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Depression, Anxiety, and Their Association to Health-Related Quality of Life in Men Commencing Prostate Cancer Treatment at Tertiary Hospitals in Cape Town, South Africa

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Abstract

Background: Comorbid depression and anxiety in men with localised prostate cancer (CaP) largely go undiagnosed and untreated and their effects on health-related quality of life (HRQOL) in men with CaP should not be underestimated. We examined the prevalence of depression and anxiety and its association with HRQOL in men about to commence treatment for CaP and the differences between treatment groups, radical prostatectomy (RP) and radiation therapy (RT).

Method: One hundred and seven participants from a longitudinal prospective observational study assessing depression, anxiety and HRQOL in men with localised CaP (DAHCaP), were used in this cross-sectional analysis. Data were collected shortly before participants were scheduled to receive their treatment. The Centre for Epidemiologic Studies Depression Scale (CES-D), the State Trait Anxiety Inventory (STAI), the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the European Organisation for Research and Treatment in Cancer Quality of Life questionnaire (EORTC QLQ-C30) and (EORTC QLQ-PR25) were used in this analysis.

Results: Symptoms of depression pre-treatment were noted in 39.3%, state anxiety 28%, trait anxiety 31.4% and prostate cancer anxiety in 12.1% of participants. Statistically significant correlations ($P \leq .05$) with the CES-D and a cluster of symptoms on the EORTC QLQ-C30 domains for Global Health ($r_s = -.35$), fatigue ($r_s = .38$), pain ($r_s = .32$), dyspnoea ($r_s = .28$), insomnia ($r_s = .30$) and finance ($r_s = .26$) and EORTC QLQ-PR25 domains for urinary symptoms ($r_s = .43$), bowel ($r_s = .43$) and hormone replacement therapy (HRT) ($r_s = .41$) were observed.
Statistically significant correlations were also noted between the STAI-S and EORTC QLQ-C30 and EORTC QLQ-PR25. No statistically significant difference was noted between treatments.

Conclusion: More men were depressed than anxious with significant associations with HRQOL prior to commencement of treatment. CaP treatments should focus not only on the prevailing indisposition but include a psychooncological and HRQOL assessment at pre-treatment in high-risk individuals.

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Introduction

Cancer is potentially a life-threatening disease involving aggressive treatments that may pose a challenge for patients psychologically. Prostate cancer (CaP) was the second most frequent and fifth leading cause of death worldwide among men in 2020.[1] In South African (SA) men CaP is the commonest cancer and the second leading cause of death (13%)[2] with a lifetime risk of 1 in 16 for developing the disease.[3]

This study was conducted within the framework of the public health care service in SA. Mayosi et al, 2014 estimated that the public health care sector in SA provided medical care to approximately 40 million uninsured individuals accounting for about 84% of the population and funded by the government.[4] The per capita spend for health care at state funded facilities in SA was estimated at $140 which is 10 times lower compared to private health care.[4] Many of these institutions face critical staff shortages, as was illustrated by the collapse of oncology services in one of the country's 9 provinces, KwaZulu Natal, in 2017, making work onerous for those committed to giving the best medical care to the public.[5,6]

A key proposition regardless of the challenges experienced by health care teams is to be alert to the psychological (depression and anxiety) needs of men with CaP and its association with HRQOL. If left untreated, psychological impairment comes at great personal and institutional cost. For instance, this has been shown to be associated with increased resource utilization and higher mortality.[7-9]

The prevalence of depression and anxiety in patients with cancer is substantially higher than that of the general population,[10] making a compelling argument for men with CaP at risk to be identified early and managed appropriately. Hartung et al, 2017 observed that in individuals with cancer, the odds of being depressed was 5 times more than that of the general population,[11] while Caruso et al,[12] in their 2016 review, highlighted that depression was 2 to 3 times more frequent in men with CaP compared to the general population. An earlier study by the Johansson group,[13] using a self-developed scale, measured depression and anxiety at 43% and 49%, respectively, while a meta-analysis of men with CaP, estimated the prevalence of depression and anxiety prior to treatment at 17.27% and 27.04%, respectively.[14]

There has been growing interest in the interrelationship between psychological dysfunction and HRQOL. An analysis examining pain in CaP patients found that those without pain had a better HRQOL,and lower levels of depression and anxiety.[15] Similarly, men with lower urinary tract symptoms (LUTS) were depressed and anxious with a poorer quality of life.[16] However, HRQOL is a multidimensional construct that includes physical, role functioning, social and psychological aspects of well-being and functioning.[17] Studies have found that depression and anxiety affect many of the HRQOL domains.[18,19] The latter comprise symptom clusters or constellations and was defined by Dodd et al,[20] 2001, as 3 or more concurrent symptoms that are related to each other and may or may not have the same etiology. Cheng and Lee[21] 2011, established that pain, fatigue, insomnia and mood disturbances was common in elderly patients receiving treatments for cancer and that this cluster affected their quality of life.

In SA, the prevalence of mood and anxiety disorders in the general population was observed at 9.7% and 15.8%, respectively.[22] Although psycho-oncological studies of CaP have been increasing elsewhere, few, if any, have explored depression, anxiety and HRQOL in South African men diagnosed with CaP. Our aims were to estimate: (1) depression and anxiety in men with localised CaP (2), the association between depression and anxiety to HRQOL, (3) whether there were differences in depression, anxiety and HRQOL between those receiving RT and RP prior to receiving treatment.

Method

Study Sample

We used baseline data obtained between June 2019 and February 2022 from 107 participants recruited into an ongoing prospective observational study examining depression, anxiety and HRQOL undergoing curative treatments for histologically diagnosed localised prostate cancer (DAHCaP) for this cross-sectional analysis. (Figure 1) Any individual fulfilling the inclusion criteria and about to receive either Radical Prostectomy (RP) or External Beam Radiotherapy (RT) was included. Consecutive sampling was used.

Description of Setting and Procedures

Participants were recruited from the 2 academic centres Tygerberg Hospital (TBH) and Groote Schuur Hospital (GSH) in the Western Cape, SA. Study data were collected pre-treatment (when participants were scheduled to come into hospital) and then twelve weekly for a year. We used demographic data, the Centre for Epidemiologic Studies Depression scale (CES-D), the State-Trait Anxiety Inventory-State (STAI-S), the State-Trait

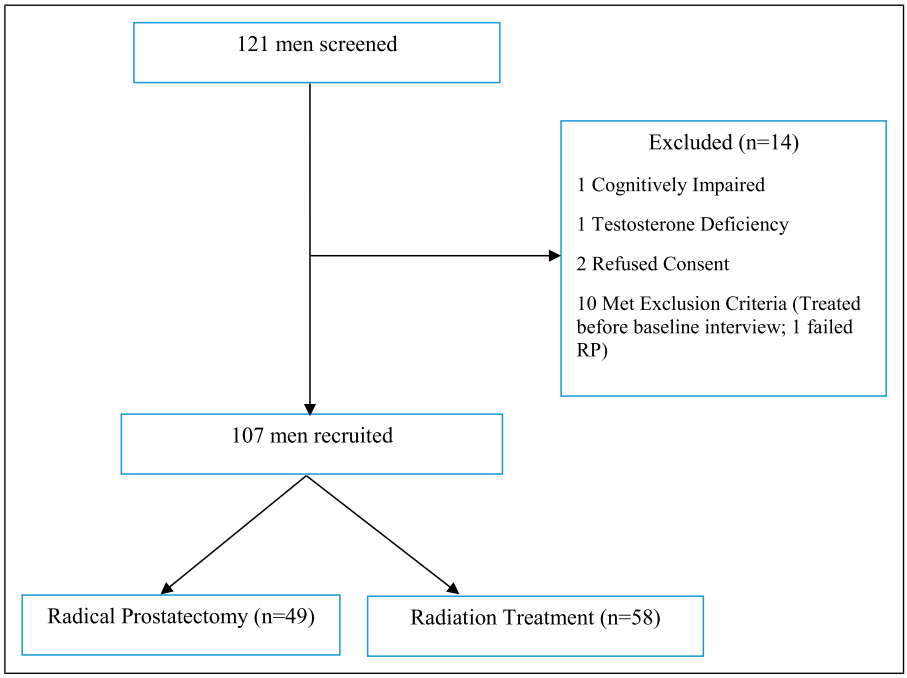

Figure 1. Flow diagram of study population. RP, Radical Prostatectomy, RT, Radiation Treatment.

Anxiety Inventory-State (STAI-T), the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and (EORTC QLQ-PR25) in this analysis. Validated self-administered questionnaires were used. Those who were unable to complete the self-administered validated questionnaire were assisted by the researcher. Study documents were available in English, Afrikaans and isiXhosa, the primary languages in this region.

Prior to the commencement of the study, clinicians involved in screening of participants were presented with an overview of the protocol. Exclusion criteria were hypogonadism, androgen deprivation treatment (ADT) or evidence of metastases.[23,24] Men with a confirmed diagnosis of hypogonadism with associated low mood were excluded.[25] Similarly, any participant on ADT was excluded as its effect on mood has been recognised.[26]

Men with either low or intermediate risk of localised CaP as per the D' Amico classification were invited by the treating clinician to participate in the study.[27] The D'Amico Classification is as follows: *Low-risk*: Prostate Specific Antigen (PSA) ≤ 10, Gleason Score (GS) ≤ 6 and clinical stage T1-T2a. *Intermediate risk*: PSA between 10 and 20, GS 7 or clinical stage T2b and *High risk*: PSA > 20, GS$\geq$ 8 or clinical stage T2c-3a.[28] High risk participants were excluded as ADT is often prescribed in these patients.[29]

Cognitive deficits in the elderly co-occur with depression and include impairment of episodic memory, speed of processing information, executive function and visuospatial ability.[30] Eligible participants underwent a pre-eligibility screening test for cognitive impairment (CI) using the 6 Item Screening (SIS) CI test.[31,32] Participants with 2 or fewer errors were invited to continue their participation. Those with a positive screen for CI were advised to visit their nearest clinic for further assessment.

Written informed consent was obtained from all eligible participants. The study was approved by Health Research Ethics Committees (HREC) of Stellenbosch University (S19/01/019) and University of Cape Town (UCT) (418/2019). Research principles outlined by the Helsinki Declaration, SA Good Clinical Practice Guidelines and the SA Research Medical Research Council (SAMRC) Ethical Guidelines for Research were followed.

The Mini International Neuropsychiatric Interview (M.I.N.I.) was used as a diagnostic instrument to assess participants for a range of psychiatric disorders such as depression, anxiety, substance use disorders, obsessive compulsive disorders etc. and was administered by a trained rater,[33] although these data are not reported here. Participants with obsessive compulsive disorder, alcohol and substance use disorders, for example, as assessed on the MINI, were excluded.

Quality checks were undertaken for missing data both on the paper and electronic version stored on REDCAP, a secure web application for managing surveys. All study data belonging to participants were de-identified using a personal identification number (PIN). The reporting of the study conforms to the STROBE guidelines.[34]

Measures

Demographic and Clinical Variables are shown in Table 1.

The Centre for Epidemiologic Studies Depression Scale (CES-D) is a 20 item self-reported scale used to measure symptoms of depression-the sum of which determines the total score. A CES-D score of ≥16 indicated symptoms of depression.[35] Responses reflect the frequency of feelings and behaviours over the past 7 days and were rated on a 4-point scale ranging from 0 (rarely or none of the time) to 3 (most or all of the time). Items number 4, 8, 12 and 16 were reverse scored, and once corrected, an overall score was calculated by summing the scores; higher scores suggest greater levels of depressive symptoms.[36]

The State Trait Anxiety Inventory (STAI) is made up of 2 separate scales and measures state anxiety (STAI-S) and trait anxiety (STAI-T)**.** STAI-S consists of 10 anxiety-absent items (reversed items) and STAI-T comprises 9 anxiety-absent (reversed items). Scores for each range between 20 to 80. STAI-S items assessed the intensity of current feelings (1 = not at all, 2 = somewhat, 3 = moderately so, and 4 = very much so) and STAI-T assessed the frequency of feelings in general (1 = almost never, 2 = sometimes, 3 = often, and 4 = almost always). A cut-off of ≥39 was used to detect clinically significant symptoms.[37] A higher cut-off ≥ 54 was also applied in this sample as has been suggested as a cut-off for older individuals.[38]

The Memorial Anxiety Scale for Prostate Cancer (MAX-PC) is an eighteen-item questionnaire with a 4-point Likert-type scale. The scale can be scored in its entirety by summing all the items or summary scores and can be grouped into CaP anxiety (11 items), prostate specific antigen (PSA) anxiety (3 items), or fear of recurrence (FOR) (4 items). It consisted of eighteen items with 4 responses and a score range between 0 to 3; a cut-off of ≥27 was used. The total scores ranged between 0 to 54.[39]

The European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-C30) comprises thirty items covering 5 functional scales, 3 symptom scales, 6 symptom items and 2 items on global HRQOL (Table 2). The scores are calculated by averaging items within the scales and transforming average scores linearly so that they range from 0 to 100. On this scale, we used a ≥20 score difference as particularly significant, ≥10 score difference as clinically significant.[40,41] Scores can detect a higher ("better") level of functioning and a higher ("worse") level of symptoms.[42]

The European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-PR25) assesses CaP symptoms and its treatments. Questions are grouped into 4 symptom scales, 2 functional scales and 5 conditional questions ie, sexual function, conditional on being sexually active (4 questions) as well as a question on use of an incontinence aid (Table 3). All items and scale scores of the

Table 1. Demographic and Clinical Variables.

	RP (%) (n = 49)	RT (%) (n = 58)	Total (%) (n = 107)	*P* value
Age in years (Median, IQR)	61 (57-66)	64 (61-69)	63 (59-68)	.016
Race				.134
Black	8.2	20.7	15.7	
Mixed ancestry	81.6	65.5	72.9	
Caucasian	10.2	13.8	12.1	
Education				.919
Primary School	22.4	25.9	24.3	
High School	61.2	58.6	59.8	
Tertiary Education	16.3	15.5	15.9	
Employment Status				.602
Formally Employed	14.3	22.4	18.7	
Unemployed/Retrenched	22.4	19.0	20.6	
Retired/Pensioner	49.0	50.0	49.5	
Casual Worker	14.3	8.6	11.2	
Marital status				.213
Life Partner	79.9	69.0	73.8	
No Life Partner	20.4	31.0	26.2	
History of Smoking	89.8	75.9	82.2	.060
History of Alcohol	93.9	81.0	86.9	.050
Medical History				
Asthma	2.0	6.9	4.7	.236
Heart Disease	20.4	25.9	23.4	.507
High Blood Pressure	65.3	63.8	64.5	.871
Diabetes	18.4	20.7	19.6	.763

Table 2. EORTC QLQ-C30 Pre-Treatment Scores Compared to Reference Values.

	RP (n = 49)	RT (n = 58)	Baseline* Reference Values	
	Median (25th, 75th Percentile)	Median (25th, 75th Percentile)	Median (IQR)	Effect Size**, *P*-value
Global Health QOL	85.71 (71.43, 92.86)	85.71 (71.43, 100.00)	75 (50, 83.3)	.01, .924
Functional Scales				
Physical Functioning	30.00 (25.00, 35.00)	30.00 (25.00, 35.00)	100 (80,100)	.08, .418
Role Functioning	25.00 (25.00, 37.50)	25.00 (25.00, 37.50)	100 (83.3,100)	.02, .823
Emotional Functioning	31.25 (25.00, 43.75)	31.25 (25.00, 43.75)	83.3 (58.3,100)	.02, .861
Cognitive Functioning	25.00 (25.00, 37.50)	25.00 (25.00, 37.50)	83.3 (83.3,100)	.06, .527
Social Functioning	25.00 (25.00, 37.50)	25.00 (25.00, 37.50)	100 (66.7,100)	.03, .795
Symptom Scales/Items				
Fatigue	33.33 (25.00, 41.67)	33.33 (25.00, 50.00)	22.2 (0, 44.4)	0, .992
Nausea	25.00 (25.00, 25.00)	25.00 (25.00, 25.00)	0	.04, .694
Pain	37.50 (25.00, 50.00)	25.00 (25.00, 50.00)	0 (0, 33.3)	.03, .724
Dysponea	25.00 (25.00, 25.00)	25.00 (25.00, 25.00)	0 (0, 33.3)	.03, .753
Insomnia	50.00 (25.00, 75.00)	25.00 (25.00, 50.00)	0 (0, 33.3)	.15, .112
Appetite	25.00 (25.00, 25.00)	25.00 (25.00, 25.00)	0	.07, .498
Constipation	25.00 (25.00, 25.00)	25.00 (25.00, 50.00)	0	.13, .180
Diarrhoea	25.00 (25.00, 25.00)	25.00 (25.00, 25.00)	0	.0, .996
Finance	25.00 (25.00, 50.00)	25.00 (25.00, 50.00)	0	.0, 1.000

A higher score for a functional scale represents healthy functioning and a higher symptom scale/item represents a higher level of symptom expression. A difference of ≥10 is considered a clinically significant difference and ≥20 as particularly significant. Ref. Values used are baseline values pre-treatment for Age (60-69)*40 **43.

Table 3. EORTC QLQ-PR25 Pre-Treatment Scores.

	RP (n = 49)	RT (n = 58)	
	Median (25th, 75th Percentile)	Median (25th, 75th Percentile)	Effect Size, *P*-value
Symptom Scales			
Urinary Symptoms	40.63 (34.38, 34.38)	37.50 (28.13, 46.88)	.17, .073
Incontinence Aid	25.00 (25.00, 25.00)	25.00 (25.00, 25.00)	.02, .861
Bowel Symptoms	25.00 (25.00, 31.25)	25.00 (25.00, 31.25)	.13, .166
*HRT Symptoms	29.17 (25.00, 37.50)	29.17 (25.00, 37.50)	.08, .393
Functional Scales			
Sexual Activity	62.50 (50.00, 75.00)	50.00 (25.00, 75.00)	.12, .201
Sexual Functioning	56.25 (43.75, 68.75)	50.00 (43.75, 62.50)	.14, .161

A higher score for a functional scale represents healthy functioning and a higher symptom scale/item represents a higher level of symptom expression. Reference values were not available at the time of writing. HRT, Hormone replacement therapy.

QLQ-PR25 were linearly transformed to a 0 to100 scale with parameters for clinical significance described as above.[40]

Statistical Analysis

The IBM SPSS version 27 (IBM Corp. Released 2020, IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp) was used. Scales were summarised using median and inter-quartile ranges by treatment group. Non-parametric Mann-Whitney tests were used to compare distributions of scale scores between groups. Statistical difference was set at $P < .05$.

Results

One hundred and seven men were included, 49 (RP) and 58 (RT). There was no group difference on demographic and clinical variables except for age, with more participants being younger in the RP group ($P = .016$) and a higher reported history of alcohol use in the RP group ($P = .050$) (Table 1). Approximately 3 quarters (72.9%) of the sample self-reported being of Mixed Ancestry, 15.7% Black and 12.1% Caucasian. Under half (49.5%) were retired/pensioners and 73.8% indicated they had a life partner. Many had received a high school education (59.8%) and

15.9%, a tertiary education. The median age (years) of the sample was 63 (IQR: 59 to 68) and per treatment group, RP 61 (IQR: 57 to 66) and RT 64 (IQR: 61 to 69) ($P = .016$). The median income/month in United States Dollars (USD) was $268.55 (IQR: 127.56 to 604.25) and per treatment group, RP $248.53 (IQR: 126.95 to 469.97) and RT 305.63 (IQR: 214.84 to 806.05).

Approximately forty percent of the sample scored ≥16 (CES-D), with 44.9% in the RP and 34.5% in the RT group although the group difference was not statistically significant. The median CES-D score was 13 (IQR: 11 to 18) and per treatment group was RP 15 (IQR: 10 to 19) and RT 13 (IQR: 11 to 18).

There were significant correlations between depression and a cluster of HRQOL symptoms. We observed the following statistically significant low to moderate correlations between the CES-D and the EORTC QLQ-C30 and EORTC QLQ-PR25. There was an inverse correlation between EORTC QLQ-C30 and CES-D for Global Health ($r_s = -.35$, $P < .01$) with those with poor Global Health being more depressed. Positive correlations between CES-D and EORTC QLQ-C30 for fatigue ($r_s = .38$, $P < .01$); pain ($r_s = .32$, $P < .01$), dyspnoea ($r_s = .28$, $P < .01$), insomnia ($r_s = .30$, $P < .01$) and finance ($r_s = .26$, $P < .01$) was noted. The following statistically significant correlations between the CES-D and EORTC QLQ-PR25 were also observed, urinary ($r_s = .43$, $P < .01$), bowel ($r_s = .43$, $P < .01$) and HRT symptoms ($r_s = .41$, $P < .01$).

Twenty-eight percent of men scored above the ≥39 cut off (STAI-S) and per treatment: 30.6% (RP) and 25.9% (RT) for state anxiety and was non-significant between treatment groups. As the median age of the sample was 63 years, we analysed the data using the higher ≥54 cut off and 3.7% scored above this. The median STAI-S score was 29 (IQR: 23 to 41). Likewise, the median score per treatment group was RP 31 (IQR: 24 to 43) and RT 28 (IQR: 23 to 41).

The following statistically significant low to moderate correlations between the STAI-S and EORTC QLQ-C30 were observed; a statistically significant negative correlation with Global Health ($r_s = -.48$, $P < .01$) which implied that those with poor Global Health were more anxious; statistically significant positive correlations between the STAI-S and EORTC QLQ-C30 for pain ($r_s = .35$, $P < .01$), fatigue ($r_s = .47$, $P < .01$), dyspnoea ($r_s = .37$, $P < .01$), insomnia ($r_s = .30$, $P < .01$) and finance ($r_s = .42$, $P < .01$) were also noted. The following statistically significant correlations between the STAI-S and EORTC QLQ-PR25 were observed with urinary ($r_s = .29$, $P < .01$), bowel ($r_s = .39$, $P < .01$) and HRT ($r_s = .33$, $P < .01$) symptoms.

Under a third (31.4%) scored above ≥39 for trait anxiety (STAI-T) and 30.6% (RP) and 25.9% (RT) per treatment group. The median trait score was 32.50 (IQR: 26 to 41). Likewise, the median score per treatment was RP 32 (IQR: 26 to 40) and RT 33 (IQR: 26 to 42). There was a statistically significant correlation between the STAI-S and STAI-T ($r_s = .39$, $P < .01$).

Just over ten percent (12.1%) reported CaP anxiety (MAX-PC) while anxiety per treatment group was reported as RP (14.3%) and RT (10.3%). The median score for the sample was 13 (IQR: 11 to 20) and similarly per treatment group median scores were RP 13 (IQR: 11 to 22) and RT 14 (IQR: 12 to 19). The median scores per treatment group for CaP anxiety, PSA anxiety and FOR were as follows; RP: CaP anxiety 4 (IQR: 0 to 14); PSA anxiety 0 (IQR: 0 to 0); FOR 8 (IQR: 5 to 12) and RT: CaP anxiety 3 (IQR: 0 to 8); PSA anxiety 0 (IQR:0 to 0); FOR 9 (IQR: 6 to 12). There was no statistical difference between treatments.

Higher scores on the EORTC QLQ-C30 and PR25 on the function scale indicates better functioning; however, a higher score on the symptom scale denotes worse symptoms. Our analysis for HRQOL showed that there was no statistically significant difference at baseline between treatment groups on the EORTC QLQ-C30 and EORTC QLQ-PR25. However, compared to the baseline reference values for the EORTC QLQ-C30 using a 10-point difference[40] (Table 2), the study sample scores were clinically significantly worse than the reference values on both functional and symptom scales except for the Global Health QOL. There was also a clinically significant difference on the symptomatic scale for pain between RP 37.5 (IQR: 25 to 50) and RT 25 (IQR:25 to 50). Similarly, a difference for insomnia was also noted between RP and RT; RP 50 (IQR: 25 to 75); RT 25 (IQR: 25 to 50). We were unable to find reference values for the EORTC QLQ-PR25 (Table 3) at the time of writing; we thus compared treatment groups using the 10-point difference. On the EORTC QLQ-PR25 there was a clinically significant difference for sexual activity between for the RP 62.5 (IQR: 50 to 75) and RT 50 (IQR: 25 to 75).

Discussion

No significant differences in demographic or clinical variables between treatment groups were observed, apart for age (RP, 61 and RT 64; $P = .016$) and a history of alcohol use ($P = .050$). We found that 39.3% of our sample had symptoms of depression, 28% state anxiety, 31.4% trait anxiety and 12.1% CaP anxiety. Compared to an earlier SA prevalence study examining common mental disorders by Herman 2009,[22] rates of depression and anxiety were higher in this cohort in line with findings from other studies, which confirms that the prevalence of anxiety and depression in men with CaP is much higher compared to the general population.[11,43]

A greater percentage of participants reported anxiety in the RP group. A recent study found that men due to undergo RP were anxious from the time of diagnosis to when they received treatment.[44] Some participants (12.1%) were anxious about their CaP as observed on the MAX-PC, with RT participants reporting fear of their cancer returning. Similar findings were noted in a recent systematic review in CaP patients done by James et al, 2022.[45] About a third of the men had trait anxiety suggesting a predisposition to anxiety.[46] Our values for

depression and anxiety correspond well with the meta-analysis done by Watts 2014.[14] No difference in depression, anxiety and CaP anxiety between treatment groups was observed.

There were statistically significant correlations between depression, state anxiety and a cluster of symptoms on both the EORTC QLQ-C30 (Global Health, fatigue, pain, dyspnoea, insomnia, and finance) and EORTC QLQ-C25 (urinary symptoms, bowel, and HRT). Untreated depression and anxiety have been shown to lower HRQOL and are associated with multiple HRQOL domains[47,48] and are referred to as clusters as identified by Dodd et al, 2001. Baden and colleagues,[49] 2020 estimated that 1 in 13 CaP survivors will experience the pain-fatigue-depressive symptom cluster, which if attended to, may help improve HRQOL. This is supported by findings from a randomised clinical trial examining mediating factors on HRQOL, which showed that pain, fatigue, anxiety and depression had a negative effect.[50] Similarly, a recent Swiss CaP survivorship study concluded that the pain, fatigue and depression cluster was associated with a poorer HRQOL.[51] An analysis of factors predicting the quality of life in men with CaP, established mental health as a predictor.[52,53] Seeman et al, 2018 showed that depressive symptoms had a significant negative effect on the QOL of men with CaP.[54] We were unable to account for the correlation between the CES-D and STAI-S with HRT symptoms despite participants not being exposed to ADT. It is possible that this may in part be attributed to late onset hypogonadism (LOH).[55] However as both clinical and biochemical features are required to be present for a diagnosis of LOH and in the absence of biochemical evaluation we cannot make this determination.[56]

Interestingly, we found more participants symptomatic for depression (38.9%) than anxiety (28.3%), consistent with findings made by others.[10,48,57] This corroborates earlier studies, which suggest the existence of a paradoxical relationship between anxiety and depression in older patients with CaP, ie, while depression appears to increase with age, anxiety decreases.[58-60] It has been proposed that physiological and psychological processes such as decreased emotional responsiveness, increased emotional control and psychological immunization are reasons why older individuals with cancer may have less anxiety and more depressive symptoms and may need more consideration.[61] Decreased anxiety in older adults with CaP have been supported by a recent study examining the effect of COVID 19 anxiety on state anxiety.[62]

Outcomes examining the relationship between depression and anxiety in older adults with CaP have been inconsistent and it has been suggested that brevity, acceptability and coverage of instruments used to measure the parameters under review, the depressive condition under evaluation and the type, stage and phase of the cancer may explain some of the variability in outcomes.[12] Furthermore, it has been suggested that the variance in estimates may be attributed to whether the interview was done by a trained psychiatrist (13%) or self-reported (4%-49%).[63,64] In addition, the wide range of estimates may in part, also, be due to the fact that the measurement of depression and anxiety in patients with cancer is challenging because of the overlapping symptomatology for both conditions that include fatigue, weight loss, sleep disturbance, loss of appetite and anxiety.[46,59]

The baseline HRQOL QLQ-C30 scores of our sample, juxtaposed with the baseline reference values for men between 60-69 years of age pre-treatment, are comparatively different. Our participants in both treatment arms rated themselves much better on the Global Health Related QOL on the EORTC QLQ-C30 but reported worse functioning and having more symptoms compared to the reference values. The latter appears to be supported by a study from SA examining contributors to HRQOL which suggested that those from disadvantaged backgrounds have a worse HRQOL.[65] It is worth noting the reference values used were obtained using pooled data from clinical and epidemiological studies and participants included in such studies may lend themselves to recruitment bias and possibly explain some of the differences.[66] Population demographics may also have contributed to the differences with participants from a lower socioeconomic setting included in this analysis. We found that RP participants reported better sexual activity on the EORTC QLQ-PR25 compared to RT group (Table 3). These results point to the likelihood that comparatively, the RP patient were younger (P = .016), and this is in agreement with findings made by Kurian 2018.[67]

The evidence from this analysis, although self-reported, has several clinical implications not only from an individual context but from a clinical services perspective. Firstly, Walker et al,[68] 2014 found that major depression was common in patients attending cancer clinics and most go untreated; particularly at risk were people that were socially deprived. Secondly, a meta-analysis drawn from 76 studies (176 863 patients) confirmed that the relative risk of mortality increased by 17% in patients with depression compared to those without.[69] Thirdly, the prevalence of sub-clinical depressive symptoms in the elderly has a significant impact on functioning and warrants clinical intervention.[70] Finally, a diagnosis of depression was associated with increased visits to the emergency room, hospitalizations and outpatient visits.[7] Similarly within the SA context, it was noted that mental disorders are not only linked to other health conditions but are amongst the costliest medical disorders in terms of the projected health expenditure needed to treat them.[8] It should be noted that some authors have argued for alternative CES-D cut-points. For instance, a systematic review which synthesized studies evaluating the accuracy of the CES-D as a screening tool for depression in the general population suggested a cut-point of 20.[71] As our study included older individuals with CaP a ≥16 cut-off was used.[72]

In conclusion, our findings suggest that SA men with CaP are ostensibly depressed and or anxious, both of which are associated with a cluster of symptoms characterized by a decreased HRQOL even before commencing treatments.

Notably we found more men with CaP reported being depressed rather than anxious.

The ramification of untreated anxiety and depression in SA men with CaP may be at an untold cost to both the individual and attending health care provider. In a recent overview of depression in CaP, Sharpley's group have strongly recommended that screening and a detailed diagnosis of depression should be included as part of urological clinical practice.[73] Given the benefit of an extended life, CaP treatments should not only focus on the prevailing indisposition but include a psycho-oncological and HRQOL evaluation of high-risk individuals thereby ensuring that those years can be purposeful.

The following are possible limitations. Participants attended a publicly funded specialist facility in SA, and therefore these results should not be generalised to other groupings (such as those with access to private health care facilities). As the data used was based on a single time point directionality could not be determined and change in well-being could therefore not be assessed. The tools used in this analysis were self-reported validated tools and therefore the reported prevalence may be higher than an interview-based study. Caution should be exercised when interpreting and generalising results given the sample size. Men with known hypogonadism were excluded from the study and therefore the influence of hypogonadism on depression, anxiety and HRQOL could not be ascertained. Participants were screened for cognitive dysfunction and those with cognitive impairment on screening were excluded. Depression and cognitive impairments are known to co-occur, especially in older adults. Inclusion of men with depression at baseline yet exclusion of those with cognitive impairment at may have contributed to sampling bias. Despite this, we believe the following to be the strengths of this study. The data was collected prior to commencement of treatments on urological functioning and symptom status to reduce the likelihood of recall bias. This study has enhanced our understanding of the psychological and HRQOL status of SA men embarking on treatment for CaP and the interrelationship between depression, anxiety and HRQOL. It also provides a springboard for the longitudinal work we are in the process of investigating.

Future Direction

These finding highlights the importance of clinicians recognizing depression and anxiety in men commencing treatment for CaP and its negative effect on a cluster HRQOL symptoms and managing appropriately prior to commencement of treatment for CaP. Future work should focus on collaborative care models that integrate multidisciplinary teams to improve access to psychological treatments and should be incorporated into treatment protocols for these patients.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

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