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Prognosis of Hydronephrosis in Cervical Cancer at the Libreville Cancer Institute

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Abstract: Introduction: In Gabon, cervical cancer is second only to breast cancer. Urological complications such as ureteral obstruction and hydronephrosis can occur in the course of this pathology. This work aimed to evaluate the impact of hydronephrosis on the overall survival of patients. Patients and Methods: the records of patients followed at the ICL from January 1, 2015, to December 31, 2019, a period of 5 years, were collected. The study included patients followed for cervical cancer and who had a complete medical record: histological evidence and extension workup. Patients not followed up at ICL were not included in the study. Results: the records of 183 patients with cervical cancer during the study period were retained. The mean age was 55.3±14.1 years, with extremes of 21 and 89 years. Stages II, III, and IV accounted for 87.4% of cancers, and stages III and IV (51.3%) represented the majority of clinical stages. In univariate survival analyses, assessed from the date of cancer diagnosis, patients with hydronephrosis during their cancer had poor survival compared with those without. Patients who had no hydronephrosis had better overall survival at three years (85%) compared with those who had developed urologic complications (54%). Conclusion: hydronephrosis has a negative effect on the prognosis of cervical cancer, and indeed, it significantly decreases the overall survival of patients with cervical cancer. Therefore, it is essential to screen them systematically to treat them as effectively as possible.

Keywords: Prognosis, Cervical Cancer, Hydronephrosis, Survival

1. Introduction

Cervical cancer remains the fourth most common cancer among women worldwide, with 604,127 new cases and 341,831 deaths estimated in 2020 [1]. In Gabon, cervical cancer ranks second after breast cancer, with a prevalence rate of 53.6/100,000 women in 2020 [1]. The evolution of this cancer can be marked by the appearance of urological complications, in particular ureteral obstruction, hydronephrosis, renal insufficiency, vesicovaginal fistula, and urinary infections. These complications appear in advanced stages of the disease and worsen the morbi-mortality of patients. [2, 3]. Some of these complications are related to the direct spread of the cervical tumor, while others develop as complications of the surgery, radiation therapy, or both [3]. Tumor infiltration of the bladder and ureters or extrinsic compression of the ureter by adenopathy leads to ureterohydronephrosis and renal failure. Thus, in 14 to 44% of cervical cancer cases, cancer-related obstructive uropathy is encountered. It is a frequent cause of mortality following this pathology [4]. Indeed, ureteral obstruction is known to be associated with a poor prognosis in locally advanced

cervical cancer [5]. There are limited data on the prognosis of ureterohydronephrosis in cervical cancer in Africa [3, 6, 7] and none concerning Gabon, hence the interest of this study. Thus, the objective of this study is to evaluate the prognosis of patients with cervical cancer complicated by hydronephrosis.

2. Patients and Methods

The study for cervical cancer was conducted among women treated at the Libreville Cancer Institute (Institut de Cancérologie de Libreville ICL). The ICL is the only national cancer treatment center in Gabon. The patients who are followed up for cervical cancer come from doctors, particularly gynecologists, from all over the country and even from neighboring countries who send them there.

Patients with a histological diagnosis of cervical cancer were included in this study. The extension workup for cervical cancer included a thoracic-abdominal-pelvic CT scan. The diagnosis of ureterohydronephrosis was made on ultrasound and/or CT scan. The clinical staging of the patients had been done based on the F. I. G. O 2018 classification.

A retrospective, longitudinal, descriptive, and analytical observational study was performed in patients followed at ICL over five years from January 1, 2015, to December 31.

The data collected from the patients retained in this study included sociodemographic characteristics, clinical characteristics including the different urological complications observed, the treatment administered, the follow-up times, and the patient's evolution.

Data collected were entered into a previously designed database using Epi info 7 software, and analysis was performed using Stata 12.0 software (Stata Corp LP, College Station, Texas 77845 USA).

Categorical characteristics were described using percentages and quantitative characteristics using the mean (±standard deviation). Comparison of proportions was performed using Pearson's Chi 2 test or Fisher's Exact test. We performed a survival analysis using the Kaplan Meier method to assess the prognosis of patients with urologic complications after cervical cancer. The comparison of the curves was made using the Log-Rank test. The significance level for all analyses was 5%.

The director of the ICL authorized this study. Access to the patients' files was restricted to the principal investigator to preserve the patients' medical information confidentiality.

3. Results

There were 183 patients with cervical cancer included during the study period. The mean age was 55.3 (±14) years.

Among the 183 patients, 84 (45.9%) had at least one urologic complication. Hydronephrosis was found in 82 (45.0%) patients; it was unilateral right in 13 (15.5%) women, unilateral left in 13 (15.5%) women, and bilateral in 56 (66.7%) women. Fifteen (17.9%) women had a vesicovaginal fistula (VVF) (Table 1). Of 82 patients with hydronephrosis, 66 (80.5%) had developed renal failure. Renal failure was either associated with hydronephrosis or related to the treatment received (radiotherapy or chemotherapy).

The anatomopathological study allowed us to distinguish three histological types of cervical cancer: squamous cell carcinoma, which represented 83.6% (153) of cases, followed by adenocarcinoma with 9.8% (18) and squamous cell carcinoma with 6.6% (12) of cases. Stages II, III, and IV accounted for 87.4% of cancers. Stages III and IV (51.3%) represented the majority of clinical stages (Table 1).

The majority of patients, 79.8% (146), had a low socioeconomic status.

Table 1. *Clinical characteristics of patients with cervical cancer at the Libreville Cancer Institute during 2015-2019.*

Characteristics	Number (n)	Proportion %
Age in years (average)	55.3±14.1	
Socio Economic Status		
Low	146	79.8
Medium and High	37	20.2
Comorbidities		
HYPERTENSION	37	16.4
Diabetes	14	3.8
HIV	40	21.5
Histology		
Squamous Cell Carcinoma	153	83.6
Adenocarcinoma	18	9.8
Squamous Cell Carcinoma	12	6.6
Cancer Stage		
I	23	12.6
II	66	36.1
III	33	18
IV	61	33.3
Urological Complications		
Left hydronephrosis	13	13.4
Right hydronephrosis	13	13.4
Bilateral rohydronephrosis	56	57.8
Vesicovaginal Fistula	15	15.4
Treatment of hydronephrosis		
JJ Catheterization	25	30.5
Nephrostomy	12	14.6
Ureterostomy	1	1.2
No Procedure	44	53.7

Out of 82 patients who developed hydronephrosis, 25 (30.5%) had received a double J catheterization and 12 (14.6%) a percutaneous nephrostomy (Table 1).

At the end of the study, 126 (68.9%) patients were alive, and 57 (31.1%) had died. Among the deceased patients, 49 (86%) had urological complications. 5-year survival was associated with the clinical stage of cervical cancer, the more advanced the stage, the worse the survival. There was a statistically significant association between 5-year survival and clinical stage (*p=0.000*). Thus, the more advanced the clinical stage, the worse the overall survival at five years (Figure 1).

Patients with hydronephrosis had poorer survival compared to those without (p=0.000) (Figure 2).

Patients with no hydronephrosis had better 5-year survival than those who developed hydronephrosis (Figure 3). Patients with hydronephrosis associated with renal failure had poor 5-year survival (39%) than those without (78%).

There was a significant association between 5-year survival and the presence of hydronephrosis associated with renal failure. Thus, the 5-year survival was significantly shorter in the presence of renal failure and hydronephrosis (p=0.003).

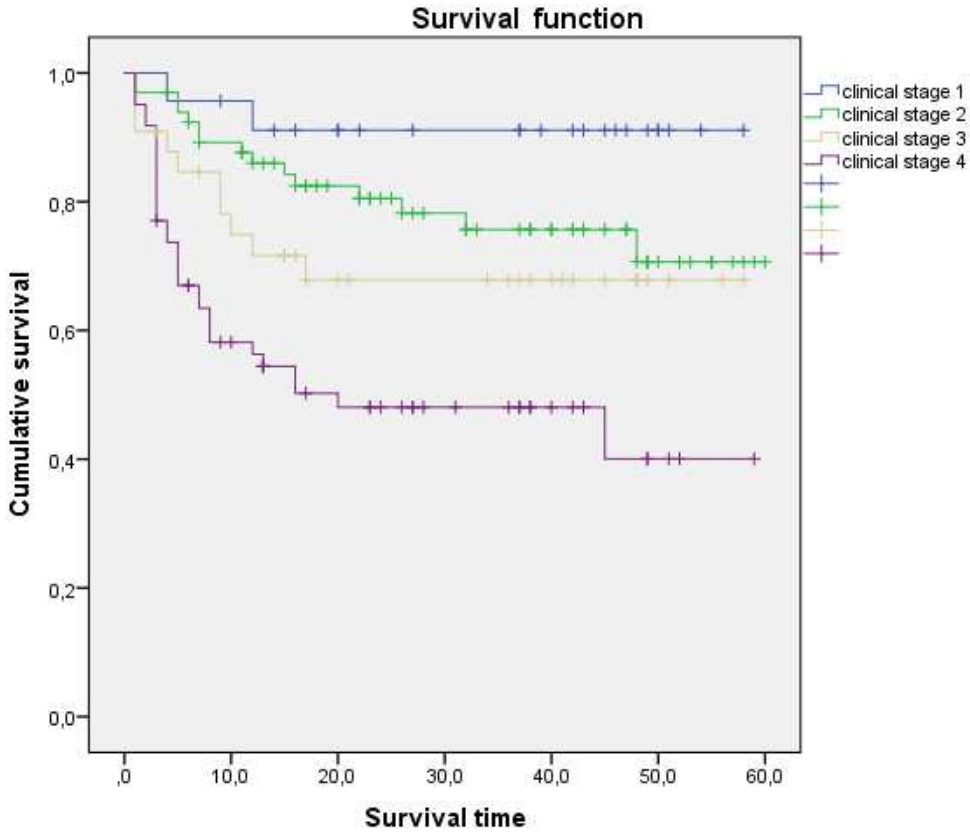

Figure 1. *60-month survival of patients according to clinical stage of cancer.*

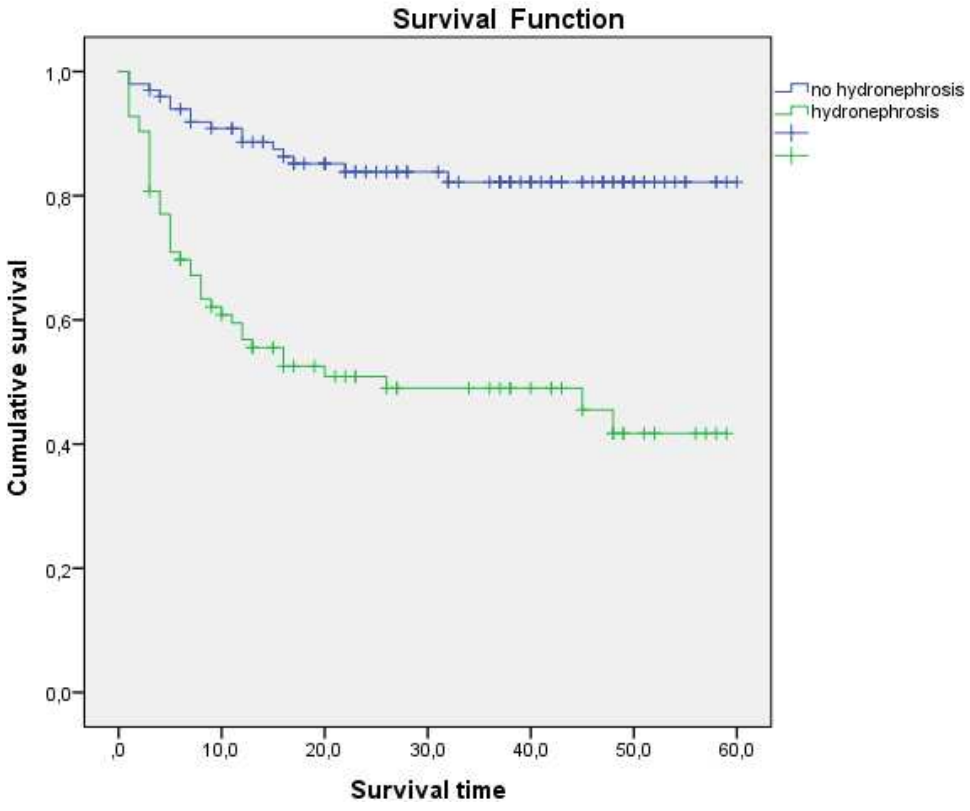

Figure 2. *60-month survival of patients with urological complications.*

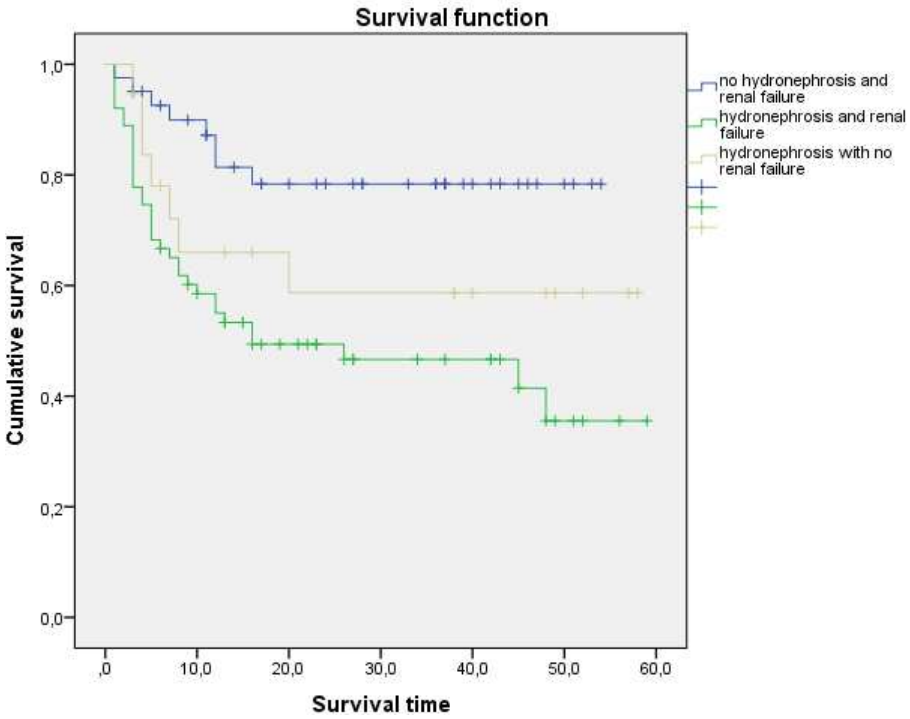

Figure 3. *60-month survival of patients without hydronephrosis and with hydronephrosis associated or not with renal failure.*

4. Discussion

In the present study, the mean age was 55.3±14.1 years, with extremes of 21 and 89 years. Our results are superior to those of Atuhairwes et al. in Uganda [3] and Lankoande et al. in Burkina-Faso, who reported a mean age of 49.4 and 48 years, respectively [8]. In France, in 2018, 40% of cervical cancer cases were diagnosed in women younger than 50 years, the median age at diagnosis was 53 years, and the highest incidence was observed in women aged 45-49 years [9]. Similarly, Bannour et al. in Tunisia found a median age of 54 years [6] with two peaks in frequency during the fourth and sixth decades of life of 28.1 and 30.2%, respectively.

The prevalence of low socioeconomic status (79.8%) in our study is lower than that of Atuhairwe et al. [3], where it was 82.7%. The same was true in the study conducted by Lankoande et al. [8], where 92.5% of the patients were without gainful occupation. Cervical cancer is most often found in the lower socioeconomic classes [8]. These low socioeconomic women often have limited income, limited access to health services, poor nutrition, and limited knowledge of health issues and preventive behaviors [8]. Poverty and ignorance about the disease have been documented as solid predisposing factors for late presentation [3].

The majority of cancers were diagnosed at advanced stages, with 51.3% of cases (stage III and IV). This result is close to that of Bannour et al. [6], who reported 56.3% of late stages.

The prevalence of urological complications was 45.9% in the present study, close to the 48.8% found by Atuhairwes et al. [3]. Similarly, Lee et al. [10] and Gloku et al. [11] reported prevalences of urological complications of 55.8% and 44.8%, respectively. The high proportion of urological complications such as hydronephrosis is due to our study's high proportion of advanced stages. In our study, 36.1% of the patients had renal failure, including 80.5% of those with hydronephrosis. However, in the study by Artuhairwe et al. [3], 17% of patients had renal failure, and women with hydronephrosis were 4 times more likely to develop renal failure.

We found a significant difference in 3-year survival between patients who developed urologic complications (54%) and those who did not (85%). This finding had also been made by Patel et al. [12], who had demonstrated in univariate survival analyses that patients with cervical cancer complicated by hydronephrosis at any time in their carcinological history had poor survival compared to those without this complication. Their 3-year survival rates were 37% and 74%, respectively, for those with and without UHN ($p=0.002$). These results are also similar to a study by Goklu et al. [11] which showed that for patients with hydronephrosis, the mean survival was significantly shortened ($p<0.05$). However, there was no significant difference in survival between patients with bilateral and unilateral hydronephrosis ($p>0.05$). Hydronephrosis has been identified as a predictor of poor survival in patients with cervical cancer [11]. In the study by Pradhan et al. [13] of 143 cervical cancer patients, 39 (27%) had unilateral hydronephrosis, and 31 (21.6%) had bilateral hydronephrosis. Survival was significantly shorter in those with hydronephrosis. According to a systematic review of the literature by Pergialiotis and al [14], the overall survival of malignant obstructive uropathy remains extremely limited in patients with limited in patients with gynecologic malignancies.

In the study of Maguire and al [15], after adjusted for stage of disease, the hazard ratio for mortality was 2, 3 times higher for cervical cancer patients who developed ureteric obstruction.

Renal function status was significant in predicting 5-year survival, and this was reduced by 39% when patients had hydronephrosis complicated by renal failure. These results indirectly reflect the negative effects of hydronephrosis on survival.

Cumulative survival at five years was 91% in stage I and 49% in stage IV —the more advanced the cancer stage, the worse the survival. The clinical stage had a significant correlation with survival ($p<0.05$). Other authors such as Hopkins et al. [2] and Pradhan et al. [13] had already made this observation. In the multivariate model of Pradhan et al. [12], the cancer stage was the only statistically significant prognostic factor ($p=0.0036$) in the survival of patients with cervical carcinoma. The clinical stage of the tumor is an important prognostic factor in the survival of these patients.

Another urologic complication, vesicovaginal fistula, was present in 8.2% of patients. Atuhairwes et al. [3] and Ramadhani et al. [7] had noted lower prevalences than ours, respectively 3.9% and 6.4%. Nevertheless, gynecological fistulas remain rare and predominate in advanced stages (stage III and IV).

Ureteral obstruction was the most common urologic complication. Thus, of the 82 patients who presented with hydronephrosis, 25 received a double J catheterization, 10 a nephrostomy catheterization, and only one a ureterostomy. The low number of procedures compared with the management of ureteral obstructions was due to; the alteration of the patient's general condition, which prevented the administration of anesthetic drugs in the operating room, the invasion and/or non-visualization of the ureteral meats at cystoscopy, which did not allow the fitting of a double J catheter and by the cost of the material (nephrostomy kit, double J catheter) and of the surgical intervention which was not negligible in patients with a low socio-economic status. This material (double J catheter, nephrostomy kit) has a high cost in our context and needs to be changed regularly, hence the difficulty for some of our patients to obtain it. In the study carried out by Goklu et al. [11], 18 patients were treated with a double J catheter and 10 with percutaneous nephrostomy. In the study by Hopkins et al. in Michigan [2], in 18 patients with obstructive renal failure, 15 patients had percutaneous nephrostomy implanted, which was the preferred procedure, and one patient had cutaneous ureterostomy. There is no consensus on the preferred method of urinary drainage nor on the ideal time to do it [12]. But Van Aardt [16] observed that nephrostomy may benefit patients with uremia and primary untreated locally advanced disease, as it may restore blood urea nitrogen levels to normal and thus, permit adjuvant treatment like chemotherapy and radiotherapy that may prolong the survival of these patients. However, the double j catheter seems to provide the most comfort in terms of social life and the precautions necessary for this equipment, unlike the nephrostomy catheter, which requires more careful maintenance. Nevertheless, the JJ catheter is not without some morbidity, as Patel et al. [11] reported. Somes authors [17] observed that patients with hydronephrosis have the same median overall survival regardless of having been submitted to urinary diversion or not, wich may be explained by baseline differences between the groups and a poor prognosis overall in that population. For them should always be performed when required because it allows to perform an adjuvant treatment.

5. Recommendations

Hydronephrosis has a worse impact on the overall survival of patients with cervical cancer. further studies should allow us to determine the ideal time to urine diversion in case of obstruction, in order to possibly improve the survival of these patients. Moreover, it is essential to look for this complication in the follow-up of these patients.

6. Conclusion

Hydronephrosis have a negative effect on the prognosis of cervical cancer. Indeed, he significantly decrease the overall survival of these patients, and their frequency increases with the clinical stage. Therefore, it is essential to detect them systematically to treat them as effectively as possible by installing a double J catheter or a percutaneous nephrostomy to reduce their deleterious effect.

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