more extensive involvement of the ureters and other adjacent organs as well (Dhani et al., 2023; Gu et al., 2022; Yossepowitch et al., 2001; Hsu et al., 2016). However, we did not find a study that supported this clinical observation with a numerical data. Most of the patients studied are diagnosed with cervical cancer at rural primary or regional hospitals who are then referred to a tertiary hospital where uro-gynecologist, oncologist and urologist are available. A significant delay is often observed during the referral process which contributes to disease advancement. In time of such a delay, ureteral obstruction will subsequently lead to obstructive nephropathy, chronic kidney disease and ultimately end-stage renal disease (ESRD). There are reports indicating a poorer overall prognosis locally advanced cervical cancer with ureteral invasion and hydronephrosis as compared to those without involvement of the ureter (Dhani et al., 2023; Salunkhe et al., 2020; Yossepowitch et al., 2001; Hsu et al., 2016; Chung et al., 2004; Matsuura et al., 2019; Song et al., 2012). Although, our study did not reveal a similar finding, it is logical to conclude that a timely decompression of ureteral obstruction not only avoids an ESRD but also minimizes the risk of stenting failure associated with the delay.

In our study, we have identified some limitations. This research analyzed the experience of the largest tertiary care center in Ethiopia. Although many patients with advanced cervical cancer are referred from all over the country to the hospital for a better care, being a single center study limited us from making a nationwide conclusion. Moreover, data regarding patients with bilateral hydronephrosis and whether a trial of bilateral stenting was done is incomplete. Being a retrospective analysis based on chart review, selection bias may also exist. We also faced data incompleteness on some of the patient charts which forced us to exclude them and reduce the size of the sample population.

5. Conclusion

As a conclusion, our study indicates that the overall failure rate of retrograde stenting in advanced cervical cancer patients is very high. This procedural failure is more likely to be encountered in patients with elevated serum creatinine and the finding of hydronephrosis. Although ureteral stent is generally the first line modality to relieve an obstructed ureter, urologists are recommended to anticipate technical difficulty and failure during trial of ureteral stenting in patients with the above negative predictors. These patients are more likely to benefit from an alternative urinary diversion procedure such as percutaneous nephrostomy tube insertion to minimize additional cost and procedural morbidity.

CRedit authorship contribution statement

Kaleab Habtemichael Gebreselassie: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tadele Aweke Adamu:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andualem Deneke Beyene:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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