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Original Article

Identification of distinct symptom profiles in prostate cancer patients with cancer-related cognitive impairment undergoing androgen deprivation therapy: A latent class analysis

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ABSTRACT

Objective: To identify latent classes of cognitive impairment and co-occurring symptoms (fatigue, pain, sleep disturbance, depression) as clusters in patients with prostate cancer undergoing androgen deprivation therapy and to explore the predictors among distinct latent classes.

Methods: A total of 228 patients with prostate cancer were recruited in this cross-sectional study. The assessment instrument included the Perceived Cognitive Impairment Scale, the Fatigue Severity Scale, the Athens Insomnia Scale, the Brief Pain Inventory, the Patient Health Questionnaire-9, the UCLA Loneliness Scale, the International Physical Activity Questionnaire - Short Form, the Charlson comorbidity index, and General Information questionnaire. The identification of different patient subgroups was done by the latent class analysis.

Results: The study identified three distinct latent classes: all low symptoms (class 1, 32%), high depression symptoms (class 2, 37.7%), and high physical symptoms (fatigue, sleep disturbance, and pain) with high cognitive impairment (class 3, 30.3%). Patients who had higher Charlson comorbidity index ($P = 0.003$) scores were more likely to be classified in class 3. Patients with higher loneliness scores ($P < 0.001$; $P < 0.001$) were significantly more likely to fall into class two or three than in class 1. However, having a higher level of physical activity ($P = 0.014$; $P < 0.001$) increased the likelihood of being in class 1.

Conclusions: This study exhibited the inter-individual variability of symptom experience in prostate cancer patients with cognitive impairment undergoing androgen deprivation therapy. The result suggests that more emphasis should be placed on screening for fatigue, sleep disturbance, and pain, and future interventions should focus on loneliness and physical activity.

Introduction

Prostate cancer (PC) is a prevalent malignant tumor that poses a significant threat to men's health worldwide. Its incidence rate is among the highest of all malignant tumors in men aged over 60 years globally, with 1,216,139 estimated emerging cases in 2020.[1] Androgen deprivation therapy (ADT) is an effective treatment for PC, and about half of patients will eventually receive ADT.[2] Consequently, ADT can cause various systemic symptoms and metabolic alterations.[3] Unfortunately, these treatment-related side effects can have a significant impact on the quality of life for PC patients and worsen the treatment burden associated with ADT.[4]

The literature on the correlation between ADT and cognitive impairment remains mixed, suggesting that other factors may contribute to cognitive impairment.[5,6] Research of symptom clusters from other cancer populations indicates robust associations between co-occurring symptoms (fatigue, sleep disturbances, pain, depression) and cognitive impairment and that patients with cognitive impairment experienced distinct co-occurring symptom profiles.[7–9] These symptoms are also prevalently reported among PC patients with cognitive impairment,

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especially following ADT.[6,10] However, exploring symptom clusters of cognitive impairment and common co-occurring symptoms remains poorly understood in PC patients undergoing ADT.[11]

Emerging research has reported that loneliness, physical activity, and comorbidity burden are correlated with cancer-related symptoms, such as psychoneurological symptoms (e.g., cognitive impairment, fatigue, sleep disturbance, pain, and depression).[8,12–14] The Symptom Interactional Framework suggests that the shared or interactive mechanisms in physiological, psychological, behavioral, or sociocultural factors may cause the symptoms to occur individually or in clusters.[15] However, research regarding comorbidity burden, loneliness, physical activity, and psychoneurological symptoms in PC patients remains scarce. PC patients who were physically inactive and who had higher comorbidity burden experienced higher levels of fatigue, pain, and depression, with a poorer quality of life.[12,13] Additionally, chronic loneliness may indirectly contribute to the progression of depression in PC patients.[16] Thus, identifying the latent class of symptom clusters with cognitive impairment as the primary symptom may provide us with a better comprehension of the symptom profile in PC patients treated with ADT. Furthermore, expanding cognitive impairment research beyond prior ADT exposure and focusing on modifiable factors has the potential to provide a new perspective for managing symptom clusters in PC patients.

Previous studies of ADT symptomatology are still predominantly in the form of individual symptoms rather than symptom clusters, which may not fully allow us to understand the symptom presentation in ADT recipients. In addition, oncology patients' symptom experiences may differ based on inter-individual variability.[17] Using a variable-centered approach to categorize symptom clusters and the subsequent placement of patients into identified categories may not provide an understanding of which survivor needs more intensive symptom management.[11] A person-centered approach, such as latent class analysis (LCA), presents an opportunity to identify subgroups of oncology patients with similarities in symptom phenotypes that distinguish them from the other subgroups.[8] The present study, for PC patients undergoing ADT, aims to identify latent classes of cognitive impairment and co-occurring symptoms as clusters using LCA in PC patients treated with ADT and to explore the predictors among distinct latent classes.

Methods

Participants

Between June 2023 and January 2024, we recruited outpatients with PC who received ADT through convenience sampling at a tertiary general hospital in Zhejiang Province, China. The inclusion criteria for participation were as follows: (a) pathologically diagnosed with prostate cancer; (b) receiving ADT and had $>$ 8 weeks of ADT[18]; (c) aged $\geq$ 18 years; and (d) aware of their condition and given consent in this study. Participants who were critically ill and had a history of cognitive impairment were excluded.

The sample size in this study followed the requirements of logistic regression analysis and was required to be at least 10 times the number of independent variables, which are 18 in this study. Thus, the minimum sample size required was 198, accounting for a possible 10% of invalid questionnaires.[9]

Measures

Sociodemographic and clinical characteristics

We collected age, body mass index (BMI), marital status, occupation, household monthly income per capita (HMIPC), and education level via self-report. Latest prostate-specific antigen (PSA), Gleason scores (prostate cancer severity score), and time since ADT via medical records were also collected. Occupation was reported based on the classifications defined by Nucci.[19]

Cognitive impairment and common co-occurring symptoms

The Perceived Cognitive Impairment scale (CogPCI): Participants' cognitive impairment was assessed using CogPCI, an 18-item subscale of The Functional Assessment of Cancer Therapy Cognitive Function (FACT-Cog, version 3).[20] In this study, the 18-item CogPCI subscale (Chinese version) was employed to measure participants' cognitive function for the past week, each with a score of 0–4. The total score ranges from 0 to 72 points, and higher scores indicate less cognitive impairment. A score of CogPCI $<$ 54 indicates cognitive impairment.[9] The reliability for the CogPCI was 0.874 in this study.

The Fatigue Severity Scale (FSS): The severity of participants' fatigue was measured by the FSS for the past 7 days, which consists of seven items.[21] Higher scores indicate more severe fatigue on a seven-point Likert scale, ranging from 0 to 7, with a total score of 9–63. A clinically significant level of fatigue was defined as an FSS score $\geq$ 36. The reliability for the FSS was 0.829 in this study.

The Brief Pain Inventory (BPI): The 3-item intensity subscale of the BPI evaluated the pain intensity of participants and was rated on a 0 ("no pain") to 10 ("pain as bad as the patient can imagine").[22] The total score is an average score of three items. The BPI score $\geq$ 4 indicates that patients have a clinically significant level of pain.[23] The reliability of the BPI was 0.923 in this study.

The Athens Insomnia Scale (ASI): The ASI was applied to measure sleep disturbance of participants.[24] Higher scores indicate more severe sleep disturbance on a four-point Likert scale, ranging from 0 to 3, with a total score of 0–24. The ASI score $>$ 6 indicates that patients have a clinically significant level of sleep disturbance. The reliability for the ASI was 0.826 in this study.

The Patient Health Questionnaire (PHQ-9): Participants' depression was measured using the PHQ-9, each with a score of 0–3.[25] The total score ranges from 0 to 27 points, and higher scores indicate more severe depression. A clinically significant level of depression was defined as a PHQ-P score $\geq$ 10.[26] The reliability for the PHQ-9 was 0.779 in this study.

Comorbidity conditions

Comorbidities were collected through a questionnaire and were checked by reviewing medical records. The Charlson comorbidity index (CCI) score included 19 different medical conditions, and each comorbidity condition was weighted according to its impact on mortality.[27] Moreover, the CCI was calculated as the sum of the comorbidity score, with a higher score indicating more severe comorbidity burden.[13]

Loneliness

The loneliness was assessed by the six-item UCLA Loneliness Scale (ULS-6).[28] The ULS-6 was formed by Chinese scholars based on the eight-item UCLA Loneliness Scale by deleting two non-lonely reverse scoring entries.[29] Each item is assigned a score of 1–4 for a total score of 6–24. A higher score indicates stronger sense of loneliness. In our research, the reliability for the ULS-6 was 0.80.

Physical activity

The seven-item International Physical Activity Questionnaire - Short Form (IPAQ-SF) was used to report the amount of time spent on physical activity of three intensities: vigorous, moderate, and walking in the past week.[30] The frequency (days/week) and duration (minutes/day) spent on each intensity of physical activity were multiplied by the metabolic equivalent (MET) values (walking = 3.3, moderate intensity = 4, vigorous intensity = 8). The total energy spent in physical activity was calculated by summing the MET min/week in individuals' light, moderate, and vigorous activities. The American Cancer Society (ACS) recommends that cancer survivors should conduct at least 150 min of moderate-intensity or 75 min of vigorous-intensity physical activity per week, equivalent to at least 600 MET minutes of physical activity every week.[31] In our research, the reliability for the IPAQ ranges from 0.72 to 0.81.

Data collection

Patient questionnaire information was collected from patients face-to-face and one-to-one using a translated Chinese version of the instrument and by three clinical nurses who had received rigorous training in advance. To ensure privacy and to avoid interruptions, the survey was conducted in the meeting room of the urology clinic. The survey comprised eight questionnaires and took approximately 20 minutes on average. The questionnaire was read, and the investigator explained some items to participants who had difficulty comprehending, and then they were checked for completeness. Finally, all questionnaires collected were kept confidential and used solely for research purposes.

Data analysis

The IBM SPSS Statistics version 26.0 and Mplus version 8.3 were used for statistical analysis. Descriptive statistics were calculated for sociodemographic characteristics, clinical characteristics, physical activity, CCI, and loneliness variables. Continuous variables were reported as the means and standard deviation (SDs), and categorical variables were presented as frequencies and percentages.

LCA was used to classify participants into different classes based on the dichotomized scores of cognitive impairment, fatigue, sleep disturbance, pain, and depression. Each symptom was dichotomized into a binary variable using the cutoff for clinical utility. The best-fitting model was determined based on model selection criteria, such as the Akaike information criterion (AIC), Bayesian information criterion (BIC), adjusted Bayesian information criterion (aBIC), entropy, Vuong–Lo–Mendell–Rubin (LMR) test, and bootstrapped likelihood ratio test (BLRT). Relatively low AIC, BIC, and aBIC values, significant P values for LMR and BLRT, and an entropy greater than 0.8 indicated the optimal number of latent classes.[32,33] Furthermore, the clinical significance of the final number of categories should be considered.[9] Following the identification of optimal latent classes, multinomial logistic regression was used to examine the predictors that distinguish between the different latent classes. The significant factors in the χ^2 and Kruskal–Wallis tests were entered into the logistic regression model to identify the final predictors. Statistical significance for all tests was indicated at $P < 0.05$.

Ethical considerations

This study was approved by the Ethical Committee of the First Affiliated Hospital of Wenzhou Medical University (IRB No. KY2023-245). Informed consent was obtained from all study participants.

Results

Participant characteristics

A total of 242 PC patients were recruited. However, 14 patients were excluded due to incomplete outpatient personal data and invalidated questionnaires. In total, 228 patients were included. Table 1 presents the sociodemographic and clinical characteristics of the total population. Most patients were married (84.2%), with a mean age of 74.46 years (SD = 6.93). In this study, most participants (44.7%) had a Gleason score of nine or higher, and about half of the patients (71.9%) were treated with ADT for more than 1 year. The average CCI was 1.88 (SD = 1.49).

Results of latent class analysis

We selected the 3-class model based on the best fit. Table 2 presents the goodness-of-fit indicators for these latent class models. The LCA results suggest that the 3-class model was preferable, with a lower BIC value than the 2-, 4-, and 5-class models and an entropy higher than 0.8. Furthermore, the LMR and BLRT had no significant difference in the 4-class mode ($P > 0.05$), demonstrating that one lower class number is present rather than the present class number. As a result, the 3-class model was selected for further analysis.

Table 1
Participant characteristics ($N = 228$).

Characteristics	*n* (%)
Age (year, mean ± SD)	74.46 ± 6.93
BMI (kg/m^2, mean ± SD)	23.89 ± 2.68
Marital status	
Married	192 (84.2)
Divorced or widowed	36 (15.8)
Occupation	
Professional or highly intellectual work	20 (8.8)
Skilled non-manual or technical work	75 (32.9)
Skilled manual work	55 (24.1)
Unskilled manual work	78 (34.2)
HMIPC	
< 3000 RMB	59 (25.9)
3000–5000 RMB	72 (31.6)
5001–10,000 RMB	76 (33.3)
> 10,000 RMB	21 (9.2)
Education level	
Uneducated	42 (18.4)
Primary or junior high schools	112 (49.1)
Senior high school or above	74 (32.5)
Physical activity	
< 600 MET min	80 (35.1)
≥ 600 MET min	148 (64.9)
Gleason score at diagnosis	
≤ 7	38 (16.7)
8	88 (38.6)
≥ 9	102 (44.7)
Latest PSA	
< 0.1 ng/ml	129 (56.6)
0.1–1 ng/ml	44 (19.3)
> 1 ng/ml	55 (24.1)
Time since ADT	
< 12 months	64 (28.1)
12–36 months	91 (39.9)
> 36 months	73 (32.0)
CCI (mean ± SD)	1.87 ± 1.49
ULS-6 (mean ± SD)	16.74 ± 2.62

ADT, androgen deprivation therapy; BMI, body mass index; CCI, Charlson comorbidity index; HMIPC, household monthly income per capita; PSA, prostate-specific antigen; ULS-6, the six-item UCLA Loneliness Scale.

Fig. 1 shows the conditional probabilities of the five symptom indicators for each latent class. Class 1 ($n = 73$, 32.0%) had the lower frequency of occurrence for all symptom indicators and was labeled "all low." Class 2 ($n = 86$, 37.7%) was designated as "high depression symptom" and demonstrated a higher frequency of occurrence for depressive symptoms among the three latent classes. Class 3 ($n = 69$, 30.3%), labeled "high physical symptoms with high cognitive impairment," showed patients in this class had a higher frequency of occurrence for cognitive impairment and physical symptoms, such as fatigue, sleep disturbance, and pain.

Differences in patient characteristics between latent classes

Table 3 summarizes the sociodemographic characteristics, clinical characteristics, physical activity, and loneliness differences between latent classes. Occupation, physical activity, CCI, and loneliness scores revealed statistically significant differences between the three latent classes ($P < 0.05$). Patients in Class 1 had a higher level of physical activity and the lowest scores of CCI and loneliness.

Predictors of identified latent classes

Table 4 reveals multinomial logistic regression of predictors for each latent class, with class 1 as the reference category. Compared to class 1, patients who had higher CCI scores (odds ratio [OR] = 1.543, $P = 0.003$) were more likely to be classified as class 3. Patients with higher

Table 2
Fit indices for LCA model.

Class	Free parameters	AIC	BIC	aBIC	Entropy	LMR (*P*)	BLRT (*P*)	Class probability
1	5	1523.972	1541.119	1525.272	–	–	–	1
2	11	1434.269	1471.992	1437.129	0.782	< 0.001	< 0.001	0.73/0.27
3	17	1404.262	1462.561	1408.682	0.836	< 0.001	< 0.001	0.32/0.30/0.38
4	23	1403.105	1481.980	1409.086	0.810	0.379	0.065	0.22/0.31/0.15/0.32
5	29	1406.005	1505.456	1413.545	0.911	0.147	0.182	0.34/0.17/0.04/0.14/0.31

aBIC, adjusted Bayesian information criterion; AIC, Akaike information criterion; BIC, Bayesian information criterion; BLRT, bootstrapped likelihood ratio test; LCA, latent class analysis; LMR, Lo–Mendell–Rubin likelihood ratio.

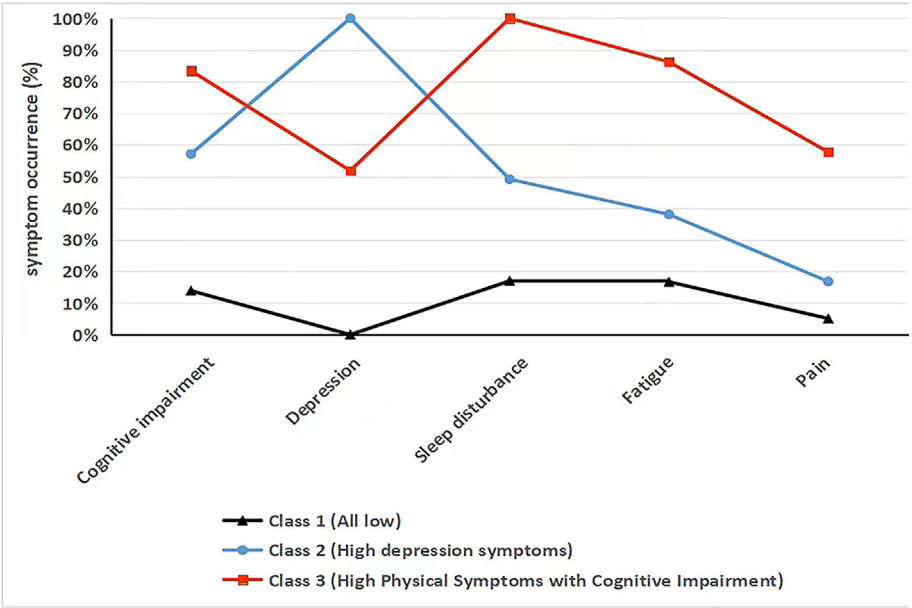

Fig. 1. Latent class profiles based on occurrence of symptoms.

Table 3
Differences in sociodemographic and clinical characteristics and scale scores between the latent classes ($N = 228$).

Variables	Class 1 ($n = 73$, 32.0%)	Class 2 ($n = 86$, 37.7%)	Class 3 ($n = 69$, 30.3%)	*P* value
Occupation, *n* (%)				0.024
Professional or highly intellectual work	7 (9.6)	6 (7.0)	7 (10.1)	
Skilled non-manual or technical work	27 (37.0)	12 (14.0)	16 (23.2)	
Skilled manual work	22 (30.1)	30 (34.9)	23 (33.3)	
Unskilled manual work	17 (23.3)	38 (44.2)	23 (33.3)	
Physical activity, *n* (%)				< 0.001
< 600 MET min	10 (13.7)	32 (37.2)	38 (55.1)	
≥ 600 MET min	63 (86.3)	54 (62.8)	31 (44.9)	
CCI (mean ± SD)	1.32 ± 1.31	1.87 ± 1.49	2.49 ± 1.44	< 0.001
ULS-6 (mean ± SD)	15.19 ± 2.71	17.59 ± 2.29	17.32 ± 2.21	< 0.001

ADT, androgen deprivation therapy; CCI, Charlson comorbidity index; MET, metabolic equivalent; SD, standard deviation; ULS-6, The 6-item UCLA Loneliness Scale.

loneliness scores (OR = 1.435, $P < 0.001$; OR = 1.372, $P < 0.001$) were significantly more likely to fall into Class two or Class three than in Class 1. However, having a higher physical activity level (OR = 0.324, $P = 0.014$; OR = 0.178, $P < 0.001$) increased the likelihood of being in class 1.

Discussion

To our knowledge, the study represents the first attempt to identify the latent class of cognitive impairment and co-occurring symptoms using LCA in PC patients undergoing ADT. Moreover, we explored the sociodemographic characteristics, clinical characteristics, CCI scores, loneliness, and physical activity, which create differences between symptom subgroups in ADT recipients.

Profiles of cognitive impairment and co-occurring symptoms

The study identified three distinct latent classes: all-low-symptom group (32.0%), high depression symptoms group (37.7%), and high physical symptoms with high cognitive impairment group (30.3%). The results suggest that ADT recipients with cognitive impairment experienced distinct symptom profiles. Patients with high cognitive impairment tend to have clinical significance such as fatigue, pain, and insomnia with probabilities of 83.4%, 57.7%, and 100%, respectively. This finding is in line with previous research on cancer that found that higher levels of fatigue, pain, and sleep disturbance were correlated with worse cognitive function.[7,9] Moreover, previous reports have confirmed the existence of subgroups of multiple psychoneurological symptoms and suggest inter-individual variability of symptom experience in cancer

Table 4
Multinomial logistic regression results: identifying the predictors of each class ($N = 228$).

Variables	Class 2 ($n = 86$, 37.7%)			Class 3 ($n = 69$, 30.3%)		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Occupation						
Professional oor highly intellectual work (reference)						
Skilled non-manual or technical work	0.395	0.097 to 1.601	0.193	0.414	0.103 to 1.668	0.215
Skilled manual work	1.238	0.327 to 4.682	0.753	0.730	0.187 to 2.854	0.651
Unskilled manual work	1.741	0.448 to 6.765	0.423	0.871	0.213 to 3.562	0.847
Physical activity						
< 600 MET min (reference)						
≥ 600 MET min	0.324	0.132 to 0.793	0.014	0.178	0.072 to 0.438	< 0.001
CCI	1.214	0.922 to 1.598	0.168	1.543	1.162 to 2.050	0.003
ULS-6	1.435	1.224 to 1.683	< 0.001	1.372	1.157 to 1.628	< 0.001

The model included occupation (professional or highly intellectual work = reference), physical activity (≥ 600 MET min = reference), CCI (unit = 1 point) and ULS-6 (unit = 1 point).
CCI, Charlson comorbidity index; CI, confidence interval; MET, metabolic equivalent; ULS-6, The six-item UCLA Loneliness Scale.

populations.[8] Notably, cognitive impairment and common co-occurring symptoms may share common biological mechanisms.[34] For example, a systematic review on cancer treatment–related psychoneurological symptoms has shown that proinflammatory immune markers and gut microbiome were associated with cognitive impairment, fatigue, sleep disturbance, pain, and depression.[35]

Predictors of different identified latent classes

This study also explored the critical predictors in identifying latent classes of symptom clusters with cognitive impairment. We found that the three latent classes revealed significant differences in the CCI scores, loneliness, and physical activity level. Patients with higher comorbidity burden were significantly more likely to belong to the high physical symptoms with the high cognitive impairment group. This finding was in line with prior research showing that the comorbidity burden of cancer patients could further aggravate the effect of treatment on cancer-related symptoms.[13] Moreover, comorbidities, such as diabetes and kidney disease, can affect cognitive function by changing the cerebrovascular structure and facilitating neurodegenerative changes.[36,37] Therefore, health care providers should give due consideration to the impact of comorbidity on the physical symptoms and cognitive functioning of PC patients before the onset of ADT and design interventions to prevent the development and worsening of comorbidity after ADT, which improves patient-centered care and treatment outcomes.

Notably, patients in the high depression symptoms group and those in the high physical symptoms with high cognitive impairment group had a higher level of loneliness than the all-low group. Our finding, that PC patients on ADT with higher levels of loneliness had higher rates of cognitive impairment and comorbid symptoms, is consistent with the previous research that has shown a positive correlation between loneliness and all of these symptoms.[14] Loneliness may also cause a state of chronic psychosocial stress characterized by pathological activation of the hypothalamic–pituitary–adrenocortical axis and impairments in immune function.[38] Chronic overactivation of this stress response, as might occur when patients consider life to arise from persistently and profoundly lacking meaningful connections, may cause or exacerbate the experience of both somatic and psychological symptoms.[39,40] Prominently, such negative impact of loneliness can inform clinical carers and researchers supporting ADT recipients of their inadequacy in care and the need for interventions to reduce the patients' loneliness and ease the symptom burden of this population.

It is well known that PC patients can benefit from adequate physical activity and physical activity may play an active role in preventing or delaying relapse, easing overall disease burden, and improving survival for the patients.[41] PC patients who achieved the ACS-recommended level of physical activity (≥ 600 MET minutes) were less likely to fall into high physical symptoms with the high cognitive impairment group and high depression symptoms group but more likely to fall into the all-low-symptom group. Importantly, this study found that adequate physical activity may be correlated with lower rates of cognitive impairment and physical symptoms. Adam et al. reported similar findings that patients in the all-low-symptom subgroup might be more active.[12] Further, the potential role of the gut microbiota linked to inflammatory pathways on psychoneurological symptom outcomes following cancer treatment in patients may be influenced by physical activity at different levels.[35,42] Interestingly, the relation between physical activity and subgroup membership was strongest between the high physical symptoms with high cognitive impairment group and all-low-symptom group (Table 4), highlighting the potential role of physical activity in cognitive impairment and physical symptoms. Furthermore, the association of adequate physical activity with low-risk cognitive impairment highlights the importance of understanding the facilitators of physical activity and further developing interventions to enhance physical activity levels for ADT recipients.

Implications for practice

Our findings demonstrate the need for health care providers to be aware that ADT recipients will experience cognitive impairment and common co-occurring symptoms. It is crucial to be proactive in providing patients with pre-emptive education programs to help them adapt to the side effects of ADT.[2] Moreover, our study suggests that ADT recipients with cognitive impairment experienced distinct symptom phenotypes, suggesting that clinicians can identify ADT recipients who are more likely to develop cognitive impairment through early assessment of patients' fatigue, sleep disturbances, pain, and depression symptoms. Also, early and effective management of cognitive impairment of ADT recipients can be achieved through symptom cluster interventions (e.g., acupressure and orthostatic decompression) tailored to individual differences and patient needs.[43] Furthermore, clinical nurses and researchers working with ADT recipients should design additional interventions for them to know the risk of adverse outcomes from comorbidity and provide evidence-based self-management strategies (e.g., adequate exercise, nutritional supplementation, stress management) to reduce the comorbidity burden of the patients. Finally, future studies should do more to understand whether reducing loneliness and promoting physical activity can prevent and mitigate the symptom clusters with cognitive impairment.

Limitations

This study has several limitations. Our study's small sample sizes limited the statistical power to detect group differences, and large samples and multicenter studies should be conducted in the future to further enhance the applicability of the findings. Additionally, due to the cross-sectional design, it is currently unknown how the identified latent classes may change over time. Future research could categorize patients

according to their evolving symptom trajectories, providing opportunities for early or preventative interventions. Our dichotomization of each symptom may cause a loss of useful information and efficacy as symptoms will likely be continuous. Furthermore, the comorbidity may have occurred after the diagnosis of PC and receipt of ADT, which may bias the findings. Finally, we only measured cognitive impairment using self-reported instruments and recommended including objective measures of cognitive function.

Conclusions

Our findings suggest that ADT recipients with cognitive impairment experience substantially distinct symptom phenotypes and multiple co-occurring symptoms, with a prevalence of high physical symptoms. Higher CCI and loneliness scores and a low level of physical activity are critical predictors of patients in the high physical symptom with high cognitive impairment group. The discovery of symptom phenotypes and influencing factors is useful in identifying PC patients undergoing ADT with high-risk cognitive impairment. In addition, health care providers should focus on cognitive function in ADT recipients who have multiple comorbidities. Future research would benefit from interventions targeting loneliness and physical activity, which may indirectly prevent and treat cognitive impairment and co-occurring symptoms in PC patients receiving ADT.

Ethics statement

The study was approved by the First Affiliated Hospital Ethical Committee of Wenzhou Medical University (IRB No. KY2023-245). All participants provided written informed consent.

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CRediT authorship contribution statement

Yongcai Liu: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft. **Qinqing Yan:** Conceptualization, Methodology, Data curation, Formal analysis. **Jieru Zhou:** Data curation, Formal analysis. **Xin Yao:** Data curation, Formal analysis. **Xiangxiang Ye:** Data curation, Formal analysis. **Wei Chen:** Data curation, Writing – review & editing. **Jian Cai:** Data curation, Writing – review & editing. **Haihong Jiang:** Critical, Writing – review & editing, Supervision. **Haiyan Li:** Conceptualization, Methodology, Writing – review & editing, Critical review and editing, Supervision. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Haiyan Li, upon reasonable request.

Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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