**Utilization of CAPRA score in the Management of patients with Prostate Cancer: The practice in Low Income Countries.**

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Abstract

**Background:**Prostate cancer is the most common cancer affecting men and causes deaths second only to lung cancer in numbers. Before making a decision regarding treatment for prostate cancer, risk stratification should be done to determine and estimate the likelihood that a given tumor will recur after treatment.The aim of this study was to assess the practicability of introducing and utilizing the UCSF-CAPRA score tool in risk assessment in a low resource setting.

**Methods:** A descriptive cross sectional hospital based study was conducted on patients with clinically localized prostate cancer at Muhimbili National Hospital, Regency and Tumaini hospitals located in Dar es Salaam,Tanzania. 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 of each category was assigned and compared with the observed treatment given.

**Results:**Among 50 patients, 27 (54%) patients had a high risk score of 6-10, followed by 17 (34%) patients with an intermediate risk score of 3-5 and 6 (12%) patients belonged to the low risk score of 0-2 CAPRA category. The majority of patients, 32 (64%) received androgen deprivation therapy. In the cohort of this study, only 6 (12%) received standard treatment as recommended by CAPRA scores while 44(88%), received inappropriate treatment.

**Conclusions:** Comparison of management approach as suggested by the UCSF-CAPRA score to what has been the practice shows only twelve percent of patients received standard treatment. Our findings have demonstrated that according to the tool, the majority of our patients can receive appropriate treatment if we adopt the use of the UCSF-CAPRA score.

**Key words.** CAPRA score, Prostate Cancer, The practice

**Introduction**

Prostate cancer incidence and mortality varies worldwide with the highest rates being reported in Scandinavia and lowest rates in China and other parts of Asia(1). In developing countries it may be less common, but its incidence and mortality has been on the rise(2).

 Clinicians must attempt to determine at the time of diagnosis which among their patients might do well with active surveillance, who should receive immediate local treatment, who requires aggressive multimodal therapy, and who should be treated presumptively for advanced disease.

All treatment options for prostate cancer carry a risk of complications, side effects and other impacts in terms of quality of life. Before making a decision regarding treatment for prostate cancer, it is important to do risk stratification to estimate the likelihood that a given tumor will recur after treatment, progress and pose a threat to life (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 either 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 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).

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.

While there is a validated prostate cancer risk assessment tool-the UCSF-CAPRA score which combines multiple risk factors, there are no data on its use in a resource poor setting. This study aimed at assessing practicality of introducing and utilizing the UCSF-CAPRA score tool in prostate cancer disease risk stratification.

**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 and Tumaini hospitals, located in Dar es Salaam, Tanzania, from June 2017 to January 2018. Ethical clearance to conduct the study was obtained from Muhimbili University of Health and Allied Sciences and the hospital’s ethical clearance committee. A data sheet including demographic data, UCSF-CAPRA score, and assigned and observed treatment modalities was used. Among UCSF-CAPRA score parameters, age was obtained from demographic data on patient records. Digit-guided prostate Trucut biopsy, 6-12 cores were obtained for histopathology, requiring information on percentage of biopsy core samples positive for cancer and Gleason score. 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. Serum PSA level was determined by Immunoassay. The clinical stage was obtained following radiological imaging, 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 three groups: low, intermediate and high risk. The recommended treatment modality of each category was assigned and compared with the observed treatment given. Data collected were cleaned, coded and descriptive analysis was done with computer using SPSS program version 20 followed by the interpretation of results.

**Results.**

**Table 1: Characteristics of the patients.**

|  |  |
| --- | --- |
| **Variable** | **No (%)** |
| **Age at diagnosis** |  |
|  < 65 | 10 (20) |
|  65 – 75 | 29(58) |
|  > 75 | 11(22) |
|  |  |
| **PSA level at diagnosis, ng/mL** |  |
|  1-6 | 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) |
|  above 34% | 22(44) |
|  |  |
| **Primary treatment modalities** |  |
|  active surveillance | 9(18) |
|  Radical prostatectomy | 9(18) |
|  Primary androgen deprivation therapy | 32(64) |

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 30,. Also the majority of patients n=28 (56%) had a T1or T2 clinical stage. Nineteen (38%) had Gleason score with secondary pattern 4or 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 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) |

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

**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**  |
| 1 | 1 (33.3) | 1 (33.3) | 1( 33.3) |
|
| 2 | 1 (33.3) | 1 (33.3) | 1 (33.) |
|
| 3 | 0 (0.0) | 2(33.3) | 4(66.7) |
|
| 4 | 1(50.0) | 0(0.0) | 1(50.0) |
|
| 5 | 3(33.3) | 2(22.2) | 4(44.4) |
|
| 6 | 1(16.7) | 2(33.3) | 3(50.0) |
|
| 7 | 1(16.7) | 1(16.7) | 4(66.7) |
|
| 8 | 0(0.0) | 0(0.0) | 3(100.0) |
|
| 9 | 1 (16.7) | 0(0.0) | 5(83.3) |
| 10 | 0(0.0) | 0(0.0) | 6(100.0) |
|  |  |  |  |
|  |  |  |  |
| 1 – 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 3 shows treatment modalities for the various CAPRA score categories. The majority n=21 (77.8%) of those in the high risk CAPRA category (6-10) received primary androgen depravation therapy while 9 (11%) underwent active surveillance and 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%) each received radical prostatectomy and active surveillance. Of

the 6 in low risk CAPRA category (0-2), 2 (33.3%) each received active surveillance, radical prostatectomy and primary androgen deprivation therapy respectively. Overall, a majority received primary androgen deprivation therapy n=32 (64%), followed by radical prostatectomy, 9 (18%) and active surveillance 9 (18%).

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

|  |  |
| --- | --- |
|  |  **No. of patients (%)** |
| **CAPRA score(s)** | **Standard treatment** | **Other treatment 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.6-10, standard treatment is multimodal therapy (radical prostatectomy and radiotherapy or Radiotherapy and hormonal therapy).

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

**Discussion**

Counseling men with a new diagnosis of prostate cancer entails many challenges, including presentation of realistic likelihoods of disease progression and mortality. These likelihoods, together with patient comorbidity, life expectancy, and preferences for treatment, should help guide planning of 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 it’s easily applied in the developed world.

 This study provides insight on the applicability of CAPRA score tool in management of localized prostate cancer in a poor resource setting.

The majority (32 out of 50) of patients were treated with primary androgen deprivation therapy. This could have resulted from the fact that androgen deprivation therapy is considered by some with limited experience in treatment of prostate cancer to be the primary treatment for most patients diagnosed with prostate cancer regardless of the stage. Specialized radiotherapy techniques e.g. cyber knife or brachytherapy are not accessible in Tanzania, and this could explain 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, 12% of the patients received standard treatment as suggest by CAPRA score tool, while 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 with 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 constrains for paying for MRI which is preferable but more expensive as compared with CT scan. This affects the results of CAPRA score. Other than standard recommended treatment modalities had been employed in management of prostate cancer, due to inaccessibility of specialized radiotherapy techniques and limited expertise in performing radical prostatectomy. This may affect decision on treatment modality to be used as observed in this study. Despite these limitations, the data are reliable and can be used as proxy for a risk- adapted treatment strategy for localized prostate cancer in our setting.

**Conclusion**

 The majority of patients were treated with primary androgen deprivation therapy regardless of the risk category. Comparison of management approach as suggested by the UCSF-CAPRA score to what has been the practice shows only twelve percent of patients received standard treatment. ? There was overtreatment of low-risk disease and under treatment of intermediate and high-risk disease. These findings support the application of the CAPRA score as a risk assessment and stratification tool for clinical practice.

**Competing interests**

The authors declare no competing interests.

**Authors’ contributions**

OES: designed the study, collected data, performed data analysis and wrote the report with a manuscript.

1OVN and CAM, participated in the study design and manuscript preparation.

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