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Bachelor's thesis in Human Movement Science
Supervisor: Xiao-Mei Mai
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Abstract

Background: The aim of this research is to investigate the effects of physical activity on quality of life and physical functioning in colorectal cancer survivors in order to provide general physical activity recommendations in rehabilitation for this population.

Methods: A systematic review was carried out using the databases Oria and Pubmed. English language articles which examined the association of PA with quality of life and/or physical functioning in colorectal cancer survivors were included.

Results: From the conducted search, nine eligible articles were identified. In general, moderate to vigorous levels of physical activity was associated with improved quality of life and physical functioning. Less evidence was found for the association with light PA levels. Physically active colorectal cancer survivors generally reported significant positive effects from physical activity, although less evidence was found on the difference in change in quality of life and physical functioning compared to non-active survivors.

Conclusions: Physical activity seems to be associated with improved quality of life and physical functioning. The association seems to be stronger the higher the physical activity level. Therefore, it might be beneficial for colorectal cancer survivors to stay physically active during rehabilitation. More research is needed to confirm the association and establish causality.

Abstrakt

Bakgrunn: Formålet med denne studien er å undersøke effektene av fysisk aktivitet på livskvalitet (eng: quality of life) og fysisk funksjon (eng: physical functioning) hos kolorektal kreft-overlevende (eng: CRC survivors) for å kunne gi generelle råd om fysisk aktivitet i rehabilitering for denne målgruppen.

Metoder: Et systematisk litteratursøk ble gjennomført i databasene Oria og Pubmed. Engelskspråklige artikler som undersøkte sammenhengen av fysisk aktivitet med livskvalitet og/eller fysisk funksjon hos kolorektal kreft-overlevende ble inkludert.

Resultat: Søket identifiserte ni studier som innfridde inklusjonskriteriene satt på forhånd. Moderat til stort fysisk aktivitetsnivå var stort sett assosiert med bedre livskvalitet og fysisk funksjon. Det ble dog funnet mindre bevis for en sammenheng dersom aktivitetsnivået var lavt. Kolorektal Kreft-overlevende som var fysisk aktive rapporterte stort sett positive effekter av fysisk aktivitet, selv om det på den andre siden ble funnet lite bevis for forskjellen

i endring i livskvalitet og fysisk funksjon sammenlignet med inaktive kolorektal kreft-overlevende.

Konklusjon: Fysisk aktivitet ser ut til å ha en sammenheng med bedret livskvalitet og fysisk funksjon. Sammenhengen ser ut til å være sterkere desto høyere aktivitetsnivå. Basert på dette, kan det være fordelaktig for kolorektal kreft-overlevende å være i fysisk aktivitet under rehabilitering. Mer forskning kreves for å bekrefte sammenhengen og stadfeste kausalitet for sammenhengen.

Background

Colorectal cancer is one of the most common cancers worldwide and its prevalence is increasing in many parts of the world (1). Survivors of colorectal cancer often experience long-term physical impairments as a result of the disease and its treatment (2). Physical activity has been identified as a promising intervention to improve physical functioning (PF) and quality of life (QoL). Past literature has studied the effects of PA and other measures such as QoL, dietary behaviors and benefits, and fatigue (3,4). As to what type of exercise would benefit the survivors short and long term is a topic which continues to be studied today. Exercises such as aerobic exercise and resistance exercise have shown to have high levels of efficacy for reducing fatigue and improving energy levels (5). Therefore, the aim of this review is to provide evidence-based recommendations on physical activity interventions to improve physical functioning and quality of life in colorectal cancer survivors undergoing rehabilitation. This review will incorporate the current literature on physical activity interventions and provide recommendations for future research and clinical practice. The findings of this review will aim to inform healthcare providers and policymakers on effective recommendations to promote physical activity in colorectal cancer survivors during rehabilitation to enhance their health and well-being. To further understand this, the definitions need to be established and defined. The QoL is defined by The World Health Organization (WHO) as “an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (6). PF refers to the ability to perform basic and instrumental activities of daily living (7,8).

Method

The studies were sourced using the online databases Oria and PubMed.

The following words were used as search terms:

“Rehabilitation” and “Colon Cancer” or “Colorectal Cancer” and “Quality of life” or “Pain” or “Fatigue” and “Exercise” or “Training” or “Physical Activity” or “Training”. From there relevant articles were extracted.

The included studies satisfied the following criteria: they included 1) quality of life questionnaire(s), 2) PA assessments and 3) outcomes of physical functioning. Studies where participants had not undergone CRC treatments or were currently undergoing chemotherapy, were excluded. Systematic reviews and studies based on meta-analyses were deemed not eligible. Only articles written in English were included.

The search conducted as described above, yielded 9 results. The sample included four randomized controlled trials (RCT), two cross sectional studies, one prospective study, one prospective cohort study and one longitudinal-experimental study. The publication dates ranged from 2008 to 2020. Characteristics for the selected studies are shown in Table 1 below.

Table 1 Included studies

| First author, year | Study design | Sample size | Cancer location, stage | QoL instruments | PF instruments |
|---------------------------------|--------------|-------------|------------------------|-----------------|---|
| Cantarero-Vil lanueva, 2016 (9) | RCT | 46 | Colon, I-III | | Trunk curl test, Back dynamometer, 6-minute walk test, Sit-and-reach test |
| Kim, 2019 (10) | RCT | 71 | Colon/rectum, II-III | FACT-C, FACIT-F | |

| | | | | | |
|---------------------------|-----------------------|-----|-------------------------------|--------------------------|--|
| Pinto, 2013 (11) | RCT | 46 | Colon/rectum, I-III | FACT-C, FACT-F | VO ₂ peak, Treadwalk test, SF-36 (PF subscale) |
| van Zutphen, 2017 (12) | Prospective cohort | 327 | Colon/rectum, I-III | | EORTC QLQ-C30 |
| Brown, 2018 (13) | RCT | 39 | Colon, I-III | FACT-C, SF-36, FSI | |
| Sellar, 2014 (14) | Prospective | 29 | Colon/rectum, I-III | | Graded exercise test (GXT) |
| Hung, 2016 (15) | RCT | 52 | Colon/rectum, I-IV | FIQL | |
| Peddle, 2008 (5) | Cross sectional | 413 | Colon/rectum, I-IV | FACT-C | |
| Park, 2020 (16) | Cross sectional | 224 | Colon/rectum/ breast, 0-IV | EORTC QLQ C-30 | |

Results

Quality Of Life

Hung et al. (15) investigated the efficacy of a pelvic floor exercise (PFE) program on improving fecal incontinence quality of life in CRC survivors after colostomy closure surgery. The participants were given an informational DVD and a pamphlet on exercises, as well as individual instruction on the execution of the exercises from a research team member. The exercises were recommended to be performed four times a day, with 20 repetitions per session. They used a Fecal Incontinence Quality of Life (FIQL) scale (17) to assess the effects of the PFE, compared to a control group with 6 different time intervals over a 9 month period. The results from the study shows that there is a significantly higher score in the PFE

group compared to the non-PFE group in the FIQL scale at some timepoints (5). The PFE group scored higher than the non-PFE group at all times, except for T9. Only T3 ($z = -2.56$, $p = 0.010$) and T6 ($z = 2.73$, $p = 0.006$) showed a significantly higher score for the PFE group.

A study (5) was conducted to examine a population of colorectal cancer survivors to see the differences of those that did and did not meet the recommended public health guidelines, which are based from the American College of Sports Medicine (18) and the American Cancer Society (19). A recommendation of 60 minutes of high intensity exercise or a moderate-high intensity exercise of 150 minutes per week for an adult. Exercise patterns were reported using a modified version of the Leisure Score Index from the Godin Leisure Time Exercise Questionnaire. QoL was assessed using the Functional assessment of Cancer Therapy-Colorectal/General(FACT-C/G). 413(100%) CRC survivors participated and only 107(25.9%) met the guideline in comparison to the 306(74.1%) participants who did not meet the guideline. FACT - C values show a significant difference between the CRC survivors that did and did not meet the public health guidelines. The one that met the guideline had a FACT - C score of 114.7 ± 12.8 ($p=0.002$) compared to ones that did not meet the guideline with a score of 108.7 ± 18.2 ($p=0.002$), and with a group difference of 6(2.3-9.8, $p=0.002$). FACT - G score shows a similar pattern to FACT - C between the groups. The group that met the guidelines show a FACT- G score of 91.8 ± 10.8 compared to those not meeting the guidelines with a score of 86.6 ± 15 , and with a group difference of 5.2(2.1-8.3, $p=0.002$). CRC survivors who met the guidelines also reported a higher score of 45 ± 7.7 ($p < 0.001$) compared to the score of 39.8 ± 11.3 ($p < 0.001$).

A cross-sectional study from 2020 (16) investigated the association between PA and QoL in stage 0-IV breast cancer and CRC survivors in Korea. 224 breast ($n=151$) and CRC ($n=73$) cancer survivors were included in the study. The study utilized the Godin Leisure-Time Exercise Questionnaire to measure PA level, and the European Organization for Research and Treatment of Cancer QLQ C-30 (EORTC QLQ C-30) questionnaire to measure QoL. The study found a significant correlation between moderate to vigorous PA and the QoL subscales “emotional functioning” ($r = 0.155$, $p < 0.05$), “fatigue” ($r = -0.176$, $p < 0.05$), “pain” ($r = -0.154$, $p < 0.05$) and “dyspnea” ($r = -0.221$, $p < 0.01$) after controlling for potential confounders. The only subscale of the QLQ C-30 where a significant correlation was found between light PA and QoL after controlling for confounders, was the “role functioning”

subscale ($r = 0.159, p < 0.05$). When looking at the QLQ C-30 as a whole, the study found a significant correlation between moderate to vigorous PA and QoL after controlling for confounders ($r = 0.311, p < 0.01$), while no correlation was found for light PA.

A randomized controlled trial from 2018 (10) investigated the effects of a 12-week exercise program on QoL in stage II-III CRC survivors. The study included 71 CRC survivors, which were randomized into either an exercise group (N=37) or a control group (N=34). The exercise group performed a home-based exercise program for 12 weeks. The exercise program included aerobic and resistance exercise. Aerobic exercise was performed in the form of walking, stationary bike or swimming. Two DVDs were provided containing instructions on resistance training, one with moderate intensity exercise, and the other with vigorous intensity exercise. The resistance exercise workout lasted for 30 minutes, and was performed at home daily. Participants were also provided a pedometer and an exercise log to track PA. QoL was assessed using the Functional Assessment of Cancer Therapy - Colorectal (FACT-C), and fatigue using the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-FS). The study found that the intervention group scored significantly better on the FACT-C after the 12 weeks compared to baseline (104.3 ± 17.5 vs. $100.5 \pm 18.1, p = 0.024$). No significant change was found in the control group (99.1 ± 19.1 vs. $97.5 \pm 19.9, p = 0.407$). However, the difference in change between the groups was not significant ($p = 0.283$). Furthermore, the intervention group reported significantly less fatigue on the FACIT-FS at 12 weeks as compared to baseline (42.6 ± 8.5 vs. $39.7 \pm 9.6, p = 0.011$), while the change in the control group was not significant (42.3 ± 7.5 vs. $41.0 \pm 8.1, p = 0.191$). The difference in change between the groups was not significant ($p = 0.212$).

Pinto et al. (11) also investigated the efficacy of a 12-week home-based PA intervention on QoL and PF in CRC survivors. The RCT included 46 stage I-III CRC survivors, which were randomized into a moderate intensity PA group and a control group. The intervention group received instructions on how to exercise at a moderate intensity, as well as a pedometer and an exercise log to monitor PA. They were further encouraged to exercise for 10 minutes on at least two days per week for the first few weeks. The exercise goal was gradually increased to 30 minutes per day at least 5 days per week for the duration of the 12-week intervention. The exercise program included aerobic exercise at 64-76% of estimated maximum heart rate. PA level was assessed through pedometer, accelerometer, exercise log, and seven-day PAR. Functional Assessment of Cancer Therapy - Fatigue (FACT-F) and FACT-C were used to assess fatigue and QoL respectively. The study found significant improvements on FACT-F

scores from baseline (39.1) in the intervention group at 3 months (42.2, 95% CI = 39.4 to 45.0, $p \leq 0.05$), 6 months (43.3, 95% CI = 40.9 to 45.8, $p \leq 0.05$) and 12 months (42.3, 95% CI = 39.9 to 44.7, $p \leq 0.05$). The control group demonstrated improvements on the FACT-F from baseline (39.1) at 3 months (41.9, 95% CI = 39.5 to 44.2, $p \leq 0.05$) and 12 months (41.8, 95% CI = 39.9 to 44.7, $p \leq 0.05$, while the scores at 6 months (40.1, 95% CI = 37.7 to 42.5, $p > 0.05$) did not significantly differ from baseline. However, the difference in change between the groups was not significant at any point. Similar findings were demonstrated in the FACT-F scores, where the intervention group showed significant improvements from baseline (105.3) at 3 months (111.3, 95% CI = 105.9 to 116.6, $p \leq 0.05$), 6 months (111.7, 95% CI = 106.5 to 116.9, $p \leq 0.05$) and 12 months (110.6, 95% CI = 105.6 to 115.8, $p \leq 0.05$). The control group also showed an improvement from baseline (105.3) at 3 months (110.8, 95% CI = 106.1 to 115.4, $p \leq 0.05$) and 12 months (110.6, 95% CI = 105.9 to 115.2, $p \leq 0.05$), but no significant change at 6 months (108.7, 95% CI = 104.0 to 113.5, $p > 0.05$). The difference in change between the groups was not significant at any point.

Brown et al. (13) examined the dose-response effect of an aerobic exercise program on health related QoL in colon cancer survivors. The study included 36 stage I-III colon cancer survivors. The participants were further divided into a control group ($n=13$), low-dose group ($n=14$) or high-dose group ($n=12$). The low-dose exercise group was instructed to exercise for 150 minutes per week and the high-dose group for 300 minutes per week for 6 months. The exercise was performed at home on a treadmill at an intensity of 50-70% of the age-predicted maximum heart rate. Participants were assessed at baseline and 6 months. Health related QoL was assessed using the Short Form Health Survey (SF36) and the Functional Assessment of Cancer Therapy-Colorectal (FACT-C), and fatigue using the Fatigue Symptom Inventory (FSI). Compared with the controls, the physical health component score of the SF-36 had improved by 1.2 ± 6.3 ($p = 0.506$) for the low-dose group, and 13.1 ± 6.5 ($p = 0.002$) for the high-dose group at 6 months ($p_{\text{trend}} = 0.002$). FACT-C scores improved by 7.6 ± 3.8 ($p = 0.048$) for the low-dose group and 6.8 ± 4.0 ($p = 0.090$) for the high-dose group compared with the controls at 6 months ($p_{\text{trend}} = 0.025$). Fatigue, as reported in the FSI, increased by 0.8 ± 3.5 ($p = 0.817$) for the low-dose group, and decreased by 6.0 ± 3.6 ($p = 0.096$) for the high-dose group ($p_{\text{trend}} = 0.045$).

Physical functioning

Park et al. (16), which methods are described earlier in the paper, also assessed the association between PA and PF. The study found a significant correlation between moderate

to vigorous PA and the PF subscale of the EORTC QLQ C-30 questionnaire ($r = .231$, $p < 0.01$) after controlling for confounders. Furthermore, the study found a linear dose-response relationship between higher PA levels and better PF. The study found no significant correlation between light PA and PF.

A randomized controlled trial from 2017 (9) aimed to investigate the effects of a lumbopelvic exercise program on health-related fitness, anthropometric measurements, and body composition in colon cancer survivors. The study included 46 colon cancer survivors (14 female, 32 male), which were further divided into a lumbopelvic exercise program group (CO-CUIDATE) and a usual care group. The lumbopelvic exercise program group participated in 90-minute exercise sessions three times per week for eight weeks. The exercise sessions included warm-up, core stabilization exercises, and stretching exercises aimed at improving isometric abdominal strength, isometric back strength, functional capacity, lower-body flexibility, weight, and anthropometric measurements. These variables were evaluated at baseline, after intervention and after 6 months. Isometric abdominal strength was assessed using the trunk curl test, isometric back strength using a back dynamometer, functional capacity using a 6-minute walk test and lower-body flexibility using a sit-and-reach test. Additionally, waist and hip circumference, and height was measured. Body composition was assessed using bioelectrical impedance. The study found significant differences in group-by-time interactions for waist circumference ($F=5.7$, $p=0.07$), functional capacity ($F=4.6$, $p=0.015$), isometric abdominal strength ($F=7.7$, $p=0.001$) and lower-body flexibility (right, $F=4.3$, $p=0.021$ and left, $F=3.6$, $p=0.034$). No significant differences were found for isometric back strength, weight, hip circumference or body composition. The study concluded that exercise programs aimed at strengthening lumbopelvic- and abdominal muscles is a promising way to increase health-related fitness in CRC survivors.

Other studies investigated other training protocols. One investigated the feasibility and efficacy of a 12 week aerobic and resistance exercise program for CRC survivors (14). The program consisted of 2 combined aerobic and resistance training sessions and 1 only aerobic session each week. All workouts had a standard 5 min warm-up and cooldown period. The Exercise was based on baseline assessment done prior and was adapted to the individual. Aerobic exercises were different between the 12 weeks. For the first 4 weeks 3 of the sessions had a continuous endurance exercise, which was performed on a cycle ergometer, 15-45 minutes on 60%-75% peak power output. Afterwards at week 5 and 6 the frequency was lowered to 2 times per week and lastly at the 7-12 week mark the exercise was reduced

to 1 time per week because of the inclusion of interval sessions. Resistance training sessions consisted of 9 exercises which were: vertical bench press, seated row(or lat pulldowns), biceps curls, triceps pulldowns, shoulder press, supine leg press, knee extension, leg curls, and partial curl ups. All resistance exercises were completed on resistance machines. Out of 29 participants in the study, all showed increased measured values. Cardiorespiratory fitness showed a lowered resting heart rate (-8 beat*min, $p < 0.001$), systolic (-5mm Hg, $p = 0.002$) and diastolic(-3mm Hg, $p = 0.040$) blood pressure was significantly lower than at the baseline start point. Body composition reported significant reduction in waist circumference(-2.1cm, $p = 0.005$) and biceps skinfold(-3.8mm, $p = 0.005$) and sum of skinfolds(-7.9mm, $p = 0.006$). The study reported no significant changes in dietary intake between the baseline and post intervention. Muscular strength and flexibility was also assessed. 1RM for bench press (+7kg, $p < 0.001$) and leg press (+26.5kg, $p < 0.001$) showed increased values.

Pinto et al. (11), which is described earlier in the paper, also investigated the efficacy of the 12-week exercise program on improving physical functioning in CRC patients. Physical functioning was assessed using the Treadwalk test, which measures the time taken to walk a mile. VO₂peak estimations were extrapolated from the Treadwalk test. In the treadwalk test the results show that the PA group showed improvements compared to the control group. The PA group had 20.4 min at 3, 19.6 min at 6, and 19.9 min at 12 months in contrast the control group performed 21.9 min at 3, 21.4 min at 6, and 21.5 min at 12 months. Between group differences were -1.5 min ($p = 0.06$) at 3, -1.8 min ($p = 0.0029$) at 6, and -1.6 min ($p = 0.003$), with the PA group outperforming the control group at all time points. VO₂peak (ml*kg⁻¹*min) had higher mean values in the PA group of 27.65 ($p = 0.435$) at 3, 28.43 ($p = 0.163$) at 6 and 27.06 ($p = 0.368$) at 12 months compared to the control group which had 23.71 ($p = 0.06$) at 3, 24.36 ($p = 0.029$) at 6, and 22.12 ($p = 0.043$) at 12 months.

A randomized controlled trial described earlier in the paper (10), also investigated the effects of the 12-week exercise program on PA in CRC survivors. This study used the Trial Outcome Index-physical/functional/colorectal (TOI-PFC) to assess physical function and well-being. The study found that PF scores had improved significantly for the intervention group post intervention as compared to baseline (66.3 ± 11.8 vs. 64.1 ± 11.2 , $p = 0.035$). The control group did not demonstrate a significant change post intervention compared to baseline (64.3 ± 12.4 vs. 63.3 ± 12.1 , $p = 0.488$). However, the difference in change between the groups was not significant ($p = 0.254$).

Van Zutphen et al. (12) investigated the relationship between PA and recovery of PF after hospital discharge in stage I-III CRC survivors (N=327). Participants' PA was assessed using the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH), and PF was assessed using the European Organization for Research and Treatment of Cancer quality-of-life questionnaire (EORTC QLQ-C30) before initiating treatment, and 6 months later. The study calculated participants' risk ratio at 6 months of not recovering to the PF they reported at baseline. The participants who increased their PA level from diagnosis to the 6 months follow up (25%; n=81), were 43% more likely to recover (relative prevalence ratio = 0.57, 95% CI = 0.39 to 0.82) to the level of PF they had before starting treatment than the participants who did not increase their PA level. Participants who reported high level of PA before starting treatment, and maintained this PA level at 6 months, were more likely to recover (relative prevalence ratio = 0.91, 95% CI = 0.65 to 1.26) to the level of PF they had before starting treatment than the participants who reported low PA level at baseline and 6 months.

Discussion

Key findings

From the nine studies included in this research, the results show that PA as an intervention for CRC survivors shows improvements in both PF and QoL. The results show there are positive improvements in PF and QoL for CRC survivors with both aerobic training, resistance training and strength training and shows increased rates of CRC survivors that meet general PA recommendations in comparison to the control groups. The results show improvements in recovery time post treatment, shortened time to regain PF and better scores in QoL questionnaires and surveys.

From a conducted search for previous literature, 3 systematic reviews have been published that look at the association between PA and QoL. From these four systematic reviews we chose to compare three of the studies with the results from this review. The remaining systematic review was excluded based on the structure of the article, which made it unclear to determine the methods and results from the review.

The results in this study show a significant positive effect on QoL from PA interventions. When comparing these results with the existing literature, two systematic reviews were found that looked at the effects of PA on QoL in CRC survivors. One of the studies from 2018 (20) shows similar results to this study, with the results being that PA interventions show a

positive effect on QoL in CRC survivors, but only looked at the results in the long term (≥ 5 years post-diagnosis). The other systematic review on the topic (21) looked at the effects of exercise interventions on CRC patients. This study found no correlation between PA interventions and QoL and fatigue scores, but found significant improvement in short term physical fitness. One of the limitations in the mentioned study is the small number of articles included to conclude the results of the study. The study includes three RCTs, where only one includes follow up after 12 months. The results from this study does disagree with our findings on the effects of PA on QoL and fatigue, but coincides with the results on the positive effects of PA on PF in the short term. In total the previous literature does mostly coincide with the results in this study, except for the results on the effects of PA on QoL and Fatigue from one of the previous studies (20).

Limitations

The studies included in this systematic review generally had large sample sizes, used validated PA, QoL and PF questionnaires and considered potential confounding factors. There are, however, some shortcomings which might limit some of the studies' ability to accurately answer the question at hand. Two of nine studies included in this review examined the relationship of PA with QoL using a cross-sectional study design. Thus, no causality can be assumed, only an association at one point in time. Additionally, one of the cross-sectional studies (16) included breast cancer survivors in addition to CRC survivors, and did not stratify results by cancer type. Thus, the CRC-specific validity of the study might be compromised.

The varying results between the studies in this article can possibly be explained by their differences in study population characteristics and instruments used to assess PA, QoL and PF. Variables such as time since diagnosis, treatment type, cancer stage and age differed between study samples, and might explain part of the differences in findings between the studies. A further limitation of some of the studies is the use, and differences therein, of subjective instruments. The majority of the studies in this review utilized questionnaires to assess QoL and/or PF. Questionnaires differed between the studies, which limits the comparability between the studies. Moreover, questionnaires were also used by several studies to assess PA, and nor was the choice of questionnaires consistent across the studies. Questionnaires are subjective measurements, and are thus affected by participants' interpretation, state of mind, personal experiences and ability to recall past events, further clouding the results.

A further limitation of this review is that none of the four studies that looked at the association between PA and PF used the same instrument to measure PF. Van Zutphen et al. (12) utilized the EORTC QLQ-C30 questionnaire, while Cantarero-Villanueva et al. (9) and Sellar et al. (14) utilized two different objective PF instruments. Pinto et al. (11) assessed PF using a combination of questionnaires and objective PF instruments. This difference in PF assessment methods limits the comparability between the studies, and might explain part of the differences between their findings.

Several of the included studies (9,10,13,14,16) excluded CRC survivors if they had certain comorbidities, for example diabetes or certain cardiovascular-, muscular- or neurological illnesses. The validity of the findings from these studies might therefore be compromised for CRC survivors suffering from said comorbidities.

To work around the aforementioned limiting factors, future research should aim to include objective assessments where this is possible, for example by quantifying PA using an accelerometer or assessing PF using objective physical tests. In order to provide more evidence on the causality of the possible relationship of PA with QoL and PF, future research should use a prospective study design, ideally in the form of RCTs. Furthermore, studies looking at implications of comorbidities on the effects of PA on QoL and PF might be warranted in order to provide more individualized recommendations. Additionally, the diversity of sample characteristics should be given more attention. In order to more easily compare different studies and get a deeper understanding of the effects of PA, future research should aim to stratify results by sample characteristics such as cancer stage, cancer location (colon vs rectum) and type of treatment. There should also be a focus to look at the results of PA on QoL and PF during both the short term and long term, as there was no literature found on the topic that had a followup longer than 12 months. This might make the results in this study only applicable for the short term effects of PA.

A final limitation of this review is that the research question and included studies might not be specific enough. Investigating the relationship of PA with both QoL and PF might make the scope of this review too broad, limiting our ability to go in depth and provide specific evidence. Because of this, investigating only one endpoint at a time, for example a sub-category of QoL, might be favorable for future research.

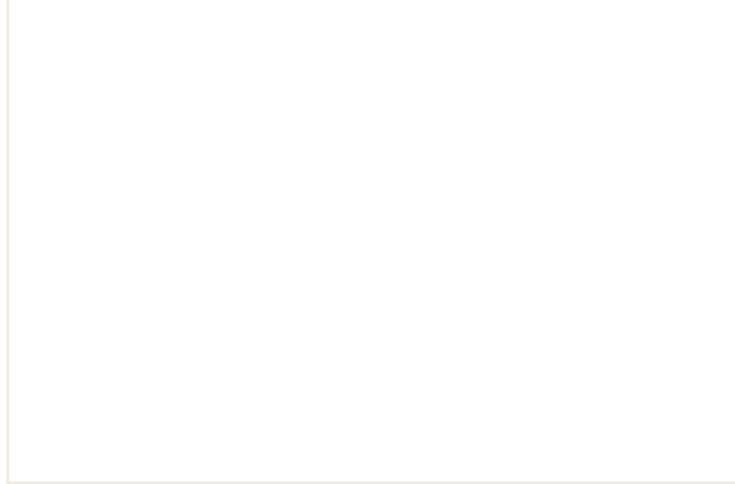
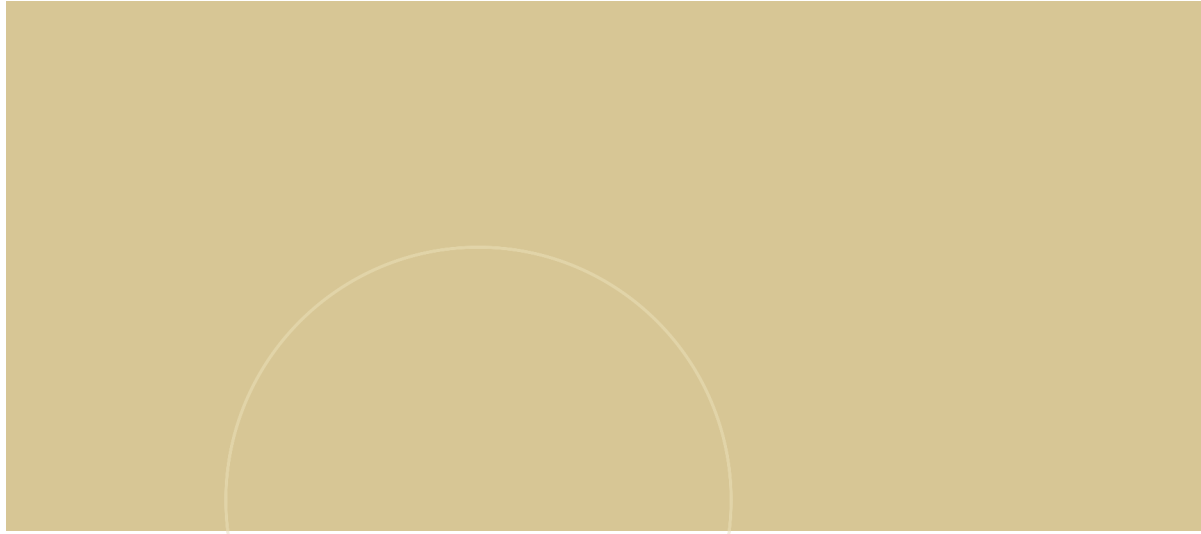
Conclusions

Although the existing evidence is not unanimous, the general findings of this review suggest a possible association of PA with QoL and PF, with some of the studies suggesting causality. Additionally, some evidence suggests a dose-response relationship, where more PA results in a larger increase in QoL and PF. Based on this, it might be beneficial for CRC survivors to be as physically active as they are able to during rehabilitation. The results in this review suggests CRC patients in rehabilitation to, if possible meet the general physical activity advice (WHO), and that a training program involving strength training, aerobic training and specific exercises such as pelvic floor training be implemented in the rehabilitation process to improve PF and QoL. More research is needed to confirm the relationship of PA with QoL and PF and establish causality for the potential association. In addition, future research should aim to investigate the optimal type and intensity of PA to further improve recommendations.

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