Original Article

Development and Initial Validation of the Novel Scale for Assessing Quality of Life of Prostate Cancer Patients Receiving Androgen Deprivation Therapy

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Abstract

Background: There has been no a specific scale to measure quality of life (QOL) for prostate cancer patients receiving androgen deprivation therapy (ADT) to date. This study aimed to develop and initially validate the scale to evaluate QOL for prostate cancer patients receiving ADT.

Methods: The scale was developed following international recommendations. Moreover, the items were all generated through literature review and referenced questionnaires. After being reviewed by expert panelists, the revised scale was formed and then completed by a convenience sample of 200 prostate cancer patients from our hospital. Explore factor analysis (EFA) was applied to test the construct validity, then split-half reliability, Cronbach's alpha, and test-retest reliability were applied to assess the reliability and stability of the scale.

Results: The revised scale contained 22 items and a total of 200 participants had completed the scale. One hundred participants were randomly selected from the total 200 participants to perform EFA with varimax rotation on the revised scale, and "hot flashes" item was deleted for low factor loading. We selected only 3 items from each factor, then, the final scale was formed with 18-items. We selected another 100 participants to perform the EFA again on the final scale. It was demonstrated that the structure with 6 factors explained 72.5% of total variance and factor loading value was above 0.40 in all items of the factors. Moreover, the split-half reliability coefficient, Cronbach's alpha, and test-retest reliability coefficient were calculated to be 0.74, 0.63, and 0.89, respectively, exhibiting good reliability on the whole.

Conclusions: The scale was identified to be a valid and reliable instrument to measure QOL for prostate cancer patients receiving ADT. Moreover, further research is needed to overcome the potential drawbacks.

Key words: Androgen Deprivation Therapy; Exploratory Factor Analysis; Prostate Cancer; Quality of Life; Scale

Introduction

Prostate cancer is the most common malignancy in men, and it is the second leading cause of cancer death in the United States and Europe.[1-3] Androgen deprivation therapy (ADT) is more and more widely used in prostate cancer patients. It has been recommended by guidelines as the first-line treatment for patients with metastatic prostate cancer and for individuals with disease recurrence after primary treatment. In addition, about 40.8% (7867 of 19,271) of patients with localized prostate cancer (Stage T1–T2) received primary ADT in the United States.[4] However, a growing body of evidence shows that ADT is associated with male climacteric symptoms: sweating, hot flashes, sexual dysfunction, fatigue, anemia, osteoporosis, and muscle loss, which lead to deterioration of quality of life (QOL) ultimately.[5,6]

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.213416

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Received: 11-04-2017 **Edited by:** Yi Cui
How to cite this article: Dun YJ, Liu HX, Yu LP, Li Q, Zhang XW, Tang X, Qin CP, Xu T. Development and Initial Validation of the Novel Scale for Assessing Quality of Life of Prostate Cancer Patients Receiving Androgen Deprivation Therapy. Chin Med J 2017;130:2082-7.

There has been a rapid increase of interest in QOL among patients with prostate cancer in the past decade. Moreover, it is now widely accepted that the impact of the particular therapeutics on QOL should be taken into consideration when the clinical decisions are made. However, there has been no a specific scale to measure QOL of prostate cancer patients receiving ADT to date. In addition, the criterion standard to assess QOL for these patients is an SF-36 questionnaire,[7] which is just a general scale that could be applicable to all people. Therefore, we do not have a proper tool to estimate the QOL of such patients. This study shed light on this hidden field and aimed to develop and initially validate a novel QOL scale designed for prostate cancer patients receiving ADT. It would help urologists and general practitioners to have an accurate understanding of our patients and improve their care.

Methods

Ethical approval

This study was approved by the Ethical Committee of Peking University People's Hospital. All participants had signed informed consent.

Item generation and scale development

We generated the items through literature review and referenced questionnaires including University of California-Los Angeles Prostate Cancer Index (PCI),[8] Expanded PCI Composite,[9] Functional Assessment of Cancer Therapy-General,[10] Functional Assessment of Cancer Therapy-Prostate cancer,[10] European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire,[11] and SF-36.[7] The scale was designed to contain six dimensions, including vitality, sexual function, hormone-related symptoms, anxiety, depression, and micturition/defecation. And, each dimension was arranged to cover 3- to 6-items. Ultimately, a pool of 27 items was generated and all items were scored from 0 (very severe) to 5 (no) according to the severity of the symptoms.

Validity testing

Content validity

Three urological oncology experts, 2 epidemiologists, 4 nurses of urology department, and 10 prostate cancer patients worked as a group to examine the scale. The criteria for content validity evaluation were as follows: (1) items were relevant to the corresponding dimensions; (2) items could be easily understood by patients surveyed. After the examination, the formed scale was arranged to be answered by participants.

Construct validity

To test the validity of the scale, 100 participants were randomly selected from our study sample of 200 participants to perform the exploratory factor analysis (EFA) with the principal component method and varimax rotation. The items with factor loading greater than or equal to 0.4 were selected from the EFA, and we chose only 3 items from each factor to form the final scale. Then, another 100 participants were selected to perform the EFA again to test the construct validity.

Reliability testing

Split-half reliability

We split the items of the scale into two parts, one part contained odd number items, and another part contained even number items, then we calculated the correlation between two parts' total scores.

Cronbach's alpha

We used Cronbach's alpha to measure the interrelatedness among the items, and a value of 0.70 and above was considered acceptable.

Test-retest reliability

To find out the stability of the scale's results, we did a test-retest reliability analysis. From the surveyed patients, we randomly selected thirty patients to answer the scale again 2 weeks after they finished their first-time survey, with a value of 0.70 and above indicating good stability.

Participants

A convenience sample of 200 prostate cancer patients diagnosed from June 2008 to June 2015 in our hospital were invited to complete the scale on January 2016. And, all participants should meet the following inclusion criteria: (1) pathologically identified primary prostate cancer, (2) had received ADT for at least 6 months, (3) had not received other treatments such as surgery, radiation and chemotherapy, and (4) capable to understand all the items in the scale and willing to complete the scale.

Statistical analysis

All data analysis was performed by SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). If data were a normal distribution, they were reported as mean ± standard deviation (SD) and analyzed with *t*-test, otherwise, they were reported as median (P_{25}–P_{75}), and analyzed with Mann-Whitney *U*-test. And, categorical variables were reported as counts and analyzed with Chi-square test. Cronbach's alpha and Pearson correlation were applied to test the reliability of the scale, while EFA was performed to test the validity of the scale.

Results

Participants characteristics

A total of 200 male participants were enrolled in this study, with a mean age of 73.91 years old. The majority of participants were Hans, married, retired. All participants had received ADT for at least 6 months, and 71.0% of them had taken it for at least 2 years. The participants receiving simple medical castration, simple bilateral orchidectomy, anti-androgen monotherapy, maximal androgen blockade, and intermittent hormone therapy accounted for 15.5%, 7.0%, 2.0%, 56.5%, and 19.0% of the entire participants, respectively. All participants had completed our revised scale. Totally, 100 participants were randomly selected to perform the EFA on the revised scale; then, another 100 participants were selected to perform the EFA again on

the final scale. The detailed information about general and clinical characteristics of the first 100 participants for the revised scale and the second 100 participants for the final scale were listed in Table 1.

Table 1: Distribution of sociodemographic and clinical characteristics of the participants (n = 200)

Characteristics	Value or n		P
	First 100 participants	Second 100 patients	
Age at diagnosis (years)	74.86 ± 6.75*	73.07 ± 7.24*	0.07
<60	3	4	0.89
60–69	20	22	
70–79	53	54	
≥80	24	20	
Ethnicity			
Han	98	99	0.56
Non-Han	2	1	
Education			
Less than high school	14	15	0.93
High school + some college	37	38	
College graduate	37	33	
Advanced degree	12	14	
Marital status			
Married	96	97	0.70
Not married	4	3	
Employment status			
Employed	3	4	0.70
Retired	97	96	
CCI score			
0	56	60	0.84
1	28	25	
≥2	16	15	
Baseline PSA values (ng/ml)	24.79 (11.48–60.30)†	20.00 (8.33–52.10)†	0.18
<10	20	30	0.26
10–20	24	21	
>20	56	49	
Gleason score			
≤6	33	32	0.98
7	38	38	
≥8	29	30	
Clinical T stage			
T1	11	10	0.91
T2	67	70	
T3	9	10	
T4	13	10	
Clinical N stage			
N0	86	90	0.38
N1	14	10	
Clinical M stage			
M0	92	88	0.35
M1	8	12	
ADT style			
Simple medical castration	15	16	0.98
Simple bilateral orchidectomy	8	6	
Antiandrogen monotherapy	2	2	
Maximal androgen blockade	57	56	
Intermittent hormone therapy	18	20	
ADT duration (months)			
6–12	5	6	0.93
13–24	23	24	
>24	72	70	

*Mean ± SD; †Median (P_{25}–P_{75}). CCI: Charlson comorbidity index; ADT: Androgen deprivation therapy; PSA: Prostate-specific antigen; SD: Standard deviation.

Content validity

The content validity of the scale was measured by the researchers group, which contained urological oncology experts, epidemiologists, nurses, and prostate cancer patients. After examination by the researchers, five items were excluded from the scale, two for irrelevant to the corresponding dimension and three for overlapped with other items. Then, a revised scale with 22 items under six dimensions was generated, as described in Table 2. All participants completed the generated 22-item scale with the responding rate at 100%, and the detailed scores of all items were also shown in Table 2.

Construct validity

A total of 100 participants were randomly selected to perform the EFA with varimax rotation on 22-items. The results showed that factor loadings of all items exceeded 0.40 at definite factors except 1-item "hot flashes". Thus, it was deleted from the scale. And, we selected only 3 items from each factor, then the final scale was formed with only 18-items, which was exhibited in Table 3 according to factor loadings from the first EFA.

Furthermore, we selected another 100 participants to perform the EFA again on the final scale with 18 items; the eigenvalues of the correlation matrix and the rotate factor pattern were demonstrated in Table 4 and 5, respectively.

Reliability testing results

We split the scale into two parts, found out that the related coefficient of the inner structure testing was 0.74 ($P < 0.001$); the Cronbach's alpha was 0.63 ($P < 0.001$), which almost achieved the standard.

And, a total of thirty patients were retested 2 weeks later, after they finished the scale. The coefficient between first total score and the retest total score was 0.89 ($P < 0.001$), indicating good stability.

Discussion

In the present study, we developed and preliminarily validated a new suitable scale for these participants. During the development of the scale, the item pool was formed according to available literature and previous scales. The evaluation from our researchers group eliminated inappropriate items further, which brought about the revised scale.

Validity and reliability studies should be undertaken to standardize a scale and confirm its ability to bring more accurate information.[12] The validity of a scale is considered to be the degree to which the scale measures what it claims to measure. Content validity demonstrates the extent which the scale represents a given objective. And, content validity evaluation often includes results from the available literature, expert consultation, and patients input derived from qualitative research.[13] In the current study, these elements were all covered, which meant that our scale had good content validity. And, construct validity refers to the extent to which operationalizations of a construct do actually measure what the theory says they do. In EFA, the model was examined on a structure with 6 factors after 4 items were removed from our scale. It was demonstrated that the structure with 6 factors consisting of 18 items explained 72.5% of total variance, and factor loading value was above 0.40 in all items of the factors. All these results

Table 2: The designed six dimensions of the revised scale and detailed items affiliated to them

Dimensions	Items	Score (mean ± SD)
Hormone-related symptoms	P1 hot flashes	3.04 ± 1.57
	P2 weight gain	4.36 ± 1.22
	P3 changed appearance	3.86 ± 1.69
	P4 breast tenderness	4.43 ± 1.35
Anxiety	P5 feeling anxious or nervous	3.81 ± 1.91
	P6 easy to lose temper	3.88 ± 1.90
	P7 lack of patience for others	4.03 ± 1.75
Depression	P8 deterioration of memory	4.01 ± 1.55
	P9 not handy in work than before	3.64 ± 1.78
	P10 feeling depressed	3.66 ± 1.96
Vitality	P11 feeling fatigued or tired	3.30 ± 1.92
	P12 poor sleep	3.89 ± 1.62
	P13 weak in spirits	3.72 ± 1.74
	P14 easy to doze off after the meals	3.75 ± 1.79
	P15 loss of energy	3.23 ± 1.92
	P16 decreased physical activity	3.52 ± 1.85
Micturition/ defecation	P17 frequent micturition	3.31 ± 1.60
	P18 difficulty in defecation	4.77 ± 0.80
	P19 difficulty in micturition	4.37 ± 1.04
Sexual function	P20 loss of libido	0.32 ± 0.80
	P21 erectile dysfunction	0.33 ± 0.87
	P22 avoiding sexual behavior	0.35 ± 0.91

SD: Standard deviation.

Table 3: Items of the final scale

Dimensions	Items
Sexual function	P21 erectile dysfunction
	P20 loss of libido
	P22 avoiding sexual behavior
Anxiety	P6 easy to lose temper
	P5 feeling anxious or nervous
	P7 lack of patience for others
Vitality	P16 decreased physical activity
	P15 loss of energy
	P14 easy to doze off after the meals
Depression	P8 deterioration of memory
	P10 feeling depressed
	P9 not handy in work than before
Hormone-related symptoms	P3 changed appearance
	P2 weight gain
	P4 breast tenderness
Micturition/defecation	P19 difficulty in micturition
	P18 difficulty in defecation
	P17 frequent micturition

demonstrated that construct validity of our scale was at an acceptable level.

Reliability is concerned with the repeatability or reproducibility of the measurement. To test reliability, we evaluated internal consistency, test-retest reliability, and split-half reliability of the scale in this study. The most widely used method for evaluating internal consistency is Cronbach's alpha. The value of Cronbach's alpha, test-retest reliability and split-half reliability all ranges from 0 to 1 and the higher the score, the more reliable the developed scale is. It has been widely established that 0.70 is an acceptable reliability value for all these coefficients. In our study, the value of test-retest reliability and split-half reliability exceeded 0.70, while Cronbach's alpha had only a value of 0.63, which was not satisfactory for internal consistency. With all these values taken into account, we can conclude the scale was approximately reliable on the whole.

Therefore, the scale was a valid and reliable scale in all statistical operations. To the best of our knowledge, the newly developed scale was the first scale aimed to assess the QOL among prostate cancer patients receiving ADT. It would provide plenty of information and assistance to urologists and general practitioners. They were able to monitor side effects of ADT via the scale and have an insight into the most serious side effects that bothered the patients. Moreover, they could change definite ADT strategy or take some intervention measures at the appropriate point to improve their QOL.

However, there were several inherent limitations to our study. First, the sample size was relatively limited, which restricted the widespread use of our scale. Further research in larger population is necessary. And, it was of great importance to recognize that our results could only apply to prostate cancer patients whose disease remained stable because men who progressed or died were censored in our study. Second, given that there was no criterion scale for prostate cancer patients receiving ADT currently, we did not test the criterion-related validity of the scale. Third, item titled "hot flashes" was eliminated from the scale for its factor loading less than 0.4 at each factor. It was reported previously that as many as 80% of men receiving ADT for prostate cancer experience hot flashes and 27% report hot flashes as the most distressing side effect of ADT.[14] And, hot flashes could be a significant impediment to QOL for men receiving ADT. The lack of this item was an important defect of our scale. Thus, further work is needed to adjust the items. Although these limitations, it is believed that this scale could be used to preliminarily evaluate QOL for prostate cancer patients receiving ADT and guide clinical practice. In addition, other researchers could gain enlightenment from our study and try to avoid inappropriateness reflected in this paper.

In conclusion, the scale showed adequate psychometric properties for application in evaluating QOL among prostate cancer patients receiving ADT. It has been identified to be a valid and reliable scale. From now on, the impact of ADT on QOL among prostate cancer patients could be evaluated comprehensively and quantified through the scale. And, more evidence of the validity and reliability of the scale would be accumulated over time as its application in more

Table 4: Eigenvalues of the correlation matrix

Factors	Eigenvalues	Difference	Proportion	Cumulative
1	3.638721	0.759374	0.2022	0.2022
2	2.879347	0.65619	0.16	0.3621
3	2.223157	0.562376	0.1235	0.4856
4	1.660781	0.263404	0.0923	0.5779
5	1.397377	0.144254	0.0776	0.6555
6	1.253123	0.342348	0.0696	0.7251

Table 5: The rotate factor pattern for the final scale with 18-items

Items	Factor 1 (sexual function)	Factor 2 (anxiety)	Factor 3 (vitality)	Factor 4 (depression)	Factor 5 (hormone-related symptoms)	Factor 6 (micturition/ defecation)
P21	0.9727	0.01937	0.06031	0.10087	0.00684	0.05065
P20	0.96937	0.00678	0.06408	0.06593	0.00635	0.03059
P22	0.96462	−0.02654	0.08461	0.11124	0.02121	0.05442
P6	−0.03998	0.95814	−0.00319	0.07597	0.00297	−0.0464
P5	0.05009	0.90694	0.01956	0.08068	−0.00236	0.0189
P7	−0.01467	0.89953	−0.0222	0.15129	0.08779	−0.01853
P16	0.07555	0.04734	0.9082	0.04104	0.02398	0.05722
P15	0.10698	−0.04878	0.87523	0.19337	0.03569	−0.06134
P14	0.01871	−0.00142	0.83552	0.01034	0.05674	0.07588
P8	0.15092	0.20378	0.0448	0.73768	0.08556	0.16507
P10	0.05599	−0.06113	0.06704	0.73519	0.01128	−0.05764
P9	0.07652	0.2826	0.12746	0.69271	0.1888	−0.01566
P3	0.02696	0.056	0.11294	0.13054	0.81011	−0.1315
P2	−0.14182	0.07037	0.092	0.29749	0.70015	−0.06589
P4	0.09602	−0.02731	−0.06374	−0.08543	0.66747	0.11332
P19	0.03526	−0.05511	0.02089	−0.02036	−0.03178	0.81444
P18	−0.10173	−0.05166	−0.04211	0.24441	−0.22149	0.58389
P17	0.22992	0.08114	0.11551	−0.1278	0.21511	0.57143

patients. Moreover, further research is needed to overcome the potential drawbacks.

Financial support and sponsorship

The study was supported by Beijing Municipal Science and Technology Project (No. Z141100002114019).

Conflicts of interest

There are no conflicts of interest.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7-30. doi: 10.3322/caac.21332.
2. Zhang HY, Cui J, Zhang Y, Wang ZL, Chong T, Wang ZM. Isoflavones and prostate cancer: A review of some critical issues. Chin Med J 2016;129:341-7. doi: 10.4103/0366-6999.174488.
3. Wang X, Wang JY, Li CM, Zhang YQ, Wang JL, Wan B, *et al.* Evaluation of the prostate imaging reporting and data system for magnetic resonance imaging diagnosis of prostate cancer in patients with prostate-specific antigen <20 ng/ml. Chin Med J 2016;129:1432-8. doi: 10.4103/0366-6999.183419.
4. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, *et al.* Survival following primary androgen deprivation therapy among men with localized prostate cancer. JAMA 2008;300:173-81. doi: 10.1001/jama.300.2.173.
5. Nguyen PL, Alibhai SM, Basaria S, D'Amico AV, Kantoff PW, Keating NL, *et al.* Adverse effects of androgen deprivation therapy and strategies to mitigate them. Eur Urol 2015;67:825-36. doi: 10.1016/j.eururo.2014.07.010.
6. Casey RG, Corcoran NM, Goldenberg SL. Quality of life issues in men undergoing androgen deprivation therapy: A review. Asian J Androl 2012;14:226-31. doi: 10.1038/aja.2011.108.
7. Wang ZY, Li T, Wang CT, Xu L, Gao XJ. Assessment of 1-year outcomes in survivors of severe acute respiratory distress syndrome receiving extracorporeal membrane oxygenation or mechanical ventilation: A prospective observational study. Chin Med J 2017;130:1161-8. doi: 10.4103/0366-6999.205847.
8. Descazeaud A, Zerbib M, Hofer MD, Chaskalovic J, Debré B, Peyromaure M. Evolution of health-related quality of life two to seven years after retropubic radical prostatectomy: Evaluation by UCLA prostate cancer index. World J Urol 2005;23:257-62. doi: 10.1007/s00345-005-0004-8.
9. Wagner AA, Cheng PJ, Carneiro A, Dovirak O, Khosla A, Taylor KN, *et al.* Clinical use of expanded prostate cancer index composite for clinical practice to assess patient reported prostate cancer quality of life following robot-assisted radical prostatectomy. J Urol 2017;197:109-14. doi: 10.1016/j.juro.2016.07.080.
10. Esper P, Mo F, Chodak G, Sinner M, Cella D, Pienta KJ. Measuring quality of life in men with prostate cancer using the functional assessment of cancer therapy-prostate instrument. Urology 1997;50:920-8. doi: 10.1016/S0090-4295(97)00459-7.
11. Guzelant A, Goksel T, Ozkok S, Tasbakan S, Aysan T, Bottomley A. The European Organization for research and treatment of cancer QLQ-C30: An examination into the cultural validity and reliability of the Turkish version of the EORTC QLQ-C30. Eur J Cancer Care (Engl) 2004;13:135-44. doi: 10.1111/j.1365-2354.2003.00435.x.
12. Capik C, Gözüm S. Development and validation of health beliefs model scale for prostate cancer screenings (HBM-PCS): Evidence from exploratory and confirmatory factor analyses. Eur J Oncol Nurs 2011;15:478-85. doi: 10.1016/j.ejon.2010.12.003.
13. Magasi S, Ryan G, Revicki D, Lenderking W, Hays RD, Brod M, *et al.* Content validity of patient-reported outcome measures: Perspectives from a PROMIS meeting. Qual Life Res 2012;21:739-46. doi: 10.1007/s11136-011-9990-8.
14. Gonzalez BD, Jim HS, Donovan KA, Small BJ, Sutton SK, Park J, *et al.* Course and moderators of hot flash interference during androgen deprivation therapy for prostate cancer: A matched comparison. J Urol 2015;194:690-5. doi: 10.1016/j.juro.2015.03.026.