Scientific Research Publishing

Surgical Science, 2022, 13, 381-400
https://www.scirp.org/journal/ss
ISSN Online: 2157-9415
ISSN Print: 2157-9407

Prostate Cancer: Risk Factors and Outcome Indicators

Cyril Kamadjou[1,2], Annie Kameni Wadeu[1], Jerry Kuitche[1], Achille Mbassi[3], Justin Kamga[4], Fru Angwafo[5]

[1]Medico Surgical Center of Urology and Mini Invasive Surgery, Douala, Cameroon
[2]Faculty of Medicine and Pharmaceutical Sciences, Department of Surgery and Specialties, University of Douala, Douala, Cameroon
[3]Yaoundé Medical and Technology Institute, Yaoundé, Cameroon
[4]Yaoundé General Hospital, Yaoundé, Cameroon
[5]Coordinator Urology Residency Program, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon
Email: cyrkamadjou@yahoo.fr

How to cite this paper: Kamadjou, C., Wadeu, A.K., Kuitche, J., Mbassi, A., Kamga, J. and Angwafo, F. (2022) Prostate Cancer: Risk Factors and Outcome Indicators. *Surgical Science*, **13**, 381-400.
https://doi.org/10.4236/ss.2022.138047

Received: July 22, 2022
Accepted: August 27, 2022
Published: August 30, 2022

Abstract

Background: Prostate cancer, which is the second most frequent cancer diagnosis made in men, more commonly occurs in the elderly. This disease is often diagnosed late in resource-limited settings, which results in people having advanced forms of the disease and a poor prognosis. This study aimed to identify factors indicative of prostate cancer aggressivity and a poor prognosis in patients with prostate cancer at a single center in Douala, Cameroon. **Methods:** We performed a retrospective study from 2015 to 2020 at the *Centre medico-chirugical d'urologie* in Douala, Cameroon, in which we included 203 patients aged 41 years to 85 years who had prostate cancer diagnosed via histopathology after either prostate biopsyor laparoscopic prostatectomy. Epi-info 7 was used for data analysis and logistic regression analyses were performed to identify factors associated with prostate cancer aggressivity and patients' outcomes (survival or mortality). **Results:** The mean age of our study participants was 64.76 ± 7.48 years. Ten patients had a contributive family history of prostate cancer. The patients presented with lower urinary tract symptoms in 61.58% of cases. All patients had serum prostate-specific antigen (PSA) levels of >4 ng/ml, 100 patients were anemic, and 36 patients had aggressive forms of the disease. Eighty-eight patients had remarkable digital rectal examination (DRE) findings. The median prostate volume, as determined via transrectal ultrasonography (TRUS), was 59 [43 - 80] ml. Fifty-nine patients had abnormal prostate echostructures, and 33 patients died during follow-up. The presence of paraplegia and the practice of professions requiring

unskilled labor were significantly associated with aggressive prostate cancer. The presence of lymphoedema, abnormal DRE findings, anemia, enlarged prostate glands (prostate volume >50 ml), and abnormal prostatic echostructures were significantly associated with both prostate cancer aggressivity and patients' outcomes. **Conclusion:** The late diagnosis of prostate cancer is a major public health problem in Cameroon because of the complications and poor prognosis of the disease at an advanced stage. Certain clinical, biological, and imaging factors are associated with prostate cancer aggressivity and a poor prognosis, whose identification could help guide clinicians in making therapeutic choices for their patients.

Keywords

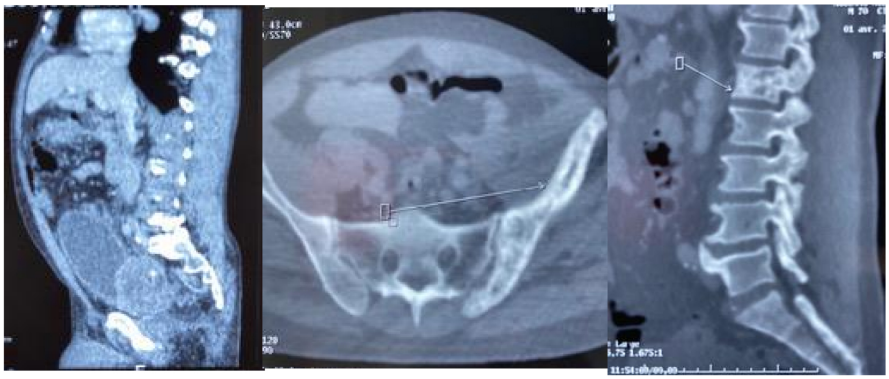
Aggressive Prostate Cancer, Early Diagnosis, Transrectal Ultrasonography, Prostate Biopsy, Prognosis

1. Introduction

Prostate cancer is the second most frequently diagnosed cancer in men and the sixth leading cause of cancer-related death among men [1]. Each year, there are more than 1,100,000 new cases of the disease, and more than 300,000 deaths occur due to prostate cancer worldwide. The disease is more common among older men, with a median age at diagnosis around age above 60 years [2]. Given that the disease is often asymptomatic in its early stages, its diagnosis is usually based on abnormal prostate-specific antigen (PSA) levels followed by a transrectal ultrasound-guided biopsy, digital rectal exam, or both [3]. CT is a widely used modality in both the diagnosis and follow-up of nearly all malignancies, but it has only a limited role in the imaging of prostate cancer owing to its poor soft-tissue contrast resolution, which does not allow precise distinction of the internal or external anatomy of the prostate. The major role of CT in patients with prostate cancer is for the detection of bony involvement and nodal staging; however, CT only detects the enlargement of involved nodes, which is a late finding in patients with prostate cancer [4]. **Figure 1** shows CT images of prostate cancer.

A CT image of metastatic prostate cancer with lymph node extension can be seen in **Figure 2**.

However, due to the poverty in Africa [5], diseases that do not immediately threaten people's well-being are often neglected and underdiagnosed, which implies that prostate cancer is often diagnosed late. According to a study conducted by Le Roux *et al.* in South Africa, 66% of the Zulu population of KwaZulu-Natal presented with either radiological evidence of metastasis or serum PSA levels of more than 100 ng/ml, and only 81 out of a possible 625 cases of prostate cancer were diagnosed early [6]. Seraphin *et al.* also reported that only 23.6% of prostate cancer cases were diagnosed at stages I and II in sub-Saharan Africa, and the



(a) (b) (c)

Figure 1. CT images of prostate cancer, including metastases. (a): Lateral view of prostatic adenocarcinoma on CT; (b): Prostate cancer with sacral bone metastasis; (c): Prostate cancer metastasis on the first lumbar vertebra.

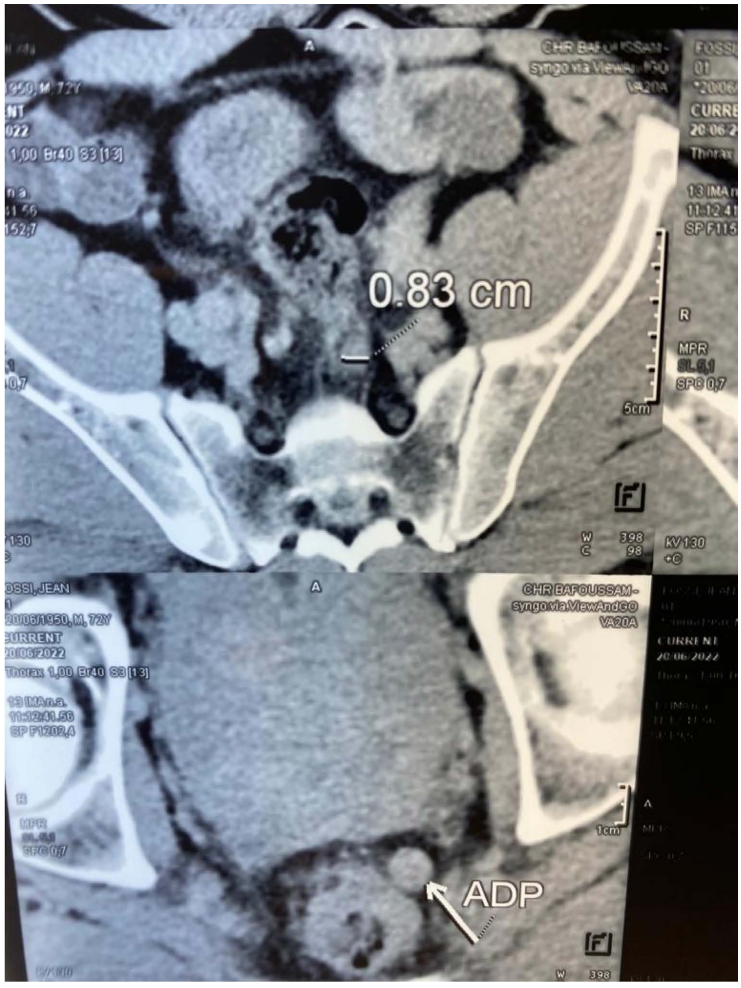


Figure 2. Metastatic prostate cancer with lymph node extension.

late diagnosis of the disease in this part of the world comes with consequences such as higher rates of disease-related morbidity and mortality [7]. Also, the prevalence of prostate cancer in sub-Saharan Africa is constantly increasing.

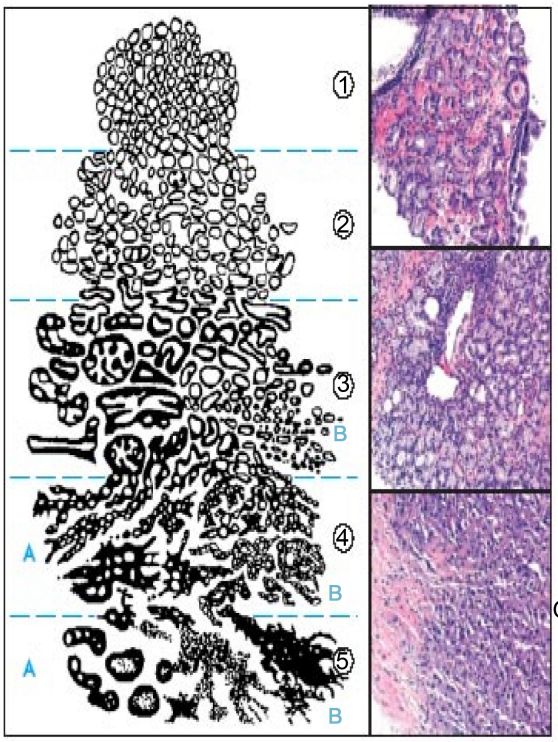
According to Ogunbiyi, prostate cancer, which affects up to 11% of the men in Nigeria, is the most common form of cancer among men in that country [8]. This steady increase in the prevalence of the condition is also accompanied by increments in the rates of disease-related morbidity and mortality. The 2013 Institute for Health Metrics and Evaluation (IHME) study further reported increasing disability-adjusted life years (DALYs) and mortality from prostate cancer, with an estimated 61% and 83% increase in DALYs and deaths from prostate cancer, respectively between 1990 and 2013 [9] [10]. In sub-Saharan Africa (SSA) alone, IHME estimated that DALYs from prostate cancer increased from 100,200 in 1990 to 219,700 in 2010, and the number of deaths also increased from 5600 to 12,300 over the same period [11] [12]. With such a huge disease burden and risk of death, it is important to identify factors indicative of prostate cancer aggressivity and a poor prognosis (usually the patient's demise). Gann identified age, African-American ethnicity, and a contributive family history as risk factors for prostate cancer [13]. Furthermore, Lietzmann and Rohrmann reported that the only firmly established non-modifiable risk factors for the condition are age, race, and a contributive family history. They also reported that the frequent consumption of dairy products and meat also enhances the development of prostate cancer and that smoking and obesity are positively correlated with prostate cancer-related mortality [14]. However, there is a paucity of studies on the risk factors and determinants of a poor prognosis of the disease in sub-Saharan Africa.

2. Materials and Methods

This is a retrospective study that was carried out from 2015 to 2020 at the *Centre medico-chirugical d'urologie* in Douala, Cameroon. We included 203 patients who had prostate cancer diagnosed via histopathology after either prostate biopsy or transurethral prostate resection (TURP) and excluded all patients with incomplete clinical records. The indications for a prostate biopsy in our study were serum PSA level >4 ng/ml and/or abnormal findings during a digital rectal examination (DRE). The data collected from the clinical records of our study participants included each patient's age, profession, year of diagnosis, body mass index (BMI), method of positive diagnosis employed, family history of prostate cancer, clinical presentation (including digital rectal examination findings), complications of the disease (including hip fractures, lymphoedema, and paraplegia), serum prostate-specific antigen (PSA) level, transrectal ultrasound (TRUS) findings (including the prostate volume and the presence of an abnormal prostatic echostructure), hemoglobin level, initial Gleason score, presence or absence of metastases, site of metastasis, histological grade, initial treatment (including radiotherapy, gosereline (zoladex) 10.8 mg, triptoreline (decapeptyl) 11.25 mg, laparoscopic prostatectomy, pulpectomy, watchful waiting, and surveillance), second treatment (including radiotherapy, docetaxel (Taxotere), abiraterone acetate (abirat), gosereline, and triptoreline), third treatment (including decetax-

el, abiraterone acetate, gosereline, and tripitoreline), total follow-up duration, and outcome (survival/death). After the diagnosis was made and the initial treatment was administered, all the patients were followed up monthly. During the monthly follow-up visits, the patients were examined and certain parameters (including the patient's weight, height, blood pressure, pulse, BMI, and hemoglobin level) were measured for follow-up. Every after three months, patients' serum PSA levels were measured as well. Normally, the PSA levels were expected to decrease; however, if they stayed constant or increased, the patients concerned were given a second treatment, and even a third if the PSA levels did not decrease. To facilitate data analyses, we classified participants' professions into four main categories. Those in the first category were skilled workers such as engineers, doctors, teachers, lawyers, magistrates, and technicians. Those in the second category were the unskilled workers such as traders, bricklayers, and drivers. Those in the third category were retired people and those in the fourth category were law enforcement officers, mainly police officers and soldiers.DRE findings were considered remarkable if the examiner felt indurations and/or nodules on the prostate gland on palpation. In our study, an abnormal echostructure was defined as the presence of hyperechoic, hypoechoic, or mixed ultrasonic patterns in certain regions of the prostate gland [15], especially the peripheries of the gland, as it has been established that prostate cancer is located in the peripheries of the gland in up to 70% of cases [16]. According to the WHO classification, A BMI of <18.5 kg/m^2 was considered underweight, 18.5 - 24.9 kg/m^2 was considered normal weight, 25 - 29.9 kg/m^2 was considered overweight, and ≥30 kg/m^2 was considered obesity (30 - 34.9 kg/m^2 was considered class I obesity, 35 - 39.9 kg/m^2 was considered class II obesity, and ≥40 kg/m^2 was considered morbid obesity) [17]. According to the WHO's definition of anemia [18], participants with hemoglobin levels of less than 13 g/dl were considered anemic. The volume of each participant's prostate gland was measured via TRUS, bearing in mind that the normal average volume in men of this age groupis 38 ml [19]. The tumors were classified using the Gleason and International Society of Urological Pathology (ISUP) grading systems, which are presented in **Figure 3**.

In this study, it was not possible to ascertain the tumor aggressivity in all the study participants since not all of them underwent surgery. So, the criteria for aggressivity in this study were the presence of metastases, serum PSA >50 ng/ml, and a Gleason score of ≥8, and patients who fulfilled these three criteria were considered to have aggressive prostate cancer. Biopsy was performed using a biopsy gun with the patients in the lateral decubitus position and under local anesthesia (using 2% Xylocaine). These biopsy samples were placed in formol inside little containers and transported immediately to the laboratory for histopathological analyses. In this study, histopathology was performed only for patients who underwent laparoscopic prostatectomy. All study participants received 500 mg of ciprofloxacin twice daily two days before and three days after a



(a)

TRANDITIONAL GLEASON SCORE	NEW GRADING SYSTEM GROUP 1
GLEASON 3+3=6 Only individual discrete well-formed glands	GRADE 1
GLEASON 3+4=7 Predominantly well-formed glands with a lesser component of poorly-formed/ fused/cribriform glands	GRADE 2
GLEASON 4+3=7 Predominantly poorly-formed/ fused/cribriform glands with a lesser component of well-formed glands	GRADE 3
GLEASON 4+4=8 Only poorly-formed/fused/ cribriform glands or -Predominantly well-formed glands with a lesser component lacking or -Predominantly lacking glands with a lesser component of well-formed glands	GRADE 4
GLEASON 9-10 Lacks gland formation (or with necrosis) with or without poorly-formed/fused/cribriform gland	GRADE 5

(b)

Figure 3. Classification of prostate cancer; (a): Gleason grading system, (b): International Society of Urological Pathology (ISUP) grading system.

biopsy.

All study data were entered into Microsoft excel 2007 and exported to Epi Info 7 for analysis. Continuous data were presented using the mean value and standard deviation for variables with normally distributed data and the median and interquartile range for variables with skewed data distributions. Categorical data were presented as frequencies and percentages. The Mann-Whitney U test and Student's t-test were used to compare continuous data for skewed and normally distributed variables, respectively, while the chi-square test was used to compare proportions between categorical variables. Kaplan-Meier survival analyses were performed to determine the five-year overall survival of our study participants. P-values of ≤0.05 were considered statistically significant. This study was approved by the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences of the University of Douala and the ethics committee of the *Centre medico-chirugicale d'urologie*, Douala, Cameroon. The requirement for informed consent was waived due to the retrospective study design.

3. Results

In this study, we included 203 patients aged 41 years to 85 years who had prostate cancer diagnosed via histopathology after either prostate biopsy or laparoscopic prostatectomy. The mean age of our study participants was 64.76 ± 7.48 years. The most predominant age group was the 61 - 70 years age group, which

accounted for 49.26% of our study participants, while the least common age groups were the 40 - 50 years and >80 years age groups, which each accounted for 1.97% of our study participants. The vast majority of our study participants (95.07%) did not declare having a family history of prostate cancer. More than half of our study participants were diagnosed in 2017 and 2018 (26.11% and 26.60%, respectively). The samples for histopathology were obtained through a prostate biopsy in 75.86% of our study participants and through TURP in 24.14% of them. The follow-up durations of our study participants ranged from 132 days to 2385 days with a median value of 951 [623 - 1278] days. The general information of our study participants is presented in Table 1.

Table 1. General information of the study participants.

VARIABLE	FREQUENCY (%)
Age (years)	
40 - 50	4 (1.97)
51 - 60	54 (26.60)
61 - 70	100 (49.26)
71 - 80	41 (20.20)
>80	4 (1.97)
Profession	
Unskilled workers	44 (21.67)
Skilled workers	84 (41.38)
Retired	71 (34.98)
Law enforcement	4 (1.97)
Family history of prostate cancer	
Yes	10 (4.93)
No	193 (95.07)
Year of diagnosis	
2015	14 (6.90)
2016	29 (14.29)
2017	53 (26.11)
2018	54 (26.60)
2019	33 (16.26)
2020	20 (9.85)
Method of sample obtention	
Prostate biopsy	154 (75.86)
TURP*	49 (24.14)
Duration of follow-up (Days)	
≤200	4 (1.97)
201 - 600	45 (22.17)
601 - 1000	61 (30.05)
1001 - 1400	52 (25.62)
>1400	41 (20.20)

*TURP = Transurethral resection of the prostate.

Regarding the initial clinical presentations of the study participants, 16.75% of them were asymptomatic, 61.58% had lower urinary tract symptoms, and 21.67% had acute urinary retention. A majority of our study participants (96.55%) had no complications; however, 1.97% of them had paraplegia, 0.49% had hip fractures, and 0.99% had lymphoedema. DRE findings were remarkable in 43.35% of study participants and unremarkable in 56.65% of study participants. The BMIs of the study participants ranged from 18.4 kg/m^2 to 42.4 kg/m^2 with a mean value of 26.98 ± 3.91 kg/m^2. Participants' PSA levels ranged from 4.28 ng/ml to 8832 ng/ml with a median value of 44.20 [16.80 - 169.30]. Participants' hemoglobin levels ranged from 6.3 g/dl to 17.0 g/dl with a mean value of 12.43 ± 2.26 g/dl. According to the participants' hemoglobin levels, 49.26% of them were anemic. Per our definition of aggressive prostate cancer (the presence of metastases PLUS serum PSA >50 ng/ml PLUS Gleason score ≥8), 17.73% of our study participants had an aggressive form of the disease. The prostate volume on ultrasound ranged from 17 ml to 450 ml with a median value of 59 [43 - 80] ml. An abnormal echostructure was found in 29.06% of our study participants. The clinical, biological, and imaging profiles of the study participants are shown in Table 2.

The Gleason scores of our participants ranged from 6 to 9. The Gleason scores of our participants ranged from 6 to 9. The most common score was 6 (3+3), which accounted for 34.98% of our study participants, while the least common score was 8 (5+3), which accounted for 1.97% of our study participants. Sixty-four (33.51%) of our study participants had metastases while 127 (66.49%) of them did not. Of the 64 patients with metastases, 8 (12.5%) had metastases in the bones only, 24 (37.5%) had metastases in the ganglions only, 30 (46.88%) had metastases in the bones and ganglions, and 1 (0.52%) each had metastases in the liver and lungs. The histological classifications for 114 (patients who underwent laparoscopic prostatectomy) out of our 203 participants were available. The most common histological grade was pT2bN0M0, which was found in 13.16% of those with available histological grades. The Gleason scores and histopathological grades of our study participants are presented in Table 3.

The initialtreatment of the patients was radiotherapy in 5.91%, gosereline 10.8 mg in 20.69%, triptoreline 11.25 mg in 10.34%, laparoscopic prostatectomy in 56.16%, pulpectomy in 5.42%, watchful waiting in 0.99%, and surveillance in 0.45% of our study participants. Out of the 203 participants that received initial treatment, 37.93% received a second treatment. Of these, 49.35% underwent radiotherapy, 11.69% received docetaxel, 25.97% received abiraterone acetate, 9.1% received gosereline, and 3.90% received triptoreline. Twenty-four (31.17%) of the 77 patients who received a second treatment went on to receive a third. Of these 24, 16.67% received decetaxel, 4.17% received abiraterone acetate, 54.17% received gosereline, and 25% received tripitoreline. Thirty-three (16.26%) of our study participants died during the follow-up period. The follow-up period varied from 132 days to 2385 days, with a median duration of 951 [623 - 1278] days.

Table 2. Clinical, biological, and imaging profiles of the study participants.

VARIABLE	FREQUENCY (%)
Initial clinical presentation	
Asymptomatic	34 (16.75)
Lower urinary tract symptoms	125 (61.58)
Acute urinary retention	44 (21.67)
Complications	
None	196 (96.55)
Paraplegia	4 (1.97)
Hip fractures	1 (0.49)
Lymphoedema	2 (0.99)
DRE findings	
Remarkable	88 (43.35)
Unremarkable	115 (56.65)
BMI ranges	
<18.5	1 (0.49)
18.5 - 24.9	61 (30.20)
25 - 29.9	96 (47.52)
30 - 34.9	39 (19.21)
35 - 39.9	5 (2.46)
≥40	1 (0.49)
Serum PSA levels (ng/ml)	
4 - 40	96 (47.29)
40.1 - 80	34 (16.75)
80.1 - 120	9 (4.43)
120.1 - 160	12 (5.91)
160.1 - 200	10 (4.93)
>200	42 (20.69)
Anemia	
Yes	100 (49.26)
No	103 (50.74)
Aggressive cancer	
Yes	36 (17.73)
No	167 (82.27)
Prostate volume (ml)	
≤20	5 (2.46)
20.1 - 40	41 (20.20)
40.1 - 60	61 (30.05)
60.1 - 80	46 (22.66)
80.1 - 100	23 (11.33)
>100	27 (13.30)
Abnormal echostructure	
Yes	59 (29.06)
No	144 (70.94)

Table 3. Gleason scores and histopathological grades of the study participants.

VARIABLE	FREQUENCY (%)
Gleason scores	
6 (3+3)	71 (34.98)
7 (3+4)	55 (27.09)
7 (4+3)	28 (13.79)
8 (4+4)	17 (8.37)
8 (3+5)	9 (4.43)
8 (5+3)	4 (1.97)
9 (5+4)	14 (6.90)
9 (4+5)	5 (2.46)
Metastasis	
Yes	64 (33.51)
No	127 (66.49)
Site of metastasis	
Bones	8 (12.5)
Ganglions	24 (37.5)
Bones and ganglions	30 (46.88)
Liver	1 (0.52)
Lungs	1 (0.52)
ISUP grade	
1	72 (35.47)
2	53 (26.11)
3	28 (13.79)
4	31 (15.47)
5	19 (9.36)
Histological classification	
pT1aNxMx	7 (6.14)
pT3aN1M0	9 (7.89)
pT2cN0M0	14 (12.28)
pT2bN0M0	15 (13.16)
pT3aN0M0	11 (9.65)
pT1bNxMx	6 (5.26)
pT1bN0M0	9 (7.89)
pT3bN1M0	8 (7.02)
pT2aNxMx	6 (5.26)
pT2aN0M0	9 (7.89)
*Others	20 (17.54)

*Others include: pT1aNOM0, pT1cNxMx, pT3aNxMx, pT2cNxMx, pT1cN0M0, pT2bNxMx, pT2bN1M0, pT3bN0M0, pT1aN0M0, pT2cN1M0, and pT1G1NxMx.

The details of the treatment, follow-up, and outcomes of the study participants can be seen in Table 4.

Table 4. Treatment, follow-up, and outcomes of the study participants.

VARIABLE	FREQUENCY (%)
Initial management	
Radiotherapy	12 (5.91)
Gosereline	42 (20.69)
Triptoreline	21 (10.34)
Laparoscopic prostatectomy	114 (56.16)
Pulpectomy	11 (5.42)
Watchful waiting	2 (0.99)
Surveillance	1 (0.45)
Second treatment	
Yes	77 (37.93)
No	126 (62.07)
Second treatment	
Radiotherapy	38 (49.35)
Decetaxel	9 (11.69)
Abiraterone acetate	20 (25.97)
Gosereline	7 (9.1)
Triptoreline	3 (3.90)
Third treatment	
Yes	24 (31.17)
No	53 (68.83)
Third treatment	
Decetaxel	4 (16.67)
Abiraterone acetate	1 (4.17)
Gosereline	13 (54.17)
Triptoreline	6 (25.00)
Final outcome	
Survival	170 (83.74)
Death	33 (16.26)
Follow-up duration (Days)	
≤200	4 (1.97)
201 - 700	53 (26.11)
701 - 1200	82 (40.39)
1201 - 1700	46 (22.66)
1701 - 2000	11 (5.42)
>2000	7 (3.45)

Concerning the factors associated with prostate cancer aggressivity, there was no significant difference between the mean age of the patients with aggressive cancer and that of patients with non-aggressive cancer (odds ratio undefined, p-value 0.70). We found significant associations between certain professions (unskilled labor; odds ratio 2.10; 95% confidence interval [0.95 - 4.66]; p-value 0.05), the presence of paraplegia (odds ratio undefined, p-value < 0.001), the presence of lymphoedema (odds ratio undefined, p-value: 0.03), a remarkable DRE (odds ratio undefined, p-value < 0.001), anemia (odds ratio 16.41; 95% confidence interval [4.84 - 55.71], p-value < 0.001), large (volume > 50 ml) prostate glands (odds ratio 5.18; 95% confidence interval [1.92 - 13.97], p-value < 0.001), and abnormal prostate echostructures on transrectal ultrasound (odds ratio 0.18; 95% confidence interval [0.08 - 0.38], p-value < 0.001), and the presence of aggressive prostate cancer. The factors associated with prostate cancer aggressivity are presented in Table 5.

Table 5. Factors associated with prostate cancer aggressivity.

VARIABLE	Aggressive cancer	Non-aggressive cancer	OR [95% CI]: P-value
Mean age (years)	65.19 ± 6.54	64.67 ± 7.69	Undefined: 0.70
Profession			
Retired	12 (16.9%)	59 (83.1%)	0.92 [0.15 - 15.46]: 0.49
Law enforcement	1 (25%)	3 (75%)	1.56 [0.16 - 15.46]: 0.54
Skilled worker	11 (13.1%)	73 (86.9%)	0.57 [0.26 - 1.23]: 0.10
Unskilled worker	12 (27.27%)	32 (72.73%)	**2.10 [0.95 - 4.66]: 0.05**
Family history			
Contributive	2 (20%)	8 (80%)	0.86 [0.17 - 4.21]: 0.56
Non-contributive	34 (17.62%)	159 (82.38%)	
Presentation			
LUTS*	25 (20%)	100 (80%)	1.52 [0.70 - 3.30]: 0.19
Acute urinary retention	11 (25%)	33 (75%)	1.79 [0.80 - 3.40]: 0.11
Paraplegia	4 (100%)	0 (0%)	**Undefined: <0.001**
Hip fracture	1 (100%)	0 (0%)	Undefined: 0.17
Lymphoedema	2 (100%)	0 (0%)	**Undefined: 0.03**
Digital Rectal Examination			
Remarkable	36 (31.30%)	69 (68.70%)	**Undefined: <0.001**
Unremarkable	0 (0%)	88 (100%)	
Anemia			
Yes	33 (33%)	67 (67%)	**16.41 [4.84 - 55.71]: <0.001**
No	3 (2.91%)	100 (97.09%)	
Prostate volume			
>50 ml	31 (25.41%)	91 (74.59%)	**5.18 [1.92 - 13.97]: <0.001**

Continued

<50 ml	5 (6.17%)	76 (93.83%)	
Prostate echostructure			
Abnormal	22 (37.29%)	37 (62.71%)	**0.18 [0.08 - 0.38]: <0.001**
Normal	14 (9.72%)	130 (90.28%)	
Obesity			
Yes	5 (11.1%)	40 (88.89%)	0.51 [0.19 - 1.40]: 0.13
No	31 (19.62%)	127 (80.38%)	

*LUTS = Lower Urinary Tract Symptoms.

Regarding the factors associated with patients' outcomes, there was no significant association between the mean age and participants' outcomes (odds ratio undefined, p-value 0.45). We found significant associations between the presence or absence of lymphoedema (odds ratio undefined, p-value: 0.02), DRE findings (odds ratio undefined, p-value < 0.001), the presence or absence of anemia (odds ratio 0.02; 95% confidence interval [0.003 - 0.16], p-value < 0.001), the volume of the prostate gland (odds ratio 0.28; 95% confidence interval [0.11 - 0.72], p-value 0.004), the prostatic echostructure (odds ratio 8.56; 95% confidence interval [3.74 - 19.61], p-value < 0.001), and the type of cancer (aggressive or non-aggressive: odds ratio 0.04; 95% confidence interval [0.02 - 0.11], p-value < 0.001) and patients' outcomes (survival or demise). The factors associated with patients' outcomes are presented in Table 6.

Table 6. Factors associated with patients' outcomes.

VARIABLE	Survival	Death	OR [95% CI]: P-value
Mean age (years)	64.59 ± 7.55	65.67 ± 7.22	Undefined: 0.45
Profession			
Retired	61 (85.92%)	10 (14.08%)	1.29 [0.58 - 2.90]: 0.34
Law enforcement	3 (75%)	1 (25%)	0.57 [0.06 - 5.70]: 0.51
Skilled worker	73 (86.90%)	11 (13.10%)	1.51 [0.69 - 3.30]: 0.20
Unskilled worker	33 (75%)	11 (25%)	0.48 [0.21 - 1.09]: 0.06
Family history			
Contributive	8 (80%)	2 (20%)	1.31 [0.26 - 6.45]: 0.51
Non-contributive	162 (83.94%)	31 (16.06%)	
Presentation			
LUTS	103 (82.40%)	22 (17.60%)	0.77 [0.35 - 1.69]: 0.33
Acute urinary retention	33 (75%)	11 (25%)	0.48 [0.21 - 1.09]: 0.06
Paraplegia	2 (50%)	2 (50%)	0.18 [0.03 - 1.36]: 0.12
Hip fracture	0 (0%)	1 (100%)	Undefined: 0.16
Lymphoedema	0 (0%)	2 (100%)	**Undefined: 0.02**

Continued

Digital Rectal Examination			
Remarkable	82 (71.30%)	33 (28.70%)	**Undefined: <0.001**
Unremarkable	88 (100%)	0 (0%)	
Anemia			
Yes	68 (68%)	32 (32%)	**0.02 [0.003 - 0.16]: <0.001**
No	102 (99.03%)	1 (0.97%)	
Prostate volume			
>50 ml	95 (77.87%)	27 (22.13%)	**0.28 [0.11 - 0.72]: 0.004**
<50 ml	75 (92.59%)	6 (7.41%)	
Prostate echostructure			
Abnormal	36 (61.02%)	23 (38.98%)	**8.56 [3.74 - 19.61]: <0.001**
Normal	134 (93.06%)	10 (6.94%)	
Obesity			
Yes	41 (91.11%)	4 (8.89%)	2.30 [0.76 - 6.94]: 0.09
No	129 (81.65%)	29 (18.35%)	
Type of cancer			
Aggressive	14 (38.89%)	22 (61.11%)	**0.04 [0.02 - 0.11]: <0.001**
Non-aggressive	156 (93.41%)	11 (6.59%)	

4. Discussion

We aimed to identify factors indicative of prostate cancer aggressivity and a poor prognosis in patients with the condition. In this retrospective study, we included 203 patients with a mean age of 64.76 ± 7.48 years, which is similar to the 68 years reported by Fofana *et al.* in the Ivory Coast in 2017 [20]. This similarity in the mean age can be explained by the fact that both studies were carried out in sub-Saharan African countries. Also, the samples were representative of the population of patients with prostate cancer in both cases. In our study, 4.93 of the participants declared having a family history of prostate cancer. This is lower than the 15% reported by Steinberg *et al.* [21]. This difference can be accounted for by the fact that Steinberg *et al.* carried out their study in the United States, a country where public awareness of the disease is much higher and the disease is often diagnosed much earlier than it is in Cameroon. In our resource-limited setting, many cases of this disease currently go undiagnosed, and deaths due to prostate cancer are often blamed either on witchcraft or natural causes since the age of onset of the condition often coincides with the life expectancy for men in this part of the world. Increasing the rate of diagnosis of this condition in Cameroon will undoubtedly increase the proportion of people who report a contributive family history. We found that the presence of LUTS (61.58%) was the most common clinical presentation of the disease. This is in line with the findings of Merriel *et al.* in 2018 [22]. The presence of these symptoms is probably

because the condition is often diagnosed at an advanced stage in this part of the globe. Studies conducted in the developed world report that early-stage prostate cancer is usually asymptomatic [23]. One of the main barriers to the early diagnosis of prostate cancer in Cameroon is that due to the low socioeconomic level of people in the country, routine checkups are not a common practice. Also, due to societal stereotypes and homophobia, people tend to shun digital rectal examinations, which are vital in the clinical diagnosis of the condition. Thus, much work needs to be done to sensitize people (especially men above the age of 50 years) and convince them to go for routine prostate examinations that will certainly increase the rate of diagnosis of the condition and also enable the condition to be diagnosed earlier. All our study participants had serum PSA levels of more than 4 ng/ml, which is in line with previous studies that recommend prostate biopsy and histopathology for patients with serum PSA levels of more than 4 ng/ml [24]. Although serum PSA at this cutoff has been reported to have a low sensitivity (20.5%), its high specificity (93.6%) makes this marker an asset in the diagnosis of the condition [25]. In our study, 49.26% of the participants were anemic. This is in line with the findings of previous studies that identify anemia as one of the features of advanced prostate cancer [26] [27]. The origin of prostate cancer-associated anemia is often multifactorial, with factors such as bone marrow metastases that lead to decreased hematopoiesis, radiotherapy that reduces bone marrow productivity, androgen deprivation therapy that takes a toll on erythropoiesis, and the chronic inflammatory state associated with the condition itself [26] [28]. We found that 17.73% of the participants had an aggressive form of the disease. This percentage is similar to the 15% reported by Ballentine Carter [29]. This similarity is probably because both studies were carried out in people of the same age group. This high prevalence of aggressive forms of the disease is undesirable as these forms are often associated with a poor prognosis. Hence, more efforts need to be put in to ensure that the condition is diagnosed early enough in our context. The median prostate volume in our study was 59 [43 - 80] ml, which is greater than the mean volume of 35.03 ± 17.41 ml in men aged 60 - 70 years reported by Zhang *et al.* in China [30]. This difference is mainly because Zhang *et al.* carried out a community-based study in which they included 1000 volunteers, irrespective of the state of health of their prostate glands, while we included 203 patients who had already been diagnosed with prostate cancer.

We found that 29.06% of our study participants had abnormal prostate echostructures indicative of prostate cancer during TRUS. This is much lower than the 50.87% reported by Maricic *et al.* in Croatia in 2010 [31]. This difference is probably because, in the developed world where resources are more available, TRUS is usually not plain but enhanced. Ultrasound techniques such as contrast-enhanced sonography using continuous harmonic imaging and intermittent harmonic imaging, as well as continuous color and power Doppler [32], are more efficient than plain ultrasonography. With such enhancements that are not

often available in our resource-limited setting, the sensitivity of ultrasonography in the diagnosis of prostate cancer will definitely be higher. In this study, 16.26% of the participants died during the follow-up period. This is lower than the 21% reported by Braga *et al*. in Brazil in 2021 [33]. This difference can be accounted for by the fact that the average age of their study participants (70.5 years) was higher than that in our study and their study participants were followed up over a longer period (13 years, from 2002 to 2015) compared to our patients who were followed up for a median duration of 951 days (2.6 years).

In this study, we identified certain factors that were significantly associated with prostate cancer aggressivity. The practice of professions that require unskilled labor was one of these factors. This is probably because these people (site laborers, gasoline station attendants, iron scrab collectors, etc.) have high professional exposure to the culprit carcinogens. This finding is corroborated by those of Sauvé *et al*., who reported that gasoline station attendants and textile processing workers had higher exposure to high-grade prostate cancer in Canada [34]. We also found that paraplegia was associated with prostate cancer aggressivity, as corroborated by R M Jameson [35]. This paraplegia is due to metastatic spinal cord compression, which is considered a serious complication of prostate cancer that only occurs in aggressive forms of the disease [36]. We also identified factors that were associated with both aggressive disease and patients' outcomes (survival or death). These factors include the presence of lymphoedema, abnormal DRE findings, anemia, enlarged prostate glands (prostate volume > 50 ml), and abnormal prostatic echostructures. Lymphoedema in prostate cancer is usually due to the presence of lymph node metastases that cause the lymph nodes to swell and block the flow of lymph and is often indicative of advanced-stage prostate cancer that has a poor prognosis [37]. Anemia is often associated with advanced prostate cancer and a poor prognosis. As mentioned earlier, anemia in men with advanced prostate cancer may be caused by several factors, including androgen deprivation, nutritional decline, bone marrow infiltration, treatment-related toxicity, and a chronic inflammatory state [26]. In our study, since the patients presented with anemia right from the onset, it was most probably due to bone marrow infiltration by metastases and the ensuing osteolysis that resulted in the attenuation of erythropoiesis and, hence, anemia. Abnormal DRE findings were also associated with cancer aggressivity and mortality. It has been well established that a DRE is an essential part of the assessment that can independently predict prostate cancer in the setting of a normal PSA level [38]; however, our findings indicate that this factor, in addition to its diagnostic value, may be useful in determining the prognosis of the condition in Cameroonian patients. We found that enlarged prostate glands (volume > 50 ml) were associated with both aggressivity and the disease prognosis. This is in line with the findings of Freedland *et al.* who suggested in their study thatprostate size may be an important prognostic variable that should be evaluated for use preoperatively and postoperatively to predict biochemical progression [39].

Lastly, we found that abnormal TRUS findings were associated with the aggressivity of the disease and patients' outcomes. To the best of our knowledge, ultrasonography is currently considered a diagnostic tool, and some studies report that it may be considered only as a diagnostic complement to serum PSA levels and DRE findings [40]. Although multiparametric MRI (mpMRI) of the prostate has been identified as a test that could mitigate prostate cancer diagnostic errors [41], its high cost and relative unavailability make it impracticable in this part of the world. As such, ultrasonography remains the modality of choice in resource-limited settings. Moreover, the findings of our study indicate that it can also be of prognostic value in Cameroonian patients. Taken together, the findings of our study indicate that even with the resources available to health care providers in our resource-limited setting, more could be done by the relevant stakeholders to diagnose prostate cancer early and prevent precarious outcomes of the condition.

However, this study has its limitations. Firstly, the retrospective study design comes with recall bias, which has a negative effect on the findings of the study. This study design also means that no causal relationship could be ascertained between the exposure and outcome variables. Secondly, all the participants of this study were recruited from the same facility, which means that the findings are not quite representative of the entire Cameroonian population. We recommend that more prospective multi-center studies be carried on this topic out to further investigate our findings.

5. Conclusion

The late diagnosis of prostate cancer is a major public health problem in Cameroon because of the complications and poor prognosis of the disease at an advanced stage. More efforts should be made to ensure the early diagnosis of the condition and improve patient outcomes. Also, there are certain clinical, biological, and imaging factors that are associated with prostate cancer aggressivity and a poor prognosis, whose identification could help guide clinicians in making therapeutic choices for their patients.

Acknowledgements

The authors thank Health Search Association for critically reviewing the manuscript.

Availability of Data and Materials

The data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics Statement

Ethical approval was obtained from the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences and the ethics committee of the *Centre*

medico-chirugicale d'urologie in Douala, Cameroon. The requirement for informed consent was waived due to the retrospective nature of the study.

Funding

The authors did not receive any funding for this study.

Conflicts of Interest

The authors have no conflicting interests to declare.

References

[1] Rawla, P. (2019) Epidemiology of Prostate Cancer. *World Journal of Oncology*, **10**, 63-89. https://doi.org/10.14740/wjon1191

[2] Tao, Z.Q., Shi, A.M., Wang, K.X. and Zhang, W.D. (2015) Epidemiology of Prostate Cancer: Current Status. *European Review for Medical and Pharmacological Sciences*, **19**, 805-812.

[3] Shore, N. (2014) Management of Early-Stage Prostate Cancer. *The American Journal of Managed Care*, **20**, S260-S272.

[4] Turkbey, B., Pinto, P.A. and Choyke, P.L. (2009) Imaging Techniques for Prostate Cancer: Implications for Focal Therapy. *Nature Reviews Urology*, **6**, 191-203. https://doi.org/10.1038/nrurol.2009.27

[5] Adeyeye, S.A.O., Ashaolu, T.J., Bolaji, O.T., Abegunde, T.A. and Omoyajowo, A.O. (2021) Africa and the Nexus of Poverty, Malnutrition and Diseases. *Critical Reviews in Food Science and Nutrition*, **1**, 1-16. https://doi.org/10.1080/10408398.2021.1952160

[6] Le Roux, H.A., Urry, R.J., Sartorius, B. and Aldous, C. (2015) Prostate Cancer at a Regional Hospital in South Africa: We Are Only Seeing the Tip of the Iceberg. *South African Journal of Surgery*, **53**, 57-62.

[7] Seraphin, T.P., Joko-Fru, W.Y., Manraj, S.S., Chokunonga, E., Somdyala, N.I.M., Korir, A., *et al.* (2021) Prostate Cancer Survival in Sub-Saharan Africa by Age, Stage at Diagnosis, and human Development Index: A Population-Based Registry Study. *Cancer Causes Control*, **32**, 1001-1019. https://doi.org/10.1007/s10552-021-01453-x

[8] Ogunbiyi, O.J. (2011) Impact of Health System Challenges on Prostate Cancer Control: Health Care Experiences in Nigeria. *Infectious Agents and Cancer*, **62**, S5. https://doi.org/10.1186/1750-9378-6-S2-S5

[9] (2015) Global, Regional, and National Age-Sex Specific All-Cause and Cause-Specific Mortality for 240 Causes of Death, 1990-2013: A Systematic Analysis for the Global Burden of Disease Study 2013. *The Lancet*, **385**, 117-171. https://doi.org/10.1016/S0140-6736(14)61682-2

[10] Vos, T., Barber, R.M., Bell, B., Bertozzi-Villa, A., Biryukov, S., Bolliger, I., *et al.* (2015) Global, Regional, and National Incidence, Prevalence, and Years Lived with Disability for 301 Acute and Chronic Diseases and Injuries in 188 Countries, 1990-2013: A Systematic Analysis for the Global Burden of Disease Study 2013. *The Lancet*, **386**, 743-800. https://doi.org/10.1016/S0140-6736(15)60692-4

[11] Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., *et al.* (2012) Global and Regional Mortality from 235 Causes of Death for 20 Age Groups in 1990 and 2010: A Systematic Analysis for the Global Burden of Disease Study 2010. *The Lancet*, **380**, 2095-2128. https://doi.org/10.1016/S0140-6736(12)61728-0

[12] Murray, C.J.L., Vos, T., Lozano, R., Naghavi, M., Flaxman, A.D., Michaud, C., *et al*. (2012) Disability-Adjusted Life Years (DALYs) for 291 Diseases and Injuries in 21 Regions, 1990-2010: A Systematic Analysis for the Global Burden of Disease Study 2010. *The Lancet*, **380**, 2197-2223. https://doi.org/10.1016/S0140-6736(12)61689-4

[13] Gann, P.H. (2002) Risk Factors for Prostate Cancer. *Reviews in Urology*, **4**, S3-S10.

[14] Leitzmann, M.F. and Rohrmann, S. (2012) Risk Factors for the Onset of Prostatic Cancer: Age, Location, and Behavioral Correlates. *Clinical Epidemiology*, **4**, 1-11. https://doi.org/10.2147/CLEP.S16747

[15] Salo, J.O., Rannikko, S., Mäkinen, J. and Lehtonen, T. (1987) Echogenic Structure of Prostatic Cancer Imaged on Radical Prostatectomy Specimens. *The Prostate*, **10**, 1-9. https://doi.org/10.1002/pros.2990100103

[16] Mitterberger, M., Horninger, W., Aigner, F., Pinggera, G.M., Steppan, I., Rehder, P., *et al*. (2010) Ultrasound of the Prostate. *Cancer Imaging*, **10**, 40-48. https://doi.org/10.1102/1470-7330.2010.0004

[17] WHO Expert Consultation (2004) Appropriate Body-Mass Index for Asian Populations and Its Implications for Policy and Intervention Strategies. *The Lancet*, **363**, 157-163. https://doi.org/10.1016/S0140-6736(03)15268-3

[18] Cappellini, M.D. and Motta, I. (2015) Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging? *Seminars in Hematology*, **52**, 261-269. https://doi.org/10.1053/j.seminhematol.2015.07.006

[19] Xia, S.J., Cui, D. and Jiang, Q. (2012) An Overview of Prostate Diseases and Their Characteristics Specific to Asian Men. *Asian Journal of Andrology*, **14**, 458-464. https://doi.org/10.1038/aja.2010.137

[20] Fofana, A., Kouame, B., Gowe, E.E., Kramo, N.A.F., Konan, K.P.G., Moro, A.C., *et al*. (2017) Cancer metastase de la prostate: Aspects socio-économiques, radiologiques et évolutifs en cote d'ivoire. *African Journal of Urology*, **23**, 281-285. https://doi.org/10.1016/j.afju.2016.11.002

[21] Steinberg, G.D., Carter, B.S., Beaty, T.H., Childs, B. and Walsh, P.C. (1990) Family History and the Risk of Prostate Cancer. *The Prostate*, **17**, 337-347. https://doi.org/10.1002/pros.2990170409

[22] Merriel, S.W.D., Funston, G. and Hamilton, W. (2018) Prostate Cancer in Primary Care. *Advanced Therapeutics*, **35**, 1285-1294. https://doi.org/10.1007/s12325-018-0766-1

[23] Oesterling, J.E. (1996) Early Detection of Prostate Cancer. Decreasing the Mortality Rate. *Minnesota Medicine*, **79**, 46-49.

[24] Eastham, J.A., Riedel, E., Scardino, P.T., Shike, M., Fleisher, M., Schatzkin, A., *et al*. (2003) Variation of Serum Prostate-Specific Antigen Levels: An Evaluation of Year-to-Year Fluctuations. *JAMA*, **289**, 2695-2700. https://doi.org/10.1001/jama.289.20.2695

[25] Ankerst, D.P. and Thompson, I.M. (2006) Sensitivity and Specificity of Prostate-Specific Antigen for Prostate Cancer Detection with High Rates of Biopsy Verification. *Archivio Italiano di Urologia, Andrologia*, **78**, 125-129.

[26] Nalesnik, J.G., Mysliwiec, A.G. and Canby-Hagino, E. (2004) Anemia in Men with Advanced Prostate Cancer: Incidence, Etiology, and Treatment. *Reviews in Urology*, **6**, 1-4.

[27] Colloca, G., Venturino, A., Vitucci, P. and Gianni, W. (2010) Management of Anaemia in Prostate Cancer. *Cancer Investigation*, **28**, 280-288. https://doi.org/10.3109/07357900903124480

[28] Boustany, R. and Zerbib, M. (2005) Anaemia and Prostatic Cancer. *Progrès en Urologie*, **15**, 604-610.

[29] Ballentine Carter, H. (2012) Differentiation of Lethal and Non Lethal Prostate Cancer: PSA and PSA Isoforms and Kinetics. *Asian Journal of Andrology*, **14**, 355-360. https://doi.org/10.1038/aja.2011.141

[30] Zhang, S.J., Qian, H.N., Zhao, Y., Sun, K., Wang, H.Q., Liang, G.Q., *et al*. (2013) Relationship between Age and Prostate Size. *Asian Journal of Andrology*, **15**, 116-120. https://doi.org/10.1038/aja.2012.127

[31] Maricic, A., Valencić, M., Sotosek, S., Oguić, R., Ivancić, A. and Ahel, J. (2010) Transrectal Sonography in Prostate Cancer Detection—Our 25 Years Experience of Implementation. *Collegium Antropologicum*, **34**, 239-242.

[32] Halpern, E.J., Ramey, J.R., Strup, S.E., Frauscher, F., McCue, P. and Gomella, L.G. (2005) Detection of Prostate Carcinoma with Contrast-Enhanced Sonography Using Intermittent Harmonic Imaging. *Cancer*, **104**, 2373-2383. https://doi.org/10.1002/cncr.21440

[33] Braga, S.F.M., Silva, R.P., Guerra Junior, A.A. and Cherchiglia, M.L. (2021) Prostate Cancer Survival and Mortality According to a 13-Year Retrospective Cohort Study in Brazil: Competing-Risk Analysis. *The Revista Brasileira de Epidemiologia*, **24**, e210006. https://doi.org/10.1590/1980-549720210006

[34] Sauvé, J.F., Lavoué, J. and Parent, M.É. (2016) Occupation, Industry, and the Risk of Prostate Cancer: A Case-Control Study in Montréal, Canada. *Environmental Health: A Global Access Science Source*, **15**, 100. https://doi.org/10.1186/s12940-016-0185-1

[35] Jameson, R.M. (1983) Paraplegia and Prostatic Cancer. *European Urology*, **9**, 267-269. https://doi.org/10.1159/000474100

[36] Nagata, M., Ueda, T., Komiya, A., Suzuki, H., Akakura, K., Ishihara, M., *et al*. (2003) Treatment and Prognosis of Patients with Paraplegia or Quadriplegia Because of Metastatic Spinal Cord Compression in Prostate Cancer. *Prostate Cancer and Prostatic Diseases*, **6**, 169-173. https://doi.org/10.1038/sj.pcan.4500641

[37] Mupamombe, C.T., LoGiurato, B., Kampel, L. and Cohen, J.M. (2018) Unilateral Upper Extremity Lymphedema in Metastatic Prostate Cancer. *Clinical Case Reports*, **6**, 1014-1019. https://doi.org/10.1002/ccr3.1367

[38] Walsh, A.L., Considine, S.W., Thomas, A.Z., Lynch, T.H. and Manecksha, R.P. (2014) Digital Rectal Examination in Primary Care Is Important for Early Detection of Prostate Cancer: A Retrospective Cohort Analysis Study. *The British Journal of General Practice*, **64**, e783-787. https://doi.org/10.3399/bjgp14X682861

[39] Freedland, S.J., Isaacs, W.B., Platz, E.A., Terris, M.K., Aronson, W.J., Amling, C.L., *et al*. (2005) Prostate Size and Risk of High-Grade, Advanced Prostate Cancer and Biochemical Progression after Radical Prostatectomy: A Search Database Study. *Journal of Clinical Oncology*, **23**, 7546-7554. https://doi.org/10.1200/JCO.2005.05.525

[40] Soggia, P., Madonia, M. and Corbu, C. (2012) Current Role of Prostatic Transrectal Ultrasound in the Diagnosis of CaP. *Urologia*, **79**, 130-134. https://doi.org/10.5301/RU.2012.9109

[41] Stabile, A., Giganti, F., Rosenkrantz, A.B., Taneja, S.S., Villeirs, G., Gill, I.S., *et al*. (2020) Multiparametric MRI for Prostate Cancer Diagnosis: Current Status and Future Directions. *Nature Reviews Urology*, **17**, 41-61. https://doi.org/10.1038/s41585-019-0212-4