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The mediating effect of activity restriction on the relationship between perceived physical symptoms and depression in cancer survivors

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Abstract

Purpose: Several studies have explored factors causing depression in cancer survivors, including perceived physical symptoms. Another critical factor in the depression symptomatology of cancer survivors is activity restriction (AR). We investigated how AR mediate the effects of perceived pain and fatigue on depression in cancer survivors.

Methods: Cancer survivors (n = 61; mean age 56.16 years) that were recruited through cancer support groups in Japan participated in this study. Participants completed a battery of questionnaires comprising demographic and clinical information, the Pain Catastrophizing Scale, the Cancer Fatigue Scale, the Activity Restriction Scale for Cancer Patients, and the Hospital Anxiety and Depression Scale.

Results: Mediation analysis indicated that AR partially mediates the effect of pain on depression. Direct paths from pain to AR, AR to depression, and pain to depression were significant ($P < .005$). Moreover, indirect paths from pain to AR, AR to depression, and pain to depression were also significant at the 95% level [0.04-0.13]. However, AR did not mediate the effect of fatigue on depression, and fatigue had a significant direct path to both AR and depression ($P < .005$).

Conclusion: This study aimed to explore the mediating effect of AR in the relationships of perceived pain and fatigue and depression in cancer survivors. We found that AR mediates perceived pain to depression, however not for perceived fatigue. In addition, because AR was experienced in the face of any survivorship period, AR may need to be treated as a long-term effect of the cancer diagnosis

KEYWORDS

activity restriction, cancer, cancer survivors, depression, fatigue, mediation analysis, oncology, pain

1 | BACKGROUND

Dramatic improvements in cancer survival rates have been achieved due to the progress made in treatment of cancer.[1] Nevertheless, many cancer survivors continue to report various psychosocial difficulties during their survivorship,[2] including concerns as the fear of recurrence, fear of death, the complicated and stressful treatment, the coexistence of depressive and anxiety symptoms, and the restriction of daily activities.[3-6] Among these psychosocial difficulties, depression is a common psychiatric disorder in cancer survivors.[5] Previous studies have reported that cancer patients with depression experience a deterioration in the quality of life (QOL) and self-control skills.[7] However, depression in cancer survivors is

known to decrease after the acute phase of the disease.[8] Therefore, psychosocial symptoms might not meet the diagnostic criteria for depression. A factor rather be targeted in cancer survivorship is activity restriction, which is known as one of the predictors of depressive symptoms in cancer survivorship.[6]

Williamson and Shaffer suggested the Activity Restriction Model, which defines AR as the restriction of daily activities after the diagnosis of a physical illness, and plays a central role in psychological adjustment.[6] Previous studies focusing on restricted activities have often operationalized AR as a health status indicator, illness severity, or depression. In the Activity Restriction Model, AR is clearly distinguished from illness severity and depressive symptoms. This distinction is emphasized because not all individuals that are seriously ill become depressed nor have restricted daily activities. The mediating role of AR could possibly explain the discrepancies in the relationship between a diagnosis of physical illness and depression, because AR could occur regardless of the level of illness severity or physical disabilities. Moreover, it is highly influenced by cognitive factors such as illness perception.[6,9] The possible interrelationships between AR and illness severity with depression have not been identified to date, nor has the AR model been tested in a population of cancer survivors.[10]

In the Activity Restriction Model, perceived pain is considered an independent variable of depression.[6] Several previous studies have attempted to explore perceived physical symptoms such as pain, as a predictor of depression in cancer populations.[11,12] Physical symptoms might include cancer-related pain and fatigue, side effects of treatment, and shortness of breath.[13,14] Among these, studies on depression symptomatology in cancer patients have focused on perceived pain and fatigue. Bamonti et al indicated that interference in daily activities of cancer patients caused by pain, rather than just the physical symptoms, was associated with the reported depression in all phases of cancer.[11] Similarly, previous studies have suggested that cancer-related fatigue and depression were strongly and longitudinally correlated.[12] However, limitations in the association between perceived physical symptoms and depression have also been reported with specific studies suggesting that the severity of pain is not necessarily related to the prevalence of depression.[15] This limitation is shared with the presented problem in the AR model.

Perceived physical symptoms and AR could result in major psychosocial problems due to current cancer policies and conditions related to survivorship care. In recent years, survivorship care led by oncologists has been decreasing because of staff shortages and the development of out-patient cancer treatment.[16] As a result, cancer patients might face many difficulties in daily life when they leave the medical setting after completing their treatment. These difficulties include concerns about death, the recurrence of cancer, as well as AR. Such difficulties become amplified because the patients only have restricted contact with their oncologists.[16] Qualitative research conducted in Australia on survivorship care conditions has reported that physical symptoms are often reported by cancer patients, although psychosocial issues are unreported, and often remain undetected and underestimated in complex oncology care situations.[17] As a result, psychological problems caused by AR are hard to detect and difficult to manage. Therefore,

further research on cancer survivors is required to develop these themes into genuine, longitudinal survivorship care.[18]

To summarize, previous literature on the investigation of depressive symptomatology in cancer survivors have the following limitations: (a) The directional relationship between perceived physical symptoms (pain and fatigue) and depression is unclear; (b) The possibility that AR plays a mediating role between the perception of physical symptoms and depression has not been investigated. Moreover, the literature on depression in cancer survivors has focused mostly on breast cancer survivors.[19] Because of these limitations in psycho-oncology literature, the current study was designed to examine perceived pain and fatigue as predictors of depression in cancer survivors and the mediating effect of AR. The results of this study are expected to increase the knowledge about the depressive symptomatology of cancer survivors, and particularly regarding the role of AR on severe difficulties experienced during cancer survivorship.

2 | METHODS

2.1 | Participants and procedure

Participants were recruited from cancer patient support groups between July 2018 and December 2018. Five patient groups agreed to participate in the present study, and each representative of the patient groups signed the contract for study participation. The study representative informed patients about the study after their monthly meetings and distributed packages each containing study information, a battery of questionnaire and pre-paid return envelope. For one of the patient groups, the questionnaire was distributed through online website managed by the patient group. From the page linked to the URL presented on the web page, participants read the explanation about the purpose of the research and answered the questionnaire package. It took around 20 minutes to answer the entire battery of questionnaires. The returning of the questionnaire was considered as their consent to participate in this study. This research was conducted with the approval of Waseda University's Ethics Review Committee on Human Studies (Accreditation Number: 2018-006).

2.2 | Measures

2.2.1 | Demographic and clinical information

Demographic and clinical information including gender, age, marital status, occupation status, type of cancer diagnosis, type of cancer treatment, cancer stage, and time since the cancer diagnosis were collected.[20]

2.3 | Perceived pain

Perceived pain was assessed by using the Japanese version of the Pain Catastrophizing Scale (PCS).[21] The PCS is a 13-item self-rating

TABLE 1 Social and medical demographic of participants (n = 61)

Demographic		n	%
Gender			
	Men	38	62.3
	Women	23	37.7
Age			
	30s	6	9.8
	40s	9	14.8
	50s	23	37.7
	60s	14	23.0
	70s	7	11.5
	Over 80s	2	3.3
Education background			
	Middle school	1	1.6
	High school	7	11.5
	Career college	7	11.5
	Junior college	6	9.8
	College	32	52.5
	Others	8	13.1
Occcupation status			
	No job	20	32.8
	Have job	31	50.8
	Others	10	16.4
Household			
	Alone	23	37.7
	Two or more	38	62.3
Cancer site			
	Prostate	37	60.7
	Breast	9	14.8
	Gastrointestinal	6	9.8
	Gynecological	4	6.6
	Blood	2	3.3
	Others	3	4.9
Years of survivorship			
	Less than two	16	26.2
	Two or more	22	36.1
	Five or more	23	37.7
Cancer treatment received			
	Radiation	33	54.1
	Surgery	32	52.5
	Chemotherapy	28	45.9
	Hormone therapy	27	44.3
	Other treatments	4	6.6
	Combined treatments	42	68.9
Cancer treatment scheduled			
	Yes	25	41.0

(Continues)

TABLE 1 (Continued)

Demographic		n	%
Cancer stage			
	I	12	19.7
	II	14	23.0
	III	10	16.4
	IV	14	23.0
	Unknown	11	18.0
Metastatic cancer			
	Yes	20	32.8
Reccurence of cancer			
	Yes	16	26.2

Note. Results of the descriptive analysis on participants' social and medical demographics are shown in Table 1. "Household" refer to the number of persons who live together in one home. "Years of Survivorship" refer to the year past since the diagnosis of cancer.

scale designed to evaluate how much pain is perceived in the daily life of patients. PCS comprises three subscales; rumination, magnification, and helplessness. Responses to each item are made on a five-point scale ranging from 0 to 4, and total pain is calculated as the sum of these subscales. Cronbach's alpha for the current sample was .95.

2.4 | Perceived cancer-related fatigue

Perceived cancer-related fatigue was assessed by the Cancer Fatigue Scale (CFS).[22] The CFS is a 15-item self-rating scale for assessing fatigue in cancer patients. This scale consists of three subscales for multi-dimensionally assessing the physical, affective, and cognitive aspects of fatigue. Each item is rated on a 5-point scale ranging from 1 to 5. The possible scores range from 0 to 28 for the physical, and 0 to 16 each for affective and cognitive subscales, with total fatigue being calculated as the sum of these scores. In the present study, the total fatigue score was tested in the mediation analysis. Cronbach's alpha for the current sample was .77.

2.4.1 | Activity restriction

AR was assessed by the Sickness Impact Profile for Cancer Patients (SIP-C),[23] which is designed to assess AR in patients after the diagnosis of cancer. SIP-C is a uni-factor scale consisting of 26 items. Responses are made by checking a checkbox lined next to each question (a 2-point, Yes or No scale). Cronbach's alpha of the SIP-C for the current sample was .84.

2.4.2 | Depression

Depression was measured by the Japanese version of the Hospital Anxiety and Depression Scale (HADS).[23] HADS is a self-assessment measure comprising 14 items, consisting of two subscales: anxiety and

depression. In this study, the depression subscale of HADS was used to assess depression in the participants. Each item in HADS is rated on a 4-point scale ranging from 0 to 3. Similar to previous studies,[24] a HADS depression score above eight points indicated possible pathology. Cronbach's alpha of HADS for the current sample was .83.

2.4.3 | Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 25. HAD[25] was used for the main mediation analysis. First, descriptive statistics were calculated to summarize the patients' clinical and demographic variables. Second, patients were tested for differences in clinical and demographical variables using one-way ANOVA. Then, Intercorrelations between study variables were calculated as the primary analysis before performing the main mediation analysis. We conducted a mediation analysis using the bootstrapping method because of the limited number of participants.

3 | RESULTS

3.1 | Descriptive analysis

Sixty-one cancer survivors participated in this study (age range 32-81 years, mean = 56.39 years, SD = 11.91). The results are presented in Table 1. It can be seen from the table that the majority of the participants are men (62.3%), had finished college (52.5%), had a job (50.8%) and lived in a household with two or more people (62.3%). Due to the majority of male participants, the most common diagnosis was prostate cancer (60.7%). The second common type of cancer was breast cancer (14.8%), which was followed by gastrointestinal cancer (9.8%). Sixteen patients had less than 2 years of survivorship (26.2%), had undergone regular check-ups by a physician during the past 3 months, and was considered as having a high risk of cancer recurrence. Most of the patients had been cancer survivors for over 2 years since the diagnosis (73.8%). Within the participants, 41.0% responded that they have pre-planned cancer treatment in the near future.

3.2 | Differences in tested variables between patient characteristics

The results of the one-way ANOVA testing for differences in the perceived pain, perceived fatigue, AR and depression between participants' social and medical characteristics are shown in Table 2. It can be seen from the table that participants with metastatic cancers reported a higher pain score compared to those that did not have such cancers (M = 24.45, SD = 10.94, P < .05). Participants that had received surgical treatment also had higher total pain scores (M = 23.03, SD = 11.66, P < .05) compared to those that did not have surgery. Furthermore, participants that lived with more than

three people had the highest total fatigue score (M = 25.29, SD = 8.75, P < .05). Similar to the total pain scores, participants that received surgical treatment for cancer had higher fatigue scores (M = 25.94, SD = 13.86, P < .001) compared to those that did not have surgery. Additionally, significant differences in AR was observed between the type of cancer treatment, such that those that received surgical treatments for cancer (M = 4.88, SD = 4.38, P < .05) had higher AR scores compared to those that did not have surgery. This result was identical to those that received chemotherapy (M = 5.18, SD = 4.13, P < .05). Finally, participants that had received surgical treatment had significantly higher scores for depression (M = 8.84, SD = 4.81, P < .001) compared to those that did not have surgery.

3.3 | Correlation analysis

From the results of the correlation analysis between study variables, predictors of depression including the perception of pain and fatigue were significantly correlated with depression (the Pearson correlation coefficient ranging between .53 and .67). Perceived pain and fatigue were also correlated (r = .59, P < .01). Additionally, AR was significantly correlated with the perceived pain and fatigue in the range of .46 to .77.

3.4 | Testing for mediators

We conducted a preliminary partial correlation analysis between perceived pain and fatigue and between AR and depression, after controlling for gender, the number of household members, the experience of cancer surgery, hormone therapy and chemotherapy as covariates. The covariates were selected from the results of an ANOVA conducted on the demographic variables, and including variables showing significant differences as covariates in the mediation analyses. Results of Pearson's correlation analyses indicated that perceived pain and fatigue were significantly correlated with depression (Pearson's r ranging between .36 and .74) and that AR was also correlated with depression (r = .55, P < .001).

Mediation analyses were conducted using the bootstrapping method, with Depression as the dependent variable of each analysis. Mediation was identified if the 95% BCa confidence intervals generated by bootstrapping did not contain a zero. The first set of analyses tested the perception of pain as the independent variable with AR as the mediating variable (Figure 1). Results indicated that AR significantly mediated the relationship between perceived pain and depression (Bootstrap SE = .073, P < .005). Moreover, perceived pain had a significant direct effect on depression ($\beta 1$ = .46, P < .001). The second set of analyses tested perceived fatigue as the independent variable with AR as the mediating variable (Figure 2). The results indicated that the relationships between perceived fatigue and depression ($\beta 1$ = .48, P < .005) was not significantly mediated by AR.

TABLE 2 Differences in pain, fatigue, activity restriction and depression scores between demographic variables (n = 61)

		Pain			Fatigue			Activity restriction			Depression		
		Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p
Gender	Men	17.16	14.31	0.14	19.34	11.13	0.06	3.47	4.01	0.44	6.92	4.02	.41
	Women	22.30	10.25		25.61	13.83		4.30	4.19		7.91	5.19	
Age	Under 40	22.50	11.36	0.54	24.83	19.70	0.20	4.67	4.63	0.79	5.50	4.76	.13
	Under 65	19.66	12.18		23.02	10.91		3.83	3.96		8.10	4.39	
	65 or older	16.00	16.35		16.50	12.82		3.29	4.36		5.71	4.30	
Occupation	Have job	19.55	11.26	0.05	23.32	12.08	0.12	4.39	4.03	0.31	8.19	4.79	.17
	No Job	22.70	13.93		22.90	13.03		3.70	4.37		6.95	4.40	
	Others	10.50	14.05		14.30	11.02		2.10	3.35		5.20	2.97	
Household	Alone	20.52	14.47	0.12	23.65	14.86	0.02	4.43	5.08	0.16	7.91	4.53	.09
	Two	13.65	11.54		14.65	10.49		2.18	3.34		5.29	3.69	
	Three or more	21.95	11.86		25.29	8.75		4.38	3.03		8.24	4.69	
Cancer stage	I, II	17.31	11.75	0.56	21.65	13.73	0.94	3.35	3.89	0.75	7.42	5.05	.97
	III, IV	21.29	14.03		22.25	12.37		4.00	4.09		7.29	4.06	
	Unknown	18.55	14.46		20.64	10.50		4.36	4.68		7.00	4.31	
Years of survivorship	Less than two	15.88	12.27	0.50	18.31	8.34	0.18	2.94	3.02	0.29	5.56	3.95	.20
	Two or more	19.55	12.81		20.32	13.57		3.32	4.58		7.77	5.28	
	Five or more	20.91	14.01		25.39	13.31		4.83	4.11		8.04	3.81	
Cancer metastasis	Yes	24.45	10.94	0.02	22.85	10.88	0.62	4.45	3.40	0.38	8.30	4.74	.22
	None	16.49	13.36		21.15	13.29		3.46	4.35		6.80	4.33	
Cancer recurrence	Yes	23.00	12.80	0.17	25.81	12.90	0.13	4.44	3.43	0.46	8.50	3.95	.21
	None	17.71	13.04		20.24	12.15		3.56	4.28		6.87	4.62	
Treatment received	Surgery	23.03	11.66	0.01	25.94	13.86	0.00	4.88	4.38	0.03	8.84	4.81	.00
	No surgery	14.76	13.38		17.03	8.85		2.59	3.37		5.59	3.41	
	Chemotherapy	24.25	10.16	0.00	26.46	12.31	0.01	5.18	4.13	0.01	8.50	4.82	.05
	No Chemotherapy	14.73	13.82		17.67	11.30		2.61	3.67		6.27	3.96	
	Radiation	14.12	12.77	0.00	18.88	12.91	0.05	3.39	4.46	0.42	6.61	3.79	.20
	No Radiation	24.96	11.01		25.04	11.30		4.25	3.57		8.11	5.13	
	Hormone	15.86	13.55	0.07	18.82	12.23	0.10	2.71	3.45	0.06	6.18	4.12	.07
	No Hormone	21.85	12.21		24.15	12.35		4.70	4.36		8.24	4.62	
Treatment scheduled	Yes	19.60	13.85	0.81	23.36	14.39	0.39	4.80	4.33	0.11	6.88	4.41	.55
	None	18.75	12.71		20.56	11.04		3.08	3.77		7.58	4.57	

Note. Results of the one-way ANOVA testing for differences in the perceived pain, perceived fatigue, AR and depression between participants' social and medical characteristics are shown in Table 2. SD, standard deviation.

4 | DISCUSSION

The primary aim of this study was to examine the mediating effect of AR between perceived physical symptoms and depression. The results indicated that AR mediated the impact of perceived pain on depression, but not the effect of perceived fatigue. The results of correlation analysis indicated a strong correlation between perceived pain and depression, perceived fatigue and depression, and AR and depression, similar to the findings of previous studies.[6,11,12]

Moreover, a mediation analysis indicated that AR partially mediated the effect of perceived pain on depression, which supported the hypothesis of this study. This result also supported the Activity

Restriction Model[6] and the contention of this study. From the mediating role of AR, there is a possibility of preventing depressive symptoms in cancer survivors through the improvement of AR. However, AR did not play a mediating role between perceived fatigue and depression, even though perceived fatigue predicted AR and depression. Therefore, improving AR in the presence of perceived fatigue might not successfully prevent depressive symptoms.

The above discussion on the relationships between perceived physical symptoms, AR, and depression, is consistent with previous psychosocial studies targeting perceived pain and fatigue in cancer survivors. Reviews on psychosocial interventions for pain show that most studies have considered the interference caused by perceived pain as the
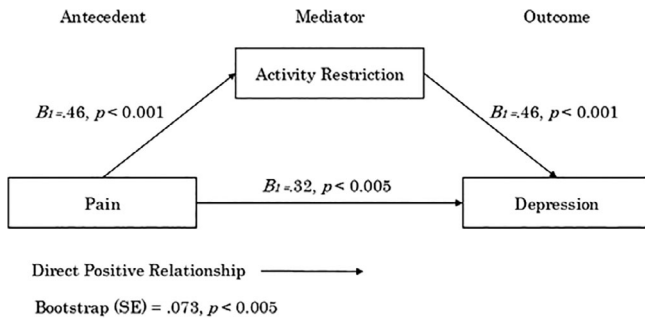
FIGURE 1 Results of the mediation analysis testing perceived pain as the independent variable, activity restriction as the mediating variable, depression as the dependent variable are shown in Figure 1. A bootstrap method was used to estimate the significance of indirect effects. SE, standard error
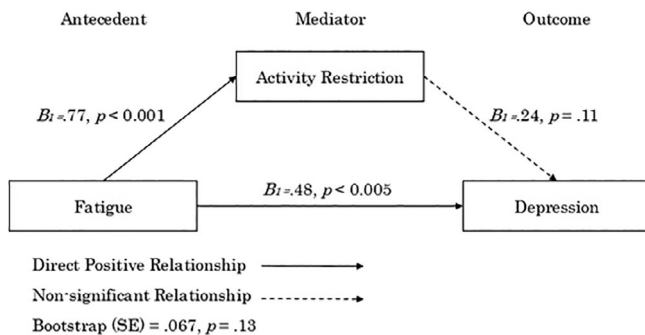
FIGURE 2 Results of the mediation analysis testing perceived fatigue as the independent variable, activity restriction as the mediating variable, depression as the dependent variable are shown in Figure 2. A bootstrap method was used to estimate the significance of indirect effects. SE, standard error

primary outcome,[26] rather than the pain itself. Applying this finding to AR caused by perceived pain suggests that treating AR could prevent depressive symptoms. In the case of perceived fatigue, however, both physical and psychological interventions focus on improving the fatigue symptom itself.[27] These studies suggest that both pain and fatigue prevention are essential aspects of the physical and the psychological well-being of cancer survivorship. However, pain and fatigue may require different perspectives on psychosocial care.

Collaterally, in order to discuss the difference in the two mediating models of each perceived physical symptoms, we explored the differences and the correlations in the social and medical demographics. From the one-way ANOVA in Table 2 indicated similar results for the two perceived physical symptoms; pain and fatigue. Participants that had received cancer treatment and participants that were in severe stages of cancer had higher perceived pain and fatigue scores, whereas participants that were employed had lower perceived pain than those without employment. However, there were differences in perceived fatigue scores. In other words, perceived pain interferes more with daily life activities, including employment, whereas cancer survivors could deal better with the interference caused by fatigue. As a result, it might be difficult to objectively recognize fatigue in cancer survivors, which makes it difficult

to conduct early treatment. Therefore, chronic perceived fatigue might lead to serious depression. In other words, caring for fatigue might be a higher priority than caring for AR in cancer patients with chronic fatigue.

The descriptive analysis of this study suggested that cancer survivors experienced AR regardless of age, gender, the stage of cancer, the severity of cancer, or years of survivorship. AR experienced by cancer survivors, which was strongly correlated with depression, was experienced in all periods of survivorship and by survivors with a wide variety of demographic characteristics. These results suggest that AR might be similar to other long-term psychosocial effects of cancer survivorship.[28] Recently, a randomized trial was conducted on behavioral activation therapy for cancer patients.[29] Behavioral activation therapy for depression (BATD) focuses on limited activities in stressful situations, which is common to AR. BATD attempts to increase overt behaviors that can be increased by reinforcing environmental contingencies, which results in improved quality of life.[30] BATD is time-limited and cost-efficient,[31] and might also be suitable for cancer survivors, who tend to lose contact with the hospital and the oncologists after the acute treatment phase.[16]

4.1 | Study limitations

Several limitations of this study should be noted. One limitation is the small sample size of this study. Another is that the data were collected only in one time-period. Further research is needed using a longitudinal design and a larger sample. The present study chose mediation analysis as the statistical method because of the small number of participants. However, simultaneously modeling of elaborate relationships, including pain and fatigue perception as predictors of depression, by using structural equation modeling, or other multivariate analyses are more desirable. Another limitation concerns the generalization of the findings to other populations. The present study relied on data gathered from members of cancer support groups and sampled cancer survivors that had completed acute cancer treatment. While there are many cancer support groups throughout Japan, not all cancer survivors participate in support groups during their survivorship. Nevertheless, not all cancer survivors participate in group activities during their survivorship. Moreover, 60.7% of the participants in this study were prostate cancer survivors. Such issues of heterogeneity in demographic factors indicate the potential for sampling bias. Finally, there are limitations in the SIP-C Scale, which was used to assess the AR of cancer survivors.[23] SIP-C had a skewed distribution, and a floor effect was seen in the histogram. Pollard and Johnston indicated that the 2-point checkbox responding style of the SIP-C has a limited range.[32] Therefore, the distribution should be improved in future studies by increasing the choices in the Likert Scale.[24]

4.2 | Clinical implications

Despite these limitations, however, the wide range of ages, cancer stages, and years of survivorship of the participants illustrate the

statistical robustness of the findings of the present study. In addition, this study tested the Activity Restriction Model[6] in the cancer survivor population for the first time. The two mediation models considering perceived pain and fatigue as the independent variables revealed that both pain and fatigue had direct effects on depression. Therefore, health professionals who deliver psychological care for cancer survivors may need to prioritize monitoring difficulties in physical symptoms. Within the monitoring process, when faced with severe fatigue, improving fatigue could also lead to improving depression because perceived fatigue did not mediate the effect of AR on depression and had a direct effect on depression. On the other hand, when faced with pain during depression treatment, it may be effective to address the interference of pain in daily activity (AR) and not solely focus on managing pain, given the mediating effect of AR in the relationship between perceived pain and depression. Although psychosocial outcomes are known to improve due to the length of survivorship,[8] the results of the present study indicated that many cancer survivors with a variety of social and medical demographics face the difficulty of AR, which shows the importance of continuous care for AR during cancer survivorship.

5 | CONCLUSIONS

This study aimed to explore the mediating effect of AR in the relationships of perceived pain and fatigue and depression in cancer survivors. From the results, we found that AR mediates perceived pain to depression, however not for perceived fatigue. While in depressive symptomatology of cancer survivors, physical symptoms tend to be treated as predictors of depressive symptoms, our study suggests that the psychological restriction of daily life activities may have a greater effect on depressive symptoms in cancer survivors. Furthermore, because AR was experienced in the context of a survivorship period, it may need to be treated as a long-term effect of the cancer diagnosis.

CONFLICT OF INTEREST
The authors have no conflict of interest to declare related to the findings of this study.

DATA AVAILABILITY STATEMENT
The data analyzed in this study are not available publicly as participants were informed that at the time of the survey, that their data would be de-identified and will be stored securely inside a locked storage media.

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