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Self-reported cognitive impairment in cervical cancer survivors: A cross-sectional study

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Abstract

Objective: Cancer-related cognitive impairment (CRCI) is a major obstacle for cervical cancer survivors, preventing the return to their social life. This study assessed the prevalence of CRCI in cervical cancer survivors and studied the association of self-reported cognitive impairment with treatment regimen and the quality of life (QoL) domains depression, anxiety, and fatigue.

Methods: Six hundred twenty one cervical cancer survivors, treated with combined chemo-radiotherapy (CCRT) ($n = 458$) or surgery only ($n = 163$) were invited in this cross-sectional study. Self-reported cognitive function was assessed using the Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog). Fatigue and psychological distress were assessed using EORTC-QLQ C30 and Hospital Anxiety and Depression Scale (HADS).

Results: Data of 254 women (40.9%) was available for the analysis. Of those, 204 (80.3%) women had received CCRT and 50 (19.7%) surgery only. In the whole cohort, 42.5% reported significant cognitive impairment. In both treatment groups cognitive complaints were significantly associated with anxiety, depression, and fatigue (all $p < 0.001$). CCRT was strongly associated with increased risk of CRCI (OR = 4.02, 95% CI = 1.57–10.25). Anxiety, depression, and fatigue increased the risk of CRCI by 13% (OR: 1.13, 95% CI 1.03–1.23), 16% (OR 1.16, 95% CI 1.04–1.28) and 2% (OR 1.02, 95% CI 1.00–1.03), respectively.

Conclusion: Almost half of the cervical cancer survivors after CCRT report significant cognitive impairment. CRCI is associated with other indicators of poor QoL, such as depression, anxiety and fatigue. An increased understanding of the specific cognitive domains affected and of the associated late effects like fatigue is crucial to customize successful interventions.

KEYWORDS
cancer, cervical cancer survivors, cognitive impairment, fatigue, gynecological cancer, oncology, psycho-oncology, psychological distress

1 | BACKGROUND

Modern cancer treatment has increased survival rates for many patients. However, survival may come at a cost, as cancer and cancer treatment itself can result in long term side effects, including cognitive impairment severely affecting daily life functions. The International Cancer and Cognition Task Force (ICCTF) has defined cancer-related cognitive impairment (CRCI) as a decline in memory, attention, concentration, and executive function among cancer patients.[1] Most studies, the majority being conducted among breast cancer survivors, report CRCI prevalence rates between 15 and 70%.[2] This prevalence varies due to the heterogeneity in study populations, methods used for cognitive assessment, and definition of cut-offs to define CRCI and therefore warrants cautiousness about the generalizability across cancer populations.

Among gynecological cancer survivors, cognitive impairment is an often reported side effect alongside with changes in bowel pattern, peripheral neuropathy and sexual dysfunction[3] and CRCI may affect up to 75% of gynecologic cancer patients treated with chemotherapy.[4,5] CRCI does not always improve with time alone, and 15-35% of cancer survivors experience cognitive problems months to years following treatment.[6-9]

Studies among patients with gynecological cancer have shown various degree of cognitive impairment both as patient-reported outcomes (PRO) and performance-based neuropsychological assessment during and after chemotherapy and we lack evidence of a definite chemotherapy-related effect on cognition.[6,8,10-13] Most of these studies are limited by their small sample size, heterogenous diagnostic groups, treatment modalities, short observation time and/or a lack of control for confounding factors. Further, the majority of these studies have primarily focused on ovarian cancer patients, an often older population with short expected survival. Younger gynecological cancer survivors report greater disease impact on family life, social activities, perceived health status and body image than older women.[14] Even minor cognitive dysfunction can significantly impact a person's ability for societal participation and employment, and interfere with normal everyday life, resulting in a decline in confidence and quality of life (QoL).[5] In particular, cervical cancer survivors are often young with a long-life expectancy who are expected to return to their personal and professional lives after treatment. CRCI might therefore be a major obstacle, as it affects most aspects of daily living and QoL.[15] A better understanding of the subjectively reported cognitive impairment and its impact on survivors' functioning in this patient population is crucial for survivorship care planning and to develop effective rehabilitation programs. Although standardized neuropsychological testing is the 'gold standard' for assessing the magnitude of CRCI,[1] the availability of neuropsychological services is often limited, especially outside neurological and psychiatric health services. Self-reported CRCI might therefore be important in identifying which patients should be referred to neuropsychological assessment and offered specialized cognitive rehabilitation.

The aim of this study was to report the frequency and severity of subjective cognitive impairment in a well characterized population of cervical cancer survivors and further explore the relationship between self-reported cognitive impairment, cancer treatment regimen, fatigue, and psychological distress reflecting depression and anxiety.

2 | MATERIAL AND METHODS

2.1 | Study population

Cervical cancer survivors between 18 and 65 years of age and tumor-free at least one year after primary treatment cessation were invited to participate, in total 621 women. The patients were identified in the validated quality assurance database for cervical cancer at the Department of gynecologic oncology, Oslo University Hospital, Norway and invitations were sent out between November 19 and December 13, 2019. Questionnaires were distributed on paper and returned to the project group by mail. All patients had received treatment for cervical cancer (FIGO stage I-IIIb[16]) between 2000 and 2018, and had either been treated with combined chemo-radiotherapy (CCRT) with minimum three cycles of concomitant cisplatin (n = 458) or surgical treatment only (n = 163). Exclusion criteria were: (a) neurological disease; (b) psychiatric comorbidity (i.e., pharmacologically treated depression/anxiety, bipolar disease, psychotic disorders); (c) secondary cancer/metastasis/recurrence.

2.2 | Self-reported cognitive function

The Functional Assessment of Cancer Therapy-Cognitive (FACT-Cog) version 3 was used to assess self-reported cognitive function. FACT-Cog is a 37-item validated PRO created specifically to assess cognitive impairment in cancer patients.[17] It consists of four subscales; perceived cognitive impairment (PCI), perceived cognitive ability (PCA), comments from others, and impact of cognitive impairment on QoL. In this study only the PCI and PCA subscale scores are reported, as recommended by the developer.[18] Higher subscale scores indicate better cognitive function (i.e., lower subjective cognitive impairment). Scores $\leq$1.5 standard deviation (SD) below normative mean on PCI (<44) and/or PCA (<9) subscales were chosen as cut-offs defining significant subjective CRCI, based on FACT-Cog normative data for healthy French women collapsed over age and education groups from the Lange et al. study.[1,19,20]

2.3 | Assessment of fatigue, anxiety, and depression

Psychological distress refers to non-specific symptoms of stress and may often reflect common mental disorders such as anxiety and depression. In this study we assessed anxiety and depression using the Hospital Anxiety and Depression Score (HADS). HADS is a commonly used self-reporting tool in clinical research and practice and is deemed both valid and reliable.[21] HADS is comprised of seven items related to anxiety (HADS-A) and seven items related to

depression (HADS-D). Items are rated on a 4-point Likert scale. According to the original HADS publication by Zigmond and Snaith a subscale score of <7 is within the normal range, whereas a subscale score between 8 and 10 indicate mild level of depression and/or anxiety; subscale scores from 11 to 14 indicate moderate level, whereas a subscale score >15 indicate severe symptom load.[21] The HADS has previously been employed as a measure of psychological distress in cervical cancer survivors.[22,23]

To assess fatigue, the European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire version 3.0 (EORTC QLQ-C30 3.0) was utilized. EORTC QLQ-C30 3.0 is a questionnaire specifically developed to assess QoL in cancer patients.[24] It consists of 30 items which include five functional scales (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, nausea and vomiting and pain), one global health status scale and six single items addressing additional symptoms. In this study only the fatigue subscale was reported.

A general questionnaire was used to collect baseline demographic characteristics (age, marital status, education, employment) as well as information on current medication. Information on the year of diagnosis as well as cervical cancer treatment was available through the institutional quality assurance database.

2.4 | Ethics

All women signed a written informed consent prior to inclusion. The study was approved by the Regional Committee for Medical Research Ethics in South-Eastern Norway (REK no. 2018/2242), the institutional review board at the Department of gynecologic oncology, Oslo University Hospital, and the data protection office at Oslo University Hospital.

2.5 | Statistical analyses

All analyses were conducted using the Statistical Package for the Social Science version 26 (SPSS 26). Missing questionnaire item data were replaced by the mean score when >50% of items were answered. Descriptive statistics were used to describe demographic and clinical characteristics of the sample. All FACT-Cog, HADS and EORTC QLQ-C30 scores were non-normally distributed ($p < 0.001$ on all Shapiro-Wilk tests), group differences in self-reported CRCI, psychological distress and fatigue were therefore analyzed by means of Independent-Samples Mann-Whitney *U* Test, and associations between self-reported CRCI and associated factors were analyzed using the Spearman's Rho correlation coefficient. Effect sizes (ES) were estimated using *r* for Mann-Whitney *U*-test, classifying ES into small (0.01–0.29), medium (0.30–0.49) and large (>0.50). A multivariate logistic regression model was fitted by forward conditional stepwise entry of independent variables to assess their predictive effect related to CCRI. Odds ratios (OR) were estimated with 95% confidence intervals (CI).

3 | RESULTS

In total 263 women responded and consented to the study (42.0%), but nine were found ineligible due to another cancer, neurologic or psychiatric comorbidities. Thus, the complete questionnaire data of 254 survivors was evaluated (40.9%). Median age in the total sample was 49.2 years (SD 8.73, range 27–65). Two hundred and four women had received CCRT and 50 women surgical treatment only with a median time since diagnosis of 7.1 years (SD 4.0, range 1–18). There were no significant differences between the treatment groups regarding age, years since diagnosis, marital status and educational level. Responders had similar age and treatment distribution as the cohort as a whole (data not shown). Employment rate was 64.5% for the total sample, with 44.2% in full and 20.3% in part time employment, compared to a general employment rate of 67% for Norwegian women in 2020.[25] However, work status ($p = 0.033$) and concurrent medication ($p = 0.005$) were significantly different between the two groups. Patients after CCRT were less likely to be fully or part time employed compared to patients treated with surgery and they also reported using more medication (mainly hormone replacement therapy). Baseline characteristics are displayed in Table 1.

In total, 108 (42.5%) of the participants reported subjective CRCI below the defined cutoff score on one or both of the chosen FACT-Cog subscales (PCI ≤ 44 and PCA ≤ 9). Compared with survivors after surgery only, patients after CCRT reported significantly more cognitive impairment; both for PCI and PCA with a median score of 49 versus 67 ($p < 0.001$) and 19.5 versus 26 ($p < 0.001$), respectively (see Table 2). There was no association between subjective CRCI and time since diagnosis and no significant correlations between age and subjective CRCI in any of the treatment groups. However, unemployed patients reported significantly more cognitive impairment compared to full or part time employed participants with median PCI score of 37.5 versus 60 ($p < 0.001$) and median PCA score 17 versus 25 ($p < 0.001$). Also, part time employed patients reported significantly more cognitive impairment compared to full time employed participants with median PCI score of 46 versus 62.5 ($p = 0.006$) and median PCA score 20 versus 27 ($p < 0.001$).

We found significantly higher scores for depression ($p = 0.002$) and fatigue ($p = 0.006$) in the CCRT group than in patients who had received surgery only. Higher prevalence rates of anxiety were also observed in the CCRT group; however, this was not significant. There was a significant correlation between both FACT-Cog subscales and anxiety ($p = <0.001$), depression ($p < 0.001$) and fatigue ($p < 0.001$), with generally large correlation coefficients.

As displayed in Table 3, a logistic regression analysis showed that chemotherapy, anxiety, depression, and fatigue were all significantly associated with subjective cognitive impairment, the strongest being chemoradiotherapy (OR = 4.02, 95% CI = 1.57–10.25, $p = 0.004$). Anxiety, depression, and fatigue increased the risk of significant subjective cognitive impairment by 13% (OR: 1.13, 95% CI 1.03–1.23, $p = 0.007$), 16% (OR 1.16, 95% CI 1.04–1.28, $p = 0.007$) and 2% (OR 1.02, 95% CI 1.00–1.03, $p = 0.002$) respectively. The model explained 40.6% (Nagelkerke R square) of the variance in subjective cognitive

TABLE 1 Sample characteristics

	Total sample (*N* = 254)		Chemoradiation (*N* = 204)		Surgery only (*N* = 50)		
	M (SD)/*N* (%)	Min-max	M (SD)/*N* (%)	Min-max	M (SD)/*N* (%)	Min-max	*p*
Demographics							
Age	49.2 (8.73)	27–65	49.3 (9.22)	27–65	48.7 (6.37)	34–62	NS[a]
Marital status							
Single	*36* (14.2%)		*31* (15.2%)		*5* (10%)		NS[b]
Married/cohabitant	*182* (71.7%)		*142* (69.6%)		*40* (80%)		
Divorced/separated	*32* (12.6%)		*27* (13.2%)		*5* (10%)		
Widowed	*4* (1.6%)		*4* (2.0%)		*0* (0%)		
Work status							0.033[b]
Full time	*111* (44.2%)		*80* (39.2%)		*31* (62%)		
Part time	*51* (20.3%)		*44* (21.6%)		*7* (14%)		
Sick leave	*40* (15.9%)		*36* (17.6%)		*4* (8%)		
Disability benefit	44 (17.5%)		*38* (18.6%)		*6* (12%)		
Unemployed	*5* (2%)		*3* (1.5%)		*2* (4%)		
Education level							NS[b]
Primary/secondary	*25* (9.8%)		*19* (9.3%)		*6* (12%)		
High school	*105* (42.1%)		*94* (46.1%)		*13* (26%)		
University/college	*122* (48%)		*91* (44.6%)		*31* (62%)		
Clinical characteristics							
Years since diagnosis	7.1 (4.00)	1–18	6.9 (4.24)	1–18	7.4 (2.59)	4–13	NS[a]
Medication (yes/no)	186/67		157/46		29/21		0.005[b]
HRT	*131* (72.0%)		*121* (77.6%)		*10* (38.5%)		<0.001[b]
Opioids	*14* (7.7%)		*10* (6.4%)		*4* (15.4%)		NS[b]
Psychofarmaca	*39* (21.4%)		*31* (19.9%)		*8* (30.8%)		NS[b]
Other	*110* (60.4%)		*90* (57.7%)		*20* (76.9%)		NS[b]

Note: Numbers in Italic are used for reporting N, non-italic are used for reporting median.

Abbreviations: HRT, hormone replacement treatment; NS, non-significant difference.

[a]Student's *t*-test.

[b]Chi-Square (x^2).

impairment caseness, and correctly classified 74.5% of cases. The assumption of multicollinearity was assessed and revealed no violation of the assumptions, as all predictor variables showed correlations below 0.70, tolerance >0.10, and variance inflation factor (VIF) <10.

4 | DISCUSSION

In this large cross-sectional study almost half of the cervical cancer survivors report cognitive impairment, with scores below the defined cut-off for significant impairment on FACT-Cog subscales PCI and PCA. The prevalence of self-reported cognitive impairment was significantly higher after CCRT compared to after surgery and we confirmed the association with other known late effects such as anxiety, depression, and fatigue.

Our findings are in accordance with the results among gynecological cancer patients reported by Zeng et al. in regards to prevalence and association with psychological distress, fatigue and treatment received (i.e., chemotherapy).[13] In that study, 62% of the participants were cervical cancer patients and all participants had just recently completed cancer treatment. Another study among cervical cancer survivors showed that cognitive functioning, assessed by EORTC QLQ-C30, remained impaired several months after chemoradiation treatment for locally advanced cervical cancer, whereas general QoL, emotional and social functioning improved during the same period.[26] Our population on average completed their treatment nearly 8 years ago, providing additional supporting evidence for long-term and persisting CRCI in cervical cancer survivors.

Van Arsdale et al. reported 60% prevalence of CRCI in a mixed gynecological cancer population and found that CRCI was

TABLE 2 Group differences in FACT-Cog PCI and PCA, HADS-anxiety, HADS depression and EORTC QLQ-C30 fatigue

	Total sample ($N = 254$) Median (IQR[a])/*n* (%)	Chemoradiation ($N = 204$) Median (IQR[a])/*n* (%)	Surgery only ($N = 50$) Median (IQR[a])/*n* (%)	*p*[b]	*r*[c]
FACT-Cog 3.0					
PCI	54.0 (34.00)	49.0 (33.00)	67.0 (25.00)	<0.001	−0.263
Above cutoff (<44)	96 (37.8%)	88 (43.1%)	8 (16%)		
Below cutoff (>44)	157 (61.8%)	115 (56.4%)	42 (84%)		
PCA	21.0 (15.00)	19.5 (13.00)	26.0 (15.00)	<0.001	−0.250
Above cutoff (<9)	12 (4.7%)	12 (5.9%)	–		
Below cutoff (>9)	241 (94.9%)	191 (93.6%)	50 (100%)		
HADS					
HADS anxiety	7.0 (7.00)	7.0 (8.00)	6.0 (8.00)	NS	−0.064
No anxiety	141 (55.5%)	110 (54.5%)	31 (62%)		
Mild anxiety (≥8)	52 (20.5%)	43 (21.3%)	9 (18%)		
Moderate anxiety (≥11)	52 (20.5%)	44 (21.6%)	8 (16%)		
Severe anxiety (≥15)	6 (2.4%)	5 (2.5%)	1 (2%)		
HADS depression	5.0 (7.00)	5.0 (6.00)	2.0 (7.00)	0.002	−0.198
No depression	177 (69.7%)	140 (68.6%)	37 (74%)		
Mild depression (≥8)	43 (16.9%)	31 (15.2%)	12 (24.5%)		
Moderate depression (≥11)	28 (11.0%)	28 (13.7%)	–		
Severe depression (≥15)	3 (1.2%)	3 (1.5%)	–		
EORTC QLQ-C30					
Fatigue	44.4 (39.89)	55.5 (33.33)	33.3 (38.89)	0.006	−0.172

Abbreviations: EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire version 3.0; FACT-Cog, Functional Assessment of Cancer Therapy-Cognitive Function version 3; HADS, Hospital Anxiety and Depression Scale; PCA, perceived cognitive ability; PCI, perceived cognitive impairment.

[a]Interquartile range.

[b]Mann-Whitney *U*-test.

[c]Effect size.

TABLE 3 Logistic regression analysis: Subjective cognitive impairment caseness

				95% CI for e^{β}	
Predictors	**β (SE)**	***p***	**e^{β} (odds ratio)**	**Lower**	**Upper**
Chemoradiotherapy	1.390 (0.478)	0.004	4.02	1.572	10.256
HADS-anxiety	0.121 (0.045)	0.007	1.13	1.034	1.233
HADS-depression	0.146 (0.054)	0.007	1.16	1.041	1.285
EORTC-QLQ C30 fatigue	0.021 (0.007)	0.002	1.02	1.007	1.035

Abbreviations: CI, confidence interval; EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire version 3.0; HADS, Hospital Anxiety and Depression Scale; SE, standard error.

associated with non-Caucasian ethnicity, uterine and vulvar cancers, lower education, older age and clinically relevant pain.[10] Unlike our results, they found no association between cognitive deficits and chemotherapy, anxiety, and depression but in line with our findings, cognitive deficits were not associated with time since diagnosis. However, this cross-study comparison is limited by the fact that the study included only very few cervical cancer survivors and used a different screening tool (Montreal Cognitive Assessment) which was not specifically developed for cancer survivors.

When comparing our CCRT group to patients receiving surgery only, a significantly larger proportion of CCRT survivors exhibit CRCI. However, cognitive impairment also occurred in approximately 16% of patients who were treated with surgery only. Similar findings have been reported in breast cancer patients where subtle cognitive

dysfunction was also observed among patients not receiving chemotherapy.[27]

It is known that self-reported cognitive dysfunction may be influenced by other factors, including psychological distress and fatigue.[28-30] As CRCI, psychological distress and fatigue represent overlapping symptoms, studies suggest that subjective cognitive measures do not solely identify cognitive impairment.[31] Our data adds to the evidence of high symptom burden in cervical cancer survivors,[32] particularly psychological distress. Also, in the surgery group, there was a high prevalence of depression and anxiety. These high distress levels may be an expression of the general insecurity cancer survivors across diagnosis and treatment modality experiences, that is, fear of recurrence, and need to be addressed in survivorship care planning.

Being able to work and return to other pre-cancer activities is a sign of recovery and an important contributor to QoL and psychological wellbeing for all cancer survivors. Zeng et al. showed that cognitive impairment was associated with unemployment, receiving chemotherapy and depressive symptoms.[13] In our total sample, 44.2% of the women reported working full-time, and employment status was significantly associated with the magnitude of self-reported cognitive impairment. Survivors after CCRT are less often employed in full- or part time work compared to survivors after surgery, indicating that late effects interfere with their working status. Several studies have recognized the influence other factors such as socioeconomic, physical (i.e., fatigue) and emotional (i.e., anxiety and depression) complaints, may have on CRCI and work ability and this is also reported as a major concern by the survivors.[15]

Assessing the patient's perspective is an important aspect of CRCI as there may be a discrepancy between physician-assessed morbidity and self-reported complaints.[34,35] Even though neuropsychological testing is considered to be the gold standard in diagnosing CRCI,[1] objective tests may fail to identify the often subtle cognitive changes associated with CRCI.[20] As a result, PROs have been recognized as a relevant outcome measure for studying CRCI.[36] Using FACT-Cog to measure self-reported complaints is beneficial to distinguish between cognitive concerns (PCI) and cognitive abilities (PCA), as these presumably reflect different aspects of self-perceived cognitive functioning. The PCA subscale is reported positively worded and can appear to cover the higher end of the symptom continuum, whereas the negatively worded PCI subscale may not measure the same construct.[35] Still, we lack knowledge on specific cognitive domain impairment as self-reported questionnaires do not assess the distinctive domains affected, but rather serve as a useful screening tool to identify patients who may benefit from additional comprehensive neuropsychological testing.

The study has several strengths. To the best of our knowledge this study is the largest and also the only study assessing CRCI in a clinically well annotated cohort of cervical cancer patients. Oslo University Hospital serves the South East Health Region of Norway, representing about two thirds of the Norwegian population. We therefore consider this study population to be representative for the Norwegian population. The large sample size made it possible to assess the prevalence of self-reported CRCI in different treatment groups. Another strength is the long period between cessation of treatment and assessment allowing us to assess the magnitude of this late effects several years after the primary treatment. We used validated state of the art instruments for the assessment of CRCI[1,20] and controlled for important confounders.

4.1 | Study limitations

There are some limitations to this study, among these the lack of longitudinal data. Using a cross-sectional study design, our study does not allow any conclusions regarding causality, other than concluding there is a significant association between the cancer treatment received and CRCI. This also applies to the other domains of QoL assessed in this study, as CRCI may be both a cause and a consequence of psychological distress and fatigue. A cancer diagnosis in itself can be a major life stressor and affect cognition. This may in part explain the CRCI prevalence among patients after surgery alone. However, no baseline data on self-reported cognitive function was available and subtle pre-existing cognitive complaints were therefore not possible to identify. The cut-offs used in this study might be regarded conservative in relation to a recent study reporting a PCI score of <60 defining 76% sensitivity and 84% specificity in order to discriminate CRCI cases from non-cases in a breast cancer population.[20]

There is also a risk of response bias in our data in that survivors who experience more treatment-related side effects may be more prone to report their complaints. The rate reported here is comparable to a study in breast cancer patients,[37] but comparable studies in gynecological cancer patients have unfortunately not reported response rates.[10,13]

4.2 | Clinical implications

A considerable proportion of cervical cancer survivors reported significant cognitive impairment after cancer treatment. In particular, survivors after chemo-radiotherapy seem to suffer from this disabling late effect, which was associated with fatigue and psychological distress. At present there are limited effective interventions targeting cognitive dysfunction following cancer treatment and there is currently no standard of care for survivors reporting CRCI. Health care professionals thus lack the necessary tools to properly care for and follow-up these women. This can lead to a neglect of CRCI and limit surveillance programs in terms of providing counselling for the psychosocial impact CRCI has on cancer survivors' “post-cancer” life. Objective neuropsychological assessment is recommended to fully understand which domains of cognitive functions are most affected, which is a precaution to customize successful treatment interventions. However, self-report is considered an important first-step assessment to identify which patients should be referred for

further cognitive evaluation. Future prospective and longitudinal studies are warranted and should include both self-reported and objective neuropsychological assessments.

5 | CONCLUSION

In conclusion, our study confirms that CRCI is a major and disabling late effect in cervical cancer survivors, particularly after CCRT. Subjective cognitive impairment is associated with other PROs such as psychological distress and fatigue, suggesting these are closely linked processes and demonstrates the complexity of diagnostical and rehabilitation needs after treatment.

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CONFLICT OF INTERESTS

The authors do not report any conflict of interest related to this work. All authors have read and approved the final manuscript.

AUTHOR CONTRIBUTIONS

Elisabeth Wang Areklett: Writing – Original draft, Data aquisition, Visualization. Elisabeth Fagereng: Statistical analysis, Writing – Review & Editing. Kjersti Bruheim: Data aquisition, Writing – Review & Editing. Stein Andersson: Methodology, Formal analysis, Writing – Review & Editing. Kristina Lindemann: Methodology, Data acquisition, Formal analysis, Writing – Review & Editing, Supervision.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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