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Feasibility of Utilizing the UCSF-CAPRA Score in the Management of Patients with Prostate Cancer: A Pilot Study in a Limited Resource Setting

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Abstract

Background: Prostate cancer is the second most common cause of dealth due to malignancy and the most common cancer in men. Risk stratification to determine the probability of recurrence is important prior to specific treatment decisions. TheUCSF-CAPRA Score Tool for Prostate Cancer Risk Assessment is effective in High Income Countries (HIC's). We hypothesized that the UCSF-CAPRA Score could successfully stratify prostate canceer patients to receive appropriate treatment in Low and Middle Income Countries (LMIC's)

Methods: A retrospective descriptive cross sectional hospital based study was conducted on patients with clinically localized prostate cancer at Muhimbili National Hospital, Regency Hospital and Tumaini Hospital in Dar es Salaam, Tanzania from June 2017 to January 2018. CAPRA scores were calculated at diagnosis from the prostate-specific antigen level, Gleason score, percentage of biopsy cores that were positive for cancer, clinical tumor stage, and age at diagnosis. The recommended treatment modality for each category was assigned and compared with the observed given treatment.

Results: Among 50 patients, 27 (54%) patients had a high risk score of 6-10, 17 (34%) patients had an intermediate risk score of 3-5 and 6 (12%) had a low risk score of 0-2 CAPRA category. The majority, 32 (64%) of patients, received androgen deprivation therapy. In the cohort of this study, only 6 (12%) received the standard treatment recommended by the CAPRA scores. Forty four (88%) received inappropriate treatment.

Conclusions: This retrospective study demonstrated that pre-treatment use of the UCSF-CAPRA score would have prevented inappropriate treatment in 88% of the study group. We conclude that use of the UCSF-CAPRA Score should be mandatory prior to initiating treatment for prostate cancer in LMIC's.

Keywords: CAPRA score, prostate cancer, limited resource setting

INTRODUCTION

Prostate cancer incidence and mortality vary worldwide, with the highest rates being reported in Scandinavia and lowest rates in China and other parts of Asia [1]. In Low and Middle Income Countries it may be less common, but its incidence and mortality has been on the rise [2]. Treatment options include active surveillance, immediate local treatment, aggressive multimodal therapy, and treatment of metastatic disease, depending on the extent of disease.

All treatment options for prostate cancer are associated with side effects, complications and risk of death. Risk stratification is important prior to specific treatment decisions to determine the probability of recurrence and progression [3, 4].

Many multivariable models have been designed in recent years to assess cancer progression risk on the basis of clinical data available at diagnosis. However, most models predict only biochemical recurrence or pathological stage, usually after single specified treatment modalities [4]. These range in complexity from a three-level categorization published by D'Amico *et al* to the monogram devised by Kattan *et al* which calculates the likelihood of recurrence as a continuous variable but requires a multi-step paper tool or a computer program to use [5, 6].

In the effort to address these limitations, University of California San Francisco (UCSF) developed Cancer of the Prostate Risk Assessment (CAPRA) score, having a calculable 0 to 10-point scale based on the prostate-specific antigen (PSA) level, Gleason score, clinical tumor stage, percentage of biopsy core samples positive for cancer, and age at diagnosis [6].

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A CAPRA score of 0 to 2 indicates low- risk. A CAPRA score of 3 to 5 indicates intermediate-risk. A CAPRA score of 6 to 10 indicates high–risk. Very low-risk tumors are often managed well with active surveillance. Low to intermediate-risk tumors generally respond well to localized treatment (surgery or radiation alone, brachytherapy with or without external-beam therapy). Intermediate to high-risk tumors often require multimodal therapy (surgery with radiation, or radiation therapy with hormonal therapy*).* Very high-risk tumors may be treated with multimodal therapy or hormonal therapy alone, and often are suitable for clinical trials of new therapeutic approaches [7, 8]. The UCSF- CAPRA score was developed by use of data from 1439 radical prostatectomy patients from the Cancer of the Prostate Strategic Urologic Research Endeavor (Cap SURE) registry [8, 11], and has been independently validated in three studies with data from the Shared Equal Access Regional Cancer Hospital registry, a multi-institutional academic cohort in Germany, and the Johns Hopkins Medical Institutes [9, 10, 11, 12]. In all three studies, the score accurately and consistently predicted pathological and biochemical outcomes.

There are no data on the use of the UCSF-CAPRA score in Low and Middle Income Countries (LMIC's). We hypothesized that the UCSF-CAPRA Score could successfully stratify prostate canceer patients to receive appropriate treatment in Low and Middle Income Countries (LMIC's)

PATIENTS AND METHODS

This was a descriptive cross sectional hospital based study that involved 50 patients diagnosed with localized prostate cancer at Muhimbili National Hospital (MNH), Regency Medical Centre and Tumaini Hospital, in Dar es Salaam, Tanzania, from June 2017 to January 2018. The study was approved by the Muhimbili University of Health and Allied Sciences Ethical Clearance Committee. A data sheet including demographic data, the UCSF-CAPRA score, and assigned and observed treatment modalities was used. Among the UCSF-CAPRA score parameters, age was obtained from demographic data on patient records. Six to 12 prostate tissue cores were taken for histopathology by digit-guided Trucut biopsy. Core biopsies were fixed in formalin, and then embedded in paraffin wax and other staining was applied according to MNH Central Pathology Laboratory protocol to identify samples positive for cancer and determine Gleason score. The serum PSA level was determined by Immunoassay. The clinical stage was obtained following pelvic MRI or CT scan. Case notes were reviewed for the treatment modalities offered to each patient.

Variables were entered into the UCSF-CAPRA score tool, a score was assigned and categorized into one of three groups: low, intermediate and high risk. The recommended treatment modality of each category was assigned and compared with the given treatment. Data collected were cleaned, coded and descriptive analysis was done with computer using SPSS program version 20 followed by the interpretation of results.

RESULTS

The mean age for the entire cohort (n=50) was 70 years with SD of 7.7. Results of PSA (ng/ml) values by categories showed the majority of patients (n=20) had a PSA above 30ng/ml,. Also the majority of patients n=28 (56%) had a T1or T2 clinical stage. Nineteen (38%) had Gleason score with secondary pattern 4 or 5. Most of the patients n=28(56%) had a percentage of core biopsy positive for cancer of less than 34%, but a broad range of patient characteristics were represented in Table 1.

Table 1: Characteristics of the patients

Variable	**No (%)**
Age at diagnosis	
<50	4 (8)
≥50	46 (92)
PSA level at diagnosis, ng/mL	
0-6	10(20)
6.1-10	5(10)
10.1-20	13(26)
20.1-30	2(4)
Above 30	20(40)
Clinical tumor stage	
T1 or T2	28(56)
T3a	22(44)
Gleason score	
No pattern 4 or 5	13 (26)
Secondary pattern 4 or 5	19(38)
Primary pattern 4 or 5	18(36)
% of biopsy cores positive for cancer	
less than 34%	28(56)
34% and above	22(44)
Primary treatment modalities	
active surveillance	9(18)
Radical prostatectomy	9(18)
Primary androgen deprivation therapy	32(64)

Table 2 below shows CAPRA score risk group results. A majority of patients, 27 (54%), had a high risk score of 6-10, 17 (34%) had an intermediate risk score of 3-5 and 6 patients (12%) belonged to the low risk score CAPRA category.

Table 2: CAPRA score risk group

CAPRA score risk group	**No. (%)**
0 – 2	6 (12)
3 – 5	17 (34)
6 – 10	27 (54)
Total	50(100)

The majority n=21 (77.8%) of those in the high risk CAPRA category (6-10) received primary androgen deprivation therapy, 9 (11%) underwent active surveillance and 9 (11%) underwent radical prostatectomy. Of those with intermediate risk CAPRA score (3-5) a majority, 9 (52.9%), received primary androgen deprivation therapy and 3 (23.5%) were primarily kept on active surveillance by follow up PSA, clinical progression and re-biopsy if positive that warranted radical prostatectomy. Of the 6 (12%) in low risk CAPRA category (0-2), 2 were kept on active surveillance and with disease progression they proceeded to radical prostatectomy. Overall, a majority received primary androgen deprivation therapy n=32 (64%), followed by radical prostatectomy, 9 (18%) and active surveillance 9 (18%).Table 3

Table 3: Distribution of Cancer of the Prostate Risk Assessment (CAPRA) scores by primary treatment type given

	No. of patients (%)		
CAPRA score(s)	**Active surveillance**	**Radical prostatectomy**	**Primary androgen deprivation therapy**
0 – 2	2(33.3)	2(33.3)	2(33.3)
3 – 5	4(23.5)	4(23.5)	9(52.9)
6-10	3(11.1)	3(11.1)	21(77.8)
Total	9(18.0)	9(18.0)	32(64)

Table 4 below shows only six (12%) patients received the standard treatment recommended by the CAPRA score while 44 (88%), received inappropriate treatment. Of those in the intermediate risk category 4 (23.5%) received standard treatment, while the majority, 13 (76.5%), received inappropriate treatment. All patients in the high risk category, n=27(100%) received inappropriate treatment.

Table 4: Comparison between standard treatment recommended by CAPRA score against treatment given*

	No. of patients (%)		
CAPRA score(s)	**Standard treatment**	**Other modalities**	**Total**
0-2	2(33.3)	4(66.7)	6(100)
3-5	4(23.5)	13(76.5)	17(100)
6-10	0(0.0)	27(100)	27(100)
Total	6(12)	44(88)	50(100)

*0-2, standard treatment is Active surveillance.3-5, standard treatment is radical prostatectomy and radiotherapy. For 6-10 standard treatment is multimodal therapy (radical prostatectomy and radiotherapy or Radiotherapy and hormonal therapy).

DISCUSSION

Counseling men with a new diagnosis of prostate cancer entails many challenges, including presentation of realistic probabilities of disease progression and death. These probabilities when combined with an assessment of patient comorbidies, life expectancy, and treatment preferences help guide planning a risk-adapted treatment strategy.

The CAPRA score is among the most extensively and independently validated risk assessment tools available for localized prostate cancer, and it performs well in terms of accuracy, generalizability, and is easily applied in the High Income Countries (HIC's).

This study provides evidence that the pre-treatment use of the UCSF-CAPRA Score has the potential to significantly reduce inappropriate treatment for prostate cancer patients in LMIC's. The majority (32 out of 50) of patients were treated with primary androgen deprivation therapy perhaps because clinicians with limited experience believe that androgen deprivation is the primary treatment for prostate cancer regardless of the stage. Specialized radiotherapy techniques e.g. Proton beam or brachytherapy are not accessible in Tanzania explaining the absence of a single patient treated by this modality. Nine patients underwent radical prostatectomy as primary treatment as it was regularly offered in one of the study centers.

In this study, only 12% of the patients received standard treatment as suggest by the calculated CAPRA score. While the majority, 88% received inappropriate treatment modalities. A majority of those in the high risk CAPRA score category (77.8%) received androgen deprivation therapy as a primary treatment modality and 11.1% were treated by radical prostatectomy and active surveillance as primary modality respectively. None of the patients received the standard treatment. Based on CAPRA risk assessment tool, patients in the high-risk category require multimodal treatment (surgery with radiation, or radiation therapy with hormonal therapy) [8, 9]. Thus most of the patients were undertreated.

The study shows that the majority of intermediate risk patients (52.9%) received androgen depravation therapy as a primary treatment. This is contrary to CAPRA risk assessment tool recommendations. Patients with intermediate risk are managed with localized treatment (surgery or radiation alone, brachytherapy with or without external-beam therapy [8, 9]. Only 23.5% of these patients received appropriate treatment based on CAPRA risk assessment tool recommendations as they were treated by radical prostatectomy.

Only one-third of low risk patients received appropriate treatment (active surveillance). Two-thirds were over treated. CAPRA risk assessment tool recommends low risk patients be managed by active surveillance [8, 9].

This study had several limitations. Different staging modalities (CT scan and MRI) were used depending on surgeon preference and financial constraints. MRI which is preferable but more expensive than the CT scan. This affects the results of the CAPRA score. Other treatments than standard recommended modalities were employed due to inaccessibility of specialized radiotherapy techniques and limited expertise in performing radical prostatectomy. This may have affected the treatment decisions. Despite these limitations, the findings in this study demonstrate that the UCSF-CAPRA score and can be successfully used in LMIC's and has the potential to improve the care of prostate cancer patients.

CONCLUSION

This retrospective study demonstrated that pre-treatment use of the UCSF-CAPRA score would have prevented inappropriate treatment in 88% of the study group. We conclude that use of the UCSF-CAPRA Score should be mandatory prior to initiating treatment for prostate cancer in LMIC's.

Competing interests

The authors declare no competing interests.

Authors' contributions

OES: designed the study, collected data, performed data analysis and wrote the first draft of the manuscript.

OVN and CAM, KM, WS contributed to the study design and manuscript preparation.

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