


ORIGINAL ARTICLE

Cancer-related fatigue and treatment burden in surgically treated colorectal cancer patients – A cross-sectional study

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Abstract

Objective: This cross-sectional study aimed to describe cancer-related fatigue (CRF) in colorectal cancer (CRC) patients who were surgically treated with curative intent, identify subgroups at risk of elevated fatigue levels and explore associations between CRF and treatment burden.

Background: CRF is a prominent symptom among cancer patients. In patients treated for CRC, CRF is associated with adjuvant treatments, low quality of life and reduced ability to self-manage.

Methods: One hundred thirty-four patients with CRC treated at a Norwegian university hospital between 2016–2018 were included. The Schwartz Cancer Fatigue Scale-6 and the Patient Experience with Treatment and Self-management questionnaires were applied for data collection. Statistical analyses included descriptive statistics and non-parametric approaches to analyse correlations and identify differences between groups. The study adhered to STROBE Statement checklist for reporting of cross-sectional studies.

Results: Median fatigue level was 10.0 (range: 7.0–13.0). Physical fatigue was higher than perceptual fatigue, with medians of 6.0 (interquartile range [IQR]: 3.0–13.0) and 4.0 (IQR: 3.0–12.0), respectively. Higher fatigue levels were associated with age <60 years, advanced cancer and adjuvant treatments. Increased CRF was significantly associated with higher treatment burden on seven of the nine dimensions, adjusted for demographic and clinical variables. The association of fatigue and treatment burden was stronger in survivors <60 years, with advanced cancer, 6–12 months since surgery or who had more comorbid conditions.

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Conclusions: This study showed patients at risk of experiencing CRF following CRC treatment. It established proof of associations between CRF and treatment burden and identified subgroups of CRC patients where this association was stronger.

Relevance to clinical practice: Screening of CRF in CRC patients can help clinicians provide individualized treatment and care to manage CRF. Clinicians should consider the association between CRF and treatment burden, especially in subgroups of CRF patients.

KEYWORDS

cancer-related fatigue, colorectal cancer, cross-sectional survey, self-management, treatment burden

1 | INTRODUCTION

Cancer-related fatigue (CRF) is a common symptom in cancer survivors. Compared with a healthy population, cancer survivors are often more fatigued, and fatigue can occur for years following primary treatment (Husson et al., 2015). Colorectal cancer (CRC) is one of the most commonly occurring cancers, with over 1.8 million new cases in 2018 (Ferlay et al., 2019). In Norway, 4332 new CRC cases were registered in 2017 (Cancer Registry in Norway, 2017), the world's fourth largest incidence rate (Ferlay et al., 2019). Fatigue is one of the most severe symptoms following treatment in CRC survivors (Han et al., 2020). High levels of CRF in CRC survivors have been associated with chemotherapy treatment, low quality of life (QoL) and a reduced ability to self-manage (Vardy et al., 2016).

Surgical tumour resection is a cornerstone of the primary treatment of CRC patients with non-metastatic disease. Although adjuvant chemotherapy is generally recommended in colon cancer patients with lymph node metastases (i.e., Dukes Stage C), neoadjuvant chemo-radiation treatment is only selectively employed according to given criteria in rectal cancer patients (Lewis & Espat, 2016). As a result of the enhanced recovery approach, CRC patients now spend less time in hospital following primary surgery (Zhuang et al., 2013). Recent reports indicate that CRC patients often feel unprepared for the period that follows after hospital treatment, experiencing increased and sometimes overwhelming self-management demands related to altered bowel function, bladder complications, sexual dysfunction, ostomy-related complications and fatigue (Lubberding et al. 2015). A large self-management workload may result in treatment burden, defined as 'the impact of health care on patients' functioning and well-being' (Eton et al., 2012), and described as the extra work created through self-care and self-monitoring, the management of therapeutic regimens, organising doctors' visits and managing transitions from hospital to home, as delegated to chronically ill patients by health professionals.

Additionally, reflecting the large proportion of CRC patients who are older (>70 years), many may suffer from other chronic debilitating conditions (Boakye et al., 2018); thus, CRC patients may experience treatment burden. Comorbidity, such as cardiovascular disorders and lung diseases, are also associated with higher risk

What does this paper contribute to the wider global community?

- This study demonstrated that cancer-related fatigue (CRF) is a problem to patients surgically treated for colorectal cancer (CRC) and identified younger patients, advanced cancer and adjuvant treatments as risk factors for experiencing CRF.
- CRF and treatment burden are positively and significantly related concepts.
- The study identified subgroups of CRC patients with a stronger association between CRF and workload dimensions of treatment burden.
- The CRC clinical pathway may include screening of patients' CRF and treatment burden levels and be extended by providing nurse-led informational, educational and psychosocial support post-hospital discharge to ameliorate CRF and treatment burden.

of post-operative complications in CRC patients >70 years of age, which may complicate recovery outcomes (Flynn et al., 2020). In a cohort study of 1017 CRC patients, one third of the patients had not returned to pre-surgical QoL levels after 5 years, and comorbidity of two or more chronic illnesses was associated with decreased QoL (Wheelwright et al., 2020). In a recent study among the same patient cohort as the current study, CRC patients reported treatment burden across several dimensions, including difficulties in accessing and understanding medical information, attending to medical appointments and monitoring their health condition and health behaviour, all of which affected their well-being (Husebø et al., 2021).

CRF adds to treatment burden by decreasing a patient's ability to perform daily life activities and self-care tasks, negatively impacting interpersonal relationships and interfering with social life roles (Jones et al., 2016). As yet, there is no empirical evidence to help clarify the reciprocal relationship between CRF and treatment burden, and gaining a broader perspective of CRC patients' experiences of treatment and self-management tasks is important. This study

investigated the incidence and characteristics of CRF in a CRC patient sample and examined the associations between CRF and treatment burden.

2 | BACKGROUND

CRF is defined as 'a distressing persistent, subjective sense of physical, emotional and cognitive tiredness related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning' (Berger et al., 2015). The CRF experience is usually captured by the use of patient-reported outcome measures (PROMs), and a large number of PROMs for CRF exist (Nordin et al., 2016). Compared with a healthy population, CRC survivors experience significantly more fatigue; in particular, short-term survivors (<5 years post-diagnosis) report substantially higher fatigue levels (Thong et al., 2013). In a recent systematic review and meta-analysis of the symptom experience in CRC survivors, compared with older patients, younger patient age and younger age at diagnosis were not found to be risk factors of fatigue (Han et al., 2020). Regarding differences between genders, female CRC patients have reported significantly higher CRF levels than male patients (Aminisani et al., 2017; Husson et al., 2015). These studies also found that comorbidity was associated with elevated CRF levels.

Patients with CRC must deal with many dimensions of treatment burden during their treatment trajectory and must balance demands with their capacity to self-manage (Husebø et al., 2021). The predominant consequences of treatment burden in patients suffering from long-term illness are impaired health and well-being (Eton et al., 2019; Lippiett et al., 2019), non-adherence to treatment and lifestyle interventions (May et al., 2014; Schreiner et al., 2020), costly readmissions (Eton et al., 2012) and burden on significant others (Sav et al., 2013). The literature on treatment burden in cancer populations is limited, and only two original studies have been conducted (Eton et al., 2019; Anderson et al. 2021). Eton et al. (2019) explored the impact of perceived treatment and self-management burden in 91 multimorbid cancer patients and found that treatment burden harmed health-related QoL. The study did not investigate the burden from generic self-management work (i.e., monitoring health, attending medical appointments and navigating problems with healthcare services). In Anderson et al. (2021), female cancer survivors reported that the impact of self-management negatively affected their general health, an association more prominent in single, multimorbid individuals, low on health literacy and who worked full time. A systematic review described treatment burden in patients with lung cancer as managing treatment side effects, burdensome cognitive decision-making processes and dealing with multiple treatment appointments, among others (Lippiett et al., 2019). The authors concluded that a clear treatment pathway with rapid access to healthcare services might reduce the post-diagnosis treatment burden.

On the basis of recent studies showing that CRF is significantly associated with increased impairment of performing

life tasks, including self-care (Jones et al., 2016), we aimed to describe CRF and explored the relationship between CRF and treatment burden in CRC patients treated with curative intent. This exploration was accomplished through the following research questions:

Research Question 1: What is the level of CRF in CRC patients treated with curative intent at a Norwegian university hospital?

Research Question 2: How does the level of CRF vary according to demographic and clinical variables?

Research Question 3: What are the associations between CRF and the different dimensions of treatment burden in this study population, and are they moderated by socio-demographic and clinical variables?

3 | METHODS

3.1 | Study design and setting

The study applied a retrospective cross-sectional design and took place in a university hospital in the south-western part of Norway in 2017–2018. The Department of Gastrointestinal Surgery offers acute and elective surgical service, and annually, more than 300 CRC patients undergo surgery at the facility. Ethical approval was obtained from the Regional Committee for Medical and Health Research Ethics and from the data protection officer at the hospital where the participants were recruited. All participants provided informed written consent and were guaranteed confidentiality and the right to withdraw from the study at any time. The patients also gave their permission to use their data obtained from the hospital's medical records. The study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cohort, case-control and cross-sectional studies (Appendix S1).

3.2 | Study population

The study sample was drawn from the electronic hospital records of individuals treated for CRC with curative intent in 2016–2018. The inclusion criteria were as follows: between 18–80 years of age, surgically treated for either colon or rectal cancer with curative intent, no distant metastases (i.e., Dukes Stages A–C; Labianca et al., 2010; National Institute for Health and Clinical Excellence (Great Britain), 2014), an elapsed time since primary surgery of 2 months to 2 years and able to speak and write Norwegian. The exclusion criteria were as follows: metastatic cancer, severe post-operative surgical complications (i.e., grade >3 according to Clavien–Dindo Surgical Complications Score; Clavien et al., 2009) or mental illness or cognitive impairment. The main reasons for non-eligibility were old age (>80 years) or metastatic cancer.

3.3 | Data collection

Two different recruitment procedures were used: (a) a request containing an information letter, consent form and the survey inventory was mailed to patients who were surgically treated between June 2016–September 2017, and (b) a study nurse recruited patients who were surgically treated between October 2017–June 2018 at their first post-operative outpatient follow-up appointment. Patients recruited at the outpatient clinic received written information, the consent form and the survey inventory and were educated by the study nurse on how to fill in the forms at home. One reminder letter was mailed to all non-responders 2 weeks following the time of recruiting. The participants did not receive any compensation for participation.

Clinical data (diagnosis, cancer stage, treatment modes, surgical complication category and number of comorbidities) were collected from the electronic hospital records. A questionnaire for collecting demographic and clinical characteristics was developed for this study, including items on age, gender, ethnicity, marital status, living conditions, education and employment.

3.4 | Measures

3.4.1 | Schwartz Cancer Fatigue Scale-6

The Schwartz Cancer Fatigue Scale-6 (SCFS-6) developed by Schwartz and Meek (1999) is a scale of six items measuring CRF on two dimensions: *physical* (i.e., worn out, tired and listless) and *perceptual* (i.e., difficulties thinking, overcome and helpless). The physical dimension is related to a decline in physical functioning, and the perceptual dimension assesses changes in mood state that may affect the patient's preparedness to take action (Schwartz et al., 2003). The scale instructions stated: 'The words and phrases below describe different emotions that can be associated with exhaustion. Please read through them and put a ring around the number that corresponds to how much these feelings have affected you in the last 2–3 days'.

The items are scored on a Likert scale of 1 (*not at all*) to 5 (*extremely*). The summed score ranges from 6–30, where higher scores indicate more fatigue. The Norwegian version of the SCFS-6 has demonstrated a Cronbach's α of 0.83 in a cancer population (Husebø et al., 2014). In the current study, the instrument obtained a Cronbach's α of 0.91.

3.4.2 | Patient Experience with Treatment and Self-management

Treatment burden was measured by the Norwegian version of the Patient Experience with Treatment and Self-management (PETS) questionnaire. PETS is a self-report measure of treatment burden for patients with chronic conditions (Eton et al., 2017). The original

PETS was translated and adapted for use in a Norwegian healthcare context by Husebø et al. (2018). The Norwegian version contains nine dimensions and 48 items. The first four dimensions—medical information (MINF; seven items), medications (MEDS; seven items), medical appointments (MAP; six items) and monitoring health (MH; two items)—pertain to the *workload* of self-management (Lee et al., 2020). The following three dimensions—relationship with others (RLO; four items), medical and healthcare expenses (MEXP; four items) and difficulties with healthcare services (HCS; seven items)—relate to *stressors* aggravating burden, whereas the last two dimensions—the role and social activity limitations (RAL; six items) and physical and mental fatigue from self-management (PMF; five items)—pertain to the *impact* of burden (Lee et al., 2020). Responses were provided using either a 4- or a 5-point Likert scale. The recall time was 4 weeks. No calculated total score is available for the PETS (Eton et al., 2017).

Initial evidence of the reliability and validity of PETS has been demonstrated in large samples of chronically ill patient populations in the United States (Eton et al., 2017, 2019; Rogers et al., 2017). The Norwegian version of the PETS has shown satisfactory Cronbach's α , ranging from 0.71–0.93 across the subscales (Husebø et al., 2021).

3.5 | Sample size calculations

A sample size of 134 provides 84% statistical power to detect correlations ≥ 0.25 using a two-tailed significance level of 0.05 (SPSS Sample Power 3.0). This sample size also allows for multivariable analysis within the rule of thumb of $N \geq 50 + 8 * IV$ (number of independent variables; VanVoorhis & Morgan, 2007).

3.6 | Data analysis

Study variables are described by frequency and percentage and by the median and interquartile range. Non-normally distributed data were revealed by applying the Kolmogorov–Smirnov test, and the non-parametric Mann–Whitney U and Kruskal–Wallis tests were used to explore differences in fatigue between groups. Spearman's rank correlation coefficient (ρ ; ρ) was used to assess the relation between fatigue and treatment burden, with and without controlling for confounding variables (age group, gender, cancer stage, treatment modality, the time elapsed since primary surgery and number of comorbid conditions). The confounding variables were determined a priori (Babyak, 2004).

Stratified analyses were performed for the statistically significant associations between CRF and PETS workload dimensions to assess possible moderating effects of socio-demographic and clinical variables. In these analyses, we controlled for all confounders except the stratifying variable.

The strength of Spearman correlations was evaluated according to Cohen's guidelines, that is, correlations of 0.10–0.29 representing small correlations, 0.30–0.49 representing medium correlations

and 0.50 and above representing large correlations (Ivarsson et al., 2013).

Data were analysed using SPSS version 25 (IBM Corp. Released, 2017), except the estimation of partial correlations was accomplished with the R package PResiduals (R Foundation for Statistical Computing; R Core Team, 2013). Missing values on subscales were handled by imputing with the mean of the remaining items in cases where <50% of the items were missing. Three cases were missing for the SCFS-6. For PETS, out of a total of 134 cases, missing cases varied from 0–31 among the subscales (MINF = 31, MEDS = 12, MAP = 2, MH = 0, RLO = 5, MEXP = 12, HCS = 30, RAL = 10 and PMF = 3). Two-sided tests were applied, and p values <.05 were considered statistically significant for all analyses. Analytical methods taking account of the two different sampling strategies were not applied.

4 | RESULTS

Of 166 eligible cancer survivors, 134 returned the written consent and the survey inventory, resulting in a response rate of 84%. Reasons for non-participation were not collected. Participant characteristics are presented in Table 1. Of the participants enrolled in the study, 62% were men, and the median age was 67 (range: 40–78 years). Forty-six per cent were surgically treated <6 months prior to taking part in the study. Regarding the cancer diagnosis, 71% were

TABLE 1 Demographic and clinical characteristics of the participants

Characteristic (N = 134)		Frequency (%)
Age group	40–59	66 (49.3)
	60–79	68 (50.7)
Gender	Male	83 (61.9)
	Female	51 (38.1)
Time since primary surgical treatment	<6 months	62 (46.3)
	6–12 months	41 (30.6)
	>12 months	31 (23.1)
Dukes cancer stage	A	39 (29.1)
	B	46 (34.3)
	C	49 (36.6)
Treatment modality	Neoadjuvant	14 (10.4)
	Adjuvant	28 (20.9)
	Surgery only	92 (68.7)
Comorbidity	Yes	100 (74.6)
	No	34 (25.4)
Number of comorbid conditions	0	40 (29.9)
	1	35 (26.1)
	2	28 (20.9)
	3	24 (17.9)
	≥4	7 (5.2)

diagnosed with Dukes cancer Stage B or C. Adjuvant systemic treatment (i.e., chemotherapy) was employed in 21% of the participants. Nearly 75% had two or more documented comorbidities in the patient records, and of those, 44% had two or more chronic conditions in addition to cancer. The results for treatment burden dimensions in this study population have been reported elsewhere (Husebø et al., 2021).

4.1 | CRF and associations with demographic and clinical variables

Total CRF, physical fatigue and perceptual fatigue in relation to the clinical variables of the CRC patient sample are presented in Table 2. The median CRF score in the included 131 patients treated for CRC was 10 (range: 6–25). Patients between 40–59 years of age reported higher fatigue levels than patients between 60–79 years of age ($p = .021$). Patients with Dukes Stage C experienced more fatigue compared with those with Dukes A and B ($p = .014$). Gender, treatment modality, the number of comorbid conditions and time elapsed since primary surgery were not significantly associated with total CRF.

Comparing physical and perceptual fatigue, the scores were highest for the subscale physical fatigue, with a median score of 6.0 vs. 4.0 for the perceptual subscale. Younger patients reported significantly higher perceptual fatigue levels than older patients (median score of 4.5 vs. 3.0, $p = .001$). Both fatigue subscales were significantly associated with cancer stage, indicating that a more severe cancer diagnosis (i.e., Dukes C) resulted in more physical (median score 7.0 vs. 5.0, $p = .028$) and perceptual (median score 5.0 vs. 3.0, $p = .011$) fatigue. Perceptual fatigue was significantly associated with treatment modality (median score 5.0 vs. 3.0, $p = .049$), showing that adjuvant treatment resulted in significantly higher levels of perceptual fatigue (Table 2). Gender, treatment modality, number of comorbidities and time elapsed since primary surgery were not significantly associated with physical or perceptual fatigue.

4.2 | Associations between CRF and treatment burden dimensions

The relationship between CRF (i.e., total, physical and perceptual) and the treatment burden was investigated using Spearman's ρ correlation coefficients (Table 3). CRF was significantly associated with treatment burden on all PETS dimensions, except for the dimension MEDS. All significant correlations were positive, indicating that patients who experienced higher fatigue levels also reported higher levels of treatment burden. Correlations were small to medium for PETS dimensions pertaining to workload and stressors and medium to large for dimensions pertaining to impact of burden. There were consistently higher correlations between the PETS domains and perceptual fatigue than between the PETS domains and physical fatigue.

TABLE 2 Total fatigue, fatigue subscales and associations with demographic and clinical variables

	CRF total ^a			Physical fatigue ^b			Perceptual fatigue ^c		
	N	Median (IQR)	<i>p</i>	<i>n</i>	Median (IQR)	<i>p</i>	<i>n</i>	Median (IQR)	<i>p</i>
Total sample	131	10.0 (6.0–25.0)	—	132	6.0 (3.0–13.0)	—	131	4.0 (3.0–12.0)	—
Age group			.021			.089			.001
40–59 years	66	11.0 (7.8–16.0)		66	6.0 (4.0–8.3)		66	4.5 (3.0–7.0)	
60–79 years	65	8.0 (7.0–12.0)		66	5.0 (4.0–7.0)		65	3.0 (3.0–5.0)	
Gender			.65			.90			.31
Male	81	9.0 (7.0–13.0)		81	6.0 (4.0–8.0)		80	4.0 (3.0–5.5.0)	
Female	50	11.0 (7.0–13.3)		51	6.0 (4.0–8.0)		50	4.0 (3.0–6.0)	
Dukes cancer stage			.014			.028			.011
Dukes A	38	8.0 (7.0–12.0)		38	5.0 (4.0–7.3)		38	3.0 (3.0–5.0)	
Dukes B	45	9.0 (6.0–12.0)		46	5.0 (4.0–7.3)		45	3.0 (3.0–5.0)	
Dukes C	48	12.0 (8.3–16.0)		48	7.0 (5.0–9.0)		48	5.0 (3.0–7.0)	
Treatment modality			.069			.13			.049
Surgery only	89	9.0 (6.0–25.0)		89	5.0 (4.0–6.5)		89	3.0 (3.0–5.0)	
Neoadjuvant	14	10.0 (7.0–13.3)		14	6.0 (3.0–9.0)		14	4.0 (3.0–5.3)	
Adjuvant	28	12.5 (8.3–17.8)		29	7.0 (5.0–9.5)		28	5.0 (3.0–8.0)	
Number of comorbid conditions			.60			.85			.062
0 condition	41	12.0 (8.0–15.5)		41	6.0 (4.0–8.5)		41	5.0 (3.0–7.0)	
1 condition	35	8.0 (6.0–11.0)		35	5.0 (3.0–6.0)		35	3.0 (3.0–5.0)	
2 conditions	30	9.5 (7.0–13.5)		31	6.0 (4.0–8.0)		30	3.5 (3.0–5.0)	
≥3 conditions	25	10.0 (8.0–14.0)		25	7.0 (5.0–8.0)		25	4.0 (3.0–5.0)	
Time since primary surgical treatment			.34			.23			.96
<6 months	61	10.0 (8.0–13.0)		61	6.0 (4.3–8.0)		61	4.0 (3.0–5.0)	
6–12 months	40	9.5 (7.3–16.0)		40	6.0 (4.0–8.8)		40	4.0 (3.0–6.8)	
12–18 months	30	8.0 (6.0–13.0)		31	5.0 (3.0–8.0)		30	3.0 (3.0–6.0)	

Abbreviations: CRF, cancer-related fatigue; IQR, interquartile range.

^aCRF measured by the Schwartz Cancer Fatigue Scale-6 (total score range: 6–30).

^bSchwartz Cancer Fatigue Scale-6 Physical subscale (score range: 3–15).

^cSchwartz Cancer Fatigue Scale-6 Perceptual subscale (score range: 3–15).

There were only minor differences between the unadjusted and adjusted analyses. Significant unadjusted associations between the treatment burden dimensions and total CRF and the CRF subscales remained significant after adjusting for the following independent variables: age group, gender, Dukes cancer stage, treatment modality, the time elapsed since primary surgery and number of comorbid conditions. The most considerable effect of adjusting was found for the association between total fatigue and the PETS domain MINF, and in particular for perceptual fatigue, with an increase in ρ from 0.34–0.43 after adjustment. Age group and treatment modality had the strongest confounding effect on the association between MINF and CRF.

4.3 | Associations between CRF and treatment burden workload domains moderated by socio-demographic and clinical variables

Stratified analyses assessing moderation from socio-demographic and clinical variables of the association between CRF and three treatment burden workload domains (i.e., MINF, MAP and MH) are presented in Table 4. It showed that age moderated the association between CRF and all three dimensions, with higher correlations among patients <60 years than for patients 60–79 years of age: partial ρ .49 ($p \leq .001$) vs. 0.32 ($p = .037$) for MINF, 0.36 ($p = .007$) vs.

TABLE 3 Unadjusted and adjusted Spearman's correlations examining the relationship between CRF and treatment burden

	SCFS-6 subscales																	
	SCFS-6 total						Physical fatigue						Perceptual fatigue					
	N	ρ	p	ρ_p	p	ρ_p	N	ρ	p	ρ_p	p	N	ρ	p	ρ_p	p		
MINF	109	0.32	.001	0.38	<.001	0.31	109	0.26	.007	0.31	.005	109	0.34	<.001	0.43	<.001		
MEDS	73	0.10	.42	0.02	.88	-.01	74	0.08	.50	-.01	.96	73	0.13	.28	0.10	.45		
MAP	122	0.27	.003	0.27	.004	0.22	123	0.23	.011	0.22	.022	122	0.28	.002	0.28	.003		
MH	111	0.29	.002	0.31	.005	0.25	112	0.24	.012	0.25	.024	111	0.34	<.001	0.37	.001		
RLO	128	0.33	<.001	0.33	.001	0.28	128	0.28	.001	0.28	.004	128	0.36	<.001	0.36	.001		
MEXP	109	0.27	.005	0.27	.011	0.21	110	0.22	.022	0.21	.047	109	0.29	.003	0.31	.004		
HCS	78	0.13	.27	0.21	.11	0.15	78	0.07	.54	0.15	.25	78	0.21	.067	0.29	.017		
RAL	123	0.46	<.001	0.46	<.001	0.41	124	0.41	<.001	0.41	<.001	123	0.49	<.001	0.49	<.001		
PMF	124	0.58	<.001	0.60	<.001	0.58	124	0.53	<.001	0.58	<.001	124	0.59	<.001	0.60	<.001		

Abbreviations: CRF, cancer-related fatigue; HCS, difficulties with healthcare services; MAP, medical appointments; MEDS, medications; MEXP, medical and healthcare expenses; MH, monitoring health; MINF, medical information; PMF, physical and mental fatigue from self-management; RAL, role and social activity limitations; RLO, relationship with others; SCF-6, Schwartz Cancer Fatigue Scale-6; ρ , Spearman correlations; ρ_p , partial Spearman correlations adjusted for age group, gender, Dukes cancer stage, treatment modality, the time elapsed since primary surgery and number of comorbid conditions.

0.00 ($p = .098$) for MAP and 0.50 ($p = .005$) vs. 0.17 ($p = .31$) for MH. Correlations were also consistently higher among women than among men. Those with no additional treatment had higher correlations between CRF and MINF and MH but not MAP. Longer time since primary surgery resulted in higher correlations between CRF and MINF. Patients with less comorbidities (0 or 1 chronic disease) had higher correlations between CRF and MAP, whereas those with 1 or 2 chronic diseases had higher correlations between CRF and MH.

5 | DISCUSSION

This study measured the levels of CRF in a sample of CRC patients surgically treated with curative intent, how the CRF level varied giving demographic and clinical variables, and explored the associations between CRF and treatment burden.

5.1 | CRF in surgically treated CRC patients

In line with earlier research, our findings confirmed that CRF is elevated among CRC patients following surgical treatment (Thong et al., 2013, 2020). Although the average CRF level of this study population equated to scores on the lower third of the scale, CRF was reported as a problem. The result compares to earlier research on CRF in Norwegian surgically treated cancer populations using SCFS-6, where women with breast cancer reported SCFS-6 levels between 10.3 (SD: ± 3.9) and 11.3 (± 4.5 ; Husebø et al., 2014). An exercise trial among American prostate cancer survivors who were on average 6 years past diagnosis found similar baseline SCFS-6 levels of 9.2 (± 3.0) to 9.9 (± 4.5 ; Winters-Stone et al., 2015), whereas a study among Canadian lung cancer patients found slightly more elevated SCFS-6 of 12.3 (± 4.4) pre-chemotherapy (Shallwani et al., 2016). Notably, in the current study, nearly 70% of the sample had received surgical treatment <6 months before responding to the survey, and nearly one third had received adjuvant chemotherapy.

In this study, physical fatigue was found to be more prominent than perceptual fatigue among the included patients, indicating an impact on physical functioning (Schwartz et al., 2003). Older CRC patients (≥ 70 years) are at particular risk of impaired physical function after surgery, and it may take months before a patient achieves pre-surgical functional status (Couwenberg et al., 2018). To improve post-surgical patient outcomes, it is now recommended a CRC patient's available pre-surgical capacity is considered by screening those at risk of declined physical functioning (Ghignone et al., 2020).

A statistically significant age difference was observed for CRF, with younger CRC patients reporting more fatigue than older patients. This confirms findings from a large longitudinal study of CRC survivors that established significant associations between fatigue symptoms and patients who were pre-retirement (≤ 65 years of age; Husson et al., 2015). Fatigue subscale analysis revealed that younger patients reported more perceptual fatigue, such as having difficulties

TABLE 4 Associations between CRF and treatment burden from MINF, MAP and MH within strata of age group, gender, Dukes cancer stage, treatment modality, the time elapsed since primary surgery and number of comorbid conditions

	MINF			MAP			MH		
	N	ρ	p	N	ρ	p	N	ρ	p
All	109	0.32	.001	122	0.27	.003	111	0.29	.002
Young	57	0.32	.017	65	0.38	.002	54	0.38	.004
Old	52	0.44	.001	57	0.13	.34	57	0.18	.17
Males	71	0.31	.010	77	0.22	.051	72	0.32	.006
Females	38	0.37	.020	45	0.37	.012	39	0.26	.11
Neoadjuvant treatment	11	0.10	.76	14	0.11	.71	13	-0.02	.95
Adjuvant treatment	26	0.21	.30	26	0.47	.015	23	0.09	.69
No additional treatment	72	0.46	<.001	82	0.22	.049	75	0.40	<.001
<6 months since operation	57	0.17	.21	55	0.15	.29	51	0.33	.017
6–12 months since operation	31	.31	.086	38	0.28	.091	32	0.31	.089
12–18 months since operation	21	0.46	.035	29	0.31	.10	28	0.13	.52
Dukes A	33	0.35	.048	36	0.16	.35	34	0.51	.002
Dukes B	36	0.27	.11	41	0.38	.014	36	0.40	.014
Dukes C	40	0.32	.047	45	0.27	.076	41	0.07	.64
No chronic diseases	33	0.14	.44	38	0.56	<.001	28	0.02	.93
1 chronic disease	26	0.49	.011	33	0.39	.025	32	0.62	<.001
2 chronic diseases	26	0.59	.001	28	-0.27	.16	27	0.27	.18
>2 chronic diseases	24	0.14	.51	23	0.23	.30	24	0.07	.75

Abbreviations: CRF, cancer-related fatigue; MAP, medical appointments; MEDS, medications; MH, monitoring health; MINF, medical information; ρ , Spearman correlations; ρ_p , partial Spearman correlations adjusted for age group, gender, Dukes cancer stage, treatment modality, the time elapsed since primary surgery and number of comorbid conditions minus the stratifying variable.

^ana = analysis not applicable due to a low N.

thinking and feeling overwhelmed and helpless (Schwartz & Meek, 1999). This may be explained by younger CRC patients undergoing more extensive post-surgery treatment, including chemotherapy (Kneuert et al., 2015). Furthermore, younger CRC patients may have more occupational and family responsibilities than older patients, which can potentially increase fatigue. Including the patient's nearest family and provide them with information adapted to the recipient's age and family role is a concern of nurses who care for CRC surgery patients (Husebø et al., 2020). Moreover, it is recommended to employ PROMs that include employment and caring for dependants when assessing cancer patients' social well-being (Catt et al., 2017).

We also found that patients with more advanced cancer and who had received adjuvant treatments appeared more fatigued, especially on the perceptual fatigue subscale. Nurses play an essential role in helping cancer patients manage their fatigue during chemotherapy treatment (Lavdaniti, 2019). Our findings suggest that nursing interventions are needed that regularly enquire about a CRC patient's fatigue experience during treatment. This should take into account the possibility that a patient's cognition may be impaired when information is delivered. Moreover, a meta-analysis showed significant effects from eHealth and mHealth interventions on CRF among cancer survivors, with interventions guided by health professionals proving to be the most effective (Seiler et al., 2017).

The CRF levels were slightly, though not significantly, lower among patients with a longer time since surgery. The lack of significance could be due to low statistical power. The slight tendency for lower CRF with time from surgery is somewhat in line with a recent meta-analysis among rectal cancer patients, which found substantial changes in CRF through the course of the illness, with CRF levels declining gradually over the 12 months following diagnosis (Wen-Pei & Hsiu-Ju, 2020). Future research should include a longitudinal study design to detect changes over time in the fatigue experience of CRC patients.

5.2 | The relationship between CRF and treatment burden in patients curatively treated for CRC

In this study, most of the treatment burden dimensions were significantly associated with CRF and the associations held after adjusting for demographic and clinical variables. Our findings also identified subgroups of CRC patients with CRF being particularly strongly associated with burden from finding and using medical information, administrating and follow-up on medical appointments and monitoring their health. These subgroups are in need of special attention and support to keep themselves sufficiently informed, to cope with a busy schedule as a patient and to register change in their health condition and symptoms of exacerbation or cancer recurrence.

Overall, the associations with treatment burden were more substantial for the perceptual fatigue dimension than for the physical dimension. Among the generic self-management tasks related to CRC treatment that were associated with CRF were retrieving

relevant health information and gaining knowledge about the illness and its treatments (i.e., PETS dimension MINF). We found that this task was associated with the patients' degree of perceptual fatigue and that the type of treatment a patient received had a confounding effect on this association. A previous study by our group revealed a non-significant association between the PETS domain MINF and treatment modality in the current sample of CRC patients (Husebø et al., 2021), which might indicate that suffering from CRF increases the workload associated with finding and understanding medical information in patients who receive adjuvant treatments. Adjuvant therapies have a toxic impact on the brain and can cause memory loss and cognitive deficiencies (El-Agamy et al., 2019), and they are associated with fatigue (Dhillon et al., 2018). Thus, CRC patients who receive chemotherapy may find it harder to engage in information seeking due to the impaired cognitive ability from CRF. Nurses are encouraged to provide patients with education and information on interventions to ameliorate fatigue (Lavdaniti, 2019). Moreover, measures to counteract the fatigue experience, such as physical activity approaches, hold the potential to increase cancer patients' chemotherapy tolerance (Hilfiker et al., 2018). Interestingly, Anderson et al. (2021) identified the impact from self-management (i.e., PETS dimensions RAL and PMF) as a mediator of effects from health literacy on cancer survivors' general health. Psycho-educational group-based nursing interventions, including cognitive-behavioural techniques and patient education, are suggested to decrease the CRF in cancer patients (Tuominen et al., 2019). In particular, comorbid cancer survivors may face multiple cancers and more general challenges; thus, cancer support programmes may evaluate the totality of self-management (Anderson et al., 2021).

The successful self-management of long-term illness requires patients to obtain information from various sources and possess a high degree of health literacy (i.e., the ability to find, understand and use health information), which may increase self-efficacy regarding self-management skills (Mackey et al., 2016). A randomised controlled trial that investigated the effects of a patient information letter at hospital discharge found significantly increased treatment comprehension and health literacy in the intervention group compared with control (Voigt et al., 2018). Jones et al. (2016) suggested that a process of individualised care planning might enable cancer patients who experience CRF to set achievable goals and could provide them with education to promote self-management strategies. By identifying the burden associated with self-management tasks of information finding, nurses are in a position to strengthen patient participation in treatment-related discussions and shared decision-making (Rogers et al., 2017).

The largest correlation was found for the PETS dimensions of physical and mental fatigue, representing the impact of treatment burden (Lee et al., 2020). Anderson et al. (2021) established negative effects from self-management on general health outcomes including fatigue in women with cancer. The direction of the relationship between the impact from treatment burden and CRF needs to be further explored, that is, whether treatment burden leads to more CRF

or whether being fatigued from cancer and its treatments affects a CRC patient's ability to deal with the work of CRC self-management.

Further, it is evident that experiencing worsening psychosocial function owing to CRC self-management (i.e., PETS dimension RAL) is significantly associated with CRF. Foster et al. (2015) suggested supporting cancer patients in building their confidence to better self-manage the consequences of cancer diagnosis and treatments, including CRF. Feasible and efficient web-based approaches may provide cancer survivors with safe and necessary CRF management tools (Myall et al., 2015). We found no statistically significant associations between treatment burden from managing medications (e.g., taking medicines as planned, refilling and adjusting medicines and multiple medicines; i.e., PETS dimension MEDS) and CRF. This may be explained by a low number of participants responding to the MEDS items, indicating that medication burden was experienced as low in relation to the cancer diagnosis.

There seem to be a particularly strong association between CRF and the burden from finding relevant medical information and from monitoring health among CRC patients who receive surgical treatment only. This may indicate a higher information need and uncertainty towards monitoring their health in CRC survivors with a less advanced cancer diagnosis. According to treatment plans, they will have less contact with specialist cancer care services compared with patients who stay longer in the healthcare system due to the need of adjuvant treatments and who may get information needs covered and health condition monitored by outpatient clinic personnel. This finding is in contrast with a study among Dutch CRC survivors, showing that survivors who received chemotherapy expressed a greater need for sustained informational support (Wieldraaijer et al., 2019). Our study suggests self-management support for CRC patients with less advanced cancer and no additional treatment following surgery who experience CRF to increase knowledge of what to expect during recovery and what and how to monitor health condition change.

In our 2020 paper on treatment burden in the same sample of CRC patients, no significant correlations were found between comorbidity and treatment burden (Husebø et al., 2020). However, the current study confirms that comorbidity in CRC patients with CRF may complicate self-management tasks of monitoring health, indicating that the presence of CRF increases the burden from monitoring health.

5.3 | Limitations

There were some limitations to this study. The cross-sectional design may limit understanding of the concept of treatment burden in CRC patients. Furthermore, the study was performed in one university hospital in Norway; therefore, the results might not be generalisable to other geographic regions. However, the governmental cancer care set-up in a national context serves as a strong guide, and our observations would likely be similar to those obtained from other regions.

The sample size may be considered small, but it was large enough to show significant correlations between CRF and treatment burden.

Moreover, the relationship between CRF and treatment burden may be affected by other confounding variables, such as the patient's depression level. It can be challenging to separate fatigue from depression, and both can compromise the daily life functioning of cancer patients (Wen-Pei & Hsiu-Ju, 2020).

Analytical methods to determine differences between groups created by different recruitment procedures were not undertaken and should be considered a weakness of the study design.

The Norwegian version of the PETS has yet to be tested for psychometric properties beyond establishing satisfactory levels of reliability. Furthermore, the original version of the PETS was developed and validated in multimorbid patient populations (Eton et al., 2017) and is not condition or diagnosis specific. The majority of the respondents of the current study reported having one other chronic condition comorbid to CRC. Thus, the burden these CRC patients experienced may also result from self-management of other chronic conditions.

Further research is warranted to establish the PETS' ability to capture the treatment burden of CRC patients. For two of the PETS dimensions (MINF and HCS), there were considerably more missing cases than for the other dimensions. This can be explained by the availability of 'does not apply to me' as a response, which was recorded as 'missing' during scoring (Eton et al., 2017).

This study included both self-reported and observational data from a single cancer type, which may be considered a strength compared with earlier research that included a range of different cancer patient populations.

6 | CONCLUSION

The study found that younger CRC patients, those with a more advanced cancer stage and those offered adjuvant treatments were at particular risk of CRF. CRF was significantly associated with several treatment burden dimensions, indicating that CRC patients who experience CRF will also likely experience burden from cancer therapies and self-management. The patient workload of finding and understanding medical information relevant to self-management of the cancer illness and treatments was particularly associated with perceptual fatigue, but this relationship was confounded by the patient's age and the treatment received. Moreover, CRC self-management's impact on the patient's well-being was strongly and significantly associated with CRF. CRC patient subgroups of younger age, no additional treatment, longer time since primary surgery and multimorbidity showed higher correlations between CRF and treatment burden.

7 | IMPLICATIONS FOR PRACTICE

This study suggests that clinicians should pay particular attention to the fatigue experience of CRC patients who are younger of age and those with more advanced disease undergoing treatments in

addition to primary, surgical procedures. Considering the short inpatient stays of people undergoing primary surgery, it can be challenging for clinicians to capture and meet patients' need for self-management support. Thus, screening patients for self-management ability and treatment burden should be considered for incorporation into the clinical pathway. Support following hospital discharge could also be extended by providing nurse-led eHealth interventions, with a focus on informational, educational and psychosocial support to strengthen the capacity for self-management and ameliorate CRF. Such interventions may especially be appropriate for younger CRC survivors, CRC survivors with advanced cancer, longer time since primary surgery or for comorbid CRC survivors.

8 | RELEVANCE TO CLINICAL PRACTICE

Screening of CRF in CRC patients can help clinicians provide individualised treatment and care to manage CRF. Clinicians should consider the association between CRF and treatment burden, especially in subgroups of CRF patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.


AUTHOR CONTRIBUTIONS

A.M.L.H., J.A.S. and A.R. contributed to the study design. A.M.L.H. contributed to the data collection. A.M.L.H., I.D. and E.B. performed the data analysis. A.M.L.H., I.D. and A.R. wrote the paper. All authors reviewed, critically commented and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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SUPPORTING INFORMATION

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