Journal of Cancer and Tumor International

10(4): 7-15, 2020; Article no.JCTI.62663
ISSN: 2454-7360

Influence of Prostate Cancer on Erectile Dysfunction in Northern Cameroon and Its Management

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Authors' contributions

This work was carried out in collaboration among all authors. Authors RTS, CNC and FDS conceived and performed the study and contributed to the acquisition of the reagents and to the preparation of the manuscript. Authors EMB, MA, AHNK and PBT contributed to data analysis and to the preparation of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2020/v10i430133
Editor(s):
(1) Sri Lakshmi Hyndavi Yeruva, Hershey Medical Center, USA.
Reviewers:
(1) Cristiane da Costa Thiago, Rio de Janeiro State University (IMS-UERJ), Brazil.
(2) Bijan Rezakhaniha, AJA University of Medical Sciences, Iran.
Complete Peer review History: http://www.sdiarticle4.com/review-history/62663

Original Research Article

Received 03 September 2020
Accepted 09 November 2020
Published 28 November 2020

ABSTRACT

Due to the lack of hospitals with adequate technical platform on one hand, and high diagnostic costs that cannot be afforded most of the population, the incidence of prostate cancer in Cameroon has increased and has great impact on people's health.

Aim: This work was undertaken with the objective to determine the impact of prostate cancer on erectile dysfunction and how to manage it.

Methodology: Sampling of the population was done in a comprehensive and non-probabilistic manner at the Urology Department of Ngaoundere Islamic Hospital, Ngaoundere, Cameroon, between June 2018 and November 2019. Of the 75 patients received, 50 of them participated in this study. Biopsies were taken from these patients to determine and confirm the form and stage of cancer followed by PSA assays. After the diagnosis was revealed, the testosterone assay was carried out in order to evaluate erectile functioning in the patients who equally completed a survey form made available to them in order to get an idea of their health history, the type of treatment followed and their lifestyle.

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Results: The mean age of the patients was 67 years, with a predominance in the 60-70 age range. 85% of the patients had a Gleason score greater than or equal to 8. Of these patients, 42% had low testosterone levels (< 2.3 ng/mL), resulting to lack of morning erection (66.6%), loss of sexual desire (43.9%), difficulty having a spontaneous erection (88%). On the other hand, erectile dysfunction was revealed in the prostate cancer patients with low testosterone levels, with a history of hypertention (16.6%), diabetes (28.5%) alcohol consumption (44%), tobacco smoking (41%) and having undergone as prostate cancer treatment involving transurethral resection of the prostate (80%) and orchiectomy (20%).
Conclusion: The major cause of erectile dysfunction observed in patients suffering from prostate cancer in Northen Cameroon can be attributed to the evolution of the disease, as well as the health history of the patients (diabetes, hypertension).

Keywords: Prostate cancer; testosterone level ; erectile dysfunction; health history.

1. INTRODUCTION

Cancers are pathologies mainly resulting from both the inability of cells to control their divisions and by the loss of mechanisms of programmed cell death. Modern lifestyle exposes us to various factors that may contribute to the activation of oncogenes [1-4], which in turn may induce disturbances in cell growth, differentiation, and apoptosis, thus, cancers [5,6].

The development of prostate cancer goes through four stages, namely : stage I, localized without symptoms; stage II, locally advanced, characterized by a local tumor compressing in certain neighboring organs causing difficulty in urinating, frequent need to urinate, and sometimes hematuria; stage III, caused damage to neighbouring lymph nodes, marked by compression in the rectum and invasion of the urethra causing lumbar pain; stage IV, metastasis, is the most dangerous, as the tumour invades the whole body and is characterized by bone pain and/or alteration of the general condition [7].

Treatment varies according to the severity of the tumour, its location, the extent of proliferation, the tumour volume and the patient's life expectancy. In most cases, a prostate tumour is known to grow slowly, therefore, different treatment options such as prostatectomy, external radiotherapy, chemotherapy, brachytherapy and cryotherapy are commonly applied. Each of these first-line therapeutic modalities has its advantages but are often associated with significant, life-altering side effects including urinary, bowel, and sexual dysfunction [8-10].

Erection is a physiological phenomenon in which the two *corpus cavernosum* dilate and become filled with blood, making the penis hard. However, erectile dysfunction may occur as a result of certain physiological disturbances. Erectile dysfunction can be defined as the inability to achieve and/or maintain an erection of sufficient quality to have satisfactory sexual intercourse [11]. This problem is encountered most often in patients with evolving prostate cancer and manifests itself as sexual impotence in which the penis fails to become or stay erect during sexual activity accompanied by decreased libido and loss of erection [12]. As a result, out of 60% of men newly diagnosed with prostate cancer, 40% already have erectile dysfunction [8].

Fighting prostate cancer equally involves the identification of its impact on men's life. It is based on this that this study was envisaged with the aim of determining the impact of prostate cancer on erectile dysfonction and its management in Northen Cameroon.

2. MATERIALS AND METHODS

2.1 Participants and Ethical Considerations

The present retrospective, cross-sectional and descriptive study was performed using historical data from the Department of Urology of Ngaoundere Islamic Hospital, Ngaoundere, Cameroon, obtained between June 2018 and November 2019. The study included all the patients whose biological assessment mentioned the performance of a prostate biopsy, with the exception of patients whose diagnosis after biopsy was a non-malignant prostate tumour. The data collected were anonymized to protect the privacy of participants.

The experimental procedures were approved by the Ethics Committee of the Faculty of Medicine

of the University of Ngaoundere and by the Institutional Review Board of Ngaoundere Islamic Hospital.

2.2 Procedures and Data Collection

Information on patients' socio-demographic characteristics and history, including exposure to prostate cancer risk factors (Lifestyle, patient clinical history and treatment types…) was obtained from the referral forms. Obtained from the individual patient files, were findings fromdigital rectal exam (DRE) performed following clinical standard procedures (assessing the volume, consistency and regularity of the prostate) as well as other clinical data relevant for the study such as the PSA (Prostate Specific antigen) level, the Gleason score and testosterone level. Then, data were anonymized. The Department of Urology of Ngaoundere Islamic Hospital obtained the Gleason scores of patients by applying Gleason classification to the anatomopathological findings of Hematoxylin & Eosin (H&E) stained prostate biopsies. The weight of the prostate determined using ultrasound was also available.

2.3 PSA (Prostate Specific Antigen) Assay

Available data on the serum PSA level were obtained using the Chemiflex flexible assay protocol in the ARCHITECT i2000SR automatic immunoassay analyzer (Abbott Diagnostics, Lake Forest, IL, USA), as recommended by the manufacturer. Briefly, 75 uL of serum was pipetted and transferred into a microcentrifuge tube containing paramagnetic microparticles coated with anti-PSA antibodies. The tube was closed and shaken vigorously for 5 min with an agitator to allow an optimal binding of the serum PSA to the anti-PSA coated microparticles. Then, after rinsing, 75 uL of acridinium-labelled anti-PSA antibody conjugate was added to the mixture and incubated at room temperature for 15 minutes. Subsequently the pre-activation and activation solutions were added to the reaction mixtures and the resulting chemiluminescent reaction was measured in relative units of URL light using immunoassay analyzer (ARCHITECT i2000SR).

2.4 Testosterone Assay

It is an immunological assay whose aim is to determine the total testosterone concentration in the human serum using the competitive immunodetection method. Initially, 30 µL of displacement reagent was pipetted and transferred to the sample mixing tube and 75µL of serum was subsequently added unto it and mixed. After closing the tube, the sample was homogenized by tube agitation and the mixture was incubated at room temperature for 3 minutes. 75 µL of this mixture was pipetted and transferred into the detection buffer tube containing the fluorescence-labelled antibody (FL). 75 µL of a sample mixture (complex) was added to the sampling well on the cartridge. This complex is responsible for migrating to the nitrocellulose matrix, where the covalent pair of testosterone and bovine serum albumin (BSA) is immobilized on a test strip, and interferes with the binding of the target material and the marked antibody (FL.).The resulting reaction was measured in relative units of light.

2.5 Statistical Analysis

The analyses of data were done by XLStat software version 2019. The $\chi 2$ test of independence was used to determine the existence of significant relationships between the testosterone and: (*i*) gleason score (*ii*) patients' lifestyle; (*iii*) patients' history of risk factors; (*iv*) treatment types. Statistical significance was set at $P < 0.05$

3. RESULTS

The population under investigation in this study consisted of 50 prostate cancer patients who are married and over 50 years of age. Before the diagnosis, we carried out a number of check-ups, including PSA assay.

3.1 PSA, Gleason Score and Testosterone Level of Patients

Table 1 shows the distribution of the study population as a function of PSA, Gleason score, testosterone level. The figure shows that 76% of patients have a PSA level ≥ 20 ng/mL and 10% have a PSA level between 10-20 ng/mL. Indeed, 40% of patients have a Gleason score ≤ 6, and 40% of patients have a Gleason score ≥8 and 20% have a Gleason score 7. In addition, 42% of patients have a testosterone level ≥ 3.5 ng/mL, and 16% have a testosterone level between 2.3-3.5 ng/mL.

3.2 Influence of Gleason Score, PSA Level on Testosterone Level

Table 2 illustrates the influence of the Gleason score and PSA level on testosterone levels. The

table shows that of the patients with low testosterone levels, 85% had a Gleason score of 8 or higher and 50% had a PSA level greater than 20 ng/mL. A significant association was found between Gleason score and testosterone level and between Gleason score and PSA level.

3.3 Influence of Lifestyle on Testosterone Levels

Table 3 illustrates the lifestyle of the patients, showing that 41% of prostate cancer patients with low testosterone levels were tobacco smokers and 42% of patients were alcohol consumers. No significant association was recorded between tobacco consumption and testosterone levels (P = 0.449) or between alcohol consumption and testosterone levels (P = 0.228).

3.4 Influence of Patient Clinical History on Testosterone Levels

Table 4 illustrates the influence of patient health history on testosterone levels, showing that 16.6% of patients with low testosterone levels had high blood pressure and 28.5% had diabetes. There was no correlation between these pathologies and testosterone levels (P=0.752 and P=0.365).

3.5 Characteristics of Erectile Dysfunction in Prostate Cancer Patients

Table 5 illustrates the characteristics of erectile function of patients with prostate cancer. It shows that 66% patients with low testosterone levels had no morning erection, 43% had loss of sexual desire and 88% had no spontaneous erection. Apart from the loss of sexual desire (P= 0.843), a correlation was noted between the other parameters and the testosterone level.

3.6 Influence of Treatment Types on Testosterone Levels

Table 6 illustrates the influence of treatment types on testosterone levels. It shows that 32.5% of prostate cancer patients who underwent transurethral resection of the prostate as treatment have low testosterone levels. 80% of prostate cancer patients who underwent orchiectomy as treatment have low testosterone levels. There was no correlation between treatment and decreased testosterone levels (P = 0.524).

Table 1. PSA, gleason score and testosterone level of patients

Variables	Characteristics	%
PSA levels (ng/mL)	< 10	14
	[10-20[	10
	>20	76
Gleason Score	<6	40
	7	20
	>8	40
Testosterone level (ng/mL)	< 2.3	42
	[2.3-3.5[	16
	> 3.5	42

Table 2. Influence of gleason score, PSA level on testosterone level

Testosterone	Gleason Score			PSA levels (ng/mL)		
levels (ng/mL)	Characteristics	(%)	P Value	Characteristics	(%)	P Value
Low	6	5	0.0001	[0-10[	25	0.0018
[1 - 2.3 [	**7**	30		[10-20[	16.6	
	> 8	85		>20	50	
Intermediary	6	25		[0-10[	12.5	
[2.3 – 3.5 [	**7**	16.6		[10-20[	16.7	
	> 8	50		>20	16.6	
Normal	6	5		[0-10[	62.5	
[3.5 – 8]	**7**	30		[10-20[	66.7	
	> 8	85		>20	33.4	

PSA: Prostate Specific antigen

Table 3. Influence of lifestyle on testosterone levels

Testosterone levels (ng/mL)	Smoking			Alcoholism		
	Characteristics	(%)	P Value	Characteristics	(%)	P Value
Low	Yes	41	0.449	Yes	44	0.228
[1 - 2.3 [	No	42		No	40	
Intermediary	Yes	18		Yes	18	
[2.3 – 3.5 [	No	29		No	20	
Normal	Yes	41		Yes	38	
[3.5 – 8]	No	29		No	40	

Table 4. Influence of patient clinical history on testosterone levels

Testosterone levels (ng/mL)	Hypertension			Diabetes		
	Characteristics	(%)	P Value	Characteristics	(%)	P Value
Low	Yes	16.6	0.752	Yes	28.5	0.365
[1 - 2.3 [	No	54.4		No	44.2	
Intermediary	Yes	16.7		Yes	14.3	
[2.3 – 3.5 [	No	18.1		No	16.3	
Normal	Yes	66.7		Yes	57.2	
[3.5 – 8]	No	27.5		No	39.5	

4. DISCUSSION

Biopsy results revealed that the majority of patients (40%) had invasive and aggressive lesions represented by a Gleason score greater than 8. This could be justified by the fact that the most affected age group is in the range (60-70) made up of people considered as elderly in Cameroon. Indeed, cellular ageing would seem to disrupt the physiology and integrity of prostate tissue, resulting in the accumulation of DNA damage and loss of control of the cell cycle by the transformation of proto-oncogenes into oncogenes or by the inactivation of tumour suppressor genes due to the effects of carcinogens [13]. A statistically significant association is observed between the Gleason score and testosterone level ($p<0.0001$) showing that the more aggressive the tumour, the lower the testosterone level. Indeed, testosterone enters the prostate cell where it is largely metabolized in the cytoplasm into dihydrotestosterone by the enzyme 5-reductase [14]. Once fixed on the androgenic stromal cell receptor, it leads to the secretion of growth factors that will directly act on the proliferation and differentiation of epithelial cells. In addition, the stroma produces FGF7 and FGF10 factors which directly stimulate epithelial cell proliferation and activate the production and secretion of PSA, which goes directly into the nucleus of the prostate cell where it is able to bind directly to the DNA, thus exerting its action on cell proliferation, leading to an increase in prostate volume [15-16]. This increase in prostate volume will block the passage of testosterone which is produced by the testicles (Leydig cell), hence the low testosterone level observed in patients with more aggressive tumour, leading to erectile dysfunction in most of them.

Prostate instrumentation or "trauma" due to cystoscopy, prostate biopsy, transurethral resection (TURP), colonoscopy, vigorous digital rectal examination (DRE) or ejaculation may cause transient increases in serum PSA. The PSA level tends to rise in men with benign prostatic hyperplasia (BPH) and is a good marker for prostate volume. PSA levels are usually elevated in men with acute bacterial prostatitis. The most valuable measurement of PSA is its change over time rather than the actual serum level. No identifiable PSA level guarantees normalcy; in addition, no specific level indicates that a biopsy should be performed [17].

Although no statistical association was observed in this study between tobacco and alcohol consumption and a drop in testosterone levels (*(P* = 0.449 *and P* = 0.228*)*), several cancer patients who use these products have low testosterone levels (41% and 42% for tobacco and alcohol respectively). Indeed, there is accumulating evidence that smoking increases the risk of fatal prostate cancer [18]. This is because the chemical compounds contained in tobacco smoke (nicotine, irritating substances, benzopyrenes, carbon monoxide) bind preferably in place of oxygen in the red blood cells. This

Table 5. Erectile dysfunction in prostate cancer patients

Testosterone levels (ng/mL)	Erectile dysfunction								
	Morning erection			Sexual desire			Erection		
	Characteristics	(%)	P Value	Characteristics	%)	P Value	Characteristics	(%)	P Value
Low	Yes	11.1	0.004	Yes	30	0.843	Absent	88.1	0.043
[1 - 2.3]	Often	14.8							
				Yes	43.9				
	No	11.1							
Intermediary	Yes	42.2		Yes	10		Absent	3.1	
[2.3 –3.5]	Often	55.1							
	No	14.9		Yes	19.5				
Normal	Yes	46.7		Yes	60		Absent	8.8	
[3.5 – 8]	Often	28.5							
				Yes	36.6				
	No	46.7							

Table 6. Influence of treatment types on testosterone levels

Testosterone levels (ng/mL)	Treatments		
	TURP (%)	Orchidectomie (%)	P-Value
Low [1 - 2.3]	32.5	80	0.524
Intermediary [2.3 –3.5]	20	0	
Normal [3.5 – 8]	47.5	20	

TURP : Transuretral resection of the prostate

leads to poor oxygenation of the penile muscles in the *corpus cavernosum*, which must become filled with blood during erection, thus leading to muscle weakness, which disturbs the erection process [19,20].

Patients with health history of diabetes and high blood pressure are more likely to develop erectile dysfonction although no significant statistical association is observed in this study. Indead, 16.6% of patients with low testosterone levels had high blood pressure and 28.5% had diabetes. Diabetes induces a generalized alteration of endothelial cell function, responsible for the decrease in nitric oxide activity [21], which acts as an activator of guanylate cyclase to cyclic guanosine monophosphate (cGMP). cGMP is a nucleotide that promotes relaxation of the smooth musculature of the penile arteries and intracavernosal tissue, contributing to penile *corpus cavernosum* engorgement and erection [22]. Its absence or decrease will thus result in the difficulty of the penis to become filled with blood in order to achieve an erection. Also, diabetes is at the origin of several cases of neuropathies which constitutes a greater risk of erectile dysfunction [23]. On the other hand, high blood pressure is an independent risk factor of erectile dysfunction and even in treated hypertensives, probably due to the conjunction of several neurogenic (noradrenaline), hormonal (angiotensin II) and hemodynamic factors that determine endothelial dysfunction. All of these phenomena lead to a decrease in oxygen supply to the *corpus cavernosum*, inducing fibrosis of the *corpus cavernosum*. This irreversibly limits the possibilities of smooth muscle relaxation and expansion of the sinusoid spaces. A failure of the veno-occlusive mechanisms is observed and this makes any rigid erection impossible [21].

In our study all patients underwent transurethral resection of the prostate which consists in reducing the size of the prostate to treat advanced cancer in patients with a life expectancy of less than 10 years. 80% of the patients underwent transurethral resection of the prostate only and did not experience erectile dysfunction a few months after the resection. Rather, small amounts of ejaculate are noticed due to the fact that as the prostate has decreased, there is less production of sperm fluid. The orchiectomy was performed in patients with metastatic prostate cancer. It is a curative treatment which consists in the total stop of production of androgenic hormones which will lead to erectile dysfunction in the long run [24]. The association between the stage of symptomatic development of prostate cancer in the body, age, and/or the presence of a co-morbidity related to smoking or the patient's lifestyle may be the reason for erectile dysfunction in prostate cancer patients.

CONCLUSION

This work was undertaken with the objective to determine the impact of prostate cancer on erectile dysfunction and its management. Results showed that 85% of patient had a Gleason score of 8 or higher and 50% had a PSA level greater than 20 ng/mL. 41% of prostate cancer patients with low testosterone levels were tobacco smokers and 42% of patients were alcohol consumers. 16.6% of patients with low testosterone levels had high blood pressure and 28.5% had diabetes. The major cause of erectile dysfunction observed in patients suffering from prostate cancer in Northen Cameroon can be attributed to the evolution of the disease as well as the lifestyle of the patients and their clinical history.

CONSENT

Filled consent forms were obtained from all of the patients.

ETHICAL APPROVAL

The experimental procedures used in this study were approved by the Ethics Committee of the Faculty of Medicine of the University of Ngaoundere and by the Institutional Review Board of Ngaoundere Islamic Hospital.

ACKNOWLEDGEMENT

Authors thank the medical professionals who provided their support in the clinical part of the study and in data analysis, in particular those of the Urology Department of Ngaoundere Islamic Hospital, Ngaoundere, Cameroon.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Available:https://doi.org/10.1007/5584_2018_264

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62663