Submitted: 13 September, 2020 Accepted: 03 November, 2020 Published: 08 January, 2021 DOI:10.31083/jomh.v17i1.320

JOMH Journal of Men's Health

Review

The association between fatigue and depression in prostate cancer patients is influenced by psychological resilience

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Abstract

Background and Objectives: Prostate cancer [PCa] patients often report an increase in fatigue, which can lead to elevated depression. Psychological Resilience [PR] has been shown to help people avoid depression arising from an increase in fatigue, but this has not previously been reported in PCa patients. **Materials and Methods:** Using an anonymous survey method, 88 PCa patients aged 44 to 88 years [M = 73.48 years, SD = 7.17 years] completed scales to measure depression, PR and fatigue. To measure changes in fatigue since before diagnosis to the time of this survey upon, participants used the "retrospective pre-test" methodology. Partial correlations were calculated for fatigue change, PR and depression to test for the effects of PR upon the association between fatigue and depression. **Results:** PR did not significantly influence the association between change in fatigue and depression at the full-scale level. However, the key aspects of PR significantly influenced the relationship for the key symptoms of depression in these men. The key aspect of PR was the patients' ability to persist; the key symptoms of depression were the ability to think clearly and to perform activities as well as they did in the past. **Conclusions:** Key aspects of PR may reduce the depressive effects of fatigue in PCa patients, suggesting possible treatment foci for assisting these men deal with this negative side effect from their diagnosis and treatment.

Keywords

Cancer; Prostate; Depression; Fatigue; Resilience

Introduction

Prostate cancer [PCa] patients have a prevalence for depression several times higher than in their non-cancer peers [1, 2], and also suffer from fatigue [3]. Depression and fatigue often occur together because fatigue can lead to depression in cancer patients [4], often lasting for at least 6 years after treatment [5]. However, some personal characteristics or traits can help these men avoid fatigue, one of which is Psychological Resilience [PR] [6]. PR is defined as the ability to "bounce back" after adversity [7], and has genetic [8] as well as learned components [9]. There is also some evidence that PR can be increased through adversity [10], including in PCa patients [11]. It may be that PR provides a counter to the depressive effects of fatigue in PCa patients.

When studying depression and fatigue, it is necessary to allow for the potential confound between data from the scales that measure these two constructs because the diagnostic criteria for Major Depressive Disorder [MDD] include "Fatigue or loss of energy nearly every day" [12]. Similarly, although the most common approach when measuring variables such as depression and PR is to use the full score from self-report inventories, these are heterogeneous constructs, comprising a series of questions about different aspects of each construct. Thus, as well as using total scores from the scales designed to measure these constructs, there is also a potential to gather valuable data regarding the underlying, core components of these variables, which can inform "individualisation" of treatment models [13] in clinical practice.

A literature searches [Google Scholar, PubMed] in June 2020 with the descriptors "prostate cancer, fatigue and psychological resilience" failed to find any studies that investigated the effects of PR on PCa patients' fatigue-related depression. Therefore, this study aimed to test for any significant associations between PR and these three variables, specifically, the possible influence of PR upon depression-related fatigue.

Due to the paucity of previous studies on these issues, no directional hypotheses could be reliably suggested. Instead, this study aimed to investigate how PR was associated with the change in fatigue since diagnosis and depression [minus fatigue] in a sample of PCa patients, and to do so using the underlying core components of scales designed to measure depression and PR, as well as the total scores from those scales.

Methods

Participants

PCa patients from four treatment centres in South East Queensland, Australia, who had biopsy-proven PCa and were attending either for treatment or for follow-up after previous treatment, received an invitation to participate in a study about "how you feel", and responded during a 3-month period from February to April, 2020. All of the treatment options had been properly considered by patients via discussion with their GP, a radiation oncologist and a urologist. The data reported in this study were part of a larger investigation into the effects of PR upon depression associated with sleep and fatigue problems, some of which have been published [11].

Measures

Background questionnaire: age [in years], living situation [with wife/partner, widowed, separated/divorced, never married], month and year of first diagnosis, past treatments and current treatments [radiotherapy, surgery, hormone therapy, none], present status of their cancer [cancer still present and undergoing initial treatment, no obvious sign of cancer [in remission], cancer re-occurring after previous treatment].

Fatigue: Patients' levels of fatigue were measured by the Fatigue Severity Scale [FSS] [14], which has previously been used to assess fatigue in cancer patients [15] and PCa patients specifically [16]. The FSS consists of nine items, to which participants respond with a rating of how much they agree with the items from 1 [Not very appropriate] to 7 [High level of agreement]. Example items include: "I am easily fatigued", "Fatigue causes problems for me" and "Fatigue interferes with my work, family or social life". Total scores range from 9 [minimum fatigue] to 63 [maximum fatigue]. Internal consistency [Cronbach alpha] for the FSS has been reported as 0.96 for patients with major illness.

The Connor-Davidson Resilience Scale [CDRISC] [17] consists of 25 items such as "I like a challenge", "When things look hopeless I don't give up", "I bounce back after illness or hardship", and "I am able to adapt to change" [17]. Responses are given on the 5-point scale of "Not true at all" [0], "Rarely true" [1], "Sometimes true" [2], "Often true" [3] and "True nearly all of the time" [4] for how the respondent felt over the past month. This produces a total score between 0 and 100, where higher scores indicate greater resilience. Scores on the CDRISC are significantly correlated [0.83] with total scores on the Kobasa Hardiness Measure and negatively correlated with total scores on the Perceived Stress Scale [-0.76]. Internal consistency is sound [Cronbach alpha = 0.89] and test-retest reliability [r = 0.87] is satisfactory [17]. A previous study with PCa patients reported internal consistency of 0.922 [6] for the CDRISC.

Depression: The Zung Self-rating Depression Scale [SDS] [18] measures 20 symptoms associated with MDD [12]. Responses are made for "the last two weeks" on a four-point scale, for "None or a little of the time" [a score of 1], "Some of the time" [2], "Good part of the time" [3] and "All or almost all the time" [4]. Total scores are from 20 to 80 and SDS scores of 40 or above indicate the presence of "clinically significant depression" [19]. Split-half reliability for the SDS has been reported as 0.81 [18], 0.79 [20] and 0.94 [21]; internal consistency is 0.84 in PCa men [22]. The SDS has been shown to possess stronger validity than the Beck Depression Inventory and the MMPI Depression Scale in male psychiatric inpatients [23]. The SDS contains one item that relates to fatigue: item 10: *I get tired for no reason.* Inclusion of this item in any test of the association between fatigue and the SDS total score might confound that relationship, and so the SDS total score was recalculated to exclude this item and thus produce a measure of SDS-minus-Fatigue, called the "SDS-F" score.

Procedure

The "retrospective pre-test" procedure [24] was adopted in this study to measure participants' change in fatigue levels from before diagnosis to the time of the survey. In this procedure, participants are asked to answer one copy of a questionnaire [in this study, the FSS] for how they feel at the present time, and another copy for how they felt at a defined point in the past. Unlike the traditional pre-test versus post-test design, the retrospective pre-test avoids such sources of invalidity as history, maturation and testing artefacts [25], and has been used in studies of depression in PCa patients [26].

Patients received a Participant Information Statement, Background Questionnaire, SDS, CDRISC and two copies of the FSS. They were asked to fill out the SDS and CDRISC and one copy of the FSS for how they felt "now", and one copy of the FSS for how they felt "before getting their diagnosis of prostate cancer". Approval for this study was received from the UnitingCare Health Human Research Ethics Committee [Approval number 2013.32.104] in accordance with the Helsinki Declaration of 1964 and confirmed in 2013. Written informed consent was obtained from all participants.

Statistical analyses

Data were analysed via SPSS 25. Subtraction of the "before diagnosis" FSS score from the "last two weeks" FSS score produced a "Change in FSS" score. Frequencies described the sample's background, treatment history and PCa status. The SDS-F score was recalculated after deletion of item 10 [relating to fatigue: see Measures]. Data were checked for normality, and internal consistency [Cronbach Alpha] was calculated for the SDS-F, CDRISC and for the FSS data. Pearson or

TABLE 1. Background data and scale data for sample of 88 prostate cancer patients who reported an increase in fatigue following diagnosis and treatment.

Variable	Sample characteristics
Age	M = 73.48 years [SD = 7.17 years], range = 44 to 88 years
Relationship status	
With wife/partner	74.40%
Widowed	11.10%
Divorced/separated	8.90%
Never married/partnered	5.60%
Time since diagnosis	M = 59.48 months [SD = 24.18 months], range = 1 to 233 months
Treatments received	
Radiotherapy	29.20%
Surgery	7.30%
Hormone therapy	11.00%
Combinations	48.80%
Surveillance	3.70%
Current treatment	
Radiotherapy	53.30%
Hormone therapy	30.60%
Combinations	11.30%
Surveillance	4.80%
Present status	
Cancer still present, undergoing treatment	34.40%
In remission [no signs]	32.20%
Cancer recurring after previous treatment	33.40%
SDS-F	M = 33.74 [SD = 8.41], range = 19-54
CDRISC	M = 79.15 [SD = 13.48], range = 41-100
FSS before diagnosis	M = 18.33 [SD = 11.67], range = 9-63
FSS at survey	M = 24.93 [SD = 15.10], range = 9-62
FSS change	M = 6.55 [SD = 12.33], range = ¯36-44

SDS-F, Zung Self-rating Depression Scale minus one fatigue-related item; CDRISC, Connor-Davidson Resilience Scale; FSS, Fatigue Severity Scale.

Spearman correlation coefficients tested for associations between SDS-F, CDRISC and Change in FSS data and between each of these scales and the background variables. Partial correlations were used to test for the mediating effects of CDRISC upon the association between change in fatigue and SDS-F scores. Scale reliability [Cronbach alpha] procedures were used to identify the "core" components for the SDS-F with this sample, called "SDS-Core". Additionally, Pearson correlation coefficients identified which CDRISC items were significantly associated with the SDS-Core. Follow-up partial correlation analyses were conducted on these "core" component versions of the SDD-F and CDRISC.

Results

Background data

A total of 88 [29.33%] PCa patients completed usable questionnaires; their background data appear in the upper section of Table 1. Internal consistency [Cronbach alpha] for the SDS-F was 0.828, CDRISC = 0.910, FSS = 0.966 at the time of the survey and 0.964 for before diagnosis. None of the background variables [including time since diagnosis] showed any significant correlations with the SDS-F score, the CDRISC score or either of the FSS scores, or for the change in FSS scores. The SDS-F, FSS and CDRISC data did not require normalising. The summary data from each scale appear in the lower section of Table 1. There was a significant increase in patients' fatigue levels measured via the FSS from before diagnosis to the time of the survey$t$ [95] = -4.898, $P < 0.001$. There were significant correlations between CDRISC and SDS-F [r = -0.423, $P < 0.001$] and CDRISC and FSS Change [r = -0.217, $P = 0.042$]; SDS-F was significantly correlated with FSS Change [r = 0.394, $P < 0.001$].

Effect of total PR upon the association between fatigue change and depression

Total scores: Partial correlations indicated that the significant correlation between FSS Change and SDS-F remained significant when the effect of CDRISC was controlled for [r = 0.339, $P = 0.001$].

Reduction of SDS-F and CDRISC to key components: In order to undertake the second aspect of this research [i.e., examination of the effects of components of PR upon specific aspects of fatigue-related depression], the total CDRISC and SDS-F scores were subdivided to identify the "core" aspects of these variables. The SDS-F contains 19 items which address a wide range of possible depressive behaviours. Not all of these contributed equally to the depression symptom profile of this

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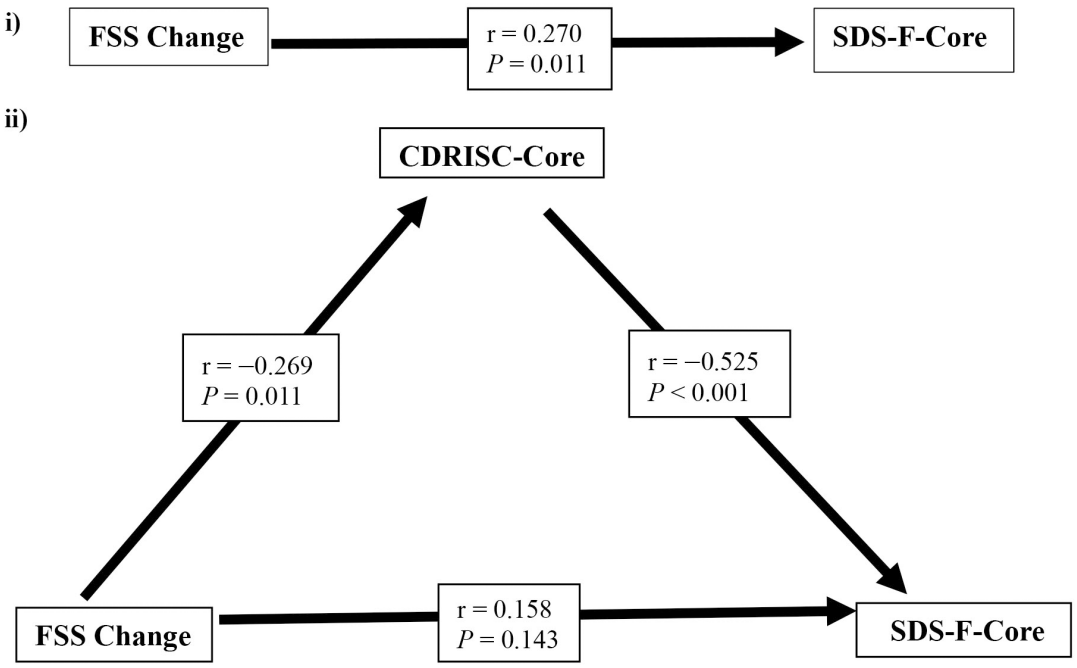

FIG. 1. Path diagrams for (i) the total effect of the independent variable FSS change on the dependent variable SDS-F-Core and (ii) the indirect effect of FSS Change on SDS-Core through the variable CDRISC-Core.

FSS Change, change in fatigue Severity Score from before diagnosis to time of survey; SDS-F Core, six SDS Core items; CDRISC Core, Connor–Davidson Resilience Scale Core items.

sample of PCa patients as indicated by internal consistency analysis of the SDS-F responses which identified the Cronbach alpha if each item was removed. This process allowed for identification of the "core" items of the SDS-F, and by applying a rule that deletion of an item must have decreased the SDS-F scale internal consistency by at least 0.005, six SDS-F items that contributed most powerfully to the internal consistency of the SDS-F were identified and their scores were summed to provide the "SDS-F-Core" subscale for this sample (Table 2).

TABLE 2. Cronbach alpha if deleted for six SDS-core items from 88 PCa patients [total scale alpha for SDS-F = 0.823].

SDS-F Items	Alpha if item deleted
11. My mind is as clear as it used to be.	0.809
12. I find it easy to do the things I used to do.	0.809
16. I find it easy to make decisions.	0.807
17. I feel that I am useful and needed.	0.81
18. My life is pretty full.	0.817
20. I still enjoy doing the things I used to do.	0.796

SDS-F, SDS minus one fatigue-related item.

The CDRISC is composed of 25 items, and the scale authors reported that these could be allocated across five underlying factors [17], supporting the heterogeneity of those 25 items. However, the factor structure of a scale can vary according to the sample [27], and the CDRISC authors did not include PCa patients in their normative sample. An alternative is to test each of the 25 items for its association with patients' depression [i.e., the SDS-F-Core]. Pearson coefficients were calculated, and CDRISC items were excluded if their p values were not less than the Bonferroni-corrected level of 0.05/25 = 0.002. CDRISC items 6, 7, 8, 12, 14, 19 and 22 met this criterion and their sum was calculated as the CDRISC-Core score. The content of these six CRISC items, plus their Pearson correlation with SDS-F-Core score, are shown in Table 3.

FSS-Change was not subject to this kind of item reduction process because the research questions posed in the Introduction assumed the total range of fatigue-related behaviours included in the FSS, because FSS Change is an indication of the change over time in the scores from the FSS.

Effect of key PR components upon the association between fatigue change and core depression symptoms

Applying partial correlations again to detect the effects of the CDRISC-Core upon the association between FSS-Change and SDS-F-Core indicated that the zero-order correlation between FSS Change and the SDS-F-Core subscale was r = 0.270, $P = 0.011$, but when CDRISC-Core was controlled for, that association reduced to non-significance [r = 0.158, $P = 0.143$]. This association is shown in Fig. 1.

TABLE 3. CDRISC-core items with significant [$P < 0.002$] correlation with SDS-F-core.

CDRISC item	Pearson r with SDS-F-core	*P*
6. I can see the humorous side of things	-0.309	< 0.001
7. I believe that coping with stress strengthens me	-0.375	< 0.001
8. I tend to bounce back after illness or hardship	-0.466	< 0.001
12. When things look hopeless, I don't give up	-0.421	< 0.001
14. When I'm under pressure, I can focus and think clearly	-0.482	< 0.001
19. I can handle unpleasant feelings	-0.347	0.001
22. I am in control of my life	-0.365	< 0.001

CDRISC, Connor-Davidson Resilience Scale; SFS-F, Zung Self-rating Depression Scale minus one fatigue-related item.

Discussion

The key aspects of PR reduced the association between change in fatigue [from before diagnosis and treatment] and the core relevant symptoms of depression. This ameliorating effect of aspects of PR upon one of the major contributors to the core of PCa depression extends the previous reports of the beneficial effect of PR on depression severity. Like PR, depression is a heterogeneous construct [12], and isolation of the core symptoms of depression as measured by the SDS enables identification of which aspects of PR might be activated in PCa patients to help them resist the depressive effects of an increase in their fatigue.

The results of this study align with some recent hypotheses regarding the complex nature of cancer-related fatigue and its treatment [28], and the treatment of comorbid disorders such as anxiety, depression and pain in PCa patients [29]. The association between fatigue and depression has been reported for some time [30] and, although some interesting hypotheses have been generated for the "causes" of fatigue in PCa patients [e.g., age, presence of depression and being treated with hormone therapy [31]], the literature search conducted for this study did not identify any previous reports about the influence of PR on the association between fatigue and depression.

The value of PR in helping people resist the depressive effects of stress has been reported by Loprinzi, Prosad, Schroeder *et al.* [32], who found that resilience training was effective in reducing stress in breast cancer patients. Similar results have been found for resilience training in military settings [33], police forces [34], business [35] and medical staff [36]. Although no reports were found regarding the effectiveness of PR training for PCa patients, this represents a potentially fruitful area for research aimed at ameliorating the depressive effects of fatigue and other PCa-related factors. It may be valuable to incorporate the findings of the current study to focus PR training upon those core aspects of resilience that were identified here (Table 3), particularly if patients present with depression that is associated with fatigue. It may also be relevant to adjust PR training to fit the particular "target" variables that patients complain about, which may include fatigue and depression, but may also be anxiety, relationship issues or specific side effects of various treatments for PCa, such as surgery, radiotherapy or hormone therapy.

Limitations of this study include the localisation of the sample and the self-selection of participants. Self-selected research participants may represent those whose emotional life [i.e., depression] is less aggravated than others [who may not feel capable of responding or interested in doing so]. No information was available regarding the PCa patients who received an invitation to participate in this study but did not accept it. The study was cross-sectional and longitudinal data would inform about any variability in the effect of PR upon fatigue-related depression. Although the scales used are well-validated, and have been used in research on PCa patients previously, self-reports may be subject to bias that could be reduced if clinical interviews were used to gather data. Finally, this study was exploratory only [due to lack of previous data on these issues] and no attempt was made to perform a formal "mediation" study, but rather to apply partial correlational analysis as an investigative process. Investigation of the exact "causal" pathways between PCa symptoms, treatment type and outcome, and fatigue and depression needs controlled trials and longitudinal studies.

Conclusions

This is the first report of the effects of particular aspects of PR on specific fatigue-related symptoms of depression in PCa patients. Although the results are confined to these restricted parameters of PR and depression, they do provide an insight into the ways that PR may act to assist these men to avoid or reduce their depression that is influenced by an increase in their fatigue. As such, these findings might be incorporated into clinical treatment settings when PCa patients present with depression, and potentially reduce the associated negative sequelae of depression in these men, such as increased suicide rate [37] and associated treatment costs [38].

Acknowledgements

The authors express their gratitude to the prostate cancer patients who participated in this research.

Funding

No funding was received for this study.

Conflict of interest

The authors declare no conflict of interest.

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