Associations of sedentary time and patterns of sedentary time accumulation with health-related quality of life in colorectal cancer survivors

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ABSTRACT

Sedentary behavior (sitting/lying at low energy expenditure while awake) is emerging as an important risk factor that may compromise the health-related quality of life (HRQoL) of colorectal cancer (CRC) survivors. We examined associations of sedentary time with HRQoL in CRC survivors, 2–10 years post-diagnosis. In a cross-sectional study, stage I–III CRC survivors (n = 145) diagnosed (2002−2010) at Maastricht University Medical Center+, the Netherlands, wore the thigh-mounted MOX activity monitor 24 h/day for seven consecutive days. HRQoL outcomes were assessed by validated questionnaires (EORTC QLQ-C30, WHODAS II, Checklist Individual Strength, and Hospital Anxiety and Depression Scale). Confounder-adjusted linear regression models were used to estimate associations with HRQoL outcomes of MOX-derived total and prolonged sedentary time (in prolonged sedentary bouts ≥30 min), and usual sedentary bout duration, corrected for waking wear time. On average, participants spent 10.2 h/day sedentary (SD, 1.6), and 4.5 h/day in prolonged sedentary time (2.3). Mean usual sedentary bout duration was 27.3 min (SD, 16.8). Greater total and prolonged sedentary time, and longer usual sedentary bout duration were associated with significantly ($P < 0.05$) lower physical functioning, and higher disability and fatigue scores. Greater prolonged sedentary time and longer usual sedentary bout duration also showed significant associations with lower global quality of life and role functioning. Associations with distress and social functioning were non-significant. Sedentary time was cross-sectionally associated with poorer HRQoL outcomes in CRC survivors. Prospective studies are needed to investigate whether sedentary time reduction is a potential target for lifestyle interventions aiming to improve the HRQoL of CRC survivors.

1. Introduction

Worldwide, there are over 3.5 million colorectal cancer (CRC) survivors (Bray et al., 2013). Due to CRC and/or its treatment, these individuals can experience persisting declines in multiple health-related quality of life (HRQoL) domains, such as physical, social, and emotional functioning (Jansen et al., 2010; Caravati-Jouvenceaux et al., 2011). As the number of CRC survivors is increasing (Parry et al., 2011), a major research priority is to identify modifiable targets for interventions aimed at improving HRQoL of survivors with persisting health problems (Demark-Wahnefried et al., 2006).

Previous cross-sectional and prospective studies in CRC survivors have shown that moderate-to-vigorous intensity physical activity (MVPA) is beneficially related to HRQoL (Johnson et al., 2009; Buffart et al., 2012; Mosher et al., 2009; Peddle et al., 2008; Grimmett et al., 2011; Lynch et al., 2008; Vallance et al., 2014; van Roekel et al., 2015). However, many CRC survivors likely struggle to exercise at these intensities, which is related to their number of comorbidities and age (Brown & Schmitz, 2014). Instead, CRC survivors spend most (≈60%) (Vallance et al., 2014) waking time sedentary (sitting/lying while awake with a low energy expenditure (Sedentary Behaviour Research Network, 2012)). A growing body of evidence (albeit, mostly cross-sectional) from general adult populations suggests that more time spent sedentary is unfavorably related to several health outcomes (Dunstan et al., 2012), including HRQoL outcomes such as overall HRQoL, physical and mental functioning, and vitality in the general population (Dempsey et al., 2014; Rosenkranz et al., 2013), and physical and social functioning in elderly individuals (Meneguci et al., 2015). Importantly, the manner in which sedentary time is accrued may also be relevant, particularly for cardio-metabolic outcomes (Healy et al., 2008; Healy et al., 2011), and also body composition and muscle quality specifically in older adults (Chastin et al., 2012). As sedentary behavior may be associated with CRC-related problems strongly affecting HRQoL, such as bowel problems and distress regarding CRC recurrence, associations of sedentary behavior with HRQoL in this population may be more pronounced than in the general population. Research into associations of sedentary time and patterns of sedentary time accumulation with HRQoL of CRC survivors is therefore timely (Lynch et al., 2013).

Prospective studies in CRC survivors have found that more time spent in leisure-time sitting (Campbell et al., 2013) and television viewing (Arem et al., 2015) (a specific sedentary behavior) were associated with increased all-cause mortality, and that television viewing was also associated with weight gain (Wijndaele et al., 2009), a higher incidence of cardiovascular disease (Hawkes et al., 2011), and reduced HRQoL (Lynch et al., 2011a). However, these studies used self-report measures of sedentary behavior, with associated biases (Boyle et al., 2015), and did not examine sedentary time accumulation patterns.

Activity monitors, including accelerometers, provide date-time stamped information about activity enabling objective assessment of sedentary time, and patterns of sedentary time accrual (accumulation of sedentary time in long uninterrupted bouts versus shorter bouts interspersed with other activities). In contrast to previous prospective studies, a recent cross-sectional study of 178 colon cancer survivors did not observe significant associations of hip-worn accelerometer-derived total and prolonged sedentary time (in uninterrupted bouts of ≥30 min) with HRQoL (Vallance et al., 2014). However, measurement error in such accelerometers may lead to failure to detect associations as their indirect classification of time as sedentary from low movement alone has low accuracy, particularly for distinguishing low energy activities with different postures, such as standing (not sedentary) from sitting (sedentary) (Berendsen et al., 2014).

Thigh-mounted monitors that measure leg position and thereby posture, have been shown to accurately distinguish sitting and lying from upright postures (including standing) (Berendsen et al., 2014; Annegarn et al., 2011), and are thereby better suited to studying associations of sedentary time and sedentary time accumulation patterns

with HRQoL. This study aimed to examine associations of sedentary time and patterns of sedentary time accumulation, measured using an accurate thigh-mounted activity monitor (Berendsen et al., 2014; Annegarn et al., 2011), with HRQoL in CRC survivors.

2. Materials and methods

2.1. Study design and participants

Data from the cross-sectional part of the Energy for life after ColoRectal cancer (EnCoRe) study was used. The EnCoRe study consists of a cross-sectional and ongoing prospective part (van Roekel et al., 2014). The cross-sectional part was conducted in CRC survivors, recruited 2–10 years post-diagnosis. Eligible individuals, i.e. persons diagnosed with and treated for stage I–III CRC between 2002 and 2010 at Maastricht University Medical Center+, the Netherlands, were preselected via the Netherlands Cancer Registry (managed by Comprehensive Cancer Centre the Netherlands). Participants were recruited between May 2012 and December 2013. Reasons for exclusion are shown in Fig. 1. The EnCoRe study has been approved by the Medical Ethics Committee of the Academic Hospital Maastricht and Maastricht University, the Netherlands. Written informed consent was obtained from all participants.

2.2. Data collection

When designing the EnCoRe study, a conceptual model was developed for studying lifestyle and HRQoL in CRC survivors (van Roekel et al., 2014), based on WHO's International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2001). Compared to the traditional biomedical concept of health and disability as separate entities with a strong emphasis on physical health, the ICF adopts a broader bio-psychosocial definition of human functioning, as a multidimensional and universal concept which includes health and disability within a single spectrum (Kostanjsek, 2011). Thus, the ICF does not only incorporate physical health components (body perspective), but also an individual's ability to perform his/her daily activities and societal role (individual and societal perspective). Further, it enables identification of environmental and personal factors and the presence of health conditions that can influence functioning. The previously developed model (van Roekel et al., 2014) was adapted for the current research question to identify relevant variables to be measured and included in data analyses (Supplementary Fig. 1).

2.2.1. Sedentary and physical activity time

The validated tri-axial MOX activity monitor (MMOXX1, upgraded version of the CAM monitor) was used for objective measurement of sedentary and physical activity time (Maastricht Instruments B.V., NL). The MOX has a high reproducibility, and excellent validity for estimating time spent in activities and postures in both controlled laboratory (100% accuracy and kappa of 0.99; compared with direct observation (Berendsen et al., 2014) and 100% accuracy compared to a standardized protocol (Annegarn et al., 2011)) and in free-living conditions (intraclass correlation coefficient of 0.98 compared with diary records (Berendsen et al., 2014) and 100% accuracy in comparison with video recording (Annegarn et al., 2011)). The monitor was waterproofed in a finger cot (VWR International B.V., NL) and attached via plaster (BSN medical, NL) to the anterior thigh 10 cm above the knee. Participants were instructed to wear the monitor 24 h/day on seven consecutive days, and to record sleep and any non-wear periods.

A customized Matlab program (Version R2012a, The MathWorks, Inc., USA) was used to classify each 1-second epoch as sedentary (sitting/lying with an energy expenditure ≤1.5 METs (Sedentary Behaviour Research Network, 2012)), standing (standing with an energy expenditure ≤1.5 METs), or physical activity (all activities with an energy expenditure >1.5 METs, including light and moderate-to-vigorous intensity activities). This was done using previously validated thresholds for parameters of
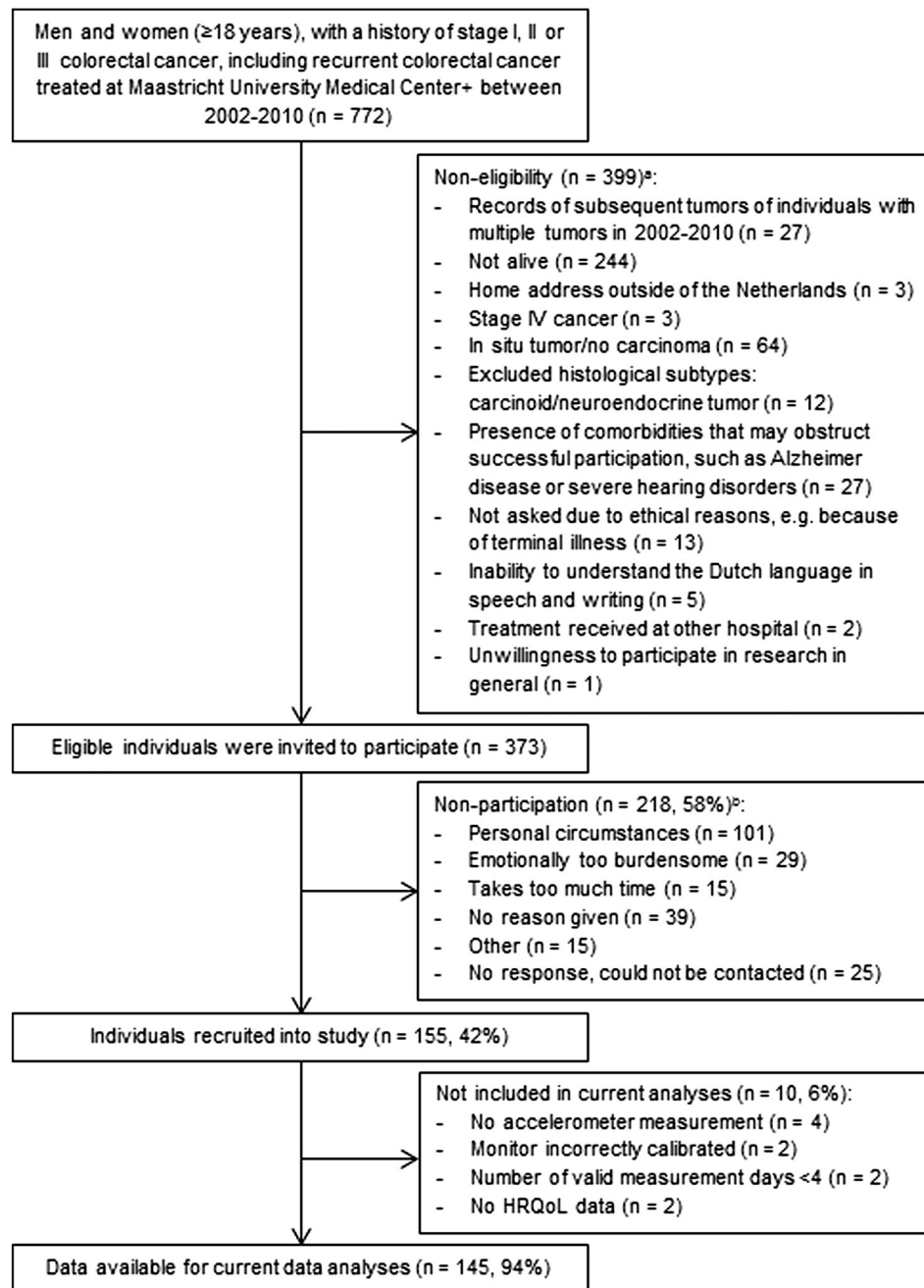
Fig. 1. Flow diagram of individuals, diagnosed with stage I–III colorectal cancer at Maastricht University Medical Center+ (2002–2010), who were included into the cross-sectional part of the EnCoRe study and analyses presented in this paper. *Footnotes*: [a]Reasons for non-eligibility are given in order of exclusion, totals do not add up because some exclusion criteria applied concurrently. [b]Totals do not add up because some individuals reported multiple reasons for non-participation.

motion intensity and orientation of the device (Annegarn et al., 2011). Time in physical activity was not further subdivided into light physical activity (1.6–2.9 METs) and MVPA (≥3 METs (Ainsworth et al., 2011)), because of a limited reproducibility of the monitor for estimating time in activities at a moderate-to-vigorous intensity (Berendsen et al., 2014). Self-reported non-wear and sleeping periods were checked by visualization of tri-axial acceleration data, with non-wear periods adjusted if necessary, and sleeping times determined if missing.

Further processing of worn waking data was performed in SAS (Version 9.3, SAS Institute Inc., USA), using a customized program with bout scoring adapted from approaches developed by the National Cancer Institute (Matthews et al., 2008). Monitor wear days with ≥10 h of waking wear time were considered valid; only participants with ≥4 valid days were included in analyses (Tudor-Locke et al., 2012). Total sedentary time (h/day), prolonged sedentary time (time accrued in sedentary bouts ≥30 min duration), and total physical activity time were calculated for each day and averaged across valid measurement days. Additionally, usual sedentary bout duration, i.e. the bout duration at which 50% of all sedentary time is accrued, was calculated for each participant using non-linear regression (Chastin & Granat, 2010; Stephens et al., 2014). A higher usual sedentary bout duration represents a more prolonged sedentary accumulation pattern. All accelerometer-derived variables, except for usual bout duration, were standardized for waking wear time, using the residuals method (Willett & Stampfer, 1986).

To reduce the impact of single-second "non-sedentary" activities within longer periods of sedentary time on estimated patterns of sedentary time accumulation, we identified sedentary bouts as all periods beginning with ≥2 consecutive seconds of sedentary time, and ending

upon ≥2 consecutive seconds of non-sedentary time. Bouts were treated as occurring on the day they began.

2.2.2. HRQoL outcomes

Cancer-specific HRQoL was measured using the valid and reliable European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30, version 3.0) (Aaronson et al., 1993; Bjordal et al., 2000). For the subscales global quality of life and physical, role and social functioning, 100-point scores were calculated (Fayers et al., 2001). Disability was assessed by the 12-item version of the ICF-based World Health Organization Disability Assessment Schedule II (WHODAS II) (van der Hoeken et al., 2000), which has good reliability and validity in different populations, including cancer survivors (World Health Organization, 2010; Posl et al., 2007). Fatigue was assessed through the 20-item Checklist Individual Strength (CIS), which was originally developed and validated in chronic fatigue syndrome patients (Vercoulen et al., 1996; Vercoulen et al., 1994), but also applied in cancer survivors (Servaes et al., 2001). The 14-item Hospital Anxiety and Depression Scale (HADS) was used to determine levels of distress (anxiety and/or depression) (Zigmond & Snaith, 1983), which has adequate psychometric properties in cancer patients (Vodermaier et al., 2009). Composite scores for each of the outcomes disability ($0 - 100$) (World Health Organization, 2010), fatigue (20–140), and distress (0–42) (Vodermaier et al., 2009) were calculated, with higher scores indicating higher levels of disability, fatigue, and distress, respectively.

2.2.3. Other factors

Socio-demographic characteristics (gender, age, education level, smoking status, paid employment) and presence of a stoma were self-reported. Body mass index (BMI, kg/m^2) was calculated from weight and height, measured by trained personnel. The number of comorbidities was assessed using the 13-item Self-Administered Comorbidity Questionnaire (Sangha et al., 2003). Clinical characteristics (cancer stage, age at diagnosis, chemotherapy/radiotherapy treatment, and tumor subsite) were collected through the Netherlands Cancer Registry.

2.3. Statistical analyses

Analyses were performed using IBM SPSS Statistics (Version 22, IBM Corporation, USA); statistical significance was set at $P < 0.05$ two-tailed. Multivariable linear regression models were used to calculate unstandardized regression coefficients (β) with 95% confidence intervals (CIs), representing the difference in mean HRQoL scores per additional unit of the independent variables. Units chosen (2 h/day for total and prolonged sedentary time; 15 min for usual sedentary bout duration) were approximately similar to one standard deviation (SD) of these variables within the sample to facilitate interpretation of results. Our minimum differences of interest were based on minimally important differences for the HRQoL outcomes (published "medium" differences for EORTC subscales (Cocks et al., 2011), and 0.5 times the SD for other outcomes scores (Revicki et al., 2008)). We defined the association to be "meaningful" (otherwise, as "small") if the difference in HRQoL outcome associated with a difference of 2 SDs in the independent variables exceeded these minimum important differences. Our choice for 2 SDs was based on the fact that this is a large but reasonable difference to occur within a population (Gelman, 2008). As the regression coefficients represented the difference in HRQoL scores per unit of the independent variables, we rescaled the minimum important differences into cut-offs that could be directly compared with the regression coefficients reported, based on this definition (Supplementary Table 1).

Potential confounders were identified a priori from our ICF-based conceptual model (Supplementary Fig. 1). These were either adjusted for in all models (age, gender, number of comorbidities, years since diagnosis, cancer stage, smoking status, and BMI) or, only when retained via backward elimination using $P > 0.2$ as cut-off for exclusion (Mickey & Greenland, 1989) (education level, paid employment, having

a partner, presence of a stoma, radiotherapy and/or chemotherapy treatment, and tumor subsite). The confounder-adjusted models were considered our main analyses. Additional models further adjusted for total physical activity and sedentary time (h/day; the latter only in usual sedentary bout duration models). Additionally, models with global quality of life as outcome were further adjusted for disability as a measure of physical ability. Potential effect modification by gender, age (<70 vs ≥70 years), number of comorbidities (≥2 vs <2), and BMI (<25 vs ≥25 kg/m^2) was explored by testing interaction terms for these variables by all independent variables ($P < 0.05$ was considered significant).

The residuals of the regression models were mostly non-normally distributed, due to non-normality in HRQoL outcomes. Therefore, findings were verified in logistic regression models with dichotomized outcomes using gender-specific medians as cut-off (Schlesinger et al., 2014). The examination of linear associations was investigated using quartile-based categories.

3. Results

3.1. Participant characteristics

In total, 373 eligible CRC survivors were invited to participate, 155 were recruited (response rate, 42%; Fig. 1), and 145 were included in the analyses. Included participants, compared with eligible survivors not included (Supplementary Table 2) were significantly younger (difference, 3.5 years; $P = 0.001$), but non-significantly different in time since diagnosis (difference, <0.01 years; $P = 0.966$), and gender ($P = 0.350$), tumor subsite ($P = 0.457$), treatment (surgery: $P = 0.550$, radiotherapy: $P = 0.176$, chemotherapy: $P = 0.138$), and stage ($P = 0.835$; all differences <10%).

Participants (91 men and 54 women, Table 1) were on average aged 70.0 years (SD, 8.7), and 5.7 years post-diagnosis (1.9). In total, 78 (54%) and 60 (41%) survivors had a history of colon and rectal cancer, respectively; seven (5%) had a rectosigmoid tumor. Most participants had a BMI in the overweight (25–29 kg/m^2, 46%) or obese (≥30 kg/m^2, 28%) category, and most (51%) reported at least two comorbidities. On average, participants spent 10.2 h/day sedentary (SD, 1.6 h, Table 2), and 4.5 h/day in prolonged sedentary time (2.3), and had a usual sedentary bout duration of 27.3 min (16.8).

3.2. Associations of sedentary time and patterns of sedentary time accumulation with HRQoL

More total sedentary time (per 2 h/day) was significantly associated with lower mean physical functioning scores (unstandardized regression coefficient (β), −7.4; 95% CI: −11.3, −3.4), and higher disability (5.5; 2.5, 8.5) and fatigue scores (8.1; 2.4, 13.8) (Table 3). Prolonged sedentary time (per 2 h/day) was significantly associated with lower mean global quality of life (−4.1; −6.9, −1.3), physical (−5.7; −8.7, −2.8), and role functioning scores (−4.5; −8.5, −0.5), and higher disability (4.4; 2.1, 6.6) and fatigue scores (7.1; 3.1, 11.1). A longer usual sedentary bout duration (per 15 min) was also significantly associated with lower global quality of life (−4.5; −7.3, −1.7), and physical (−5.7; −8.7, −2.7) and role functioning scores (−4.9; −8.9, −0.8), and higher disability (4.5; 2.2, 6.8) and fatigue scores (7.2; 3.1, 11.2). Most significant associations observed were of a meaningful magnitude (Supplementary Table 1), except for associations with physical and role functioning. The analyses with dichotomized HRQoL outcomes showed largely the same results as our main analyses except with wider CIs, indicating that the non-normality of residuals had not influenced our results (Supplementary Table 3). The examination of linear associations was also supported, with no additional associations detected using quartiles (Supplementary Table 4).

After further adjustment for physical activity time, most significant associations observed remained significant, except for associations of

Table 1
Socio-demographic and clinical characteristics of included colorectal cancer survivors (n = 145), diagnosed with stage I–III colorectal cancer at Maastricht University Medical Center+ (2002–2010).

Characteristic	n	%
Age, years		
Mean	70.0	
SD	8.7	
Years since diagnosis		
Mean	5.7	
SD	1.9	
Gender		
Men	91	62.8
Women	54	37.2
Tumor subsite		
Colon	78	53.8
Rectosigmoid	7	4.8
Rectum	60	41.4
Cancer stage[a]		
I	40	29.2
II	50	36.5
III	47	34.3
Treatment with chemotherapy		
Yes	75	51.7
No	70	48.3
Treatment with radiotherapy		
Yes	55	37.9
No	90	62.1
Number of comorbid conditions		
None	35	24.1
1	36	24.8
≥2	74	51.0
Stoma (colostomy/ileostomy)		
Yes	24	16.6
No	121	83.4
BMI, kg/m^2		
Mean	27.6	
SD	4.3	
Education level		
Low	37	25.5
Medium	48	33.1
High	60	41.4
Smoking status		
Current	16	11.0
Former	98	67.6
Never	31	21.4
Partner		
Yes	118	81.4
No	27	18.6
Paid employment		
Yes	24	16.6
No	121	83.4

Abbreviation: SD, standard deviation.
[a] Data missing for 8 participants.

usual sedentary bout duration with physical functioning (attenuated by 39%) and role functioning (attenuated by 6%), which became non-significant after adjustment for physical activity and sedentary time. Upon adjustment for disability, associations of prolonged sedentary time and usual bout duration with global quality of life became small and non-significant (Supplementary Table 5).

Effect modification was significant only by gender, and only of associations with physical functioning ($P < 0.01$, Supplementary Table 6). Specifically, associations with physical functioning were non-significant and small in men, but were significant and meaningful in women for total and prolonged sedentary time (−12.7; −17.9, −7.5; and −10.3; −14.1, −6.5, respectively), and a longer usual sedentary bout duration (−8.6; −12.2, −5.1).

4. Discussion

This is one of the first studies investigating whether objectively assessed sedentary time and sedentary time accumulation patterns were cross-sectionally associated with HRQoL in CRC survivors. We

Table 2
Descriptive statistics for accelerometer and health-related quality of life (HRQoL) outcome variables in included colorectal cancer survivors (n = 145), diagnosed with stage I–III colorectal cancer at Maastricht University Medical Center+ (2002–2010).

Characteristic	Mean	SD
Accelerometer data		
Number of valid days	6.8	0.6
Waking wear time, h/day	15.3	0.8
Sedentary time, h/day[a]	10.2	1.6
Prolonged sedentary time, h/day[a] (in bouts with duration ≥30 min)	4.5	2.3
Usual sedentary bout duration, min[b]	27.3	16.8
Standing time, h/day[a]	3.4	1.2
Physical activity time, h/day[a]	1.7	0.7
HRQoL outcomes (scale)[c]		
Global quality of life (0–100)	77.6	18.3
Physical functioning (0–100)	80.7	20.6
Role functioning (0–100)	83.4	25.3
Social functioning (0–100)	89.3	18.3
Disability (0–100)[d]	12.5	15.6
Fatigue (20–140)[e]	56.1	27.2
Distress (0–42)[e]	8.3	6.0

Abbreviation: SD, standard deviation.
[a] Standardized for daily waking wear time using residuals method.
[b] Bout duration at which 50% of total sedentary time is accrued.
[c] Higher scores indicate higher levels of quality of life, physical, role, and social functioning, and disability, fatigue, and distress.
[d] Data missing for 4 participants.
[e] Data missing for 2 participants.

observed that greater sedentary time was significantly associated with poorer physical functioning, disability, and fatigue. Prolonged patterns of sedentary time accumulation (more prolonged sedentary time and/or longer usual sedentary bout duration) were also significantly and adversely associated with these outcomes, and with global quality of life and role functioning. Most associations were of a meaningful magnitude. We did not observe any significant associations with distress or social functioning. For social functioning, meaningful effect sizes were generally not included in 95% CIs, indicating that a meaningful association in the overall CRC survivor population is unlikely based on our results. For distress, however, the sample size was insufficient to obtain conclusive findings, with 95% CIs containing meaningful effect sizes.

Results of previous studies investigating associations of sedentary time with HRQoL in cancer survivorship cohorts are inconsistent, possibly due to the diversity of sedentary time and HRQoL measures applied as well as differences in populations studied (sample size and characteristics such as age, gender, and cancer treatment). Similar to our findings, a longitudinal study of 1266 CRC survivors reported unfavorable associations between self-reported television viewing time, and overall HRQoL, physical, social, emotional, and functional well-being, and CRC-specific symptoms (Lynch et al., 2011a). In contrast, a cross-sectional study in 710 breast cancer survivors found no significant associations of self-reported total sitting time with physical, role, and mental functioning, and fatigue (George et al., 2013). In a cross-sectional study of 178 colon cancer survivors no significant associations were observed of total or prolonged sedentary time, assessed by a hip-worn accelerometer, with overall HRQoL, CRC-specific symptoms, a combined score for CRC-specific symptoms, physical and functional well-being, and fatigue (Vallance et al., 2014). Similarly, a cross-sectional study in 358 breast cancer survivors observed no significant associations of hip-worn accelerometer-derived sedentary time with cancer-specific HRQoL domains, depression, anxiety, and fatigue severity, although an association with longer fatigue duration was found (Phillips et al., 2015). The limited validity of the hip-worn accelerometer in assessing sedentary time (Berendsen et al., 2014) may have contributed to their null findings. Similar to our findings, in 54 mixed cancer survivors (including CRC), unfavorable significant cross-sectional associations were observed of higher sedentary time, assessed with thigh-mounted activity monitors, with physical HRQoL and general health, but not mental HRQoL and social

Table 3
Adjusted results of multivariable linear regression models investigating associations of sedentary time and patterns of sedentary time accumulation with health-related quality of life scores[a] in colorectal cancer survivors, diagnosed with stage I–III colorectal cancer at Maastricht University Medical Center+ (2002–2010).

	Global quality of life (n = 137)		Physical functioning (n = 137)		Role functioning (n = 137)		Social functioning (n = 137)		Disability (n = 133)		Fatigue (n = 135)		Distress (n = 135)	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Sedentary time, per 2 h/day[b]														
Multivariable adjustment[c]	−2.9	−6.8, 1.0	−7.4	−11.3, −3.4	−4.7	−10.1, 0.8	−1.6	−5.6, 2.5	5.5	2.5, 8.5	8.1	2.4, 13.8	0.5	−0.8, 1.8
With adjustment for physical activity time	−1.3	−6.7, 4.1	−5.6	−11.2, −0.1	−5.2	−12.7, 2.4	−2.3	−7.9, 3.4	5.4	1.1, 9.6	8.4	0.5, 16.3	−0.2	−2.0, 1.7
Prolonged sedentary time, per 2 h/day[b,d]														
Multivariable adjustment[c]	−4.1	−6.9, −1.3	−5.7	−8.7, −2.8	−4.5	−8.5, −0.5	−1.5	−4.4, 1.5	4.4	2.1, 6.6	7.1	3.1, 11.1	0.8	−0.1, 1.8
With adjustment for physical activity time	−4.5	−8.2, −0.9	−4.5	−8.3, −0.7	−5.3	−10.5, −0.1	−2.0	−5.8, 1.9	4.1	1.2, 7.1	8.0	2.7, 13.2	0.7	−0.5, 1.9
Usual sedentary bout duration, per 15 min[e]														
Multivariable adjustment[c]	−4.5	−7.3, −1.7	−5.7	−8.7, −2.7	−4.9	−8.9, −0.8	−0.8	−3.8, 2.2	4.5	2.2, 6.8	7.2	3.1, 11.2	0.8	−0.2, 1.7
With adjustment for physical activity and sedentary time	−5.0	−8.6, −1.4	−3.5	−7.2, 0.3	−4.6	−9.7, 0.6	−0.3	−4.1, 3.6	3.2	0.3, 6.0	6.1	0.8, 11.4	0.7	−0.5, 2.0

Abbreviations: β, unstandardized regression coefficient (representing the difference in mean health-related quality of life score per unit increase of the independent variables); CI, confidence interval.

[a] Higher scores indicate higher levels of quality of life, physical, role, and social functioning, and disability, fatigue, and distress.

[b] Standardized for waking wear time (h/day) using residuals method.

[c] Adjusted for waking wear time (h/day), age (years), gender, number of comorbidities (0/1/≥2), smoking status (current/previous or never), time since diagnosis (years), cancer stage (I/II/III), body mass index (kg/m^2), paid employment (yes/no; only models with disability as outcome), partner (yes/no; only models with disability and fatigue as outcome), stoma (yes/no; only models with physical, role, and social functioning, and disability and distress as outcome), tumor subsite (colon/rectum, with rectosigmoid classified as rectum; only models with physical and role functioning, and disability as outcome).

[d] Average time spent in sedentary bouts with ≥30 min duration per day.

[e] Bout duration at which 50% of total sedentary time is accrued.

functioning (George et al., 2014). This could imply that the associations we observed could also occur in other cancer survivorship cohorts. Further research applying thigh-mounted monitors in different cancer survivor cohorts will be necessary to further investigate associations of sedentary time with the HRQoL outcomes examined in the current study.

Nearly all significant associations observed between sedentary time and HRQoL showed limited attenuation and remained significant upon adjustment for physical activity. From one perspective, this implies associations of sedentary time with HRQoL are unlikely to be due to confounding by physical activity. From another perspective, these models indirectly imply a potential importance of standing for HRQoL, as they treat as fixed both total physical activity (of a light- and moderate-to-vigorous intensity; excluding standing) and total waking wear time using adjustment, and all remaining non-sedentary time is standing (Mekary et al., 2009). Other emerging evidence, including one longitudinal study (Blair et al., 2014) and previous findings from this population (van Roekel et al., 2015), further supports favorable associations of self-reported light intensity physical activity, independent from MVPA, with physical functioning (van Roekel et al., 2015; Blair et al., 2014) and other HRQoL outcomes in CRC survivors (van Roekel et al., 2015). Interventions targeting reductions in overall and prolonged sedentary time, primarily by increasing low-energy expenditure activities such as standing, have been shown to be feasible and acceptable in older adults at similar ages as CRC survivors (Gardiner et al., 2011). Such interventions may prove a useful adjunct to MVPA promotion for CRC survivors, many of whom encounter difficulties in performing recommended amounts of MVPA (Brown & Schmitz, 2014). Furthermore, our findings and results from previous studies indicate that cancer survivors spend the majority of their time sedentary (61–69% of total waking wear time (Vallance et al., 2014; Phillips et al., 2015; Lynch et al., 2010; Lynch et al., 2011b)), and their sedentary behavior levels are higher than in the general population (Kim et al., 2013). This further illustrates that reducing sedentary time could be an important target for intervention.

Strengths of our study included the objective, accurate and posture-based measurement of sedentary time using the MOX activity monitor, and the in-depth analyses of sedentary time accrual. In addition, our ICF-based conceptual model facilitated a comprehensive HRQoL assessment in domains relevant to CRC survivors, and identification of important contextual factors. However, there are also limitations to consider. In particular, the cross-sectional design of our study limits our ability to draw conclusions about the direction of associations or causality. The association of sedentary behavior with HRQoL in CRC survivors is likely to be reciprocal and to result in a downward spiral of more sedentary time causing a lower HRQoL and vice versa. Nevertheless, interventions that promote physical activity (and thereby possibly reduce sedentary behavior) can improve HRQoL in cancer survivors (Mishra et al., 2012), potentially by breaking this downward spiral. However, few intervention studies have been conducted exclusively in CRC survivors and these have mostly shown null results (Lynch et al., 2016). This is likely caused by a lack of knowledge on which type of intervention would be effective in this older population. Therefore, to enable development of tailored interventions for CRC survivors, prospective data are needed to investigate the temporal direction of associations of different types of activities with HRQoL, and to further study how disability as a measure of physical ability influences associations of prolonged sedentary time with global quality of life. Due to the limited reproducibility of the MOX at moderate-to-vigorous intensity levels, we could not differentiate between light physical activity and MVPA and could only adjust for total physical activity. Further research using activity monitors that are more reliable at higher intensities is recommended. Additionally, participants differed in age and perhaps other (non-measured) characteristics from non-participants, which limits the generalizability of our results, as findings may have been impacted by selection bias. The sample size was not selected a priori with the present research questions in mind but mostly appeared adequate, except regarding distress as an outcome. Larger studies are necessary to further investigate associations with distress.

In conclusion, our cross-sectional analyses showed that sedentary time, particularly prolonged sedentary time, was significantly and detrimentally associated with HRQoL outcomes in CRC survivors. Prospective studies are needed to provide more convincing evidence as to whether reducing prolonged sedentary time is a suitable target for lifestyle interventions aiming to improve CRC survivors' HRQoL.

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Conflicts of interest statement

Transparency document

The Transparency document associated with this article can be found, in the online version.

Acknowledgments

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