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FOR THE LATEST IN WORLDWIDE SUPPORTIVE CANCER CARE

IN THIS ISSUE: Van Blarigan and colleagues discuss adherence to the American Cancer Society’s published exercise and nutrition guidelines. Zhang’s team perform a meta-analysis exploring the effect of acupuncture on cancer-related fatigue symptoms. In a narrative review by Sheill et al., considerations for exercise prescription among patients with bone metastases are reviewed. Wakefield and colleagues discuss the meaning of patient empowerment for adults in advanced stages of illness. And lastly, Kleckner et al., perform a review of exercise for toxicity management.

PHYSICAL ACTIVITY AND NUTRITION

Van Blarigan, E.L., Fuchs, C.S., Niedzwiecki, D., et al.

Association of survival with adherence to the American Cancer Society nutrition and physical activity guidelines for cancer survivors after colon cancer diagnosis

JAMA Oncology (2018), 4(6):783-790. doi:10.1001/jamaoncol.2018.0126

ABSTRACT | Importance: The American Cancer Society Nutrition and Physical Activity Guidelines for Cancer Survivors (ACS guidelines) include maintaining (1) a healthy body weight; (2) physical activity; and (3) a diet that includes vegetables, fruits, and whole grains. It is not known whether patients with colon cancer who follow these guidelines have improved survival.

Objective: To examine whether a lifestyle consistent with the ACS guidelines is associated with improved survival rates after colon cancer.

Design, Setting, and Participants: This prospective cohort study included 992 patients with stage III colon cancer who were enrolled in the CALGB 89803 randomized adjuvant chemotherapy trial from 1999 through 2001. Data for the present study were analyzed between November 2016 and December 2017.

Exposures: We assigned an ACS guidelines score for each included patient based on body mass index; physical activity; and intake of vegetables, fruits, whole grains, and red/processed meats (score range, 0-6, with higher score indicating healthier behaviors). Secondarily, we examined a score that also included alcohol intake in addition to the other factors (range, 0-8). Lifestyle was assessed during and 6 months after chemotherapy.

Main Outcome and Measures: Hazard ratios (HRs) and 95% confidence intervals (CIs) for disease-free, recurrence-free, and overall survival. **Results:** Of the 992 patients enrolled in the study, 430 (43%) were women, and the mean (SD) age was 59.6 (11.2) years (range, 21-85 years). Over a 7-year median follow-up, we observed 335 recurrences and 299 deaths (43 deaths without recurrence). Compared with patients with a 0 to 1 ACS guidelines score (n = 262; 26%), patients with a 5 to 6 score (n = 91; 9%) had a 42% lower risk of death during the study period (HR, 0.58; 95% CI, 0.34-0.99; P = .01 for trend) and improved disease-free survival (HR, 0.69; 95% CI, 0.45-1.06; P = .03 for trend). When alcohol consumption was included in the score, the adjusted HRs comparing patients with scores of 6 to 8 (n = 162; 16%) vs those with scores of 0 to 2 (187; 91%) were 0.49 for overall survival (95% CI, 0.32-0.76; P = .002 for trend), 0.58 for disease-free survival (95% CI, 0.40, 0.84; P = .01 for trend), and 0.64 for recurrence-free survival (95% CI, 0.44-0.94; P = .05 for trend).

Conclusions and Relevance: Having a healthy body weight, being physically active, and eating a diet rich in vegetables, fruits, and whole grains after diagnosis of stage III colon cancer was associated with a longer survival.

INSPIREHEALTH’S INTERPRETATION: The American Cancer Society (ACS) has published Nutrition and Physical Activity Guidelines for Cancer Survivors. Not surprisingly, suggestions include maintenance of a healthy body weight, regular physical activity, and eating a diet rich in vegetables, fruit and whole grains. The purpose of this study was to see if patients with stage III colon cancer who followed the guidelines had improved survival. This study was a prospective cohort design and included 992 patients with stage III colon cancer. A prospective cohort design gathers data from a group of patients (the cohort), then

follows those patients over a period of time. Patients were given questionnaires regarding diet, activity, and height/weight (from which body mass index (BMI) was calculated) during and six months after chemotherapy. Scores ranging from 0-6 were calculated with higher scores indicating healthier behaviours/stricter adherence to the guidelines. Secondary scores from 0-8 that included alcohol were also calculated. Assessed outcomes included overall survival (the time from survey one to death), disease-free survival (occurrence of a new primary colon tumour or death from any cause), and recurrence-free survival (time to tumour recurrence or new primary colon tumour or death from colon cancer only). Results indicated that in comparison to those scoring 0-1, those scoring 5-6 had a 42% lower risk of death, 31% improved disease-free survival, and 22% improved recurrence-free survival during the study period.

Interestingly, the authors raised the typically accepted “healthy” BMI (weight in kg divided by height in metres squared) from 18.5-24.9 to 23-29 because that range has been associated with increased survival in colorectal cancer patients. The authors acknowledge that this finding may represent “reverse causation” since weight loss may be a marker of cancer progression. Additionally, they used moderate alcohol consumption as being “healthier” than either abstinence or heavier drinking. When alcohol was added to the scoring system, those scoring 6-8 vs 0-2 (≤ 1 drink per day for women or ≤ 2 drinks per day for men) had a 51% lower risk of death. This finding is in contrast to other researchers who suggest that less/no alcohol may improve cancer survival. For physical activity, benefit was observed with approximately 150 minutes per week of moderate activity. Diets including ≥ 5 servings of vegetables and fruits per day and choosing whole over refined grains were associated with improved colon cancer survival. Low consumption of red and processed meat did not appear to diminish survival. This was a surprising finding because red meat consumption has been associated with the development of colon cancer, but in this study, not with increased mortality from colon cancer. The authors wonder if higher protein intake may benefit colon cancer survivors.

Overall, the 5-year survival probability was 85% for those with stricter adherence to the guidelines compared to 76% for patients with poorer adherence. Taking all factors into consideration, the authors summarize that a healthy body size, regular, moderate physical activity, and a diet rich in vegetables, fruits and whole grains improves insulin sensitivity, decreases inflammation and increases Vitamin D levels, all of which are associated with improved colon cancer survival.

ACUPUNCTURE AND CANCER-RELATED FATIGUE

Zhang, Y., Lin, L., Huiling, L., et al.

Effects of acupuncture on cancer-related fatigue: A meta-analysis

Supportive Care in Cancer (2018), 26, 415–425

ABSTRACT | Purpose: This study was designed to critically evaluate the effect of acupuncture on cancer-related fatigue (CRF). **Methods:** Seven databases (Cochrane Library, Embase, Medline, Web of Science, CBM, Wanfang, and CNKI) were systematically reviewed from inception to November 2016 for randomized controlled trials (RCTs). Two reviewers critically and independently assessed the risk of bias using Cochrane Collaboration criteria and extracted correlated data using the designed form. All analyses were performed with Review Manager 5. **Results:** Ten RCTs, including 1327 patients (acupuncture, 733; control, 594), meeting the inclusion criteria for the meta-analysis were identified. Acupuncture had a marked effect on fatigue in cancer patients, regardless of concurrent anti-cancer treatment, particularly among breast cancer patients. The meta-analysis also indicated that acupuncture could significantly mitigate CRF compared with sham acupuncture or usual care. Acupuncture for 20–30 min/session three times/week for two or three weeks, twice weekly for two weeks and weekly for six weeks, and weekly for six weeks had substantial effects on CRF. Six RCTs reported the occurrence of adverse events, whereas five reported none. The remaining study reported some manageable events, including spot bleeding and bruising. **Conclusions:** Acupuncture is effective for CRF management and should be recommended as a beneficial alternative therapy for CRF patients, particularly for breast cancer patients and those currently undergoing anti-cancer treatment.

INSPIREHEALTH'S INTERPRETATION: Cancer-related fatigue (CRF) is a long-term effect of cancer treatments that can affect over 50% of cancer patients, which can greatly influence overall quality of life and daily functioning. Pharmacological approaches to CRF have not shown consistent benefit, and some medications have undesirable side effects. Acupuncture has been used as a treatment for CRF and has shown positive results. The purpose of this study was to summarize the research of the effect of acupuncture on CRF symptoms. In this paper, researchers performed a meta-analysis (statistical analysis of multiple studies) of ten randomized controlled trials all comparing acupuncture treatment to either a control or to sham acupuncture (where acupuncture needles are used but not for the function of treating CRF). Across these studies, a total of 1327 patients were included (733 acupuncture and 594 control). Patients ranged between 51 and 64 years old, and diagnoses were primarily breast cancer. The frequency of acupuncture sessions ranged from one to three times per week over a period of two to ten weeks. Five studies used sham acupuncture as a comparison and eight also compared acupuncture to usual care. Overall, studies showed significant improvement in CRF symptoms with acupuncture over both sham acupuncture and usual care. Adverse effects were limited and mild, including local spot bruising and minor bleeding. This paper indicates that acupuncture can be a safe and effective way to help treat CRF symptoms with very few side effects. InspireHealth offers weekly acupuncture to patients to support CRF and other treatment-related side effects.

EXERCISE AND BONE METASTASES

Sheill, G., Guinan, E.M., Peat, N., et al.

Considerations for exercise prescription in patients with bone metastases: A comprehensive narrative review

Physical medicine and rehabilitation (2018), 10(8), 843-864

ABSTRACT | Metastatic disease is a frequent complication of advanced cancer, with bone representing one of the most common sites of metastatic occurrence. Patients with bone metastases receive long-term systemic treatments that have a significant attritional impact on muscle strength, fatigue, and physical functioning. Physical rehabilitation involving exercise and physical activity prescription has a considerable role in counteracting these changes; however, exercise is often perceived as a contraindication in the presence of bone metastases due to concerns about aggravating skeletal related events. This article examines the physical sequelae of bone metastases and outlines the factors for consideration with exercise prescription in metastatic bone disease, including bone health, pain levels, and oncologic treatment. This article includes a comprehensive review of the evidence from trials of exercise prescription in this population, including the efficacy and safety outcomes of exercise interventions. Exercise interventions for patients with bone metastases are associated with positive physical and self-reported outcomes. Studies reviewed reporting adverse events did not find a high fracture incidence with exercise in comparison with control participants, or an association between exercise and fracture risk. The need to individualize exercise prescription and adapt exercises to patient ability were reinforced in all papers reviewed. Exercise prescription to patients with bone metastases does involve complex decision making; however, a number of tools are available that may inform both the assessment of patients and the prescription of exercise.

INSPIREHEALTH'S INTERPRETATION: While it is well established that physical activity (PA) is beneficial for cancer patients throughout a diagnosis, the authors of this paper set out to summarize the evidence of the impact of exercise in patients with bone metastases. Bone is one of the most common sites of metastases with incidence ranging from 14-90% of cancer patients depending on the type of primary cancer. There are two types of bone lesions: osteoblastic lesions are characterized by unhealthy bone building up in an area, while osteoclastic lesions are characterized by bone destruction in an area. Risks associated with bone metastases include an increased risk of breaking bones as well as spinal cord compression as a result of a broken bone or a bone growth into the vertebral column. The main symptom of bone metastases is pain, as well as reduced physical function and overall quality of life. Analgesics (pain killers), radiation, bone-modifying medications such as bisphosphonates, and surgery are all treatments used to manage bone metastases.

As survival rates improve and more people are living longer with bone metastases, it is important to consider what factors can improve functional capacity and quality of life. Muscle strength, physical function, and PA are often reduced after a cancer diagnosis and treatment, and various symptoms such as nausea and fatigue pose barriers to PA participation. Those with bone metastases also face a higher risk of fracture. The authors emphasize the importance of educating those at risk about the benefits of regular and safe PA which can outweigh the risks of fracture. Specific safety precautions do exist, such as avoiding activities that cause increased pain, avoiding exercises that create shear force in an area with a bone lesion, high impact activities, and heavy lifting. The authors propose a framework that takes factors into account, including location and size of lesions which can help to classify the level of risk for a fracture and guide an appropriate exercise prescription. Eleven studies were included in this review with a total of 593 patients. Aerobic, resistance, and combination aerobic/resistance exercise programs were all well-tolerated by participants and led to positive effects including greater bone mineral content, walking speed, strength, and improved pain and fatigue. In the interventions, exercises were adapted if needed to ensure patient safety.

The authors conclude that patients with bone metastases would benefit from regular exercise that is individualized and prescribed (and where possible supervised) by an exercise professional experienced in cancer rehabilitation. InspireHealth Exercise Therapists develop individualized exercise programs that are safe for anyone with a diagnosis, taking into consideration all current conditions including bone metastases.

PATIENT EMPOWERMENT AND ADVANCED ILLNESS

Wakefield, D., Bayly, J., Selman, L.E., et al.

Patient empowerment, what does it mean for adults in the advanced stages of a life-limiting illness: A systematic review using critical interpretive synthesis

Palliative Medicine (2018), 32(8), 1288-1304.

ABSTRACT | **Background:** Patient empowerment, defined as 'a process through which people gain greater control over decisions and actions affecting their health' (World Health Organization) is a key theme within global health and social care strategies. The benefits of incorporating empowerment strategies in care are well documented, but little is known about their application or impact for patients with advanced, life-limiting illness(s). **Aim:** To identify and synthesise the international evidence on patient empowerment for adults with advanced, life-limiting illness(s). **Design:** Systematic review (PROSPERO no. 46113) with critical interpretive synthesis methodology. **Data sources:** Five databases (MEDLINE, Embase, CINAHL, PsycINFO and

Cochrane) were searched from inception to March 2018. Grey literature and reference list/citation searches of included papers were undertaken. Inclusion criteria: empirical research involving patients with advanced life-limiting illness including descriptions of, or references to, patient empowerment within the study results. **Results:** In all, 13 papers met inclusion criteria. Two qualitative studies explored patient empowerment as a study objective. Six papers evaluated interventions, referencing patient empowerment as an incidental outcome. The following themes were identified from the interpretive synthesis: self-identity, personalised knowledge in theory and practice, negotiating personal and healthcare relationships, acknowledgement of terminal illness, and navigating continued losses. **Conclusion:** There are features of empowerment, for patients with advanced life-limiting illness distinct to those of other patient groups. Greater efforts should be made to progress the empowerment of patients nearing the end of their lives. We propose that the identified themes may provide a useful starting point to guide the assessment of existing or planned services and inform future research.

INSPIREHEALTH'S INTERPRETATION: The authors reviewed 13 papers with patients in advance stages of their diseases, including cancer to learn more about patients' understanding of empowerment and what factors or interventions could help them feel empowered. The findings suggested that self-identity (belief about them) is an important factor and was represented by self-esteem, self-image and ideal-self. For patients, maintaining routines related to personal care, having autonomy and involvement in important decisions helped with their self-esteem. Having a regular schedule made them feel in control and empowered; however, the sense of control was lost when schedules were imposed by others in a non-negotiable way. Receiving respect, being included, acknowledged and have privacy was also seen as empowering. Challenges included changes (and loss) of physical appearance and social life. The loss of physical appearance and function was a threat for confidence and caused ideas of loss of power, identity and capabilities. Learning to cope with the changes, and having hope felt empowering.

For some patients acknowledging disability and death was helpful, while others found empowered when communicating the need of avoidance of those topics. This is an important finding, as it confirms the relevance of listening to our own-self and doing what feels right for us, versus the approach of "one size fits all". Keeping a healthy lifestyle was seen as positive and desirable, and felt like a way to regain control. Having individual goals towards a healthier lifestyle was important; it also helped to avoid guilt when broader goals were not met. The role of healthcare professionals was also presented in the paper. Patients identified wanting to know more about the cause of certain symptoms, how to manage them and what to expect given their disease, treatment, etc. Empowerment was achieved when patients were listened to, supported and included in the decision making process. Patients preferred to take decisions in partnership with healthcare professionals, rather than on their own. The authors indicated the importance of healthcare education being delivered in a sensitive, unrushed, empathic, honest, inclusive and personalized way, adapting to changes in capacities, capabilities and priorities of each patient.

EXERCISE AND TOXICITY MANAGEMENT

Kleckner, I.R., Dunne, R.F., Asare, M., et al.

Exercise for toxicity management in cancer: A narrative review

Oncology & Hematology Review (2018) 14(1), 28–37

ABSTRACT | Although the treatment of cancer is more effective now than ever, patients with cancer still face acute and chronic toxicities such as fatigue, cardiotoxicity, pain, cognitive impairment, and neurotoxicity. In this narrative review, we briefly discuss the use of exercise for toxicity management in patients with cancer, biological mechanisms underlying the toxicities and the effects of exercise, barriers that patients- especially underserved patients-face in adopting and adhering to exercise programs, and new technologies to overcome barriers to exercise. Our conclusions and clinical suggestions are: (1) exercise is safe and effective for treating many toxicities; (2) patients can benefit from a variety of exercise modalities (e.g., walking, cycling, resistance bands, yoga); (3) exercise should be started as soon as possible, even before treatments begin; (4) exercise should be continued as long as possible, as a lifestyle; and (5) barriers to exercise should be identified and addressed, (e.g., continually encouraging patients to exercise, using mobile technology, advocating for safe communities that encourage active lifestyles). Future research should inform definitive clinical guidelines for the use of exercise to ameliorate toxicities from cancer and its treatment.

INSPIREHEALTH'S INTERPRETATION: This paper summarizes the scientific evidence demonstrating the important role exercise plays in managing cancer and cancer treatment-related toxicities. Toxicities are the harmful side effects of either cancer itself or cancer treatment (chemotherapy, radiation, or hormone therapy). These side effects can be physical, psychological, or social, and may be acute or chronic. Fatigue, pain, cardiotoxicity, cognitive impairment, neurotoxicity, sleep disturbances, bone damage, metabolic toxicity, and psychological distress are categorized as high priority toxicities and are the main side effects examined in this review. Pharmacological treatments that are used to address these side effects usually target one toxicity or biological pathway. Exercise has a positive impact on more than one toxicity through more than one pathway, and therefore is a valuable treatment in managing symptoms of these toxicities.

The studies reviewed in this paper examined the impact of various exercise interventions on cancer and treatment toxicities before, during, and after cancer treatment. The exercise interventions employed before and during treatment were a minimum

of three sessions per week, and included both aerobic (at least 30 minutes per session) and strength exercises. Pre-treatment exercise interventions led to improved recovery and function after surgery as well as less damage to the heart (cardiotoxicity) from chemotherapy. Exercise interventions during chemotherapy and radiation were also effective in reducing cardiotoxicity and pain, and exercise done throughout bone radiation reduced bone damage. During chemotherapy, participation in an exercise program resulted in less cognitive impairment (learning, memory, attention) and reduced neurotoxicity (damage to the brain). Post treatment, walking three days per week for 40 minutes (in combination with counselling) reduced psychological distress and sleep disturbances, and a combination aerobic and strength program reduced fatigue. A strength-based exercise program also improved fitness, symptoms of fatigue, and quality of life in men taking hormone therapy. Studies examining mindfulness-based physical activity found that practicing yoga or tai chi reduced fatigue during chemotherapy. Post treatment, doing yoga twice per week reduced fatigue and improved symptoms of cognitive impairment and sleep disturbances, and three sessions of Tai Chi per week improved bone health, strength, fitness, and quality of life.

The authors of this paper also summarize the biological mechanisms through which exercise exerts these positive effects. Cancer and cancer treatments chronically stress the immune system and negatively impact inflammatory pathways in the body. Dysregulation of these pathways can have negative effects on hormone pathways that regulate metabolism, shifting the balance to a “breakdown” environment in the body. When muscles contract however, they release proteins that ultimately trigger anti-inflammatory effects in the body. Through a different pathway, strength-based exercise appears to promote a building environment supporting the body to heal, rebuild, and recover from toxicities that it has been exposed to by upregulating certain genes. Because different modes of exercise may act on unique biological pathways to impact the toxicities, it is recommended to incorporate more than one type of physical activity into an exercise program. The authors also emphasize that exercise programs should be progressive, focus on moderate intensity regardless of the type of activity, be supervised, and be tailored to each person’s individual needs.

The authors of this paper conclude 1) that a variety of exercise modes are safe and effective for managing side effects of cancer and cancer treatment, 2) an appropriate exercise program should be started as soon as possible and continued as long as possible ideally creating a lifelong physical activity habit, and 3) successful physical activity participation is supported by engaging community partners and health professionals in identifying and reducing barriers.

This paper makes a strong case for the importance of exercise prescription alongside standard cancer treatments. InspireHealth’s exercise programs support patients at all stages of a diagnosis to optimize function, recovery, and overall quality of life.

InspireHealth provides patients with the knowledge, tools, and services to support their overall health during and after cancer treatment. Our medical doctors value conventional cancer treatments such as chemotherapy, radiation, and surgery. At the same time, they recognize the importance of supporting health, immune function, body, mind, and spirit.

InspireHealth’s programs are supported by current research and can be safely integrated with patient’s conventional treatments.

InspireHealth’s *Research Updates* are compiled by Rachel Mark, M.A. (kin)—with guidance from the editorial board—using InspireHealth’s Research Information System, a unique supportive cancer care knowledge management database. The editorial board includes: Dr. Janice Wright, MD, CEO, Dr. Hannah Nette, MD, Dr. Lori McFarlane, MD, Emily Medd, M.Sc., and Terry Heidt, M.Sc. For more information, email info@inspirehealth.ca

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