MANAGEMENT, OUTCOMES AND SURVIVAL OF PATIENTS WITH OBSTRUCTIVE UROPATHY DUE TO CERVICAL CANCER ADMITTED AT KENYATTA NATIONAL HOSPITAL (2014 – 2019)

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STUDENT'S DECLARATION

I declare that this dissertation is my original work and has not been submitted for the award of any degree at any other institution.

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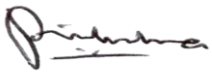
Signature:  **Date:** 03/06/2023

DEPARTMENTAL APPROVAL

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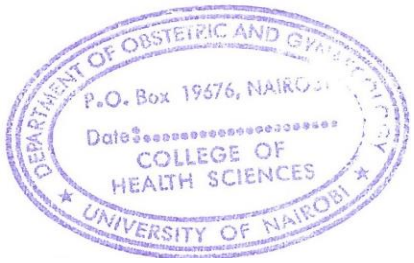

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LIST OF ABBREVIATIONS

FIGO:	International Federation of Gynecology and Obstetrics
GLOBOCAN:	Global Cancer Incidence, Mortality, and Prevalence.
HPV:	Human Papilloma Virus.
KNH:	Kenyatta National Hospital.
PI:	Principal Investigator
SPSS:	Statistical Package for the Social Sciences.
UoN:	University of Nairobi.
WHO:	World Health Organisation
HEM:	Hemolysis
PCN:	Percutaneous Nephrostomy
PNH:	Percutaneous Nephrostomy and hemodialysis
Obs/Gyn:	Obstetrics and Gynecology

ABSTRACT

Background: Uterine cervical cancer is associated with long-term infection of the Human Papilloma Virus in 99% of cases. It is the second most common cancer in women in Kenya after breast cancer. The advanced stage of cervical cancer is a common presentation and is associated with complications like obstructive uropathy. Percutaneous nephrostomy and hemodialysis are mostly done to relieve the obstruction and uremia. Controversy still exists on the benefits of interventions to manage obstructive uropathy compared to no intervention and their impact on overall survival duration.

Objective: To determine management, outcomes, and survival of patients with obstructive uropathy due to cervical cancer admitted at Kenyatta National Hospital (2014 – 2019)

Study Design: Descriptive Retrospective Cohort Study.

Study Population: These were 127 patients with obstructive uropathy due to cervical cancer who were managed at Kenyatta National Hospital between 2014 to 2019.

Methodology: A retrospective analysis of 127 patients with a diagnosis of obstructive uropathy due to cervical cancer were included. The proportion of patients who underwent nephrostomy, hemodialysis, or no intervention was determined. The outcome of treatment was evaluated in terms of whether they went on to undergo chemoradiation, chemotherapy alone, radiotherapy alone, or no treatment thereafter. The overall and specific interventions' two-year survival rate was determined.

Results: The two-year overall survival rate was 50.4%. The estimated proportions of post-diagnosis procedures done were (95% confidence interval) double j stent 1 ([CI] 0.0%–10.1%), hemodialysis19 (14.8% CI 6.3%–24.1%), PCN 55(43.0% (CI 3 4.4%–52.2%), PCN + hemodialysis 19 (15.6% (CI 7.0%–24.9%) and no intervention 33 (25.8%% (CI 17.2%–35.1%). Specific overall two-year survival rates as per intervention done was (95% CI) PCN 35(54.7% (43.8-67.5), HEM11(17.2%(6.3-30), PNH7(10.9%(0.0-23.7) no intervention 10(15.6%(4.7 -28.4%).

Conclusion: Obstructive uropathy negatively impacts the prognosis of advanced cervical cancer. Percutaneous nephrostomy was the best choice to relieve the obstruction and it impacted the two-year survival rate and whether the patient underwent palliative or definitive treatment.

1.0 CHAPTER ONE: INTRODUCTION

1.1 Introduction

Cervical cancer is linked to long-term infection with Human Papillomavirus (HPV) in 99% of the cases. Worldwide, it is ranked 4th in both incidence and cancer-related mortality amongst women with approximately 570,000 new cases and 310,000 reported deaths annually **(WHO 2018)**

In East Africa, the estimated incidence and mortality rate is 40.1 and 28.6 per 100,000 respectively the highest in the world and above the world's average of 13.3 and 7.3 per 100,000. **(GLOBOCAN,2020).**

In Kenya, a diagnosis of cervical cancer contributes to 5236 (12.4%) of all new cancer cases and 3211 (11.9%) cancer deaths annually. It ranks second after cancer of the breast amongst cancers affecting women. It has an incidence rate of 31.3 and a mortality rate is 20.6 per 100,000. **(GLOBOCAN,2020).**

Patients presenting when the cancer has already spread is a common problem in Kenya and other Lower- and Middle-Income Countries where a cure is hard to achieve. **(WHO,2018b).** In Uganda, Tanzania, and Morocco the patients who presented in FIGO stage II B and above were 66%, 64%, and 55% respectively **[1,2,3]** The burden is greater in Kenya with 80% of patients presenting in FIGO stage II B and above at the time of diagnosis. **[4,5]**

Cervical cancer stages IIb, III, and IV are managed by chemotherapy, radiotherapy, and brachytherapy. There's a limited role of surgery in these patients. One of the most common complications of cervical cancer is obstructive uropathy which leads to hydronephrosis and pelvic pain due to inflammation of the kidneys, ureters, and the surrounding structures. This may lead to delay in management as chemotherapy drugs are mostly nephrotoxic and there's a need to correct the renal function before initiation or resumption of treatment.

Obstructive uropathy in cervical cancer patients is due to the malignant spread or external compression of the distal ureters leading to obstruction, hydronephrosis, and consequently kidney failure. A rise in pressure in the ureters leads to changes in renal blood flow, glomerular filtration, and tubular function. A significant reduction in glomerular filtration rate and the ability of the renal tubules to transport sodium, potassium, and protons impairs the kidney's function of concentrating and diluting urine. Obstructive uropathy can also be caused by pelvic fibrosis due to the effect of radiotherapy in the management of the disease.

Uremia as a result of obstructive uropathy causes severe morbidity and mortality in cervical cancer patients.[6] Obstructive uropathy predisposes the patient to recurrent urinary tract infections (UTIs) and electrolyte imbalance which worsens the patient's condition.

Procedures done to treat obstructive uropathy include placement of ureteric stents, percutaneous nephrostomy, and hemodialysis. Placement of ureteric stents is usually the first line of management of obstructive uropathy but it becomes technically difficult to perform in the setting of bulky disease and needs the intervention of urologists.[7] In the context of external compression, percutaneous nephrostomy is a relatively easier procedure but carries an increased risk of infections and impairment of quality of life.[7] Ureteric stenting and percutaneous nephrostomy may lead to significant delays in treatment due to infections, pain, or the need for the replacement of a failed device.[8] Hemodialysis can be done to correct the renal derangement before percutaneous nephrostomy is done.

The first publication describing percutaneous nephrostomy was in 1955 by *Goodwin et al*. It has been used as a primary option for temporary or long-term solutions to obstructive uropathy. It is the most common urinary diversion method practiced. It aims to improve renal function and enable the patient to get tumor-specific palliative or at times curative treatment.[9] Controversy exists on the benefits of percutaneous nephrostomy in relieving renal failure due to obstructive uropathy. There are no guidelines for predicting long-term outcomes.[10]The obstruction can lead to infection and there will be reduced antibiotic penetration to the kidney due to accumulation of purulent material. It becomes an attractive alternative for relieving the obstruction, allowing specimen collection and institution of antibiotic therapy.

Percutaneous nephrostomy's expected complications include; infection of the catheter, incision site bleeding, peri catheter leaks, sepsis, and slippage of the catheter which usually requires replacement. Contraindications to Percutaneous nephrostomy tube placement are severe hyperkalemia which requires correction by hemodialysis before insertion, patients with bleeding disorders, and uncooperative patients. The cost of performing percutaneous nephrostomy is also prohibitive to most patients admitted to KNH due to obstructive uropathy secondary to cervical cancer.

Survival duration post nephrostomy tube insertion is largely dependent on the age, metastasis, and Eastern Cooperative Oncology Group(ECOG) performance status. Advanced age (>60 years), metastasis beyond the true pelvis, and ECOG performance status of 4 are associated with poor prognosis and a median survival duration of 2 months. The risks and benefits of urinary diversion in these patients with obstructive uropathy should be considered carefully

Table 1:ECOG Perfomance Status

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

Malignant obstructive uropathy in cervical cancer patients is associated with a median survival duration of less than a year despite urinary diversion and further management. Patients with small tumor size, creatinine levels <260micromol/l, and good performance status should be selected for urinary diversion procedures and then radical treatment afterward. Other patients should be offered upfront palliative radiation without urinary diversion[12]

Advanced cervical cancer patients without obstructive uropathy have a better prognosis than those with obstructive uropathy. There is conflicting data on the benefits of urinary diversion in patients with obstructive uropathy and the impact on their survival duration compared to those who don't undergo diversion. The survival duration of these patients is dependent on multiple factors. No standardized or universally accepted criteria exist on which patients would benefit from urinary diversion and impact on their survival duration.

2.0 CHAPTER TWO: LITERATURE REVIEW

The cervix is 2 to 3 cm long. It is divided into two parts. A lower end that bulges through the anterior vaginal wall also known as ectocervix and a supravaginal portion that is attached to the body of the uterus. A central canal runs through it and connects the uterine cavity via internal os and the vaginal opening via external os.[11]

The ectocervix is lined by stratified squamous non-keratinized epithelium. In contrast, the endocervix is lined with columnar cells with tubular mucous glands secreting alkaline mucus into the lumen. The junction between the two epithelia is called the squamocolumnar junction. Pre-puberty the functional squamocolumnar junction lies within the cervical canal. In puberty, due to hormonal influences, the columnar epithelium extends over the ectocervix as the cervix everts shifting the squamocolumnar junction into the vaginal portion of the cervix.[12] This exposes the columnar epithelium to the harsh vaginal acidic environment and may undergo physiological metaplasia into a tougher metaplastic squamous epithelium.[12] The new squamocolumnar junction formed is internal to the original one creating a zone of unstable epithelium between the two junctions called the transformation zone.[12] Postmenopausal uterine structures involute shifting the squamocolumnar junction towards the endocervix.

The genesis of cervical cancer is mostly in the transformation zone. Human Papillomatous Virus infection poses the greatest risk factor for the development of cervical cancer. Infection with HPV commonly occurs in sexually active women. However, around 90% of HPV infections resolve without treatment with no sequelae. Around 5% of HPV infections will lead to the development of Cervical Intraepithelial Neoplasia (CIN) grade 2 or 3 lesions within 3 years of infection. Approximately 20% of CIN grade 3 lesions progress to invasive cancer within 5 years and around 40% within 30 years. A small proportion of HPV infections progress to cervical cancer, other factors are involved in the carcinogenesis progression. The type and duration of HPV infection play a role in predisposition to CIN. HPV types 16 and 18 are classified as high-risk and cause 75% of cervical cancer globally. Other high-risk HPV like 31 and 45 cause another 10%.[13] Women with multiple sexual partners or women whose sexual partners have multiple sexual partners increase the risk of HPV infection.[14] Immunocompromised states like Human Immunodeficiency Virus (HIV) infection and poor nutritional status increase the risk of transformation into cervical cancer. Smoking cigarettes both present and past increases the risk two to three times of developing invasive cancer.[15] HIV infection increases the risk of developing cancer of the cervix and is associated with a more rapid progressive disease.[16] The use of oral contraceptives for about 5 to 9 years is

associated with a threefold increase in the incidence of cervical cancer.[17] Women infected with HPV and have carried multiple pregnancies (7 or more full-term pregnancies) have four times the risk of developing cervical cancer compared to nulliparous women.[17] Changes in the expression of some genes have been linked to the development of cervical cancer. Tumor necrosis factor (TNF) is involved in initiating cell apoptosis, and the genes *TNF G-308, TNFa-8, TNFa-572, TNFa-857,* and *TNFa-863* have been associated with a higher incidence of cervical cancer.[18] Polymorphism of *Tp53*gene which is involved in apoptosis and gene repair has also been associated with an increased risk of HPV infection transforming into cervical cancer. Genetic changes account for less than 1% of cervical cancer cases.

Histological subtype frequency according to a Kenyan study evaluating advanced cervical cancer patients undergoing radiotherapy in KNH showed that squamous cell carcinoma (89.9%) and adenocarcinoma (5.6%) were the most common subtypes. Squamous carcinoma tumor grade frequency was; well differentiated (21%), moderately differentiated (39%), and poorly differentiated at (32%).[5] Other histological subtypes are rare and include adenosquamous, small cell carcinoma, neuroendocrine tumor, villoglandular adenocarcinoma, and glassy cell carcinoma.

There are generally two staging systems for cervical cancer; FIGO and Tumour Nodes and Metastasis (TNM). In FIGO staging it involves imaging and/or pathological findings, clinical assessment of tumor size, and disease extent. It doesn't involve the surgical staging.

TNM	FIGO	Description
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis		Preinvasive carcinoma
T1	I	The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)
T1a	IA	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion < 5 mm[a]
T1a1	IA1	Measured stromal invasion depth of < 3 mm
T1a2	IA2	Measured stromal invasion depth ≥ 3 mm and < 5 mm
T1b	IB	Invasive carcinoma with measured deepest invasion of ≥ 5 mm (greater than Stage IA), lesion limited to the cervix uteri[b]
T1b1	IB1	Invasive carcinoma with measured deepest stromal invasion of ≥ 5 mm, and greatest dimension of < 2 cm
T1b2	IB2	Invasive carcinoma with greatest dimension of ≥ 2 cm and < 4 cm
-	IB3[d]	Invasive carcinoma with greatest dimension of > 4 cm
T2	II	The carcinoma invades beyond the uterus, but has not extended into the lower third of the vagina or to the pelvic wall
T2a	IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	IIA1	Invasive carcinoma with greatest dimension of < 4 cm
T2a2	IIA2	Invasive carcinoma with greatest dimension of ≥ 4 cm
T2b	IIB	With parametrial involvement but not up to the pelvic wall
T3	III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes[c]
T3a	IIIA	The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
T3b	IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
N[d]	IIIC[d]	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
	IIIC1[d]	Pelvic lymph node metastasis only
	IIIC2[d]	Para-aortic lymph nodes metastasis
T4	IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum (the presence of bullous edema is not sufficient to classify a case as Stage IV)
	IVA	Spread to adjacent pelvic organs
M1	IVB	Spread to distant organs

Figure 1:TNM (8th Edition) and FIGO (2018) Classification of cervical cancer (from refs. 26, 31)

According to a study done by Maranga et al in 2013 at KNH, at diagnosis, the frequency of per FIGO stage was stage IA (2.2%), IB (7.3%), IIA (8.5%), IIB (29.9%), IIIA (16.1%), IIIB (25.6%), IVA (7.3%) and IVB (3.1%) **[5]**

Cervical cancer screening is normally done using a Papanicolaou smear. Cells in the endocervix, transformation zone, and ectocervix are collected, stained, and examined under the microscope for any precancerous changes or cervical dysplasia. Abnormal results are analyzed and reported according to the Bethesda System 2014.

There are various cancer treatment options depending on the stage. Stage IA a cone biopsy of the cervix or radical trachelectomy is done for those who desire fertility. Simple or radical hysterectomy can be done with or without radiation if pelvic lymph nodes are involved in those who don't desire fertility. Stage IB radical trachelectomy and lymph node dissection are done for those who desire fertility. Radical hysterectomy with chemotherapy afterward is a treatment option. Radiation (external beam and brachytherapy) with concurrent chemotherapy is an

option for those not healthy enough for surgery or those who don't want surgery. Cervical cancer stage IIA treatment options include radical hysterectomy and pelvic or para-aortic lymph node dissection with concurrent chemoradiation afterward or radiation alone. For cancer of the cervix stage IIB, III, and IV, the treatment of choice is chemoradiation. Chemotherapy involves cisplatin, carboplatin, and fluorouracil.

Obstructive uropathy i.e. hydronephrosis is classified as stage IIIB. The tumor has spread from the cervix to the pelvic walls and may have involved the ureters leading to obstruction, hydronephrosis, and later renal impairment. Hydronephrosis may be due to the external compression of the ureters by the bulky tumor in the pelvis. Patients who have undergone radiotherapy may present with obstructive uropathy thereafter due to pelvic fibrosis. Bilateral hydronephrosis is almost always present with renal injury compared with those with unilateral hydronephrosis.[19] Immediate decompression is needed to relieve the obstruction in bilateral hydronephrosis. [20] If the obstruction is not relieved the patient may end up with uremia, electrolyte and water imbalance, altered consciousness, and death.[21]

Hydronephrosis is classified into 4 grades according to the Society of Fetal Urology (SFU)

Table 2:Grades according to the Society of Fetal Urology (SFU)

Grade 0	Normal examination with no renal pelvis dilation
Grade I	Mild renal pelvis dilation only.
Grade II	Moderate renal pelvis dilation including a few calyces
Grade III	Renal pelvis dilation with visualization of all the calyces, which are uniformly dilated, and normal renal parenchyma.
Grade IV	The renal pelvis and calyces have a similar appearance as grade III, plus thinning of the renal parenchyma.

Bilateral hydronephrosis has a worse outcome than unilateral hydronephrosis.[22]

There has been great debate about the significance of treating obstructive uropathy and the overall survival duration of patients with late-stage cervical cancer. In *2006, Radecka et al* observed that the median survival time of oncology patients was 255 days when percutaneous nephrostomy was used as the treatment option regardless of the primary site of the disease.[20] In *2018, Mashadi et al* retrospectively observed that the Death Risk value was 2.43 times higher in patients who did not undergo percutaneous nephrostomy compared to those who did. Of the 70 patients studied the median overall survival duration was 203 days in patients who

underwent Percutaneous Nephrostomy compared to 75 days in those who had no intervention.[23] In *2019, Texeira* studied whether percutaneous nephrostomy improved the quality of life in patients with obstructive uropathy due to cancer of the cervix. Fifty patients were retrospectively evaluated who had percutaneous nephrostomy tube successfully inserted and there was recovery of renal functions in all of them. Quality of life improved significantly in the first week and first month but wasn't sustained at three months as shown by a 42% mortality rate. At 9 months the mortality increased to 90%.[24]

Percutaneous nephrostomy tube insertion is associated with improvement of the kidney function. In 2018, *Zawadski et al* evaluated renal function pre and post-percutaneous nephrostomy tube insertion in cancer of the cervix patients with obstructive uropathy. Of the 27 patients followed up 55.5% recovered their renal functions. It was concluded that recovery of the renal functions was dependent on the degree of hydronephrosis and the creatinine clearance pre-procedure. In 2008, *Dienstmann R* analyzed 50 cervical cancer women who had percutaneous nephrostomy due to obstructive uropathy. Improvement of renal functions was noted in 60% of patients. Median creatinine levels pre and post-percutaneous nephrostomy insertion were 6.4 and 3.7 mg/dL respectively ($P < 0.05$). Median survival in patients with improvement of renal function after percutaneous nephrostomy insertion was 10.0 weeks compared to 2.6 weeks in those without improvement of renal function (log-rank, $P = 0.01$). Twenty-nine patients (58%) succumbed due to renal failure.[25]

Percutaneous nephrostomy tube insertion has also been performed to relieve obstruction and underlying renal dysfunction to enable patients to continue with palliative and at times therapeutic chemoradiation. In *2017, Van Aardt et al* observed this. Seventy patients were retrospectively studied, 44 were percutaneous nephrostomy inserted and 26 were conservatively managed. In the percutaneous nephrostomy group, 73% (of 26 with complete files) renal functions improved. Eleven patients (42%) completed palliative radiotherapy, 5 (19%) started therapeutic radiotherapy and 3 (15%) started chemotherapy. In the conservative group, 13 (59%) of 22 received palliative radiotherapy, and 4 (18.1%) started chemotherapy. Nevertheless, the Median Overall Survival duration in the percutaneous nephrostomy group was 120 days. Percutaneous nephrostomy improves the renal function to enable the patients to complete or start their definitive treatment but the Mean Overall Survival duration wasn't significantly improved.[26] In *2016, Beckta et al* conducted a retrospective study on whether urinary diversion facilitated the use of aggressive therapy without adversely affecting overall treatment time. The No diversion group had 63 patients and the diversion group had 19 patients. median overall survival duration was 79% in the no-diversion group compared to 60% in the

diversion group (P=0.139) at 22 months. The mean overall treatment time was 60.8 days in the diversion group compared to 65.8 days in the diverted group (P=0.182). The values were statistically not significant. Urinary diversion did not cause any significant delays in overall treatment time and provided a similar expected overall survival time.[27]

The role of percutaneous nephrostomy in recurrent disease is debatable. In *2016, Vasquez et al* evaluated the role of insertion of percutaneous nephrostomy in newly diagnosed versus recurrent disease in late-stage cervical cancer in patients with similar complications. The Median Overall Survival rate was 22.7 months in both groups, 19.2 months in the recently diagnosed group, and 28.1 months in the recurrent disease group (P=0.059). Percutaneous Nephrostomy was safe and improved renal functions but its use in recurrent disease should be individualized according to the patient's health status..[28]

Evidence of the best urinary diversion procedure to be done remains compelling. *Ku et al* observed that the possibility of failure of insertion of a ureteric stent was higher compared to percutaneous nephrostomy.[29] On the other hand, percutaneous nephrostomy is associated with high rates of urinary tract infections 20 to 50% and catheter dislodgement 10% to 40%.[30,31,32]Infections are usually mild or moderate and don't impact quality of life. *Gadducci et al* suggested that Percutaneous Nephrostomy had a limited role in patients with recurrent disease. Patients with primary disease may be alleviated until definitive treatment with chemoradiation is completed.[33]

Survival duration after nephrostomy due to obstructive uropathy is affected by multiple factors. *Perri et al.,2019* observed that the mean survival duration after urinary diversion was 11(0-67)months. Diabetes mellitus, ascites, and ECOG performance >1 were noted to impact negatively on survival. They proposed a prognostic Index based on the above factors to select patients who would benefit from urinary diversion. Other significant complications observed in the study included pyelonephritis, sepsis, and severe hematuria[36]

Noegroho et al. 2021, observed that age, metastasis, and ECOG performance impacted the survival duration of the patients. Based on age, those below 40 years had a survival rate of 6 months, 40-60 years 5 months, and those > 60 years 2 months. The median survival length of patients with metastatic disease was 2 months (1-5) months compared to those with non metastatic disease which was 5 (1-17) months[11].

2.1 Study Justification

Treatment of cervical cancer poses a healthcare burden. Despite efforts to educate the masses and decentralize screening services to tertiary medical facilities most patients present to the hospital when the disease is in stage II B and above. The overall survival duration at these stages is significantly reduced. Obstructive uropathy is a poor prognostic factor and interventions to relieve the obstruction are generally expensive and mostly palliative. Some studies noted that the mean overall survival time post-intervention compared to those who did not have any interventions done did not vary significantly.[25]

There's a paucity of local data to support the benefits of urinary diversion. This study aimed to show the impact of post-diagnosis interventions on palliative or definitive treatment of the disease. My proposed study will help get local data to compare with other similar studies worldwide. The study will inform evidence-based practice and the algorithm in the oncology ward to standardize how patients are classified with obstructive uropathy and management to optimize survival in advanced cancer of the cervix.

2.2 Research Question

What are the management, outcomes, and survival of patients with obstructive uropathy due to cervical cancer admitted at Kenyatta National Hospital between 2014 to 2019?

2.3 Objectives

2.3.1 Broad Objectives

To determine the management, outcomes, and survival of patients with obstructive uropathy due to cervical cancer admitted at Kenyatta National Hospital between 2014 to 2019.

2.3.2 Specific Objectives

Amongst the patients presenting with obstructive uropathy due to cervical cancer at KNH between 2014 – 2019;

a) To determine the two-year overall survival rate.
b) To determine the proportions of patients who underwent nephrostomy, hemodialysis, or no intervention.
c) To determine the outcome of patients who underwent nephrostomy, hemodialysis, or no intervention.

2.3.3 Secondary Objective

a) To determine the specific overall survival rate of patients who underwent nephrostomy, hemodialysis, or no intervention.

2.4 Conceptual Framework

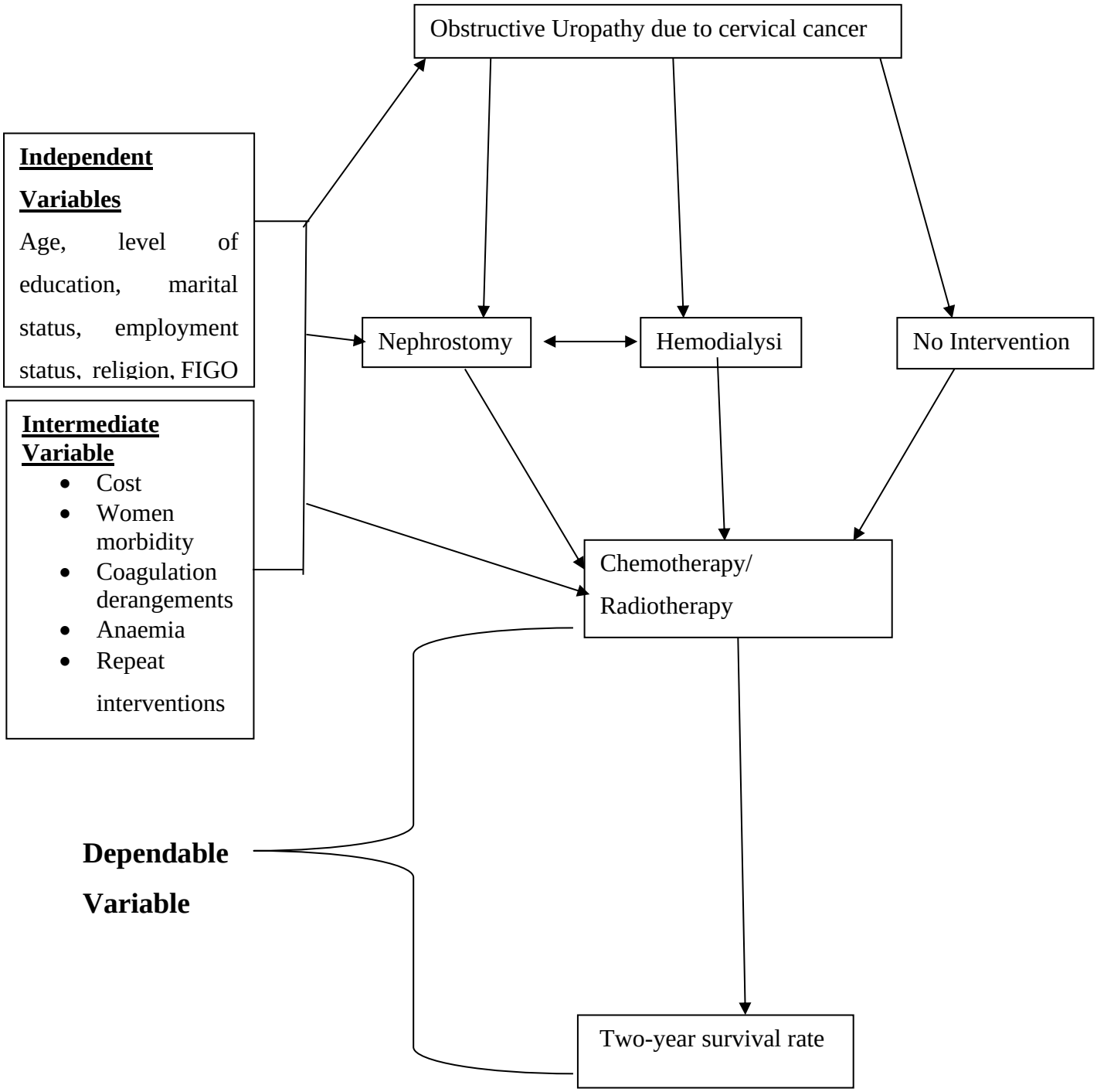

Figure 2: Conceptual Framework

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study Design

Descriptive Retrospective Cohort Study.

3.2 Study Area

The study was conducted at Kenyatta National Hospital in the Obstetrics and Gynecology, Interventional Radiology, and Records departments.

3.3 Study Population

These were all patients presenting obstructive uropathy due to cancer of the cervix being managed at Kenyatta National Hospital between 1st January 2014 and 31st December 2019.

3.3.1 Inclusion Criteria

a) Patients with obstructive uropathy due to cervical cancer confirmed by imaging.
b) Patients with cervical cancer FIGO stage II b and above.
c) Histological diagnosis of cervical cancer.
d) Files with complete records

3.3.2 Exclusion Criteria

a) Patients who had a Percutaneous Nephrostomy tube inserted outside KNH.
b) Files with missing records.

3.4 Sample Size Calculation

All files from the Records department at Kenyatta National Hospital with a diagnosis of Obstructive uropathy due to cancer of the cervix stage 2b to stage 4b between 2014 to 2019 meeting the eligibility criteria were selected for the study. A sample size of 127 was achieved.

3.5 Sampling Technique

A consecutive sampling technique was used. All patient files meeting the eligibility criteria were selected from 2019 backward each year till 2014.

3.6 Study Tool

A data abstraction tool was used to collect data from patients' medical records.

3.7 Study Procedure

Patients' medical files were retrieved from the Records Department in Kenyatta National Hospital. All files with a diagnosis of obstructive uropathy secondary to cervical cancer were retrieved. Consecutive sampling was done and all files meeting the eligibility criteria were selected.

The two-year overall survival rate of patients with obstructive uropathy due to cervical cancer was calculated irrespective of whether they had an intervention or not.

The files that fulfilled the eligibility criteria were further analyzed and the proportion of patients who underwent nephrostomy, hemodialysis, or no intervention was calculated.

The outcomes were evaluated:

- Nephrostomy group – time when it was done was recorded. Was it done after starting chemoradiation, radiotherapy alone, chemotherapy alone, or hemodialysis? The FIGO stage at the time the nephrostomy was recorded. If treatment had not been started, the time duration between the time of diagnosis of obstructive uropathy and when the nephrostomy tube was inserted was established. Post nephrostomy, the proportion of patients who went on to start or continue chemoradiation was calculated. The two-year survival rate of those who underwent treatment or not post-nephrostomy will be determined. Those who underwent repeat nephrostomy tube insertion will be recorded and reasons noted.
- Hemodialysis group – The time it was done was recorded. Was it done before chemoradiation, chemotherapy alone, radiotherapy alone, or pre or post-nephrostomy tube insertion? FIGO stage at the time of hemodialysis was recorded. The proportion of patients who underwent nephrostomy post-hemodialysis was calculated. The proportion who went for chemoradiation after hemodialysis was determined. The two-year survival rate was calculated.
- No intervention group – The reasons for not intervening to relieve obstructive uropathy were noted. Their two-year survival rate was also calculated.

3.8 Quality Control

The principal investigator verified every data collection form to confirm the data was entered correctly. The research assistants were trained on proper case definitions and supervised at the beginning to ensure collected data was recorded properly.

3.9 Data Management

Filled data-collecting forms were stored under lock and key in the Principle investigator's computer. It was protected by a password only known to the principal investigator. Variables were abstracted from patient's files and data from laboratory, radiological, and radiochemotherapeutic reports. Approval was sought from KNH-UoN ethics and research committee to conduct patient follow-up to ascertain the selected patient's status if the information is missing from the file. All patient details were de-identified and code numbers were allocated. Data collected was immediately fed into a computer database and analyzed using statistical packages for social science version 26 software.

3.10 Data Analysis

Analysis was done using the Statistical Package for Social Sciences (SPSS) version 26 software. Data analysis entailed running descriptive statistics such as means, standard deviation, medians, interquartile range, frequencies, and percentages and presenting them in tables. To answer the specific objectives of the study, inferential analysis will be done as follows:

Table 3: How Inferential analysis will be done

To determine the 2-year overall survival duration.	Kaplan Meier statistics were used to determine the two-year overall survival of patients. Cox regression was used for comparative analysis.
To determine what proportions of patients who underwent nephrostomy, hemodialysis, or no intervention.	Frequency distributions with percentages were used and the Exact Clopper Pearson method was used to compute 95% confidence intervals.
To determine the outcome of patients who underwent nephrostomy, hemodialysis, or no intervention.	Frequency distribution was calculated and the chi-square test and multinomial regression will be used for comparative analysis.

3.11 Ethical Consideration

The study was carried out in Kenyatta National Hospital after approval by the UoN-KNH Ethics and Research Committee. Permission to carry out the study was sought from the KNH administration: Obstetrics and Gynecology, Interventional Radiology, and Records departments. Confidentiality was maintained with the data collected only accessible to the PI. Study numbers were assigned to the eligible case records instead of patient names to enhance confidentiality.

4.0 CHAPTER FOUR: RESULTS

4.1 Study Flow Chart

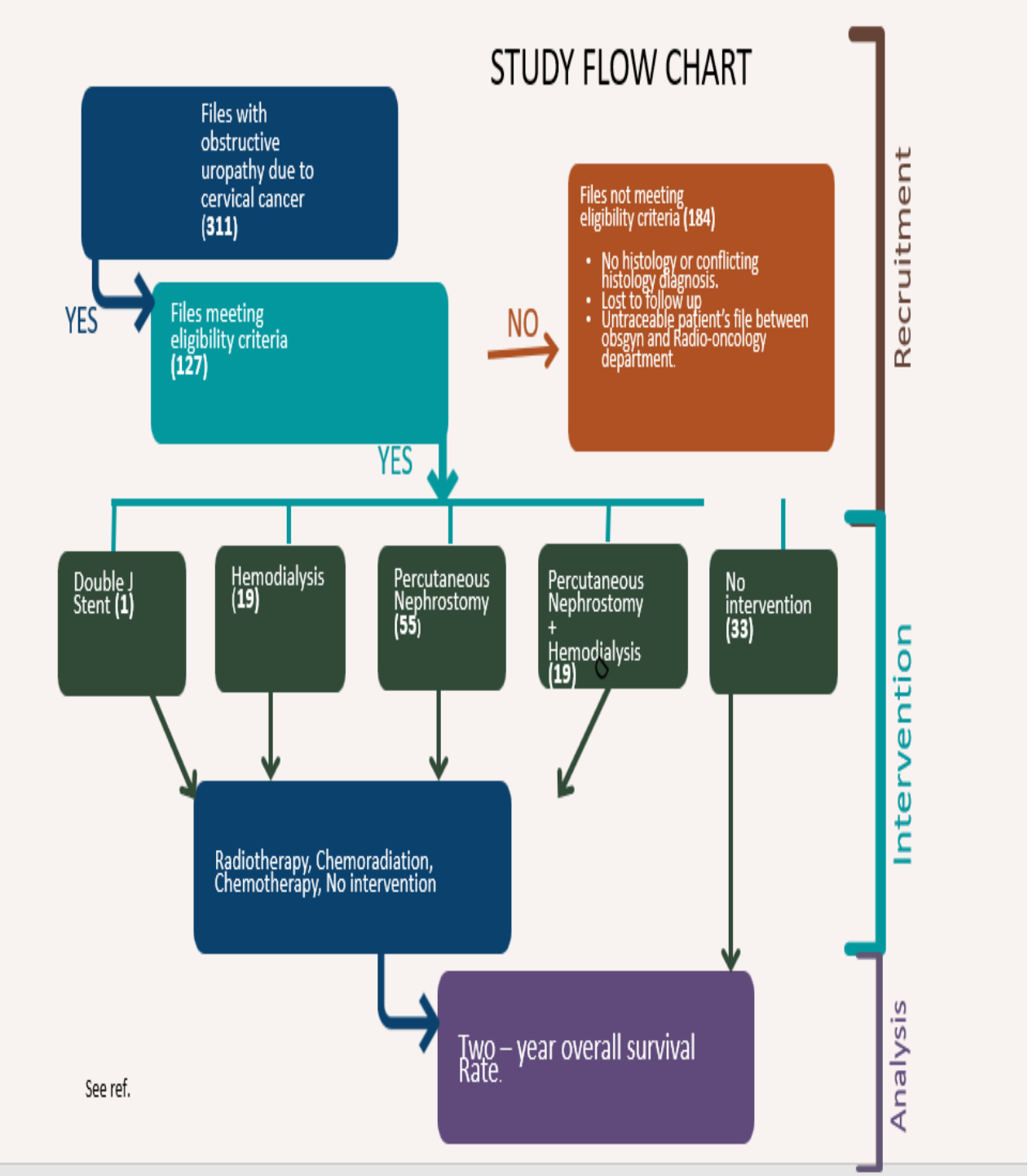

Figure 3:study flow chart from recruitment to analysis. It also shows reasons why some files did not meet the eligibility criteria

Table 4:Socio-demographic characteristics of study patients with obstructıve uropathy due to cervıcal cancer at Kenyatta National Hospital, Nairobi, 2014 – 2019

Characteristic	Level	All patients	Survival status (rate)		
			Yes	No	*p*-value[1]
All patients N (%)		127	64 (50.4)	63 (49.6)	
Age (years)	Median (IQR)	48.0 (17.0)	48.5 (15.0)	48.0 (18.0)	0.929
Age group (years)	27-39	36 (28.3)	17 (26.6)	19 (30.2)	0.784
	40-49	30 (23.6)	17 (26.6)	13 (20.6)	
	50-60	41 (32.3)	19 (29.7)	22 (34.9)	
	60+	20 (15.7)	11 (17.2)	9 (14.3)	
Marital status	Married	84 (66.1)	40 (62.5)	44 (69.8)	0.454
	Other[2]	43 (33.9)	24 (37.5)	19 (30.2)	
Religion	Christian	117 (94.4)	59 (95.2)	58 (93.5)	1.000
	Muslim	7 (5.6)	3 (4.8)	4 (6.5)	
Level of education	No formal education	21 (16.8)	8 (12.9)	13 (20.6)	0.510
	Primary	66 (52.8)	34 (54.8)	32 (50.8)	
	Secondary	32 (25.6)	18 (29.0)	14 (22.2)	
	Tertiary institution	6 (4.8)	2 (3.2)	4 (6.3)	
Employment status	Casual labourer	10 (8.0)	4 (6.5)	6 (9.5)	0.896
	Formal-employment	6 (4.8)	3 (4.8)	3 (4.8)	
	Self-employment	22 (17.6)	10 (16.1)	12 (19.0)	
	Unemployed	87 (69.6)	45 (72.6)	42 (66.7)	

[1] *p*-value from the Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon/Mann-Whitney U test for continuous variables, two-sided; bold *p*-values indicate statistical significance ($p<0.05$). 2Single, divorced, separated.

4.2 Sociodemographic Characteristics of Patients

The data were abstracted from records of a total of 127 patients. The median (interquartile range [IQR]) age at the time of diagnosis was 48.0 (17.0) years and 66.1% were married. Patients having no formal education, in primary, secondary, and tertiary institutions comprised 16.8%, 52.8%, 25.6%, and 4.8%, respectively. Christianity was the most common religion and most patients were unemployed. The sociodemographic characteristics of these groups stratified by two-year survival status are detailed in Table 4, and by post-diagnosis interventions (double j stenting, hemodialysis (HEM), percutaneous nephrostomy (PCN),

percutaneous nephrostomy + hemodialysis (PNH), and no ıntervention) are summarized in Supplementary Table 1 (S1) in Appendix III. The groups were statistically indifferent ($p>0.05$), that is, they demonstrated greater similarity among their demographic groups in both two-year survival and post-diagnosis intervention comparative analyses.

4.3 Clinical and Gynaecological Characteristics Of The Study Population

The patients were mostly parous women of 3-5 parities (61.6%). The majority of the patients belonged to the International Federation of Gynecology, Obstetrics (FIGO) stage IIIb (62.7%). There was a statistically significant difference in distribution by FIGO classes in terms of two-year survival categories ($p=0.024$). The data is summarized in Table 5 and S2 in Appendix III. About a quarter of the women were HIV-positive (24.4%) and 11.6% had a history of Papanicolaou test. The most common histological subtype was squamous cell carcinomas at 96.9%. The most common comorbidities were anemia, deep vein thrombosis (DVT), and hypertension comprising 42.3%, 17.6%, and 14.9%, respectively.

Table 5. Clinical and gynecological characteristics of study patients with obstructıve uropathy due to cervıcal cancer at Kenyatta National Hospital, Nairobi, 2014 – 2019

Characteristic	Level	Total	Survival status (rate)		
			Yes	No	*p*-value[3]
All patients N (%)		127	64 (50.4)	63 (49.6)	
Parity	≤2	22 (17.6)	12 (19.4)	10 (15.9)	0.848
	3-5	77 (61.6)	38 (61.3)	39 (61.9)	
	≥6	26 (20.8)	12 (19.4)	14 (22.2)	
FIGO[4] staging	IIb	6 (4.8)	1 (1.6)	5 (8.1)	**0.024**
	IIIa	2 (1.6)	1 (1.6)	1 (1.6)	
	IIIb	79 (62.7)	38 (59.4)	41 (66.1)	
	IVa	31 (24.6)	22 (34.4)	9 (14.5)	
	IVb	8 (6.3)	2 (3.1)	6 (9.7)	
HIV[5] status	Negative	72 (56.7)	34 (53.1)	38 (60.3)	0.391
	Positive	31 (24.4)	18 (28.1)	13 (20.6)	
HIV+ve, highest CD4[6] count	Median (IQR)	480.0 (252.0)	508.5 (257.0)	252.0 (57.0)	0.091
HIV-ve, lowest CD4 count	Median (IQR)	236.0 (163.0)	229.0 (297.5)	244.0 (87.5)	0.866
History of pap smear	No	84 (88.4)	44 (89.8)	40 (87.0)	0.755
	Yes	11 (11.6)	5 (10.2)	6 (13.0)	
Histological type	Adenocarcinoma	4 (3.1)	3 (4.7)	1 (1.6)	0.619
	SCC [7]	123 (96.9)	61 (95.3)	62 (98.4)	
Comorbidities[8]	AKI	13 (5.9)	7 (6.2)	6 (5.5)	0.119
	Anaemia	94 (42.3)	43 (38.4)	51 (46.4)	
	CKD	26 (11.7)	8 (7.1)	18 (16.4)	
	Diabetes	5 (2.3)	3 (2.7)	2 (1.8)	
	DVT	39 (17.6)	21 (18.8)	18 (16.4)	
	Hypertension	33 (14.9)	21 (18.8)	12 (10.9)	
	None	12 (5.4)	9 (8.0)	3 (2.7)	

[3] *p*-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon/Mann-Whitney U test for continuous variables, two-sided; bold *p*-values indicate statistical significance ($p<0.05$).

[4] FIGO, International Federation of Gynecology, Obstetrics.

[5] HIV, human immunodeficiency virus.

[6] CD4, cluster of differentiation 4; IQR, interquartile range.

[7] SCC, squamous cell carcinomas

[8] AKI, acute kidney injury; CKD, chronic kidney disease; DVT, deep vein thrombosis. The sum may not total 127 due to multiple co-morbidities.

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4.4 Proportions of Patients Who Underwent Nephrostomy, Hemodialysis, or No Intervention

The estimated proportions of post-diagnosis procedures were double J stent insertions 0.8% (95% confidence interval [CI] 0.0%–10.1%), HEM 14.8% (CI 6.3%–24.1%), PCN 43.0% (CI 34.4%–52.2%), PCN +HEM 15.6% (CI 7.0%–24.9%) and 25.8%% (CI 17.2%–35.1%) for No intervention. Percutaneous nephrostomy was the most common obstructive uropathy intervention (Table 6).

Table 6:Distribution of patients who underwent nephrostomy, hemodialysis, or no intervention at Kenyatta National Hospital, Nairobi, 2014 – 2019

Intervention procedure	Percent Estimates[9] and Confidence Interval (CI)	
	Frequency	Estimate (95% CI)
Double J stenting	1	0.8 (0.0–10.1)
Hemodialysis	19	14.8 (6.3–24.1)
Percutaneous Nephrostomy	55	43.0 (34.4–52.2)
Percutaneous Nephrostomy + Hemodialysis	19	15.6 (7.0–24.9)
No Intervention	33	25.8 (17.2–35.1)

[9] Multinomial estimates and confidence intervals by the Sisonglaz method.

4.5 The Outcome of Patients Who Underwent Nephrostomy, Hemodialysis, Or No Intervention

Post-diagnosis treatment based on the Kaplan-Meier method indicated that the median duration of treatment for patients who underwent HEM only was seven weeks, while those who underwent PCN only were 12 weeks (Figure 2). The median post-diagnosis time, defined here to be the time at which the time-to-treatment probability curve crosses 50%, was undefined implying that it was greater than 50% at the last time-point for patients who underwent PNH. The undefined median here suggests that the median post-diagnosis time-to-treatment was longer for patients in the PNH stratum. The Log-rank test (p=0.024) for comparisons also shows that there was a statistically significant difference in time-to-treatment rates for the three intervention strata.

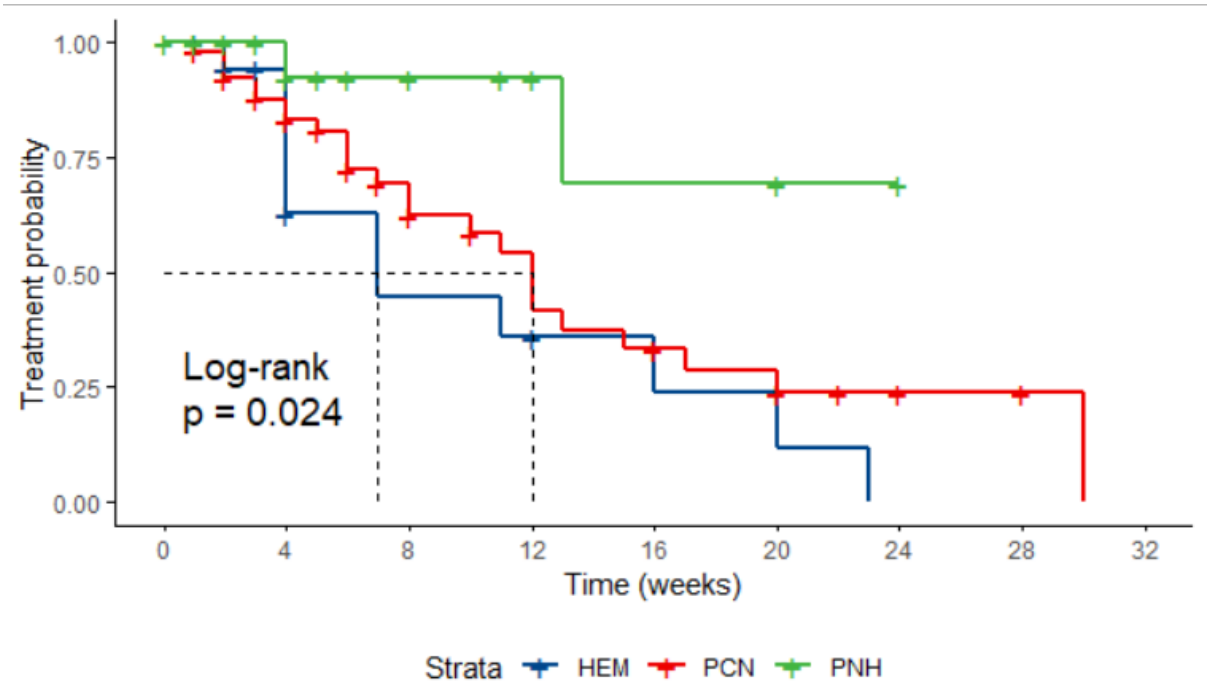

Figure 4:Kaplan Meir time-to-treatment curves for patients who underwent hemodialysis (HEM), percutaneous nephrostomy (PCN), and percutaneous nephrostomy + hemodialysis (PNH) presenting at Kenyatta National Hospital, Nairobi, 2014 – 2019.

To provide insights into the outcomes, this study further investigated the reasons why some patients did not undergo interventions. Overall, the reasons for lack of intervention were more of a clinical nature (78.9%; 56/71) than socioeconomics (financial: mostly widowed/separated, no formal education/primary or unemployed, see Table 7) or gynecological (women of >3 parity) suggesting the presence of competing risks at clinical presentation precluding potential occurrence of post-diagnosis supportive intervention. As aforestated, the most frequent reasons were due to anemia (46.5%), death before intervention (26.8%), and financial issues 19.7%. Anemia and death/succumbing before any intervention were more common in FIGO class III and IV as critically ill patients develop deranged coagulation as a result of homeostatic abnormalities and renal dysfunction. The overall and stratified distribution of reasons is presented in Table 7 below.

Table 7:Frequency distribution of reasons for no intervention stratified by socioeconomic, clinical, and gynecological information at the Kenyatta National Hospital, Nairobi, 2014–2019

Label	Levels	Anemia	Death[10]	Financial	CD[11]	DVT[12]	Inf./RD[13]	LTFP[14]
All N (%)		33 (46.5)	19 (26.8)	14 (19.7)	2 (2.8)	1 (1.4)	1 (1.4)	1 (1.4)
Marital status	Married	25 (56.8)	12 (27.3)	5 (11.4)	0 (0.0)	1 (2.3)	1 (2.3)	0 (0.0)
	Separated	2 (40.0)	1 (20.0)	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Single	5 (45.5)	2 (18.2)	4 (36.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Widowed	1 (9.1)	4 (36.4)	3 (27.3)	2 (18.2)	0 (0.0)	0 (0.0)	1 (9.1)
Education	None	6 (50.0)	2 (16.7)	3 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
	Primary	19 (47.5)	12 (30.0)	6 (15.0)	2 (5.0)	0 (0.0)	1 (2.5)	0 (0.0)
	Secondary	5 (35.7)	5 (35.7)	4 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Tertiary	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)
Employment	Casual labourer	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Self-employed	6 (46.2)	3 (23.1)	3 (23.1)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)
	Unemployed	26 (50.0)	14 (26.9)	8 (15.4)	2 (3.8)	0 (0.0)	1 (1.9)	1 (1.9)
Parity	≤2	5 (62.5)	2 (25.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	3-5	19 (42.2)	13 (28.9)	10 (22.2)	2 (4.4)	0 (0.0)	1 (2.2)	0 (0.0)
	6+	8 (47.1)	4 (23.5)	3 (17.6)	0 (0.0)	1 (5.9)	0 (0.0)	1 (5.9)
FIGO[15] class	II	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	III	23 (46.9)	15 (30.6)	9 (18.4)	0 (0.0)	1 (2.0)	1 (2.0)	0 (0.0)
	IV	6 (35.3)	4 (23.5)	5 (29.4)	2 (11.8)	0 (0.0)	0 (0.0)	0 (0.0)
HIV[16] status	Negative	18 (41.9)	13 (30.2)	10 (23.3)	0 (0.0)	1 (2.3)	1 (2.3)	0 (0.0)
	Positive	6 (40.0)	4 (26.7)	3 (20.0)	2 (13.3)	0 (0.0)	0 (0.0)	0 (0.0)
Survival	No	18 (40.0)	15 (33.3)	8 (17.8)	2 (4.4)	1 (2.2)		1 (2.2)
	Yes	15 (57.7)	4 (15.4)	6 (23.1)			1 (3.8)	

[10] Death, death/succumbed before any intervention

[11] CD, coagulation derangement.

[12] DVT, deep vein thrombosis.

[13] Inf./RD, infection and renal dysfunction.

[14]LTFP, loss to follow up.

[15] FIGO, International Federation of Gynecology, Obstetrics

[16] HIV, human immunodeficiency virus

Table 8 below summarizes the distribution of treatment outcomes by post-intervention procedures, FIGO staging, and two-year survival according to obstructive uropathy procedures performed. Double J stent insertion was done on one patient who also survived in the two-year follow-up period. Of all the post-diagnosis treatments provided, radiotherapy was the most common (27.3%) followed by repeat nephrostomy due to blockage of tubes at (16.2%). Of the

19 patients who had percutaneous nephrostomy + hemodialysis, 63.6% died within the two-year follow-up period suggesting how critical the patients were.

Generally, two-year survival was moderately higher (42.6% vs. 57.4%) with post-diagnosis interventions done but differed by type of intervention (p=0.011). Among 61 patients who had FIGO class III b cervical cancer, 50.8% (31/61), 24.6% (15/61), and 23.0% (14/61) had PCN, PNH, HEM, and Double J stent insertion, respectively (row proportions not shown in Table 8).

Table 8:Frequency distribution of treatment outcomes, International Federation of Gynecology and Obstetrics staging and two-year survival according to procedures done at the Kenyatta National Hospital, 2014–2019
Table 5.

Variable	**Level**	**All patients N (%)[17]**	**Procedures performed[18], n (%)**				
			Double J stenting	**HEM**	**PCN**	**PNH**	***p*-value[19]**
Post-intervention	None	40 (40.4)	1 (100.0)	12 (63.2)	25 (46.3)	2 (8.0)	–
	Chemoradiation	9 (9.1)	–	2 (10.5)	5 (9.3)	2 (8.0)	
	Chemotherapy	7 (7.1)	–	1 (5.3)	6 (11.1)	0 (0.0)	
	Radiotherapy	27 (27.3)	–	4 (21.1)	18 (33.3)	5 (20.0)	
	Nephrostomy	11 (16.2)	–	–	–	16 (64.0)	
FIGO[20] Staging	IIb	3 (3.2)	0 (0.0)	0 (0.0)	3 (5.6)	0 (0.0)	0.904
	IIIa	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	
	IIIb	61 (64.9)	1 (100.0)	14 (73.7)	31 (57.4)	15 (75.0)	
	IVa	25 (26.6)	0 (0.0)	4 (21.1)	17 (31.5)	4 (20.0)	
	IVb	4 (4.3)	0 (0.0)	1 (5.3)	2 (3.7)	1 (5.0)	
	All N (%)	95	1 (1.1)	19 (20.0)	55 (57.9)	20 (21.1)	–
Two-year survival	Yes	54 (57.4)	1 (100.0)	11 (57.9)	35 (63.6)	7 (36.8)	**0.011**
	No	40 (42.6)	0 (0.0)	8 (42.1)	20 (36.4)	12 (63.2)	
	All N (%)	94	1	19	55	19	

[17] The totals may not sum to 95 or column total where there are missing data, where data is a subset without "no intervention", and in situations where the data was pivoted longer for multiple post-diagnosis interventions in a patient: chemoradiation, chemotherapy, radiotherapy, nephrostomy, and no intervention.
[18] HEM, hemodialysis; PCN, percutaneous Nephrostomy; PNH, percutaneous Nephrostomy + Hemodialysis.
[19] Where applicable, *the p*-value from the Chi-square test or Fisher's exact test for categorical variables, two-sided; bold *p*-values indicate statistical significance ($p<0.05$).
[20] FIGO, International Federation of Gynecology and Obstetrics.

Z4.6 Survival Rates of Patients Who Underwent Nephrostomy, Hemodialysis, Or No Intervention

In the two-year follow-up period, patients who underwent percutaneous nephrostomy survived more than other post-diagnosis intervention groups (54.7%, 95% confidence interval [CI] 3.8%–67.5%). Two-year all-cause mortality was more prevalent in patients who had no post-diagnosis intervention (36.5% [95% CI 25.4%–50.6%]). Table 9 summarizes the survival

Table 9:Survival rates of patients who underwent nephrostomy, hemodialysis, or no intervention, stratified by survival status

Procedure	**Percent Estimates[21] and Confidence Interval (CI)**			
	Two-year survival		**Two-year all-cause mortality**	
	n	**Estimate (95% CI)**	**n**	**Estimate (95% CI)**
Double J stenting	1	1.6 (0.0–14.3)	0	0.0 (0.0–14.1)
Hemodialysis	11	17.2 (6.3–30.0)	8	12.7 (1.6–26.8)
Percutaneous Nephrostomy	35	54.7 (43.8–67.5)	20	31.8 (20.6–45.9)
Percutaneous Nephrostomy + Hemodialysis	7	10.9 (0.0–23.7)	12	19.1 (7.9–33.2)
No Intervention	10	15.6 (4.7–28.4)	23	36.5 (25.4–50.6)

[21] Multinomial estimates and confidence intervals by the Sisonglaz method.

The median post-diagnosis treatment time for patients who survived (two-year survival) was 16 weeks, against 11 weeks for patients who died (two-year all-cause mortality). There seemed to be no post-diagnosis treatment advantage for patients who survived in the two-year compared with those who died (log-rank test p=0.56), showing that the groups did not differ significantly. Figure 2 below shows that the longer time between diagnosis to intervention did not correspond to two-year all-cause mortality.

[21] Multinomial estimates and confidence intervals by the Sisonglaz method.

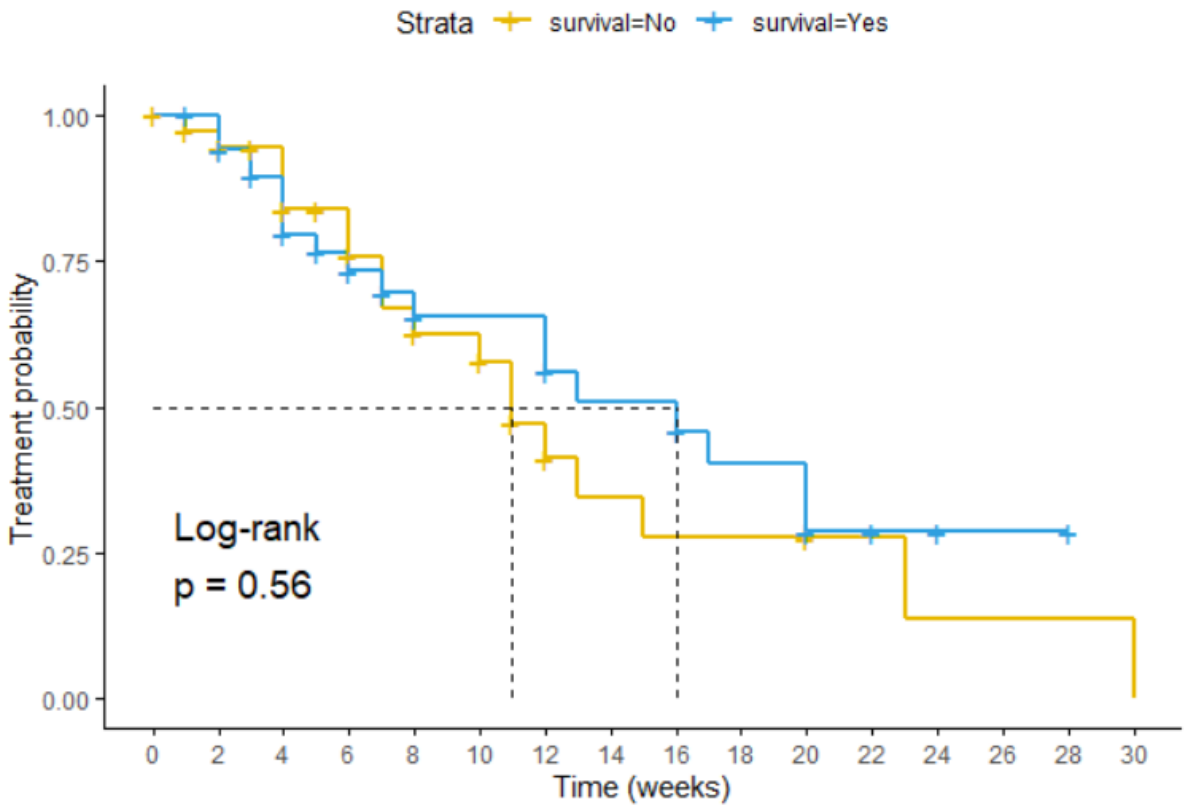

Figure 5:Kaplan-Meier curve for post-diagnosis treatment probability for patients who underwent nephrostomy, hemodialysis interventions stratified by two-year survival

4.7 Unadjusted And Adjusted Odds Ratio Of Two-Year Survival

In the univariable logistic regression model, single women had higher odds of two-year survival (odds ratio [OR] 3.95, 95% confidence interval [CI] 1.29-14.84, p=0.024) compared with married women. In comparison with patients who did not undergo any post-diagnosis intervention, patients who underwent PCN had greater odds of two-year survival (OR 4.02, 95% CI 1.64-10.49, p=0.003). Similarly, in the multivariable-adjusted analysis, single patients had 5.83 times the odds of two-year survival (95% CI 1.65-25.45, p=0.010) compared to married patients. Moreover, PCN had higher two-year survival odds (AOR 5.37, 95% CI 1.95-16.22, p=0.002) than no intervention. All other variables in the univariable and multivariable-adjusted logistic regression model were not statistically significant (Table 10).

Table 10:The univariable and multivariable-adjusted odds ratio for two-year survival (n=127)

Variable	Level	2-year survival		Unadjusted odds ratio (OR)			Adjusted odds ratio (AOR)[22]		
		No (%)	Yes (%)	OR	95% CI	*p*-value	AOR	95% CI	*p*-value
Marital status	Married	44 (53.0)	39 (47.0)	Ref.			Ref.		
	Separated	5 (55.6)	4 (44.4)	0.90	0.21-3.64	0.885	1.18	0.24-5.89	0.836
	Single	4 (22.2)	14 (77.8)	3.95	1.29-14.84	**0.024**	5.83	1.65-25.45,	**0.010**
	Widowed	10 (62.5)	6 (37.5)	0.68	0.21-2.00	0.487	1.02	0.28-3.55	0.974
Parity	≤2	10 (45.5)	12 (54.5)	Ref.			Ref.		
	3-5	39 (51.3)	37 (48.7)	0.79	0.30-2.05	0.629	0.98	0.33-2.83	0.965
	≥6	14 (53.8)	12 (46.2)	0.71	0.22-2.23	0.563	0.81	0.22-2.95	0.752
FIGO class[23]	IIb/IIIa/IIIb	47 (54.7)	39 (45.3)	Ref.			Ref.		
	IVa/IVb	15 (38.5)	24 (61.5)	1.93	0.90-4.24	0.096	2.02	0.86-4.91	0.113
Comorbidity Score (0–4)	Mean (SD)	1.7 (0.8)	1.6 (1.0)	0.85	0.57-1.26	0.428	0.81	0.51-1.28	0.370
Procedure[24]	NON	23 (69.7)	10 (30.3)	Ref.			Ref.		
	HEM	8 (42.1)	11 (57.9)	3.16	0.99-10.63	0.055	3.65	1.00-14.35	0.054
	PCN	20 (36.4)	35 (63.6)	4.02	1.64-10.49	**0.003**	5.37	1.95-16.22	**0.002**
	PNH	12 (63.2)	7 (36.8)	1.34	0.40-4.43	0.629	1.80	0.48-6.82	0.383

[22] Stepwise multivariable logistic regression with covariate entry threshold of p=0.15 from the univariable model. Clinically and gynaecologically important variables such as comorbidity as a score (range: 0 to 4 comorbidities), FIGO class, and parity were also entered. Ref., referent group for comparison. *p*-value from Logistic regression; two-sided; bold p-values indicate statistical significance (p<0.05). 95% CI OR = 95% confidence interval of odds ratio (OR).

Number in dataframe = 127, Number in model = 123, Missing = 4, AIC = 168.7, C-statistic = 0.739, H&L = Chi-sq (8) 7.87 (p=0.446).

[23] FIGO, International Federation of Gynecology and Obstetrics classification.

[24] NON, No intervention; HEM, Hemodialysis; PCN, Percutaneous Nephrostomy; PNH, Percutaneous Nephrostomy + Hemodialysis

Table 11:The unadjusted and covariate-adjusted odds ratio for two-year survival as a function of time between diagnosis and intervention

		Two-year survival		Unadjusted odds ratio	Adjusted odds ratio
Label	**Levels**	**No (%)**	**Yes (%)**	**OR (95% CI, *p*-value)**	**AOR (95% CI, *p*-value)**
Hemodialysis (n=19)					
Duration (weeks)	Median (IQR)	4.0 (5.0)	4.0 (7.5)	0.97 (0.83–1.13, p=0.696)	1.10 (0.90–1.43, p=0.373)
Age (years)	Median (IQR)	45.5 (9.8)	43.0 (13.0)	0.97 (0.88–1.07, p=0.568	0.99 (0.84–1.22, p=0.944)
FIGO class	IIb/IIIa/IIIb	7 (50.0)	7 (50.0)	1.00	1.00
	IVa/IVb	1 (20.0)	4 (80.0)	4.0 (0.44–89.4, p=0.263)	2.82 (0.18–119, p=0.494)
HIV status	Negative	6 (60.0)	4 (40.0)	1.00	1.00
	Positive	1 (14.3)	6 (85.7)	9.0 (1.0–207.9, p=0.081)	9.02 (0.73–265, p=0.118)
Comorbidity score	Median (IQR)	2.0 (1.2)	2.0 (1.0)	0.58 (0.15–1.95, p=0.390)	0.46 (0.05–2.66, p=0.407)
Percutaneous Nephrostomy (n=55)					
Duration (weeks)	Median (IQR)	6.0 (8.0)	5.0 (7.0)	0.99 (0.92–1.08, p=0.882)	1.0 (0.91–1.10, p=0.970)
Age (years)	Median (IQR)	54.0 (27.8)	49.0 (18.0)	0.99 (0.94–1.04, p=0.690)	1.02 (0.96–1.09, p=0.511)
FIGO class	IIb/IIIa/IIIb	15 (42.9)	20 (57.1)	1.00	1.00
	IVa/IVb	4 (21.1)	15 (78.9)	2.81 (0.82–11.4, p=0.116)	3.73 (0.70–25.14 0.140)
HIV status	Negative	9 (32.1)	19 (67.9)	1.00	1.00
	Positive	6 (40.0)	9 (60.0)	0.71 (0.19–2.68, p=0.607)	1.05 (0.24–4.96, p=0.945)
Comorbidity score	Median (IQR)	1.0 (1.0)	1.0 (1.0)	0.70 (0.35–1.32, p=0.279)	0.57 (0.22–1.33, p=0.209)
Treatment received	None	11 (44.0)	14 (56.0)	1.00	1.00
	Chemoradiation	2 (40.0)	3 (60.0)	1.18 (0.17–10.2, p=0.869)	0.45 (0.03–5.98, p=0.548)
	Chemotherapy	1 (16.7)	5 (83.3)	3.93 (0.53–81.2, p=0.241)	1.09 0.08 27.83 0.949)

		Two-year survival		Unadjusted odds ratio	Adjusted odds ratio
Label	**Levels**	**No (%)**	**Yes (%)**	**OR (95% CI, *p*-value)**	**AOR (95% CI, *p*-value)**
	Radiotherapy	6 (33.3)	12 (66.7)	1.57 (0.45–5.77, p=0.482)	2.11 (0.42–12.6, p=0.376)
Percutaneous Nephrostomy + Hemodialysis (n=20)					
Duration (weeks)	Median (IQR)	5.5 (8.2)	4.0 (8.5)	1.03 (0.9–1.19, p=0.637)	0.96 (0.75–1.17, p=0.703)
Age (years)	Median (IQR)	50.0 (16.5)	48.0 (22.5)	0.98 (0.91–1.06, p=0.682)	0.93 (0.77–1.06, p=0.328)
FIGO class	IIb/IIIa/IIIb	9 (64.3)	5 (35.7)	1.00	1.00
	IVa/IVb	3 (60.0)	2 (40.0)	1.20 (0.13–9.91, p=0.865)	8.01 (0.11–3393, p=0.40)
HIV status	Negative	8 (61.5)	5 (38.5)	1.00	1.00
	Positive	3 (60.0)	2 (40.0)	1.07 (0.11–8.90, p=0.952)	0.22 (0.01–3.36, p=0.314)
Comorbidity score	Median (IQR)	1.5 (1.2)	1.0 (2.5)	1.49 (0.68–3.57, p=0.334)	2.98 (0.75–31.1, p=0.222)
Treatment received	None	1 (50.0)	1 (50.0)	1.00	1.00
	Nephrostomy + Chemoradiation/Radiotherapy	2 (40.0)	3 (60.0)	1.50 (0.04–57.1, p=0.810)	0.09 (0.00–19.2, p=0.420)
	Nephrostomy/ Chemoradiation/Radiotherapy	9 (75.0)	3 (25.0)	0.33 (0.01–10.2, p=0.482)	0.02 (0.00–3.21, p=0.201)

Table 12:Table S1. Sociodemographic characteristics of study patients with obstructıve uropathy due to cervıcal cancer, stratified by procedures done at Kenyatta National Hospital, Nairobi, 2014 – 2019

Label	Level	All patients	Procedure performed[25]					
			JJ stent	HEM	PCN	PNH	None	*p*-value[26]
All N (%)		127	1 (0.8)	19 (14.8)	55 (43.0)	20 (15.6)	33 (25.8)	
Age (years)	Median (IQR)	48.0 (17.0)	51.0	44.0 (10.5)	50.0 (20.0)	47.5 (16.8)	43.0 (18.0)	0.614
Age	27-39 years	36 (28.1)	0 (0.0)	5 (26.3)	14 (25.5)	5 (25.0)	12 (36.4)	0.501
	40-49 years	31 (24.2)	0 (0.0)	8 (42.1)	11 (20.0)	6 (30.0)	6 (18.2)	
	50-60 years	41 (32.0)	1 (100)	4 (21.1)	17 (30.9)	7 (35.0)	12 (36.4)	
	60+ years	20 (15.6)	0 (0.0)	2 (10.5)	13 (23.6)	2 (10.0)	3 (9.1)	
Marital status	Married	85 (66.4)	1 (100)	8 (42.1)	41 (74.5)	15 (75.0)	20 (60.6)	0.081
	Other [27]	43 (33.6)	0 (0.0)	11 (57.9)	14 (25.5)	5 (25.0)	13 (39.4)	
Religion	Christian	118 (94.4)	1 (100)	17 (94.4)	53 (96.4)	20 (100.0)	27 (87.1)	0.279
	Muslim	7 (5.6)		1 (5.6)	2 (3.6)		4 (12.9)	
Level of education	Secondary	32 (25.4)	1 (100)	5 (27.8)	17 (31.5)	3 (15.0)	6 (18.2)	0.128
	None	21 (16.7)		2 (11.1)	8 (14.8)	7 (35.0)	4 (12.1)	
	Primary	67 (53.2)		11 (61.1)	27 (50.0)	7 (35.0)	22 (66.7)	
	Tertiary	6 (4.8)			2 (3.7)	3 (15.0)	1 (3.0)	
Employment status	Unemployed	88 (69.8)	1 (100)	13 (72.2)	35 (64.8)	15 (75.0)	24 (72.7)	0.858
	Casual labourer	10 (7.9)		2 (11.1)	4 (7.4)	1 (5.0)	3 (9.1)	
	Formal employed	6 (4.8)		1 (5.6)	3 (5.6)	2 (10.0)		
	Self-employed	22 (17.5)		2 (11.1)	12 (22.2)	2 (10.0)	6 (18.2)	

[25] HEM, hemodialysis; PCN, percutaneous nephrostomy; PNH, Percutaneous Nephrostomy + Hemodialysis; None, No Intervention.
[26] *p*-value from the Chi-square test or Fisher's exact test for categorical variables and the Kruskal-Wallis test for continuous variables, two-sided; bold *p*-values indicate statistical significance ($p<0.05$).
[27] Single, divorced, separated.

Table 13:Gynaecological characteristics of study patients with obstructıve uropathy due to cervıcal cancer, stratified by procedures done at Kenyatta National Hospital, Nairobi, 2014 – 2019

Variable	Level	All patients	Procedure performed[28]					
			JJ stent	HEM	PCN	PNH	None	*p*-value[29]
All patients N (%)		128	1 (0.8)	19 (14.8)	55 (43.0)	20 (15.6)	33 (25.8)	
Parity	≤2	22 (17.5)		6 (31.6)	8 (14.8)	6 (30.0)	2 (6.2)	0.305
	3-5	77 (61.1)	1 (100)	10 (52.6)	33 (61.1)	10 (50.0)	23 (71.9)	
	≥6	27 (21.4)		3 (15.8)	13 (24.1)	4 (20.0)	7 (21.9)	
FIGO class	IIB	6 (4.7)			3 (5.6)		3 (9.1)	0.807
	IIIA	2 (1.6)			1 (1.9)		1 (3.0)	
	IIIB	80 (63.0)	1 (100)	14 (73.7)	31 (57.4)	15 (75.0)	19 (57.6)	
	IVA	31 (24.4)		4 (21.1)	17 (31.5)	4 (20.0)	6 (18.2)	
	IVB	8 (6.3)		1 (5.3)	2 (3.7)	1 (5.0)	4 (12.1)	
HIV status	Negative	73 (70.2)	1 (100)	10 (58.8)	28 (65.1)	14 (73.7)	20 (83.3)	0.364
	Positive	31 (29.8)		7 (41.2)	15 (34.9)	5 (26.3)	4 (16.7)	
HIV+ve, highest CD4 count	Median (IQR)	480.0 (252.0)	–	518.0 (47.0)	480.0 (294.5)	266.0 (0.0)	307.0 (57.0)	0.337
HIV-ve, lowest CD4 count	Median (IQR)	236.0 (163.0)	–	236.0 (225.0)	252.0 (342.0)	164.5 (57.5)	244.0 (0.0)	0.841
History of pap smear	No	85 (88.5)	1 (100)	11 (78.6)	40 (88.9)	14 (87.5)	19 (95.0)	0.611
	Yes	11 (11.5)		3 (21.4)	5 (11.1)	2 (12.5)	1 (5.0)	
Histological type	SCC	124 (96.9)	1 (100)	19 (100.0)	53 (96.4)	19 (95.0)	32 (97.0)	1.000

[28] HEM, hemodialysis; PCN, percutaneous nephrostomy; PNH, Percutaneous Nephrostomy + Hemodialysis; None, No Intervention.

[29] *p*-value from the Chi-square test or Fisher's exact test for categorical variables and the Kruskal-Wallis test for continuous variables, two-sided; bold *p*-values indicate statistical significance ($p<0.05$).

5.0 CHAPTER FIVE: DISCUSSION, CONCLUSION & RECOMMENDATIONS

5.1 Discussion

Obstructive uropathy is one of the more common complications of advanced cervical cancer. İt impacts negatively on the prognosis of the disease. In 2022 *Damian et al* concluded that the mean overall survival was 19.2 months and 10 months in patients with unilateral and bilateral obstructive uropathy respectively. [38] In 2013 a study by *Maranga I.O et al* showed a two-year survival rate of <20%[5]. This is in contrast to our findings which noted that 50.4% of our study population were still alive at two years after diagnosis of advanced cervical cancer. This could be due to advances, more accessibility, and increased frequency of the post-diagnosis interventions being done at Kenyatta National Hospital.

The median age at the time of diagnosis in our study was 48 years. This is comparable to *Van Aardt et al. 2017, Patel 2015et al., and Texeira et al. 2019* which were 49.5, 49, and 48 years respectively. The most prevalent histological type in our study was Squamous cell carcinoma at 96.9%. This is similar to *Maranga IO 2013, Elizabeth et al. 2021, and Damian et al. 2022* who found 89.8%, 98%, and 90.1% respectively.

There is a need to relieve the obstructive uropathy and subsequent hydronephrosis to correct the renal dysfunction [26]. This allows the patients to undergo the planned treatment which is mostly for palliative or definitive chemoradiation.[28] The two-year survival rate post-diagnosis of those who had intervention in our study was 57.4% compared to those who didn't. This is in line with *Mashadi et al.,2018* findings where the death risk was 2.43 times higher in patients who did not undergo PCN compared to those who did. This is in contrast to *Goklu et al 2015* which showed that the patients with hydronephrosis who underwent nephrostomy or not had similar Mean Overall Survival duration.[39] This could be explained by the baseline differences between the groups and the overall poorer prognosis of their study population.

The most commonly performed intervention post-diagnosis of obstructive uropathy was percutaneous nephrostomy tube insertion at(PCN alone 43% and PNH 16%) in our study. This is comparable to *Paula de Souza et al. 2016* and *Maguire et al. 2019* where it was noted that Percutaneous nephrostomy was the most commonly performed intervention at 69% and 68% respectively. İn 2019 *Tan S et al 2019*[40] compared the use of ureteral stenting and percutaneous nephrostomy tube insertion and concluded that PCN had fewer complications and was better in bulky disease.

Reasons for not undergoing interventions to manage obstructive uropathy were more clinical 78.9% than socioeconomic. Anaemia 46.5% and death before intervention 27% were more common reasons compared to financial issues at 19.7%. this is in contrast to *Yang YR et al 2021*[41] where the leading comorbidities were Diabetes, Hypertension, and chronic kidney disease. This can be explained by the differences in study site and population (high-income vs. lower-income countries). Delays in blood transfusion were common in our study populations which impacted whether the post-diagnosis interventions were done in particular percutaneous nephrostomy where a hemoglobin level of >10g/dl is needed before the procedure is done.

they had to undergo hemodialysis after PCN insertion. In 2017 *Van Aardt et al* 10% of the patients did not commence treatment post intervention. Of the patients who underwent PCN 57% went on to get treatment. Around 10% of patients post percutaneous nephrostomy insertion patient's renal functions did not improve and they went on to have hemodialysis. In 2005 *Romero et al* noted that 60.5% of the patients who underwent PCN due to malignant ureteric obstruction went home and were ready to undergo the planned treatment. These studies resonate with our findings in terms of the patients who went on to get treatment after interventions and those who went for hemodialysis after worsening renal functions. Percutaneous nephrostomy was the most common intervention and this could explain why many patients in this group went on for post-intervention treatment.

The two-year survival rate analyzed as per intervention was 64%, 58%, and 36.8% for percutaneous nephrostomy, hemodialysis, and percutaneous nephrostomy+ hemodialysis respectively. The two-year survival rate in those who didn’t undergo any intervention was 15.6%. There was statistical significance in the two groups AOR ($p = 0.002$). In 2018 *Mashadi et al* noted the median overall survival of 44 patients who underwent percutaneous nephrostomy was 203 days with a probability of survival at 6 months at 56.9% and 12 months at 31%. The median survival of 26 respondents who did not undergo percutaneous nephrostomy was 75 days with a chance of survival at 6 months 26.6% and 12 months 10% by 31.1%. There was a significant association between percutaneous nephrostomy and survival ($p = 0.0470$, $\alpha = 0.05$. This study had similar conclusions to ours in that the patients who did not undergo any intervention had a worse prognosis compared to those who did. It differed in the survival rates in the intervention group which was lower in their study. This could be due to differences in the sample size population and the short duration of follow-up in their study which was 1 year.

5.2 Conclusion

Malignant obstructive uropathy due to advanced cervical cancer impacts negatively on the prognosis of the disease. In our study, we found a two-year survival rate of 50.4%. This was higher compared to most studies but most of them were not evaluating the two-year survival.

There are various interventions done to relieve the obstruction. In our study at Kenyatta National Hospital and indeed worldwide percutaneous nephrostomy tube insertion was the most commonly performed post-diagnosis intervention to relieve the obstruction. For those whose renal functions did not improve hemodialysis was afforded to them and the combination of the two procedures made up for the second most performed procedures.

In our study, we noted that it significantly improved the two-year survival rate compared to those who did not undergo any intervention or when compared to other modalities used to manage obstructive uropathy like hemodialysis.

It was also noted that post-diagnosis intervention improved most patients' condition and they went on to receive palliative or definitive treatment compared to those who did not undergo any intervention. The percutaneous nephrostomy insertion group had the most patients going on to get definitive or palliative treatment. Radiotherapy alone was the most performed treatment modality. In our study, clinical reasons contributed the most to why patients did not undergo post-diagnosis interventions compared to financial reasons. Anemia was the most prevalent condition hampering interventions. It was also noted that some patients died while awaiting interventions to be done. However, these two factors didn’t have a significant statistical impact on the two-year survival rate.

The two-year survival was higher in the intervention group compared to the No intervention group. Percutaneous nephrostomy statistically significantly increased the two-year survival of the patients. Those who did not undergo any interventions had a poorer prognosis.

The majority of our patients (88%) did not have a Papanicolaou smear done at the time of diagnosis. Most of the patients in our study were HIV-negative. These factors didn't have statistical significance on the two-year survival rate.

At the time of diagnosis, most patients presented at FIGO stage III b. It was noted that the two-year survival rate was significantly and statistically impacted by the stage at diagnosis. Stage III b and above had a worse prognosis.

5.3 Study Limitations

Due to the retrospective nature of the study missing data was a common occurrence. Some files had conflicting data on histological type and FIGO staging. Most patients were treated in at least two departments in the hospital with different file numbers. Some patients were lost in between the departments like a patient seen in the obstetrics and gynecology department and was sent to for radiotherapy in the radio oncology department and the file could not be traced between the two departments. Some patients were lost to follow-up. Upon calling their contact phone numbers or those of their next of kin registered in the patient's file we could not get a reply. We could not assess their 2-year survival rates. Adaption of the FIGO staging system in 2018 further subclassified stage III into a, b, and c with the latter having a poorer prognosis. Some files may have been lost to stage III c during collecting data.

5.4 Recommendations

Harmonizing patient records between the Obstetrics and Gynecology and Radio-oncology departments for ease of follow-up of patients after discharge from one department. Many patients' files could not be traced from one department to another. Prompt and timely blood transfusion to reduce delays in doing post-diagnosis interventions. Anemia was the most found clinical reason for not undergoing timely interventions or no intervention at all. Review the pricing of post-diagnosis procedures to make them more accessible to more patients with obstructive uropathy. Financial reasons also played a role in patients not undergoing the necessary interventions to relieve the obstruction. Public sensitization to increase awareness about cervical screening to capture any cervical abnormalities early**.** The rate of pap smear done at the time of diagnosis was very low.

5.5 Declaration of Competing Interest

There were no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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APPENDICES

Appendix I: Data Abstraction Sheet

Section A: Socio-Demographic Data

Study Number: ..... **Age:** .....

Marital Status: ☐ Single ☐ Married ☐ Divorced ☐ Separated
☐ Widowed ☐ Not Indicated

Religion: ☐ Christian ☐ Muslim ☐ Not indicated ☐ Others
If Others, specify …….

Education Level: ☐ Primary ☐ Secondary ☐ Tertiary Institution
☐ No Formal Education ☐ Not Indicated

Employment Status: ☐ Formal Employment ☐ Self-Employment
☐ Casual laborer ☐ None
☐ Not Indicated

Section B: Clinical Characteristics

Parity: ☐ ≤ 2 ☐ 3-5 ☐ ≥ 6 ☐ Not indicated

FIGO Classification: ☐ IIb ☐ IIIa ☐ IIIb ☐ IIIc ☐ IVa ☐ IVb

HIV STATUS: ☐ **HIV Positive**

If positive:

Highest CD4 count recorded …….. ☐ Not Recorded

Lowest CD4 count recorded ……. ☐ Not Recorded

☐ **HIV Negative**

☐ **Not Indicated**

History of Pap Smear: ☐ Yes ☐ No ☐ Not indicated.

Histological Type: ☐ SCC ☐ Adenocarcinoma ☐ Others

If others, specify ……

Comorbidities: ☐ Hypertension ☐ Diabetes ☐ Anaemia ☐ Deep Venous Thrombosis ☐ None ☐ Others

If others, specify ……

……

Procedure Done: ☐ Percutaneous Nephrostomy ☐ Hemodialysis ☐ Percutaneous Nephrostomy + Hemodialysis ☐ No Intervention ☐ Others

If others, specify …….

What is the time duration between diagnosis and the start of intervention?

☐ Nephrostomy …….. weeks

☐ Hemodialysis ……. weeks

Post Nephrostomy, did the patient proceed to get further treatment?

☐ Yes ☐ No

If yes, what treatment did she receive? ☐ Chemotherapy ☐ Radiotherapy ☐ Chemoradiation ☐ None

Did the patient have a repeat Nephrostomy?

☐ Yes ☐ No

If yes, how many times?.....

Reason(s)……

……..

If the patient had hemodialysis, did she get ☐ Chemotherapy ☐ Radiotherapy ☐ Chemoradiation ☐ Nephrostomy ☐ No Intervention?

Did the patient have repeat hemodialysis at a different time from the one specified above?

☐ Yes ☐ No

If yes, how many times?

Reason(s) …….

……..

Reasons for No Intervention ☐ Financial ☐ Anemia ☐ Coagulation derangement ☐ Others

If others, specify reason …….

……

…….

Point of 1st intervention

		Nephrostomy	Hemodialysis	P value
Pre	Chemotherapy			
	Radiation			
	Chemotherapy			
	Chemoradiation			
post	Chemotherapy			
	Radiation			
	Chemoradiation			
FIGO Staging	IIb			
	IIIa			
	IIIb			
	IIIc			
	IVa			
	IVb			

Appendix II: KNH/UoN-ERC Letter of Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel (254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/348

30th September, 2021

Dr. Edwin Mwabe Mochama
Reg. No.H58/7461/2017
Dept. of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 30 SEP 2021 P.O. BOX 20723 - 00202 NAIROBI KNH/UoN ERC

Dear Dr. Mochama

RESEARCH PROPOSAL: MANAGEMENT, OUTCOMES AND SURVIVAL OF PATIENTS WITH OBSTRUCTIVE UROPATHY DUE TO CERVICAL CANCER ADMITTED AT KENYATTA NATIONAL HOSPITAL (2012-2019) (P519/06/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 30th September 2021 – 29th September 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoNERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
vii. Submission of an executive summary report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L CHINDIA
SECRETARY, KNH- UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Obstetrics and Gynaecology, UoN
Supervisors: Prof. Ojwang' Shadrack B., Dept. of Obstetrics and Gynaecology, UoN
Prof. Peter Michoma, Dept. of Obstetrics and Gynaecology, UoN