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Comparison of the effects of a supervised exercise program and usual care in patients with colorectal cancer undergoing chemotherapy.


**BACKGROUND:** Although exercise has been addressed as a promising therapy for cancer adverse effects, few studies have evaluated the beneficial effects of exercise for colorectal cancer (CRC) patients during chemotherapy. **OBJECTIVE:** The purpose of this study was to compare the effects of supervised-exercise intervention with those of usual care on cardiorespiratory fitness, muscle strength, fatigue, emotional distress, sleep quality, and quality of life (QoL) in patients with CRC undergoing chemotherapy. **METHODS:** Patients with stage II or III CRC admitted for adjuvant chemotherapy were allocated to either a supervised-exercise group that received a combined aerobic and resistance exercise program or a “usual care” control group for 12 weeks. The outcomes, QoL, muscle strength, cardiorespiratory fitness, emotional distress, physical activity, fatigue, and sleep quality, were assessed at baseline and after intervention. **RESULTS:** Significant interactions between intervention and time were observed for the role functioning and pain subscales of QoL and physical activity level. The time main effects were significant for the secondary outcomes: hand-grip strength, cardiorespiratory fitness, physical activity level, and physical functioning, role functioning, social functioning, fatigue, and pain subscales of QoL. **CONCLUSION:** Compared with usual care, the supervised exercise demonstrated larger effects than usual care on physical activity level and role functioning and pain subscales of QoL. **IMPLICATIONS FOR PRACTICE:** Supervised-exercise program is suggested to be incorporated as part of supportive care to promote the cardiorespiratory fitness, muscle strength, physical activity level, and QoL of patients with CRC undergoing chemotherapy.

**INSPIREHEALTH’S INTERPRETATION:** The benefits of appropriate exercise throughout cancer treatment are well-noted in the scientific literature. This study compared an exercise intervention to usual care for patients diagnosed with colorectal cancer who were undergoing chemotherapy. Participants were 45 males and females aged 18 years and older with a confirmed diagnosis of colorectal cancer. These individuals had undergone elective, abdominal colorectal surgery, and were currently receiving either in- or out-patient adjuvant chemotherapy. Participants chose whether they wanted to be part of the supervised exercise intervention group, or the usual care group. The exercise group included supervised moderate intensity aerobic and resistance training two times per week across 12 weeks. Sessions lasted between 40 and 60 minutes. Across the trial, the intensity of exercise was increased as permitted from 40% to 55% of maximum heart rate. Participants in the usual care...
Higher intakes of total calcium (dietary and supplemental equal or greater than 500mg daily) and milk (equal or with calcium, vitamin D or dairy product intake and mortality prior to a colorectal cancer diagnosis. Following diagnosis, it was found that higher intakes of total calcium (dietary and supplemental equal or greater than 500mg daily) and milk may be associated with lower colorectal cancer incidence, but their impacts on colorectal cancer survival are unclear. We evaluated associations of calcium, vitamin D, and dairy product intakes before and after colorectal cancer diagnosis with all-cause and colorectal cancer-specific mortality among colorectal cancer patients.

**Patients and Methods:** This analysis included 2,284 participants in a prospective cohort who were diagnosed with invasive, non-metastatic colorectal cancer after baseline (1992 or 1993) and up to 2009. Mortality follow-up was through 2010. Pre-diagnosis risk factor information was collected on the baseline questionnaire. Post-diagnosis information was collected via questionnaires in 1999 and 2003 and was available for 1,111 patients.

**Results:** A total of 949 participants with colorectal cancer died during follow-up, including 408 from colorectal cancer. In multivariable-adjusted Cox proportional hazards regression models, post-diagnosis total calcium intake was inversely associated with all-cause mortality (relative risk [RR] for those in the highest relative to the lowest quartiles, 0.72; 95% CI, 0.53-0.98; P trend = .02) and associated with marginally statistically significant reduced colorectal cancer-specific mortality (RR, 0.59; 95% CI, 0.33 to 1.05; Ptrend = .01). An inverse association with all-cause mortality was also observed for post-diagnosis milk intake (RR, 0.72; 95% CI, 0.55 to 0.94; Ptrend = .02), but not vitamin D intake. Pre-diagnosis calcium, vitamin D, and dairy product intakes were not associated with any mortality outcomes.

**Conclusion:** Higher post-diagnosis intakes of total calcium and milk may be associated with lower risk of death among patients with non-metastatic colorectal cancer.

**InspireHealth’s Interpretation:** Nutritional guidelines may vary based on different chronic health issues. In the case of cancer, specific types of cancer may influence body weight, lean body mass, as well as immune and digestive health, and as a result, there may be varying dietary guidelines, recommendations, and research findings. Although the literature pertaining to dairy intake and cancer is controversial, some studies have shown a positive relationship between calcium, vitamin D and some dairy products with a reduced risk of developing cancers. This study adds some preliminary information into supervised exercise programs throughout chemotherapy among colorectal patients; however, the design of this study makes it difficult to attribute its results directly to the intervention due to bias created from non-randomization, as opposed to randomized group assignment. Participants could choose the exercise group because they wished to increase activity, or perhaps because they were already quite active, and would have enjoyed the benefits of being in an exercise program. On the contrary, participants could choose to be in the usual care group because they had no desire to exercise, or because they were already active, and therefore did not feel that they required the additional support of a supervised exercise program. Physical activity was also not restricted among the usual care group, which would have provided for a true control group within the study. Since overall physical activity went up in the exercise group, and slightly decreased in the usual care group, it could be assumed that the overall changes related to physical conditioning and quality of life could be attributed to the intervention. It is important to remember, that this cannot be confirmed due to the nature of the study. Overall, this study helps to support the current literature pertaining to the benefits of maintaining an active lifestyle even during chemotherapy. An InspireHealth Exercise Therapist can work with you to create an activity plan for all stages of the cancer journey.
Plasma vitamin D concentration influences survival outcome after a diagnosis of colorectal cancer.


PURPOSE: We investigated whether the plasma level of 25-hydroxyvitamin D (25-OHD) after a diagnosis of colorectal cancer (CRC) influences survival outcome. PATIENTS AND METHODS: We prospectively studied 1,598 patients with stage I to III CRC. We sought association between plasma 25-OHD and stage-specific survival and tested for interaction between 25-OHD level and variation at the vitamin D receptor (VDR) gene locus. Blood was sampled postoperatively, and plasma was assayed for 25-OHD by liquid chromatography-tandem mass spectrometry. VDR polymorphisms (rs1544410, rs10735810, rs7975232, rs11568820) were genotyped, and haplotypes were inferred by using BEAGLE software. We tested for association between survival and 25-OHD, VDR genotype/haplotype, and after applying a VDR genotype-25-OHD interaction term. We conducted Kaplan-Meier survival analysis and used Cox proportional hazards models to estimate adjusted hazard ratios (HRs).

RESULTS: We found strong associations between plasma 25-OHD concentration and CRC-specific (P = .008) and all-cause mortality (P = .003). Adjusted HRs were 0.68 (95% CI, 0.50 to 0.90) and 0.70 (95% CI, 0.55 to 0.89), respectively (highest v lowest 25-OHD tertile), particularly in stage II disease (HR, 0.44; P = .004 for CRC-specific mortality). We detected gene-environment interactions between 25-OHD concentration and rs11568820 genotype for CRC-specific (P = .008) and all-cause (P = .022) mortality, number of protective alleles (P = .004 and P = .018, respectively), and GAGC haplotype at the VDR locus for all-cause mortality (P = .008). CONCLUSION: In patients with stage I to III CRC, postoperative plasma vitamin D is associated with clinically important differences in survival outcome, higher levels being associated with better outcome. We observed interactions between 25-OHD level and VDR genotype, suggesting a causal relationship between vitamin D and survival. The influence of vitamin D supplementation on CRC outcome will require further investigation.

INSPIREHEALTH’S INTERPRETATION: This study examined the connections between plasma levels of 25-hydroxyvitamin D (blood levels of vitamin D) and survival among patients with stage one to three colorectal cancer. These researchers followed 1598 patients who had undergone surgery with the hopes of eliminating the cancer (while some patients did undergo chemotherapy following their surgery, it was not part of their original treatment plan). Blood samples of vitamin D included both dietary vitamin D intake and the vitamin D absorbed by the skin from direct sunlight. The blood samples were taken from patients somewhere between 53 and 200 days following surgery, with the median being 105 days. Patients were then followed up either until death, or until the study’s data collection finished in 2013. Researchers also looked at variations in genetics at the receptor level of the cell. Samples found that almost 50% of patients were vitamin D deficient, and an additional 27% of patients were at high risk for deficiency. Of the 1598 patients, there were 363 deaths as a result of colorectal cancer, and 168 deaths due to other causes. For those dying of colorectal cancer, survival time following surgery was a median of 5.5 years for stage I, 3.4 years for stage II, and 2.7 years for stage III. This study also found that higher levels of vitamin D were strongly related to lower cancer-related and all-cause mortality. There were some significant findings between certain genetic receptors and mortality.

This study is clinically relevant as it helps to strengthen the already known relationship between vitamin D levels and cancer development, and prognosis. When making choices, it is always best to pay attention to how your body feels. Holistic Nutritionists at InspireHealth are able to meet with you to further to discuss dairy, or any other nutrition and supplement related questions that you may have.
survival. Further research is needed which looks at supplementation of vitamin D, as the levels from this study were only synthesized through food and through the skin from direct sunlight. This study took place in Scotland which boasts a similar climate the west coast of British Columbia. That being, we likely do not receive enough sunlight per year in order obtain the optimal blood levels of vitamin D. Physicians at InspireHealth can talk to you about supplementation, and information on food sources for vitamin D is available through our nutritionists. InspireHealth is also running a clinical trial looking at vitamin D supplementation among stage IV colorectal cancer patients. If this is something that you are interested in participating in, please contact InspireHealth.


Association of change in physical activity and body weight with quality of life and mortality in colorectal cancer: a systematic review and meta-analysis.


PURPOSE: A systematic review and a meta-analysis were performed to assess the associations between change over time in physical activity and body weight and quality of life and mortality in colorectal cancer patients. METHODS: The PubMed, Embase, and Cochrane Central Register of Controlled Trials databases were searched for English language articles published between January 1, 1990 and October 7, 2013. These articles reported results for changes in physical activity and body weight, assessed at pre- to post-diagnosis or at post-diagnosis only. A random effects model was used to analyze pooled quality of life and mortality estimates. RESULTS: Seven eligible studies were identified and analyzed. Increased physical activity was associated with higher overall quality of life scores (N = 3 studies; standardized mean difference (SMD) = 0.74, 95% confidence interval (CI) = 0.66–0.82), reduced disease-specific mortality risk (hazard ratio (HRpooled) = 0.70, 95% CI = 0.55–0.85), and reduced overall mortality (HRpooled = 0.75, CI = 0.62–0.87) (N = 2 studies). Weight gain was not associated with disease-specific (HRpooled = 1.02, CI = 0.84–1.20) or overall (HRpooled = 1.03, CI = 0.86–1.19) mortality (N = 3 studies). CONCLUSIONS: Increased physical activity was associated with improved quality of life, a reduced risk of colorectal cancer, and overall mortality rate. Given the paucity of the literature published on this topic, this finding should be interpreted with caution.

INSPIREHEALTH’S INTERPRETATION: To date, this is the first literature review to investigate changes in physical activity and body weight over time and their associations with quality of life and mortality among colorectal cancer survivors. The studies included in this review were required to assess physical activity and body weight at least twice, which allowed for tracking a change in these variables over time (i.e., longitudinal studies). Seven studies in the scientific literature met the author’s criteria. Although there were seven studies included in this review, the variables measured were not the same in all studies and therefore, some analyses only included three or five studies. An increase in physical activity pre- to post- diagnosis was found to decrease cancer-related mortality by 20% (pooled results from two relevant studies) and decrease overall mortality by 24% (pooled results from the same two relevant studies). An increase in physical activity was also found to significantly increase quality of life among the three observational studies included in this review. No significant differences were found among the three studies that assessed changes in body weight and disease-specific or overall mortality.

This review was quite limited in that few relevant studies in the literature were available to include in the analyses. Therefore, the results should be interpreted with caution. Due to the paucity of studies available, the results from any one study could greatly influence the pooled hazard ratios (pooled hazard ratios are the combined results of all studies). As well, there were large differences in the time intervals between initial and follow-up assessments between the studies. Such a review may have been premature in order to assess changes in physical activity and body weight among colorectal survivors. More research is necessary to further investigate non-statistical trends showing that an increase in physical activity improved quality of life and decreased cancer-specific and overall mortality.


Curcumin enhances the effect of chemotherapy against colorectal cancer cells by inhibition of NF-κB and Src Protein Kinase Signaling Pathways.


OBJECTIVE: Development of treatment resistance and adverse toxicity associated with classical chemotherapeutic agents highlights the need for safer and effective therapeutic approaches. Herein, we examined the effectiveness of a combination treatment regimen of 5-fluorouracil (5-FU) and curcumin in colorectal cancer (CRC) cells. METHODS: Wild type HCT116 cells and HCT116+ch3 cells (complemented with chromosome 3) were treated with curcumin and 5-FU in a time- and dose-dependent manner and evaluated by cell proliferation assays, DAPI staining, transmission electron microscopy, cell cycle analysis and immunoblotting for key signaling proteins. RESULTS: The individual IC50 of curcumin and 5-FU were
PATIENTS AND METHODS: From a cohort of adults without colorectal cancer at baseline in 1992-1993, we identified 2,293 participants who were diagnosed with invasive, non-metastatic colorectal cancer up to mid-2007. At baseline, before their cancer diagnosis, and again after their cancer diagnosis, participants completed detailed questionnaires that included information concerning recreational physical activity and leisure time spent sitting. RESULTS: During a maximum follow-up of 16.1 years after colorectal cancer diagnosis, 846 patients with colorectal cancer died, 379 of them from colorectal cancer. Engaging in 8.75 or more metabolic equivalent (MET) hours per week of recreational physical activity (equivalent to approximately 150 minutes per week of walking) compared with fewer than 3.5 MET hours per week was associated with lower all-cause mortality (pre-diagnosis physical activity: relative risk [RR], 0.72; 95% CI, 0.58 to 0.89; post-diagnosis physical activity: RR, 0.58; 95% CI, 0.47 to 0.71). Spending 6 or more hours per day of leisure time sitting compared with fewer than 3 hours per day was associated with higher all-cause mortality (pre-diagnosis sitting time: RR, 1.36; 95% CI, 1.10 to 1.68; post-diagnosis sitting time: RR, 1.27; 95% CI, 0.99 to 1.64). CONCLUSION: More recreational physical activity before and after colorectal cancer diagnosis was associated with lower mortality, whereas longer leisure time spent sitting was associated with higher risk of death.
INSPIREHEALTH'S INTERPRETATION: The benefits of exercise during and after cancer treatment and diagnosis have been well documented as being both safe and well tolerated by patients. Further to this, research has indicated that greater levels of physical activity can improve response to cancer treatment, reduce time to completion of chemotherapy and improve outcomes. This cohort study observed the effects of 60 versus 150 minutes of weekly physical activity, as well as three hours or less versus six hours or more of time spent sitting during leisure-time on all-cause mortality before and after a colorectal cancer diagnosis on 2,293 men and women. Participants were identified from the Cancer Prevention Study-II Nutrition Cohort. Questionnaires were used for participants to self-report minutes per week of physical activity and leisure-time spent sitting.

The results from this study revealed some very interesting and significant figures. First, results from pre-diagnosis leisure-time sitting revealed that those who sat for more than six hours per day during their leisure-time were at a 36% higher risk of all-cause mortality compared to those who sat for less than three hours. Post-diagnosis surveys revealed that leisure-time sitting for greater than six hours resulted in a 27% increased risk of all-cause mortality compared to those who sat for less than three hours per day. Pre-diagnosis physical activity questionnaires indicated that being physically active for 150 minutes or more per week reduced risk of all-cause mortality by 28% when compared with engaging in less than 60 minutes of physical activity per week. Interestingly, a greater protective effect was observed with those individuals who were the most physically active post-diagnosis. Post-diagnosis results indicated that those who were physically active for 150 minutes or more per week reduced their risk of all-cause mortality by 42% compared with those who were physically active for 60 minutes or less per week.

The results of this study show how both becoming and/or remaining physically active after a diagnosis of colorectal cancer has greater benefits than those associated with exercising prior to a diagnosis alone. The body of research on exercising and its benefits following a diagnosis is growing with positive relationships observed between physical activity and improved health outcomes. InspireHealth offers exercise classes and programming for patients and support members.