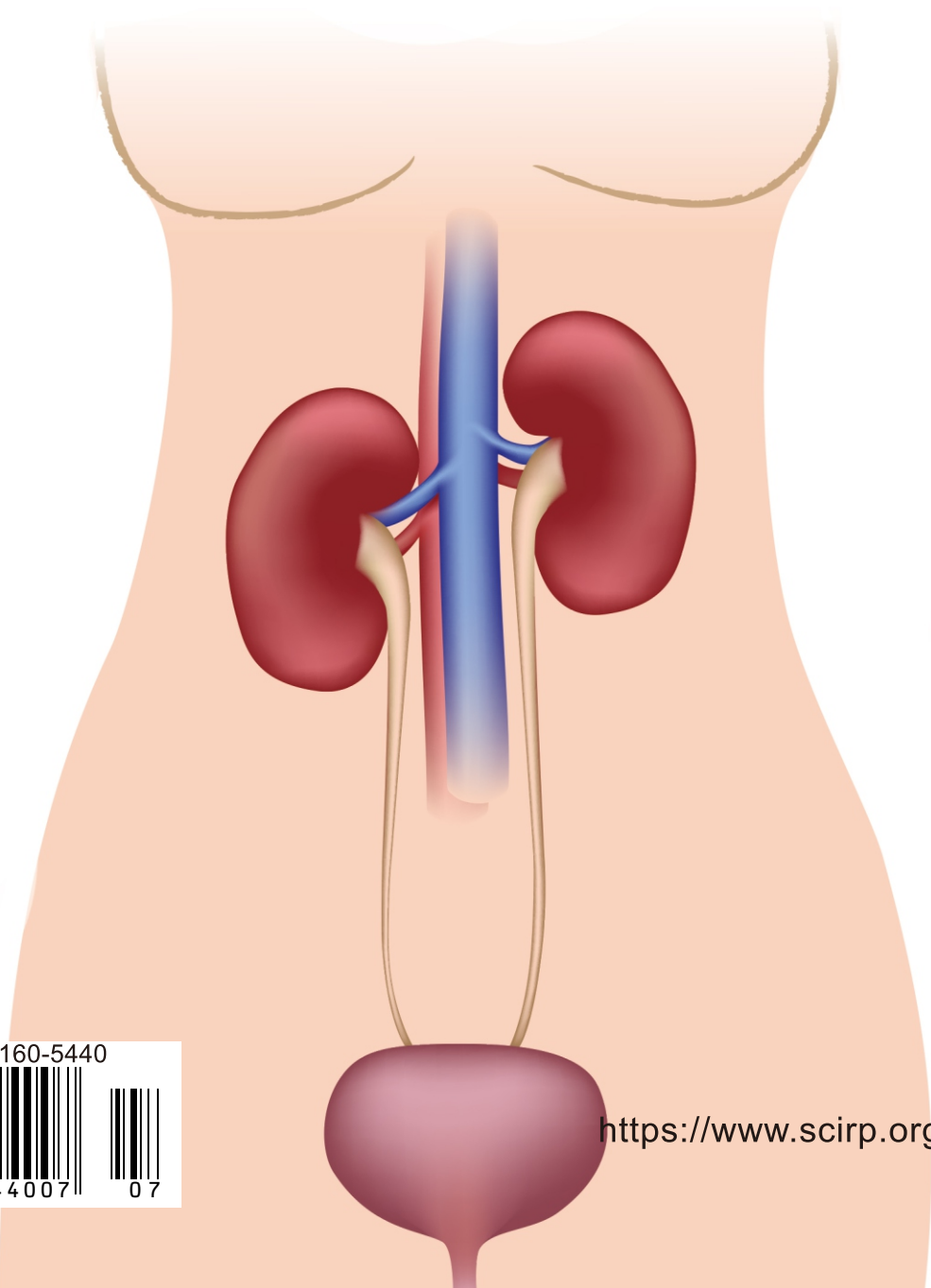


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Urinary Lithiases: Epidemiological, Clinical and Therapeutic Aspects of 164 Cases at Sheikh Zayed Hospital in Nouakchott—Mauritania

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Abstract

Urinary lithiases occupy an important position with respect to urological activities in our department. In our Sahel region, lithiasic pathology represents 40% in urology in Senegal [1]. In Mauritania, we did not find a study evaluating the prevalence of this pathology. The frequency and gravity are variable. The objective of the study was to report the clinical profile and the results of management of urinary lithiasis in our environment. **Materials and Methods:** We conducted a retrospective, descriptive study spanning over two years (April 2015 to March 2017) in the urology department of Sheikh Zayed Hospital in Nouakchott. All patients operated for urinary lithiasis during this period were included in the study. The operative techniques used were semi rigid ureteroscopy, extra corporeal lithotripsy, open surgery. Our center did not have flexible ureteroscopy and percutaneous nephrolithotomy. The indications were lithotripsy for calculations lower than 20 mm of low density. Bigger than 20 mm were by open surgery. Semi rigid ureteroscopy for distal ureteral calculi. Medical treatment or monitoring for non-obstructive calculi is less than 7 mm. Urine drainage by JJ probe or nephrostomy are performed. We excluded all patients with lithiasis for the medical treatment. The result was good when absence of lithiasis residues was less than 7 mm and removal of the obstruction. **Results:** A total of 164 patients were found. The average age was 41 years, and F/M ratio was 1/10. Considering geographical origin, 82% of patients came from rural areas. The presenting complaint was mainly Lower Urinary Tract Symptoms (56%) and Renal Colicky Pain (31%). The bladder and kidneys were the most common (respective 45% and 35%) sites of stone location. Bilateral stones were 18%. Staghorn stones constituted 6% of the cases. Non steroidal anti-inflammatory treatment was administered in 82% of cases, while antibiotic therapy was administered in 32% of cases. Complications occurred in open surgery about 11% like parietal infection and

residual stones. 0.6% of ESWL got uretere obstruction that needed jj catheter. 4% of cystolithotomy had infection. **Conclusion:** Urinary lithiasis often consults at the complication stage. Minimally invasive techniques are limited in our service and offer less complication.

Keywords

Lithiasis, Urinary

1. Introduction

The epidemiological and therapeutic profile of urinary lithiasis depends on several factors including socioeconomic status of the country, level of medical care and climatic conditions [1]. This profile undergoes constant change. In Mauritania, few data is available on urinary lithiasis, which has an important place in the urologic activities carried out in our department. In our Sahel region, lithiasic pathology represents 40% in urology activity in Senegal [1]. Localization of stone is diverse and the treatment modalities are rapidly changing with technological evolution. The objective of our study was to report the clinical profile and the results of management of urinary lithiasis in our context.

2. Patients and Methods

We conducted a two-year retrospective study between April 2015 and March 2017 in the urology department of the Sheikh Zayed Hospital in Nouakchott. Our department has a small capacity of 12 beds, three urologists, and one resident. It is situated at the outskirts of Nouakchott with a high population density. All patients operated in our unit were included in the study. Diagnostic methods were uroscanner for lithiasis of the upper urinary tract. Ultrasound coupled with conventional radiology in bladder stones. The operative techniques used were semi rigid ureteroscopy, extra corporeal lithotrithy, open surgery. Our center did not have flexible ureteroscopy and percutaneous nephrolithomy. The indications were lithotrithy for calculations lower than 20 mm of low density. Bigger than 20 mm were by open surgery. Semi rigid urestroscopy for distal ureteral calculi. Medical treatment or monitoring for non-obstructive calculi and less than 7 mm. urine drainage by jj probe or nephrostomy are performed. We excluded all patients with stones treated medically. The result was good when absence of lithiasis residues less than 7 mm and removal of the obstruction Parameters studied was, age, localization, obstruction, choice of treatment, complications. Statistics analysis was IPSS.

3. Results

We treated 164 cases of urinary lithiasis, which represent of 28.1% of all patients operated in our department, and these involved several localizations of the uri-

nary system. The bladder (45%) and kidneys (35%) were the most frequent localizations (**Figure 1**). The mean age was 41 years and ranged from 2 to 84 years. The majority were in the range 20 - 40 years age with 43.9% of cases (**Figure 2**). The F/M ratio was 1/10. For geographical origin, 82% of patients came from rural area. The presenting complaints were mostly renal colicky pains (31%) and lower Urinary Tract Symptoms (52%) of cases were incidentally discovered during routine analysis (**Table 1, Figure 1**). Biological complications were found in 35% of cases (anemia, high creatinin); three of them were in chronic renal failure currently undergoing dialysis for renal parenchyma laminated following obstruction. Dilatation of the urinary tracts was observed in 37% of cases. Localization was bilateral in 18% of cases. Staghorn stone was found in 6% of cases (**Figure 3** and **Figure 4**), and one patient had the bladder completely filled

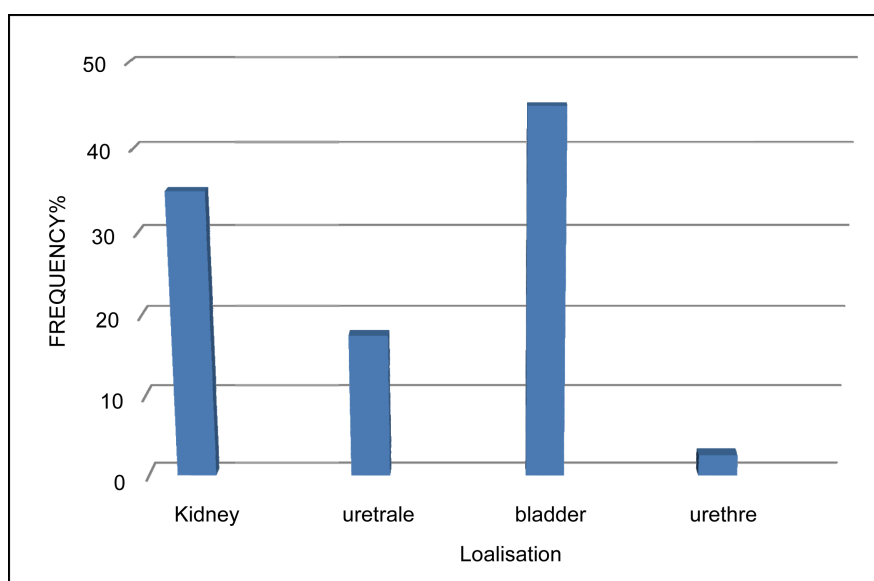


Figure 1. Localization of the stones in the urinary tract.

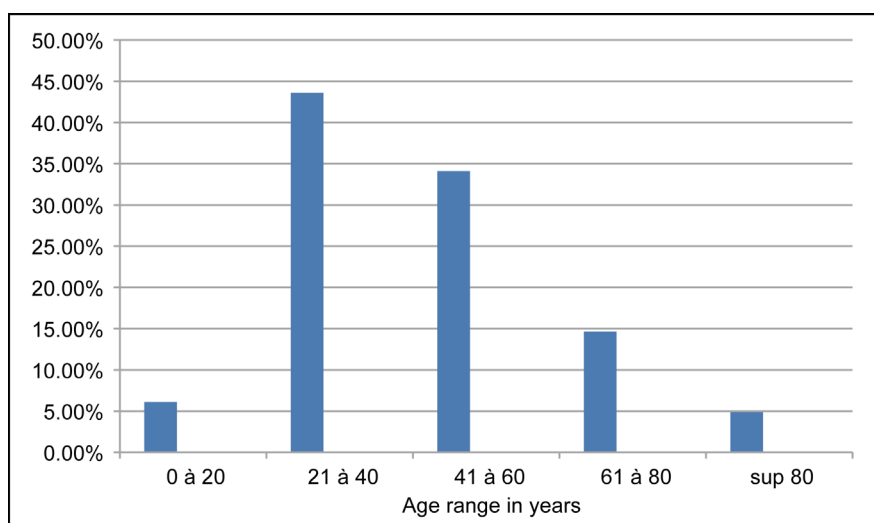


Figure 2. Distribution of patients according to age.

with a huge stone with severe bilateral uretero pyelocaliceal dilatation. The etiology of the stone was unknown in 48%, metabolic analysis for stone necessary for determine etiology. Bladder neck and prostatic obstruction in 35%, urethral stricture 10%, and ureteropelvic junction obstruction in 3.75% of cases. Urethral stricture and bladder neck contracture were the etiological factors associated with the huge stone which completely filled the bladder in one patient. The stone extracted weighed 480 g. (**Figure 5**). Before surgery, 38.7% of patients had received antibiotic treatment, specifically quinolones. Antibiotic therapy based on

Table 1. Distribution of patients according to presenting complaint.

Renal colicky pains	Lower Urinary Tract Symptoms	Hypogastric pain	Haematuria	Incidental finding	total
41.2%	25%	22.5%	8.7%	2.5%	100%



Figure 3. Bilateral radio-opaque stag-horn stone on a plain radiograph.



Figure 4. Bilateral staghorn after removal by open surgery.

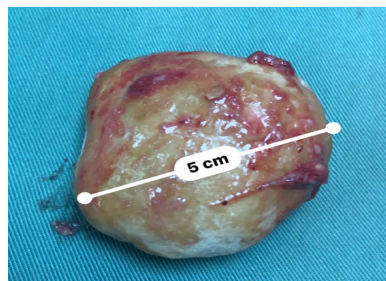


Figure 5. Bladder stone.

cytobacteriological examining or clinical signs of urinary tract infection. Non-steroidal anti-inflammatory drugs were prescribed to 80% of patients. Anti-inflammatory drugs are prescribed for analgesic purposes and apart from contraindications. Open surgery was performed in 87% of the patients, while 8 patients were re-treated using Extracorporeal Shock Wave Lithotripsy (ESWL).

Postoperative complications included hemorrhage in 2 cases of staghorn stone requiring blood transfusion. Two cases of residual kidney stones were secondarily treated with ESWL. Three patients developed a vesico-cutaneous fistula requiring prolonged bladder drainage and a long hospital stay. Abdominal wall infection was found in 3.7% of cases.

4. Discussion

Urinary stone disease varies according to climatic zones, feeding habits and the quality of drinkable water. In Congo, Odzebe [2] reported 68 cases over 4 years and Zoung-K [3] in Cameroon 118 cases over 4 years. Countries in Sahel seem to be more exposed than those in Central African region. In Senegal, Y Tfeil [4] found 30 children with urolithiasis over a 2-year period. The mean age varies between 30 - 50 years in the literature [5] [6]; Odzebe [2] found a mean age of 53 years. Majority of our patients were young, and age from 20 to 60 years was the mostly affected age range. Sex ratio varies according to different authors F/M 1/8 to 1/10 [4] [7]. Lower urinary tract symptoms were the most frequent presenting complaint followed by renal colicky pains.

The bladder was the common (45%) site of stone localization in this study. In Cameroon, 42% of bladder stones against 39% of renal stones [2]. Ureteral localization is very rare but with the remarkable symptom [8]. Staghorn are more frequent in our series, the authors find 01% to 04% [9] [10]. Bilateral urinary stones were 21% to Mali [11].

Imaging investigations usually reveal the diagnosis; ultrasonography usually done as first choice, coupled with plain kidney-ureter-bladder (KUB) radiography and or a computerized tomography urography scan (CTU) were the diagnostic tools in our series and in the literature [12] [13] [14]. Intravenous Urography was rarely requested. Staghorn stone and bilateral stone localization were common and required a search for etiology [15] [16]. There was a patient who presented with a poor general state carrying a huge stone occupying the entire bladder cavity on a urethral stricture. A 480 g stone adherent to the bladder wall was extracted. The etiological factors were sedentariness, lack of drinking water in rural areas, consumption of red meat; the hot and dry climate of the Sahel. Delay in consultation is an aggravating factor, favoring the occurrence of complications. Medical treatment with Non-steroidal Anti-inflammatory Drugs (NSAID) has been reported to between 48% to 72% in some series [17] [18]. Antibiotic treatment is used in cases of fever, cloudy or purulent urine, or positive urine culture [19] [20]. Microorganism commonly encountered includes *Proteus*, *K. Pneumoniae*, *Staphylococcus* and *E coli* [20]. In current practice, treat-

ment of urolithiasis is oriented towards minimally invasive techniques including ureteroscopy, ESWL and percutaneous nephrolithotomy (PCNL) [8] [19] [21]. Open surgery is reserved for some complex stones [22]. In our context, open surgery still has a major role due to the lack of minimally invasive equipments. All types of urinary drainage techniques were used in our series in emergency. Drainage in cases of obstruction was performed as a means of relief while awaiting surgery [23]. Hemorrhagic complications following conventional open surgery are reported to be rare in the literature [18] [24]. Vesicocutaneous fistula and wound infections are common, attributable to urine infection complicating urolithiasis [18] [25]. Postoperative drainage could be maintained until the urinary tract is completely sealed [25].

5. Conclusions

Urolithiasis is common in Mauritania, a country located in Sahel region, which is hot and dry. The quality of drinkable water is below standard in certain parts of the country. The feeding habits are based on red meat essentially, and a sedentary life style is some factors which favour the occurrence of stone.

Delayance before consultation and the absence of imaging equipments in all the cities could account for the occurrence of complex stones and the frequency of functional renal complications. Stone disease could be prevented by improving hygiene and dietary life style measures, curable by the development of non or minimally invasive therapeutic modalities.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Metastatic Prostate Cancer under Androgen Deprivation Therapy: Factors Influencing Castration Resistance

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Abstract

Objective: To evaluate the factors predicting the time to progression to castration-resistant in metastatic prostate cancer under Androgen Deprivation Therapy (ADT) in our center. **Patients and Methods:** This is a retrospective, descriptive, analytical study in a single center over a period of 2 years. It has interest patients followed for metastasized prostate cancer under ADT. The parameters studied were: epidemiological, clinical, paraclinical, prostate specific antigen (PSA) nadir, time to nadir (TTN) and their link with the castration resistance. **Results:** The frequency of castration resistant prostate cancer was 28 patients per year. The mean age was 70.4 ± 7.9 years. An ECOG score ≥ 3 was more common as was the cT2c stage. The median of the initial total PSA was 489.6 ng/ml (203.3; 1653.2). All patients had adenocarcinoma. The International Society of Urological Pathology (ISUP) 1 was more frequent. Bone metastases were more frequent. The medians of nadir, TTN and the castration resistance were 19.3 ng/ml (3.7; 102.1), 5.5 months (3; 9) and 11 months (6; 15.3), respectively. The Eastern Cooperative Oncology Group (ECOG) score, clinical stage, metastatic site, the nadir and its TTN influenced the DSR. Age, lymph node involvement, initial total PSA and Gleason score did not influence the castration resistance. **Conclusion:** ADT should be initiated as soon as possible before an attack of general and/or clinical stage advanced to delay resistance. A drilling should be associated with this hormone therapy as much as possible because of its gain on resistance.

Keywords

Cancer, Prostate, Androgen Deprivation Therapy, Resistance, Prognoses

1. Introduction

Prostate cancer is the most common cancer in older men, the second leading cause of cancer death after lung cancer and the fourth leading cause of cancer death in the general population [1]. In Senegal, most prostate cancers are diagnosed in locally advanced or metastatic stage [2] [3]. ADT the effects of which have been known for several years, is the cornerstone of the treatment of metastatic prostate cancer [4]. Bilateral pulpectomy remains the most common method in our context [2]. The hormone-sensitivity is limited in time and the biochemical progression usually takes place between 18 and 36 months after the start of hormone therapy [5]. Ten to 20% of prostate cancers progress to castration-resistant prostate cancer (CRPC) within 5 years of diagnosis, and more than 84% of newly diagnosed metastatic cancers would be CRPC [6]. The resistance to castration of metastatic prostate is now likely to be treated with new molecule. The CRPC poses a therapeutic problem in developing countries because of the accessibility and cost of these new molecules used at this stage. The objective of this study was to evaluate the factors predicting the time to progression to castration-resistant in metastatic prostate cancer under Androgen Deprivation Therapy (ADT) in our center.

2. Patients and Method

This is a retrospective, descriptive, analytical and single-center study, collecting the records of patients followed for metastasized prostate cancer between January 1, 2016 and December 31, 2017. ADT was: either medical, using analogues of luteinizing hormone-releasing hormone (Goserelin, triptorelin) or surgical, using bilateral testicular pulpectomy. A non-steroidal antiandrogen (bicalutamide) was used to complete the androgen blockade. The definition of CRPC in the CCAFU Oncology Recommendations 2016-2018 was used [7]. The general condition was evaluated by the ECOG (Eastern Cooperative Oncology Group) performance status score. Patients who had metastatic prostate cancer on hormone therapy with a complete history were included. Patients with metastatic prostate cancer receiving hormone therapy with an incomplete or unrecognized record and those with localized or metastatic prostate cancer without hormone therapy were not included. The parameters studied were: frequency, age, general condition, clinical T stage, initial total prostate specific antigen (PSA), International Society of Urological Pathology (ISUP) score 2014, lymph node involvement, metastatic sites, total PSA nadir and its TTN and their link with the castration resistance. IBM SPSS Statistics Viewer 20 software was used for statistical analysis. Prognostic factors were assessed by a multivariate analysis with the Chi-2 test

and the p value < 0.05 was considered to be statistically significant. The data were collected on a survey form from the files of patients followed in consultation or hospitalized in our department for metastatic prostate cancer under hormone therapy.

3. Results

Seventy-eight patients were included. Among them, 56 patients had CRPC. The frequency of CRPC was 28 per year. The mean age was 70.4 ± 7.9 years. The most common age groups were those between 60 and 70 and those between 70 and 80. A deterioration of the general condition with a higher ECOG score ≥ 3 was observed in 59% of patients. The clinical T stage of the tumor classified cT2c was more common, found in 55% of the patients followed by the stage cT4 observed in 36%. The median total PSA rate before treatment was 489.6 ng/ml (203.3 and 1653.2 ng/mL). Eighty-six percent (86%) of patients had a total PSA greater than 100 ng/ml. An adenocarcinoma was objectified in all patients and the ISUP score 1 was more common, found in 33% of patients. Fifty-one percent (61%) of patients did not have a regional lymph node assessment and regional lymph node involvement observed in 38% of thoracoabdominal-Computed Tomography (CT) patients. Bone metastases were more frequent, objectified in 43.6% of patients with bone scintigraphy. The median total PSA nadir was 19.3 ng/ml (3.7 and 102.1 ng/ml). The median TTN was 5.5 months (3 and 9 months). The median of the castration resistance was 11 months (6 and 15.3). Eighty-seven percent of the patients had surgical castration. This surgical castration was associated with a drilling in 19% of patients. The patients, who had surgical castration associated with drilling, had less resistance compared to the other patients (**Table 1**). This type of treatment influenced significantly ($p = 0.003$) the castration resistance. The deterioration in general condition with an ECOG ≥ 3 , total PSA nadir and its TTN, Metastatic sites and Clinical stage T influenced the castration resistance with significant p (**Table 1** and **Table 2**). The patients classified CT4 were 3 times more likely to develop resistance than others with odds ratio of 3.4 and a confidence interval 1.0 to 11.3. Patient age ($p = 0.120$), lymph node involvement ($p = 0.14$), initial total PSA rate, ISUP score did not affect the castration resistance with p which were not significant (**Table 3**).

4. Discussion

The frequency of castration resistant cancer is high in our center. This high frequency can be explained by the fact that our patients often come for consultation only at the late stage, therefore already metastasized [2] [3] [8]. In the literature, almost all prostate cancers progress to castration resistance to increasing serum PSA despite castrate levels of testosterone and progress to metastases [6]. Ten to 20% of prostate cancers progress to CRPC within 5 years of diagnosis, and more than 84% of newly diagnosed metastatic cancers are thought to be CRPC [5] [9]. The epidemiological profile of CRPC is difficult to determine due to the lack of

Table 1. Distribution of the type of treatment, the Gleason score and clinical stage based the castration resistance.

		Slice at castration resistance				Total	p
		Not resistant	<5	5 - 10	>10		
Type of treatment	Medical castration	4	1	0	4	9	0.003
	Surgical castration	9	3	27	15	54	
	Surgical castration + drilling	9	2	3	1	15	
	Total	22	6	30	20	78	
Score ECOG	0	0	0	1	0	1	0.010
	1.0	9	0	3	1	13	
	2.0	8	1	5	4	18	
	3.0	5	4	13	7	29	
	4.0	0	1	8	8	17	
	Total	22	6	30	20	78	
Clinical T stage	cT2b	0	0	0	4	4	0.019
	cT2c	16	3	8	16	43	
	cT3c	2	1	0	0	3	
	cT4	4	2	12	10	28	
	Total	22	6	20	30	78	

Table 2. Distribution of metastatic sites according to castration resistance.

		Slice at castration resistance				Total	P
		Not resistant	<5	5 - 10	>10		
Metastasis	M1a	0	0	0	1	1	0.04
	M1b	5	3	14	12	34	
	M1c	12	3	6	2	23	
	MX	5	0	10	5	20	
	Total	22	6	30	20	78	

Table 3. Distribution of the total PSA slice before treatment, the total PSA nadir tranche and the TTN according to castration resistance.

			Slice at castration resistance				Total	P
			Not resistant	<5	5 - 10	>10		
Slice total PSA	PSA < 100		1	0	4	3	8	0.500
	PSA ≥ 100		21	6	26	17	70	
	Total		22	6	30	20	78	
Slice total PSA nadir	<5		11	0	8	3	22	0.030
	5 - 10		11	6	22	17	56	
	Total		22	6	20	30	78	
Slice TTN	<2		1	3	1	1	6	0.000
	[2 - 5]		10	3	6	14	33	
	>5		11	0	23	5	39	
	Total		22	6	30	20	78	

standardized diagnostic models, reporting methods for CRPC and inconsistent terminology [10]. The average age of our series was similar to the average age of 73.3 ± 9.3 years found by Rigaud J *et al.* [11] when setting up their hormone therapy. Age was not a prognostic factor for the resistance that occurred in our series, which was consistent with the results of Mulders *et al.* [12]. However, Emrich *et al.* [13] found that age was a prognostic factor in their series. A deterioration in the general condition with an ECOG score of 3 more frequently objectified in our series could be explained by the fact that, this cancer is characterized in our regions by its diagnosis most often late, at a locally advanced or metastatic stage [3] [14]. This deterioration of the general condition was a prognostic factor in our series, as it was in most of the major series in the literature in single or multivariate analysis [15] [16] [17] [18]. Several African authors have also shown that this deterioration of the general condition with an ECOG score greater than or equal to 2 decreases survival [3] [14]. The clinical stage T2c was more frequent in our series which confirms that the tumor was advanced at diagnosis. The clinical stage of the tumor was an important prognostic factor, which was comparable to the results of Emrich *et al.* [13]. However Rigaud *et al.* [11] and Mulders *et al.* [12] had concluded that the clinical stage T of the primary tumor was not a prognostic factor. The level of total PSA before treatment did not influence the castration resistance as shown by Rigaud *et al.* [11]. In contrary, the results of Robinson *et al.* [19] showed that this pre-treatment total PSA level was a prognostic factor in patients treated with androgen suppression for prostate cancer. ISUP score has a disputed prognostic value in the case of advanced prostate cancer treated with hormone therapy. For some, the ISUP score has no influence on survival [12] [13] [18] but for others, a low ISUP score was a factor of good prognosis on survival in uni and multivariate analysis [17] [20]. The high Gleason (ISUP 4 and 5) score is a factor in the poor prognosis of prostate cancer in a study by Sine *et al.* [21] in Senegal and Gagnat *et al.* [22] in France. Indeed this hypothesis is confirmed by our series where the Gleason score (ISUP score) influenced the castration resistance. There was no significant difference between whether or not there was regional lymph node involvement, unlike Halabi *et al.* [23] who found in their study influence. The absence of regional lymph node assessment in our series could be explained by the fact that the patients were seen at an advanced stage with an impairment of renal function probably due to an invasion of the ureteral meatus making difficult the extension assessment by a thoraco-abdominal CT. It could also be explained by the lack of financial means of some patients in our regions.

An impact of the metastatic site on the castration resistance in our series has been proven by several authors in the literature [22] [23].

The PSA nadir was a significant influence on the castration resistance in our series that has been confirmed by several authors in the literature [9] [19] [22] [24] [25]. The median TTN in our series was short compared to those found in the literature. In effect Gagnat *et al.* [22] reported a median of TTN to 13.1

months. Most of the patients in our series had a prostate cancer already metastasized castration resistant which could explain this short time observed in our series. The study by Choueiri *et al.* [24] showed for the first time that the TTN was a significant prognostic factor for overall survival in metastatic prostate which complies our results. Currently in the literature several authors confirmed this impact on the occurrence of resistance [22] [26].

5. Conclusion

At the metastatic stage, ADT should be started as soon as possible before general involvement and/or an advanced clinical stage to delay resistance. Drilling for a cytoreduction must also be done as much as possible because of its gain on the occurrence of resistance to castration of metastatic prostate cancer under ADT.

Conflict of Interest Statement

All the authors do not have any possible conflicts of interest.

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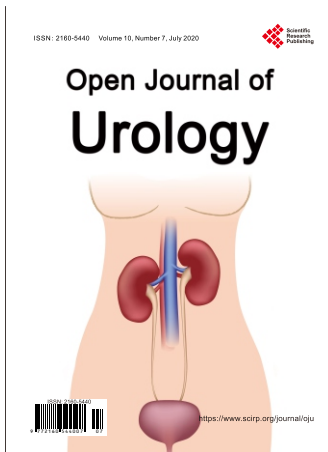
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