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Physical Activity, Bowel Function and Quality of Life among Rectal Cancer Survivors

Robert S. Krouse, MD^{1,2,3}, Christopher S. Wendel, MS⁴, David O. Garcia, PhD⁵, Marcia Grant, PhD⁶, Larissa K. F. Temple, MD⁷, Scott B. Going, PhD⁸, Mark C. Hornbrook, PhD⁹, Joanna E. Bulkley, PhD⁹, Carmit K. McMullen, PhD⁹, and Lisa J. Herrinton, PhD¹⁰

¹University of Pennsylvania School of Medicine; 3400 Spruce St., Philadelphia, PA 19104

²Leonard Davis Institute of Health Economics should be 3641 Locust Walk, Philadelphia, PA 19104

³Cpl. Michael J. Crescenz VA Medical Center; 3900 Woodland Ave., Philadelphia, PA 19104

⁴University of Arizona College of Medicine; 1501 S. Campbell Ave., Tucson, AZ 85724

⁵University of Arizona College of Public Health; 1295 N. Martin Ave., Tucson, AZ 85724

⁶City of Hope/Beckman Research Institute, Division of Nursing Research and Education; 1500 East Duarte Road, Duarte, CA 91010

⁷University of Rochester Medical Center, Division of Colorectal Surgery; 601 Elmwood Ave., Box SURG, Rochester, NY 14642

⁸University of Arizona College of Agriculture and Life Sciences, Department of Nutritional Sciences; 1177 E. 4th Street Shantz Bldg., Rm 309 Tucson, AZ 85721

⁹Kaiser Permanente Center for Health Research; 3800 N. Interstate Ave., Portland, OR 97227

¹⁰Kaiser Permanente Division of Research; 2000 Broadway, Oakland, CA 94612

Abstract

Purpose—Physical activity (PA) is positively associated with numerous health benefits among cancer survivors. This study examined insufficiently-investigated relationships among PA, health-related quality of life (HRQOL), and bowel function (BF) in rectal cancer survivors.

Corresponding Author: Robert S. Krouse, MD, University of Pennsylvania Perelman School of Medicine, 4 Silverstein, 3400 Spruce St., Philadelphia, PA 19104, (215) 823-5880, (215) 823-4309 fax, robert.krouse@va.gov.

Compliance with Ethical Standards

Disclosure of potential conflicts of interest: The authors declare that they have no conflicts of interest.

Research involving Human Participants and/or Animals: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: This study was approved by the UA Institutional Review Board (IRB) and the IRBs at both Kaiser Permanente sites in accordance with assurances filed with and approved by the U.S. Department of Health and Human Services. Informed consent was considered to be received by return of the completed survey; a statement of this principle was included in the study invitation letter.

Methods—RC survivors (n=1,063) five years from diagnosis in two Kaiser Permanente Regions were mailed a multidimensional survey to assess HRQOL and BF. PA was assessed by a modified Godin-Leisure Time Exercise Questionnaire. PA minutes were categorized into weighted categories based on guidelines: 1) not active (zero PA minutes); 2) insufficiently active (1–149 PA minutes); 3) meeting guidelines (150–299 PA minutes); and 4) above guidelines (≥ 300 PA minutes). Relationships of PA with HRQOL and BF were evaluated using multiple linear regression, stratified by sex and ostomy status for BF. Types of PA identified as helpful for BF and symptoms addressed were summarized.

Results—Response rate was 60.5%. Of 557 participants, 40% met or exceeded PA guidelines, 34% were Not Active, and 26% were Insufficiently Active. Aerobic activities, specifically walking and cycling, were most commonly reported to help BF. Higher PA was associated with better psychological wellbeing and multiple SF12 scales, worse BF scores in men with ostomies, and better BF scores in women.

Conclusions—Meeting or exceeding PA guidelines was associated with higher HRQOL. Although the BF findings are exploratory, they suggest women may benefit from increased PA, whereas men with ostomies may face challenges that require more study. Identifying PA strategies that will lead to improved patient compliance and benefit are needed.

Keywords

Rectal Neoplasms; Bowel Function; Physical Activity; Health-Related Quality of Life; Survivorship

Background

Rectal cancer (RC) has been estimated to affect nearly 40,000 people in the U.S in 2016 [1]. Trans-abdominal surgical extirpation is commonly employed for most Stage II and III rectal cancers. The most common decision-making factor for the surgical procedure is whether a patient will have an anastomosis with or without a temporary intestinal stoma (ostomy), or a permanent ostomy. This decision depends on several factors, most importantly the distance of the tumor from the anal sphincters. Radiotherapy and chemotherapy, typically in the neoadjuvant setting, also is commonly utilized for RC treatment for locally advanced tumors (T3 and/or nodal involvement).

RC treatments have many implications for survivors' health-related quality of life (HRQOL) [2, 3]. In addition, there are clearly differences based on gender [2, 4]. Specifically, RC survivors with anastomosis experience variable degrees of bowel function (BF) changes after their cancer treatment(s) [5, 6]. Loss of bowel control is universal for people with ostomies, although some are able to attain a certain measure of control utilizing irrigation techniques [7], and ostomy pouching systems can help manage this loss of bowel control. Regardless of the surgical procedure utilized, RC survivors may experience persistent bowel problems. One potential strategy to improve HRQOL and BF is to increase physical activity (PA).

PA is associated with numerous health outcomes such as improved cardiorespiratory fitness, reduced fatigue, and higher quality of life among cancer survivors [8–16]. Further, PA has been shown to be safe and effective in reducing many negative side effects of treatment for

cancer survivors and promoting better overall health [17]. As RC survivors are often younger [18] and living longer than in the past, a healthy lifestyle, including appropriate level of PA, is likely to provide long-term benefits. As with other chronic disease sufferers, PA also may improve a sense of well-being [19, 20], and provide the means for RC survivors to regain a sense of autonomy [21], as well as connection to and control over their bodies, countering the invasive, depersonalizing, and loss-of-control nature of major bowel surgery [22]. Despite the many benefits of PA, RC survivors often suffer many long-term and late effects of their treatments [2, 23] which may pose barriers to engaging in PA. Examples of problems that can inhibit PA include hernia [24], skin problems [24], fistula [3], neuropathy [25, 26], and pain [26]. Other barriers to PA may include fear of stool leakage, having an ostomy, and persistent fatigue [27]. Notably, the role PA may play in improving HRQOL and BF for RC survivors is understudied [2, 23]. A broader understanding of RC survivor patterns of PA, and the association of PA to BF could lead to targeted PA interventions for these cancer survivors. Therefore, the purpose of this study was to examine relationships among PA, HRQOL and BF in RC survivors.

Methods

Participants

Surveys were mailed to 1,063 RC survivors (5 years post-diagnosis who had a major proctectomy excluding transanal only excisions) during 2010–2011. Survivors were members of two Kaiser Permanente regions: Northern California and Northwest. Survey packets included scannable forms developed at the University of Arizona (UA) Cancer Center programmed with Teleforms 10.3 (Copyright 2007 Cardiff). Two weeks after mailing, individuals who had not returned the questionnaire were contacted by phone (up to ten attempts). If they were interested, individuals were asked to complete the questionnaire and return it in the provided postage-paid envelope, or if they preferred, to answer the questionnaire items over the phone. Patients refusing participation were no longer contacted. Medical history items were extracted from the Kaiser Permanente electronic medical record, including length of time since surgery, Surveillance, Epidemiology, and End Results (SEER) general summary stage, radiation treatment, chemotherapy, and the Charlson-Deyo comorbidity index [28].

QOL and Bowel Function

A multidimensional survey was constructed using elements from several validated instruments. Surveys included the City of Hope Quality of Life-Colorectal Cancer (COH-QOL-CRC), the SF-12v2 Health Survey, and the Memorial Sloan-Kettering Cancer Center Bowel Function Index (BFI) [29, 30]. Using both HRQOL measures allowed the assessment of both general (SF-12v2) and RC-specific (COH-QOL-CRC) aspects of HRQOL. The BFI produces a total score as well as three subscales: Dietary (the degree to which certain food or liquids, or limitation thereof, affect the number of bowel movements per day), Urgency/Soilage (frequency of garment soilage, use of padding due to stool leakage, and altering activities because of bowel function), and Frequency (diarrhea or loose stools, number of bowel movements per day, use of medicines to decrease number of bowel movements, and ability to get to the toilet on time). The UA research team modified the COH-QOL-CRC for

subjects with anastomosis by changing question stems to refer to surgery rather than ostomy and deleting eight inapplicable items, as well as adapted the BFI for subjects with ostomies by changing five items to refer to emptying the ostomy bag and deleting two inapplicable items. Both adaptations demonstrated strong internal consistency reliability and concurrent validity, and factor analysis supported construct validity of Urgency/Soilage and Dietary scales on the BFI ostomy version [29, 31].

The multidimensional survey was scored based on published instrument-specific rules [30, 32–34]. COH-QOL-CRC items and scales range 0 to 10 with 10 indicating better QOL; scales were derived by arithmetic mean of non-missing items for overall HRQOL and subscales (physical, psychological, social, and spiritual wellbeing). BFI subscales (Dietary, Urgency/Soilage, and Frequency scales) were derived by summation of relevant items scores and Total BFI score was the sum of all item response scores. For missing items on the BFI, we substituted the mean of the non-missing items in the subscale for the missing item. The Frequency scale of the BFI was not calculated for the ostomy group, as it has not been validated in this population [29]. Total BFI score for the ostomy group was rescaled to have the same range as in the anastomosis group. A higher BFI score denotes better function with ranges Total BFI 14–70, Urgency/Soilage 4–20; Frequency (defined only for anastomosis group) 6–30, and Dietary 4–20. The SF12v2 Health Survey was scored with QualityMetric scoring software (QualityMetric Inc., Lincoln, RI) to derive norm-based scores (mean of 50 and standard deviation of 10 in the standard 1998 U.S. general population), for the scales Physical Component Score (PCS), Mental Component Score (MCS), Physical Function, Role Physical, Body Pain, General Health, Vitality, Social Function, Mental Health, and Role Emotional. Six individual items of a priori interest from the COH-QOL-CRC also evaluated were control (“Do you feel like you are in control of things in your life?”), pain related to ostomy/anastomosis surgery, leakage from ostomy pouch, skin problems, sleep problems, and constipation.

Physical Activity

PA was assessed with a modified version of the Godin Leisure-Time Exercise Questionnaire (GLTEQ) [35]. The GLTEQ is a validated self-reported measure of the frequency of light-intensity, moderate-intensity, and vigorous-intensity leisure time PA and is commonly used in oncology research [36]. In fact, a recent systematic review by Amireault et al., [36] found it has been used for 212 English-written published articles among cancer survivors between 1997 and 2014; 16 of these studies were in colorectal cancer survivor populations. The GLTEQ has also used to classify cancer survivors as active (e.g., 150 minutes/week of moderate-vigorous intensity activity), insufficiently active (e.g., <150 minutes/week of moderate-vigorous intensity activity), and not active (e.g. 0 mins/week of moderate-vigorous intensity activity [37]. Amireault et al. also validated the GLTEQ to classify breast cancer survivors (n=199) into active (150 min/week) and insufficiently active (<150 min/week) categories based on moderate-vigorous intensity activity. [37]. The GLTEQ and accelerometer classified 33.8 and 27.2 % of participants as active, respectively (agreement = 70.8 %). Sensitivity and specificity values were 75.3% and 58.5%, respectively. The authors concluded that the GTLEQ can be used to classify cancer survivors into PA categories in

reference to PA guidelines. Overall, these findings support the use of the GTLEQ classification coding system for PA at the group level for cancer survivors.

Participants were asked to recall, for a typical week in the past month, the number of times per week and average amount of time per exercise session of light (minimal effort, no sweating), moderate (not exhausting, light sweating), and vigorous (heart beats rapidly, heavy sweating) PA that lasted at least 15 minutes and was performed during free time. Average weekly PA time within each category of exertion was derived by multiplying the session duration by the frequency. The American Cancer Society (ACS) and the American College of Sports Medicine (ACSM) recommend that cancer survivors perform 75 mins/week of vigorous activity, 150 mins/week of moderate PA, or an equivalent combination [38, 39] (i.e., 1 minute of vigorous activity is considered equivalent to 2 minutes of moderate activity). Following methods described by Trinh et al. [40], a weighted index we will call “weighted PA minutes” was calculated as moderate-exertion time plus 2 times vigorous-exertion time. Weighted PA minutes were categorized into four categories based on PA guidelines: 1) not active (zero weighted PA minutes); 2) insufficiently active (1–149 weighted PA minutes); 3) meeting guidelines (150–299 weighted PA minutes); and 4) above guidelines (≥ 300 weighted PA minutes) [32, 39–42]. Thus, the weighted PA-minute categories, including “not active,” do not take into account free-time activities at the light activity level or baseline daily activities that occur outside of free time.

An additional question about PA and bowel function was also utilized: “Since your operation/ostomy, are there any exercises or activities that have helped with your bowel function?” Participants who responded “yes” were asked to write-in up to three activities they found helpful and report bowel function symptoms helped by each activity. Fixed choice responses were common bowel function symptoms cited by RC survivors in exploratory focus groups and enumerated prior to development of the survey, and participants could write-in any additional symptoms. Types of PA and symptoms helped were analyzed descriptively. Activities were categorized into aerobic (e.g., walking, biking), anaerobic (e.g., yoga, Pilates), and general (e.g., gardening, housework). If the respondent wrote in a symptom that was not listed, it was recoded and grouped with another category if sufficiently similar. For example, many subjects wrote in “regularity” (or words to that effect) that we combined with the fixed choice “predictability,” and other responses suggested a new category of “general well-being.”

Statistical Analysis

Subject characteristics were summarized for each of the four weighted PA-minute categories, reporting mean and standard deviation for most continuous measures, median and interquartile range (IQR) for PA measures, and column percentage for categorical measures. Continuous measures included age at the time of survey, years since surgery, body mass index (BMI), average weekly minutes of PA within each exertion level, COH-QOL-CRC scales and selected items, SF12v2 Health Survey scales, and BFI scales. Categorical variables included sex, non-Hispanic white (Y/N), income over \$50,000 (Y/N), college graduate (Y/N), married/partnered (Y/N), ostomy status, Charlson-Deyo score ≥ 2 (Y/N), age ≥ 50 at diagnosis (Y/N), radiation treatment (Y/N), chemotherapy treatment (Y/N), and

tumor stage (Local, Regional, Distant). The four weighted PA-minute categories were ordinal. Subject characteristics were compared across weighted PA-minute categories with one-way ANOVA for continuous measures, the Kruskal-Wallis test for weekly minutes of PA within each exertion level, and chi-square (or Fisher's exact) test for categorical measures. A p-value of less than 0.05 was considered statistically significant. All analyses were performed with Stata 14.0 (College Station, TX: StataCorp LP).

Since there is evidence that health benefits are associated with weighted PA-minute categories, our primary analysis was performed with multiple linear regression on HRQOL and BF outcomes with indicator variables for weighted PA-minute categories (referenced to Not Active category) as independent variables of interest. Normality of residuals was evaluated by inspection of histograms and Q-Q plots against the normal distribution within weighted PA-minute categories, evaluation of potential outlier influence, and the Shapiro-Wilk test and skewness/kurtosis test. As no suitable normalizing transformation of outcomes was found, we confirmed that significant findings from linear regression were also significant using the Kruskal-Wallis test and pairwise comparisons between PA categories via Mann-Whitney U tests.

Potential effect modification by sex, ostomy status (based on previously reported observations [2]), and comorbidity (Charlson score ≥ 2 , based on plausibility that comorbidity burden could explain differences in both PA and HRQOL) was tested with interaction terms between weighted PA-minute indicator variables and these three candidate variables. First, we constructed separate models with 2-way interactions between PA and each candidate variable. Next, if evidence of interaction was found in any 2-way models, we constructed models with 3-way interactions between PA, the significant candidate variable, and one of the remaining candidate variables. We reverse coded candidate variables to evaluate all 2-way interactions in the 3-way models. An interaction term with $p < .05$ was considered significant effect modification, requiring that further analysis be stratified by that variable. Because tests of interactions are often underpowered, interaction terms with $p < .10$ and qualitative interaction indicated by different directions of effects between groups are presented as corroborative evidence of interaction.

Participant characteristics that were significant across weighted PA-minute category (as well as BMI, chemotherapy, radiation treatment, and cancer stage, based on clinical plausibility) were evaluated as potential confounders and were retained in models if statistically significant ($p < .05$) or if covariate presence changed an indicator coefficients of weighted PA-minute category by more than 10 percent. Covariates retained were age, sex, years since surgery, ostomy status, income over \$50,000, and Charlson-Deyo score ≥ 2 . We reported adjusted means (standard error) of HRQOL and BF outcomes by weighted PA-minute category, as well as significant mean differences with 95% confidence intervals from the Not-Active group. We evaluated trends across weighted PA-minute categories with a nonparametric test for trend across ordered groups [43, 44]. For COH-QOL-CRC and SF12v2 scales, tests by weighted PA-minute category, as well as confirmatory pairwise Mann-Whitney U tests, were Bonferroni-corrected for three comparisons, and p-values for trend tests across weighted PA-minute categories were Bonferroni-corrected for 15 scales. However, as the first reported use of a newly validated version of the BFI for RC survivors

living with an ostomy [29], the analysis of PA and BF was considered exploratory and alpha adjustment for multiple comparisons was not performed.

To evaluate clinical importance, we used the empirical rule effect size (ERES) method [45] to derive minimally important differences (MID), defined as 8% of the range of the scale. The MID was 0.88 for mCOH-QOL-CRC scales and individual items, 8.0 for SF-12v2 scales (0–100 scales rather than norm-standardized scores), 4.5 for Total Bowel Function, 1.3 for BFI Urgency/Soilage, 1.9 for BFI Frequency, and 1.3 for BFI Dietary. Although norm-standardized scores are not suitable for the ERES, a two-point or greater difference on the SF-12v2 PCS and MCS is considered the MID [46].

Results

The overall response rate was 60.4% (574 respondents/950 eligible). Twenty participants were excluded from the analysis due to missing PA responses on the survey. As expected, weekly PA at each exertion level (light, moderate, and vigorous) were strongly associated with weighted PA-minute categories (Table 1). Overall, 40% met or exceeded ACS/ACSM PA guidelines, with 190 (34%) Not Active, 145 (26%) Insufficiently Active (median weighted PA minutes 60 IQR 42.5–95), 72 (13%) Meeting Guidelines (median weighted PA minutes 210 IQR 180–240), and 150 (27%) Above Guidelines (median weighted PA minutes 510 IQR 400–920). As shown in Table 1, greater weighted PA-minutes were associated with being younger at survey completion, having fewer years since surgery, having a college degree, higher income, being married or partnered, and having a comorbidity burden score below 2. The proportion with an ostomy across weighted PA-minute categories was not significant ($p=.08$). Exercises or activities that reportedly helped participants with bowel function are shown in Table 2. Of the 140 participants who reported at least one PA that helped bowel function, walking was the most common (76%; 107/140), followed by bicycling (7%; 10/140), gardening/yard work (6%; 9/140), and swimming (6%; 8/140). In general, aerobic exercises were the most commonly reported helpful PAs and the most common symptoms helped were constipation (54%; 75/140), predictability/regularity (39%; 55/140), and gas (22%; 31/140).

Physical Activity and HRQOL

Adjusted quality of life scores by the four weighted PA-minute categories are presented in Table 3. Average outcomes generally rose across the first three weighted PA-minute categories and reached a plateau in the Above Guidelines category. Participants in any of the three active weighted PA-minute categories had significantly better average psychological well-being compared to the Not Active category and there was a significant trend across increasing PA category. The mean difference for psychological well-being in the Above Guidelines group was .55 (95% CI .23 – .88). Mean total QOL in the Above Guidelines category was significantly better than in the Not Active category (mean difference .43, 95% CI .10 – .76). Each active weighted PA-minute groups had significantly better SF12v2 scores that exceeded the MID compared to the Not Active group (mean difference for Above Guideline group shown), and there was a significant trend across increasing PA category, for the Physical Component Score (6.0, 95% CI 3.9 – 8.1), Physical Function (7.0, 95% CI 4.8 –

9.3), Role Physical (4.5, 95% CI 2.5 – 6.5), General Health (5.8, 95% CI 3.5 – 8.2), Vitality (5.7, 95% CI 3.6 – 7.8), and Social Function (3.7, 95% CI 1.4 – 5.9). The mean difference for Role Emotional in the Meet Guidelines group was 3.8 (95% CI .82 – 6.7). All significant contrasts shown in Table 3 were also significant with non-parametric tests. The Mental Component Score exceeded the MID in each active weighted PA-minute category compared to the Not Active category, but was not statistically significant. No significant interaction was observed between weighted PA-minute category and sex, ostomy status or comorbidity (Charlson score = 2).

Analysis of selected COH-QOL-CRC items (not shown in Tables) indicated a significantly greater sense of control (over things in life) in those Meeting Guidelines (mean difference .77, 95% CI .16 – 1.4) and Above Guidelines (mean difference .82, 95% CI .32 – 1.3). In addition, pain related to ostomy/anastomosis surgery was significantly better in those Meeting Guidelines (mean difference .84, 95% CI .16 – 1.5) and Above Guidelines (mean difference .72, 95% CI .18 – 1.3). Mean differences for control and pain did not exceed the MID of .88. No significant differences were found between weighted PA-minute categories for the following COH-QOL-CRC items: leakage from ostomy pouch, skin problems, sleep problems, and constipation. Although differences were not statistically significant, men with ostomies had consistently worse adjusted scores for leakage from pouch (−0.2, −0.9, −0.6, on 10 point scale), whereas women with ostomies had predominantly better adjusted scores (+1.0, +1.0, −0.3) for Insufficiently Active, Meeting Guidelines, and Above Guidelines (compared to Not Active), respectively.

Physical Activity and Bowel Function

Adjusted BFI scores for each of the weighted PA-minute category are shown in Table 4, separately by sex and by ostomy within men, based on the evaluation of interactions. In models with 2-way interactions, significant interactions were observed between sex and the Above Guidelines category for Total BF ($p=.005$), Urgency/Soilage ($p = .025$) and Dietary score ($p = .05$), but not Frequency ($p=.24$). No significant interaction was observed between ostomy or comorbidity and weighted PA-minute categories in 2-way interaction models. In models with 3-way interactions of weighted PA-minute category, sex, and ostomy status, we observed a significant sex by ostomy effect on Total BF (indicating that in the referent Not Active group, having an ostomy is associated with almost 4 point improvement in men compared to women, $p=.02$). In men, we observed ostomy-PA interactions denoting that BF worsened with increasing PA in men with ostomies, which was significant for total BF in the Above-Guideline group ($p=.03$) and had $p < .10$ for Urgency/Soilage in Above-Guideline ($p=.097$) and Meeting-Guideline ($p=.077$) groups. No significant ostomy-PA interaction was observed in models restricted to women. Qualitatively, men with ostomies had consistently worsening scores on all BF scales with increasing PA, whereas men with anastomosis had essentially no change or slightly improved scores on all BF scales with increasing PA. By contrast, women with either ostomy or anastomosis had consistently higher scores on all BF scales with PA (with two exceptions suggesting no change out of 12 dummy variables in the anastomosis group). We observed no significant interaction between PA, sex, and comorbidity in 3-way models. Therefore, findings are presented for men separately by ostomy status and for women combined ostomy and anastomosis.

Among men with an ostomy, the mean scores for Above Guidelines were significantly lower (worse) compared to Not Active and exceeded the MID for Total BF (mean difference -6.1 , 95% CI -2.0 to -10.2), Urgency/Soilage (mean difference -1.6 , 95% CI $-.20$ to -2.9), and Dietary (mean difference -1.9 , 95% CI $-.42$ to -3.4), and there was a significant trend of worse function across increasing PA category for all three BF outcomes. Among men with anastomosis, no significant contrast or trend was observed across weighted PA-minute categories. However, the consistency of positive mean differences from not active suggested no association of worse BF with higher PA in men with anastomosis. Among women, mean Total BF for the Above Guidelines category was significantly greater (better) compared to Not Active (mean difference 3.50 , 95% CI $.04$ – 7.0). Urgency/Soilage bowel function exceeded the MID in the Meeting Guidelines and Above Guidelines categories. There was a significant trend of better function across increasing PA category for both Total BF and Urgency/Soilage in women. We observed no significant association for Frequency or Dietary score and weighted PA-minutes in women. Significant contrasts shown in Table 4 were also significant with non-parametric tests.

Discussion

Bowel function has overwhelming implications for HRQOL for RC survivors [30]. Changes in BF are often not addressed by clinicians [47], and RC survivors are left to discover their optimal modalities to control their BF. These may include modifications in diet, medications and supplements, meal-related behaviors, and PA [48]. Our survey was designed to probe these trial-and-error adaptations that RC survivors make to control their BF [29]. A broader understanding of RC survivor patterns of PA and use of PA to improve their BF could lead to targeted interventions for these cancer survivors.

Our findings indicate that higher levels of PA may improve HRQOL, particularly a colorectal cancer-specific measure of psychological well-being, as well as a consistent and broad array of general measures of physical function, including pain. However, a randomized controlled trial would be necessary to definitively make recommendations for RC survivors. These results are important, as colorectal cancer survivors, including those living with ostomies, have been shown to be more likely to report significant limitations in physical health than age-matched persons in the general population [49]. A qualitative study showed the importance of PA for both men and women, especially those who had lower HRQOL scores; it seemed of greater importance for women with higher HRQOL, although the sample set was small [4]. Our findings also suggest that higher levels of PA may improve BF in RC survivors, particularly among women. Further, nearly 40% of RC survivors in this study were achieving or exceeding ACSM/ACS PA guidelines. Importantly, higher levels of PA are related to HRQOL and BF in this group, particularly among women. Lynch et al. showed women with a stoma having decreased levels of PA, but meeting PA guidelines was associated with being male [50]. Importantly, it is estimated only one-third of cancer survivors achieve PA guidelines [51–53]. Walking was identified as the preferred PA mode to improve BF. This activity is the most utilized PA by other cancer survivor populations as well [54, 55]. Other aerobic activities such as swimming and biking were also undertaken by RC survivors. In order to facilitate the optimal uptake of PA interventions among RC survivors, individual preferences should be recognized and supported.

An exploratory analysis was conducted in an effort to explain the differences observed between men and women living with ostomies in the association between PA and the Urgency/Soilage scale of BFI. Men with ostomies who engaged in higher PA levels appeared to report worse leakage at the ostomy seal, but women with ostomies did not. Men with ostomies at higher PA levels also had worsening scores on the dietary BFI scale, indicating that certain foods or drinks increased bowel movement frequency or that they limited certain foods or drinks to control bowel movement frequency. No such association was observed in women with ostomies. These patterns may relate to findings of previous studies reporting that patients with ostomies receive little to no education about diet and nutrition status to avoid obstruction [56]. This is an important issue to address with RC patients with ostomies, who may fear equipment-related issues, or those with anastomosis who may suffer from frequent bowel movements or anal leakage. It is interesting that RC survivors in this study who had higher levels of PA reported greater control in their life. Improved personal autonomy and self-control can lead to greater work, volunteer, and leisure activities, which could further enhance HRQOL [17, 21]. Therefore, clinicians should alert RC patients to potential challenges with PA and inform them that they likely will be able to participate in PA.

Strengths of this study include a well-characterized study sample of 574 RC survivors and the use of several validated measures [29, 35]. Several limitations of this report should be noted. First, PA is based on self-report data, which are subject to recall bias [57]. Utilization of objective data, as measured by body-worn sensors (e.g., accelerometers), would also help to better understand PA effects for those that are active, but below ACS/ACSM guidelines. In addition, body-worn sensors would integrate other activities of daily living, such as occupational time, which would lead to better assessment of total PA. Second, temporal relationships between PA, HRQOL, and BF could not be documented. We cannot rule out the possibility that RC survivors with better BF or HRQOL found it easier to engage in moderate/vigorous PA. Third, the effects of aging or other co-morbidities over time cannot be completely captured. Despite controlling for age, comorbidity burden, time since surgery, and other potential confounders in our analysis, the cross-sectional nature of our study limits our ability to make causal inference. Fourth, although the ACS/ACSM guidelines emphasize the importance of achieving a certain level of moderate/vigorous PA outside of leisure time and activities of daily living, it is possible that the health benefits of light PA are not negligible. By evaluating an outcome that is tailored to the ACS/ACSM guidelines, we may be missing the impact of light activity and are unable to evaluate a sedentary subgroup that engages in essentially no PA of any intensity. Finally, while this study population was diverse, it may not represent minorities and underserved populations, geographic variability, or other factors. Thus, a randomized, controlled trial large enough to evaluate sub-populations based on gender and stoma status is needed to definitively evaluate the benefits of PA for BF in a diverse sample of RC survivors.

The potential effect of PA on BF for RC survivors is novel and important. While our data suggests benefit for women, the discrepancy with men who have ostomies must be considered. While BF benefit for males, especially those with ostomies, cannot be confirmed, it is clear that many males are still exercising at or above guidelines. Many men must derive value from PA as they continue to actively exercise. As negative BF effects in

men with ostomies seem most extreme in those that exercise above guidelines, one can envision precautions taken to ensure these activities are accomplished and enjoyable. These may be as simple as, for example, exercising only near bathrooms, ensuring emergency kits are readily available, and shaving hair around stomas to limit wafers dislodging when sweating.

As RC survivors' lifespans are increasing, it is important to focus on modifiable lifestyle behaviors to ensure longer, more productive, healthier, and happier lives. The findings of this study indicate that higher levels of PA may be related to better HRQOL and BF in RC survivors, particularly among women. In addition, aerobic activities, such as walking, were reported as preferred activity modes to reduce symptoms related to BF. Prospective studies are needed to test PA strategies that will lead to improved RC survivor compliance and benefit.

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Table 1

Participant characteristics by physical activity category

	Not Active weighted PA min = 0/wk (n=190)	Insufficiently Active weighted PA min = 1-149/wk (n=145)	Meeting Guidelines weighted PA min = 150-299/wk (n=72)	Above Guidelines weighted PA min = 300/wk (n=150)	p-value
Age, mean (SD)	75.7 (10.3)	72.1 (11.3)	71.2 (9.9)	71.3 (11.1)	<.001
Sex, % male	52.1	64.1	58.3	65.3	.03
Non-Hispanic white, %	17.6	17.0	23.9	22.1	.21
Income > \$50,000/year, %	32.0	52.6	51.5	48.9	.004
College graduate, %	25.7	43.0	50.8	47.3	<.001
Married/partnered, %	55.0	70.1	63.9	72.3	.003
Permanent ostomy, %	39.5	25.5	30.6	29.3	.08
Body Mass Index, mean (SD)	27.5 (6.1)	28.1 (6.1)	27.1 (6.3)	26.6 (4.4)	.11
Charlson-Deyo comorbidity score 2, %	29.5	21.4	18.1	12.0	<.001
Age 50 at diagnosis, %	16.3	22.1	23.6	27.3	.02
Years since surgery, mean (SD)	14.2 (7.0)	12.7 (5.9)	12.3 (6.0)	12.7 (6.0)	.02
Radiation Treatment, %	40.5	40.7	38.9	36.7	.45
Chemotherapy, %	50.5	55.9	54.2	45.3	.33
Stage, %					
In situ/local	50.0	46.9	48.6	54.0	.67 ^a
Regional	46.3	48.3	44.4	43.3	
Distant	1.1	2.1	0	0.7	
Unknown	2.6	2.8	6.9	2.0	
PA per week in past month					
Light minutes, median (IQR)	30 (0-120)	100 (30-210)	120 (30-240)	120 (0-420)	<.001
Moderate minutes, median (IQR)	0	60 (30-90)	180 (100-210)	315 (150-450)	<.001
Vigorous minutes, median (IQR)	0	0 (0-0)	0 (0-37.5)	120 (0-225)	<.001

PA min = “physical activity minutes” calculated as moderate minutes/week + 2 × vigorous minutes/week

SD = standard deviation

IQR = interquartile range

Fisher's exact test

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Physical Activities Reported to Help Bowel Function and Symptoms Improved (n=140)^a**Table 2**

		Symptoms helped						
Exercise/activity	Participants Reporting	Constipation/ obstruction/ bloating	Predictability/ regularity	Gas	Diarrhea	Urgency	General wellbeing	
Total (any helpful exercise)	140	75	55	31	8	7	17	
Walking	107	64	44	18	1	4	9	
Bicycling	10	8	2	2	0	0	2	
Gardening/ Yard Work	9	5	3	2	0	0	1	
Swimming	8	5	2	1	0	0	3	
Yoga	6	8	1	3	1	2	0	
Weight Lifting	6	2	3	0	0	0	2	
Jogging	5	3	0	2	1	0	1	
Golf	5	4	2	1	0	0	0	
Other	14	3	6	3	4	1	0	
Aerobic	124	68	51	27	4	4	16	
Anaerobic	34	19	15	11	2	4	5	
Daily Activities	11	6	4	2	0	0	4	
Other	18	9	4	8	3	1	4	

^aParticipants could report more than one PA and more than one symptom per activity

Table 3

Health Related Quality of Life by PA Guideline Categories

	Not Active weighted PA min = 0 /wk (n=190)	Insufficiently Active weighted PA min =1– 149/wk (n=145)	Meeting Guidelines weighted PA min =150– 299/wk (n=72)	Above Guidelines weighted PA min 300/wk (n=150)
	Adjusted mean (SE) ^d			
COH-QOL-CRC				
Total QOL	7.3 (.11)	7.6 (.12)	7.7 (.17)	7.7 (.12) ^d
Physical Wellbeing	7.2 (.14)	7.6 (.16)	7.8 (.23)	7.7 (.16)
Psychological Wellbeing ^c	7.4 (.11)	7.8 (.12) ^d	7.9 (.17) ^d	7.9 (.12) ^e
Social Wellbeing	7.3 (.16)	7.7 (.19)	7.8 (.26)	7.6 (.18)
Spiritual Wellbeing	7.1 (.15)	7.3 (.18)	7.3 (.25)	7.4 (.17)
SF12v2				
Component summary scores ^b				
Physical Component Score ^c	40.9 (.71)	44.7 (.80) ^{e,f}	47.5 (1.1) ^{e,f}	47.1 (.79) ^{e,f}
Mental Component Score	50.4 (.70)	52.8 (.79) ^f	53.3 (1.1) ^f	52.4 (.78) ^f
Health domain scales ^b				
Physical Function ^c	40.6 (.75)	44.9 (.85) ^{e,f}	48.0 (1.2) ^{e,f}	47.7 (.84) ^{e,f}
Role Physical ^c	42.2 (.67)	45.6 (.76) ^{e,f}	46.8 (1.1) ^{e,f}	46.8 (.75) ^{e,f}
Body Pain	46.2 (.78)	48.3 (.89)	50.3 (1.2) ^{d,f}	48.6 (.87)
General Health ^c	43.3 (.79)	47.1 (.89) ^{e,f}	49.2 (1.2) ^{e,f}	49.2 (.88) ^{e,f}
Vitality ^c	47.0 (.71)	50.2 (.80) ^{e,f}	53.4 (1.1) ^{e,f}	52.8 (.79) ^{e,f}
Social Function ^c	46.0 (.75)	50.3 (.85) ^{e,f}	51.4 (1.2) ^{e,f}	49.8 (.84) ^{e,f}
Mental Health	51.6 (.62)	53.5 (.70)	53.7 (.98)	53.6 (.69)
Role Emotional	44.9 (.80)	47.8 (.91) ^d	48.8 (1.3) ^{d,f}	47.5 (.89)

COH-QOL-CRC = City of Hope Quality of Life-Colorectal Cancer

PA min = “physical activity minutes” calculated as moderate minutes/week + 2 × vigorous minutes/week

^a Predicted mean (SE) adjusted for age, sex, years since surgery, ostomy status, income over \$50,000, and Charlson-Deyo score 2^b Norm-based scores with mean = 50 and SD = 10^c p < 0.05 Trend across ordered weighted PA-minute categories, Bonferroni adjusted^d p < 0.05 compared to completely sedentary group, Bonferroni adjusted^e p < 0.01 compared to not active group, Bonferroni adjusted^f Exceeds minimally important difference (MID) compared to not active group (0.88 for mCOH-QOL-CRC scales, 2.0 for PCS and MCS, 8.0 on 0–100 scale for health domain scales)

Table 4

Bowel Function by PA Guideline Categories

	BFI Scale ^a	Not Active weighted PA min = 0/wk (n=190)	Insufficiently Active weighted PA min = 1-149/wk (n=145)	Meeting Guidelines weighted PA min = 150-299/wk (n=72)	Above Guidelines weighted PA min = 300/wk (n=150)
		Adjusted mean (SE) ^b			
Men Ostomy (n=117)	Sample size	N = 46	N = 24	N = 18	N = 29
	Total Bowel Function ^c	58.4 (1.3)	57.2 (1.7)	55.5 (2.0)	52.5 (1.6) ^{d,f}
	Urgency/Soilage ^c	17.6 (.43)	17.1 (.58)	16.6 (.67)	16.2 (.52) ^{e,f}
	Dietary ^c	15.8 (.46)	15.6 (.63)	15.1 (.72)	13.8 (.57) ^{d,f}
Men Anastomosis (n=215)	Sample size	N = 53	N = 69	N = 24	N = 69
	Total Bowel Function	51.0 (1.4)	52.6 (1.2)	53.5 (1.9)	51.0 (1.2)
	Urgency/Soilage	14.7 (.57)	15.4 (.48)	15.9 (.80)	14.9 (.50)
	Frequency	21.5 (.63)	22.6 (.53)	22.4 (.88)	21.8 (.55)
Women Combined ^g (n=225)	Dietary	14.8 (.51)	14.6 (.43)	15.2 (.72)	14.3 (.45)
	Sample size	N = 91	N = 52	N = 30	N = 52
	Total Bowel Function ^c	52.4 (1.0)	54.1 (1.4)	54.9 (1.8)	55.9 (1.4) ^d
	Urgency/Soilage ^c	15.7 (.39)	16.1 (.53)	17.0 (.69) ^f	17.0 (.52) ^f
	Frequency	22.6 (.55)	22.3 (.71)	23.1 (.85)	24.0 (.73)
	Dietary	14.2 (.38)	15.2 (.51)	14.0 (.67)	14.8 (.50)

Weighted PA min = "weighted physical activity minutes" calculated as moderate minutes/week + 2 × vigorous minutes/week

SE = Standard Error of regression coefficient

^a Higher BFI score denotes better function; Total BFI score range 14–70; Urgency/Soilage range 4–20; Frequency (defined only for anastomosis group) range 6–30; Dietary range 4–20^b Predicted mean (SE) adjusted for age, years since surgery, income over \$50,000 (Y/N), Charlson-Deyo score 2 (Y/N), and ostomy status (for analysis of women only)^c p < 0.05 Trend across ordered weighted PA-minute categories^d p < 0.01 compared to not active group^e p < 0.05 compared to not active group^f Exceeds minimally important difference (MID) compared to not active group (4.5 for Total Bowel Function, 1.3 for BFI Urgency/Soilage, 1.9 for BFI Frequency, and 1.3 for BFI Dietary)

$\bar{g}$ Combined women with ostomy and anastomosis because contrasts with not active had consistent direction

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