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SHORT REPORT

SIGNIFICANCE OF NON-UROLOGICAL CLINICAL INDICES IN MANAGEMENT OF PROSTATE CANCER

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Abstract

Background: To have a re-look at the common non-urological features of prostate cancer with a view of determining if the non-urological presenting symptoms in patients with carcinoma of the prostate are of any significance or use as applicable indices in their management, especially in developing countries.

Method: Twenty-seven patients with carcinoma of the prostate and twenty patients with benign prostatic enlargement presenting over a five-year period were studied. From the data on both groups of patients, the sensitivities, specificities, predictive values, and usefulness indices of the non-urological symptoms of carcinoma of the prostate were determined.

Result: The commonest non-urological symptoms of carcinoma of the prostate were constipation, pedal oedema, weight loss, waist pain, abdominal pain/discomfort, generalized body weakness, and inability to walk. All the symptoms were of relatively poor sensitivity and negative predictive value, but specificity and positive predictive value were relatively high, and were remarkably so for pedal oedema, weight loss, generalized body weakness, inability to walk, and chest pain. None of the symptoms was found to be useful in the management of the patient as none attained the minimum acceptable usefulness index.

Conclusion*:* Non-urological symptoms of carcinoma of the prostate are not useful indices for the detection and management of CAP. Efforts should be made to ensure provision of the minimal facilities for the management of carcinoma of the prostate in healthcare facilities in the developing countries.

Mots clé : Prostate, cancer, symptômes, non urologiques

Résumé

Fond : Pour une revue plus profonde des dispositifs non urologiques communs du cancer de prostate avec une vue de déterminer si les symptômes de présentation non urologiques dans les malades présentant le carcinome de la prostate sont de n'importe quelle importance ou employés en tant qu'index applicables dans leur traitement, particulièrement dans les pays en voie de développement.

Méthode : Vingt-sept malades de présentant le carcinome de la prostate et vingt malades présentant l'agrandissement prostatique bénin sur une période de cinq ans ont été étudiés. À partir des données sur les deux groupes de patients, les sensibilités, les spécificités, les valeurs prédictives, et les index d'utilité des symptômes non urologiques du carcinome de la prostate ont été déterminés.

Résultat : Les symptômes non urologiques les plus communs du carcinome de la prostate étaient constipation, oedème de pédale, perte de poids, douleur de taille, douleur abdominaux, faiblesse généralisée de corps, et incapacité de marcher. Tous les symptômes étaient de sensibilité relativement faible et valeur prédictive négative, mais la spécificité et la valeur prédictive positive étaient relativement hautes, et étaient remarquablement ainsi pour l'oedème de pédale, perte de poids, la faiblesse de corps généralisée, l'incapacité de

marcher, et la douleur de coffre. Aucun des symptômes n'est considère utile dans le traitement du malade endant qu'aucun n'atteignait l'index acceptable minimum d'utilité.

Conclusion : les symptômes Non urologiques du carcinome de la prostate ne sont pas des index utiles pour la détection et le traitement du CAP. Des efforts devraient être faits pour garantir la disposition de l'équipement minimal du traitement de carcinome de la prostate dans le centre de soins médicaux dans les pays en voie de développement.

Introduction

Carcinoma of the prostate (CAP) can present with clinical symptoms that may be urological (urinary) or non-urological. Diagnosis of CAP is commonly based on the findings from digital rectal examination (DRE), prostate specific antigen (PSA) estimation, transrectal ultrasound (TRUS) and prostate biopsy.[1] Symptoms generally are well recognized as reliable bases for diagnosis in surgical diseases, hence the use of symptom indices and scores in the evaluation of illnesses like thyroid dysfunction,[2] benign prostatic enlargement (BPE) [3,4] and erectile dysfunction.[5] Urological symptoms, which are usually lower urinary tract symptoms (LUTS), are well recognized in prostate diseases on presentation and are valuable in the management of the patients. Non-urological symptoms in prostate diseases are mostly considered to be non-specific and thus thought to be of little relevance in the management of CAP. It is true that the detection methods of CAP, both early and advanced, have greatly improved especially with the introduction of PSA estimation and advanced technological investigations like the CT scan and MRI, but in the vast developing world, these diagnostic modalities are not usually readily available. In most parts, they are totally unavailable. Thus heavy reliance is still placed on clinical acumen and clinical indices for the detection and monitoring of patients' illnesses, if such patients would ever receive any medical care.

This study is aimed at having a re-look at the common non-urological features of CAP with a view of determining their significance in the management of patients with CAP in our environment.

Patients and Method

Consecutive patients who presented at the Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Nigeria between January 1993 and December 1998 were retrospectively studied. All the patients included in the study had clinical and histological diagnoses of CAP. The demographic characteristics of the patients and their presenting symptoms were recorded. All symptoms that were LUTS were regarded as "urological" and all other symptoms were "non-urological".

A control group of patients were selected from consecutive patients who also presented during the same period with BPE. The control group also had clinical and histological diagnosis of BPE. The demographic characteristics and the presenting symptoms of this control group of patients were also recorded.

From the data on both groups of patients, the sensitivities, specificities, predictive values, and the usefulness indices of the non-urological symptoms of CAP were determined. In this study, the sensitivity, specificity, and predictive values determined were as defined by Schecter,[6] and the clinical usefulness index was as used by Eskelinen et al. [7] Sensitivity was defined as the number of patients with CAP who had non-urological presenting symptoms, divided by the total number of patients with CAP. Specificity was defined as the number of the control patients (patients with BPE) without non-urological symptoms, divided by the total number of the control patients. The positive predictive value was defined as the number of patients with CAPs who had the non-urological presenting symptoms, divided by the sum of such patients and the number of patients with BPE who had the non-urological presenting symptoms. The negative predictive value was defined as the number of patients with BPE who did not have non-urological symptoms, divided by the sum of such patients and the patients with CAP who did not present with the non-urological symptoms. The usefulness index is defined as d x (d – r), where d is the incidence of the finding in the disease (= sensitivity), and r is the incidence of the finding in the reference population (1 – Specificity). It runs coherently from –1 to 1 and tests where usefulness index is over 0.35 are regarded as useful.

Results

Twenty seven patients with CAP and 20 patients with BPE who met the criteria for inclusion in the study were analysed.

The mean age of the patients with carcinoma of the prostate was 69.7 (SD 9.2) years, range 56-87 years, and with BPE was 71.2 (SD 6.0) years, range 60-86 years.

All the patients had DRE, prostatic acid phosphatase estimation, x-ray of the lumbosacral spine and pelvis, and a biopsy of the prostate. The biopsies were either transrectal or trans-perineal Trucut needle biopsy, or incision/excision biopsies done during open surgeries. One patient only had prostate specific antigen estimation during the period of study. Trans-rectal ultrasound was not done in any of the patients.

Of the 27 patients with CAP, 22 (81.5%)

had advanced disease (15 stage T3 M1, 7 T3 M0), 5 had early disease. Clinical stage was determined by DRE and recorded according to the UICC classification.[8]

Non-urological and urological presenting symptoms in patients with CAP are shown in table 1. The commonest symptoms were constipation, pedal oedema, weight loss, waist pain, abdominal pain/discomfort, generalized body weakness and inability to walk. The commonest urological symptoms were inability to pass urine (urinary retention), difficulty in passing urine (dysuria, straining), increased daytime frequency and nocturia.

The non-urological and urological presenting symptoms in patients with BPE are shown in table 2. Non-urological presenting symptoms in CAP with their calculated sensitivities, specificities, positive predictive values, negative predictive values, and usefulness indices are shown in table 3. All the symptoms are of relatively poor sensitivity and negative predictive value, but specificities and positive predictive values are relatively high, being remarkably so for pedal oedema, weight loss, generalized body weakness, inability to walk and chest pain, all of which attained values of 100%. However, the usefulness indices for all the symptoms are far less than 0.35 and thus the symptoms are not clinically useful in the management of CAP.

Table 1: Presenting symptoms of patients with carcinoma of the prostate

Symptoms	Non-urological		Symptoms	Urological	
	No.	%		No.	%
Constipation	6	22.2	Inability to pass urine	11	40.7
Bilateral pedal oedema	6	22.2	Difficulty in passing urine (straining, dysuria)	9	33.3
Weight loss	6	22.2	Increased diurnal frequency, nocturia	9	33.3
Abdominal pain, discomfort	4	14.8	Hesitancy	6	22.2
Generalized body Weakness	3	11.1	Poor stream, terminal dribbling of urine	6	22.2
Inability to walk	3	11.1	Urgency	3	11.1
Generalized body Swelling	2	7.4	Feeling of incomplete emptying	3	11.1
Generalized body aches, pain	2	7.4	Pussy urine	1	3.7
Loin pain	2	7.4	Haematuria	1	3.7
Chest pain	2	7.4			
Right groin Swelling	1	3.7			
Insomnia	1	3.7			
Anal protrusion	1	3.7			
Fever	1	3.7			
Palpitations	1	3.7			
Cough, breath-lessness	1	3.7			
Erectile dysfunction	1	3.7			

Table 2: presenting symptoms in patients with benign prostatic enlargement

Symptoms	Non-urological		Symptoms	Urological	
	No.	%		No.	%
Abdominal pain	8	40	Inability to pass urine(urinary retention)	12	60
Constipation	2	10	Difficulty in passing urine	7	35
Waist pain	2	10	Frequency, nocturia	7	35
Generalized body aches, pain	2	10	Urgency	6	30
Anal protrusion	11	55	Feeling of incomplete emptying	6	30
Loin pain	1	5	Poor stream, terminal dribbling	5	25
			Hesitancy	5	25
			Haematuria	3	15

Table 3: Sensitivity, specificity, predictive values, usefulness index of non-urological symptoms of CAP

Symptom	CAP (n) %	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Usefulness index
Constipation	22.2%(6)	22	90	75	46.2	0.03
Bilateral pedal oedema	22.2%(6)	22	100	100	48.8	0.049
Weight loss	22.2%(6)	22	100	100	48.8	0.049
Waist pain	14.8%(4)	14.8	90	66.7	43.9	0.001
Abdominal pain/discomfort	14.8%(4)	14.8	60	33.3	34.3	-0.037
Generalized body weakness	11.1%(3)	11.1	100	100	45.5	0.012
Inability to walk (paraplegia or paraparesis)	11.1%(3)	11.1	100	45.55	45.5	0.012
Generalized body swelling	7.4%(2)	7.4	100	100	44.4	0.005
Generalized body aches & Pains	7.4%(2)	7.4	90	50	41.9	0.002
Loin Pain	7.4%(2)	7.4	95	66.7	43	0.002
Chest pain	7.4%(2)	7.4	100	100	44.4	0.005

CAP = Carcinoma of the prostate

Discussion

One may wonder why there is the need to study the significance of clinical symptoms since there are advanced biochemical and technological techniques to detect and diagnose CAP. Nevertheless, we still believe that careful history taking and physical examination are still invaluable to a clinician, especially in the developing countries.

In urology, symptoms have been developed mainly for use in patients with LUTS suggestive of benign prostatic obstruction.[3, 4] Since both CAP and BPE are common causes of LUTS, it will be valuable to identify and project any presenting symptoms of CAP which are not LUTS, and which may be useful in detecting CAP, and in monitoring the progress of the disease.

Sensitivity and specificity are measures of a diagnostic feature's validity; the higher these values are, the better the feature at detecting the presence or absence of disease.[4] To have a useful role in screening for CAP, the relevant non-urological presenting symptoms should have a specificity and sensitivity close to 100%. In this study, this condition has not been fulfilled as there is a generally low diagnostic sensitivity for all the presenting symptoms, even though specificity is high for pedal oedema, weight loss, and generalized body weakness, inability to walk, generalized body swelling and chest pain. It is therefore not surprising that their usefulness indices fell below the minimum value for clinical usefulness.

Positive predictive value represents the probability of a patient having a given disease when the symptom is present and negative predictive value represents the probability of not having the disease when the symptom is absent. From this study, the positive predictive value is also high for all the symptoms that attained high specificity for CAP, but also remarkably so for pedal oedema, weight loss, generalized body weakness, inability to walk, generalized body swelling and chest pain. The negative predictive value is however low for the entire non-urological symptoms, with none attaining up to the 50% value. These findings are also inconsistent with the requirements for clinical usefulness of these symptoms, thus rendering them insignificant in the management of these patients.

Because most of the studied patients had advanced CAP (81.5%), the usefulness of the symptoms may relate more to advanced disease than to the early disease. In this environment however, most cases present late, just as it is in other studies from Africa. [9 - 11] Absence of prostate cancer screening and early detection programs and absence of access to medical care have been identified as some of the factors responsible for this late presentation of CAP. [10] The development and application of clinical indices as was envisaged before this study will no doubt enhance case-finding in developing countries by creating a high index of suspicion amongst practitioners, thus reducing the period of pre-treatment morbidity.

Our inference from this study, is that though the presenting symptoms of pedal oedema, weight loss, generalized body, body weakness, paraplegia or paraparesis, generalized body swelling and swelling and chest pain may be common findings in advanced CAP, they are nonspecific features of advanced diseases, not just of CAP. In CAP, they may just be expressions of the weight of morbidity, and reflections of patients' performance and efficacy of outcome measures. They are not clinically useful in the detection, and not significant in the management of CAP.

Since the common presenting non-urological symptoms have no significant impact on the initial diagnosis of CAP, reliance has to continue meanwhile on DRE, PSA estimation, TRUS, prostate biopsy, and advanced technological investigations like CT scan and MRI regardless of the cost implications for the developing countries. Therefore, pressure has to be put on the stakeholders in health policy making and administration, and positive efforts made to ensure

that the minimal modalities needed for the diagnosis and other aspects of the management of CAP are provided in healthcare facilities. Otherwise, many cases of CAP will remain undiagnosed or misdiagnosed.

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