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RESEARCH UPDATES OCTOBER 2017

FOR THE LATEST IN WORLDWIDE SUPPORTIVE CANCER CARE

IN THIS ISSUE: Wu and colleagues explore the impact of physical activity participation both pre- and post-diagnosis on survival benefits among colorectal cancer patients. Owen's team reviews the literature pertaining to lifestyle support to help mitigate the potential side effects of androgen deprivation therapy among prostate cancer patients as they relate to bone health and body composition. Ricker and Hauss explore the clinical role of an anti-inflammatory diet. Danhauer et al. report on the benefits of yoga therapy for cancer patients currently in treatment. Lastly, the Into the Vault study provides discussion related to the management of radiation therapy side effects using complementary medicine.

PHYSICAL ACTIVITY AND SURVIVAL BENEFITS

Wu, W., Guo, F., Ye, J., et al.

Pre- and post-diagnosis physical activity is associated with survival benefits of colorectal cancer patients: a systematic review and meta-analysis

Oncotarget (2017), 7(23), 52095-52103

ABSTRACT | Objective: Physical activity is associated with reduced risk of colorectal cancer. However, whether physical activity could impart cancer patients' survival benefits remains uncertain. The aim of this study is to systematically evaluate the relationship between physical activity and colorectal cancer mortality. **Results:** Our meta-analysis included 11 studies involving 17,295 patients with a follow-up period ranging from 3.8 to 11.9 years. Results indicated that physical activity was inversely associated with overall (RR = 0.81, 95% CI = 0.72–0.91) and colorectal cancer-specific mortality (RR = 0.79, 95% CI = 0.71–0.89) before the diagnosis of cancer, respectively. For physical activity after diagnosis, the pooled RRs of colorectal cancer-specific and total mortality were 0.77 (95% CI, 0.63–0.94) and 0.71 (95% CI, 0.63–0.81), respectively. Similar inverse associations between exercise and prognosis were found among colorectal cancer survivors who had high level exercise compared with those who had low-level exercise or were inactive. There was no obvious evidence for publication bias among studies. **Materials and Methods:** We performed a systematic data search in PubMed, Cochrane Library databases and Web of Science for relevant articles before Jan 2016. We adopted adjusted estimates to calculate pooled relative risks (RRs) with 95% confidence intervals (CI) by the random-effects model. The publication bias was assessed by Begg's test. **Conclusions:** Our meta-analysis provides comprehensive evidence that physical activity, whether before or after the diagnosis of colorectal cancer, is related to reduced overall and cancer-specific mortality. Our findings may have significant public health implications and more prospective randomized clinical trials should be warranted to certify this protective association.

INSPIREHEALTH INTERPRETATION: This paper is a meta-analysis, combining the results from 11 studies examining the effect of physical activity (PA) on the risk of mortality (death) in colorectal cancer survivors. Colorectal cancer is one of the most common cancers, and while survival rates have been rising, it is important to identify factors that can improve the long term prognosis. These selected studies met specific inclusion criteria, and were all observational cohort studies, meaning that data was collected from the same participants at various time points over several years. Many variables were controlled for including participant characteristics, follow up period, and stage of cancer. Self-reported PA participation was examined both before (eight studies) and after (seven studies) cancer diagnosis. Results show that for PA participation before diagnosis and after cancer diagnosis, exercisers had reduced risk compared to non-exercisers for cancer-related mortality and all-cause mortality. Furthermore, high exercisers had a lower risk compared to low exercisers for cancer-related mortality and all-cause

mortality. Again, this effect was observed for PA participation before and after cancer diagnosis. Overall, this paper confirms that PA participation both before and after a colorectal cancer diagnosis is associated with improved survival outcomes, and higher levels of PA are more beneficial compared to lower levels of PA. The major limitation of this paper is that the authors did not report what criteria they used for defining exercisers vs non-exercisers and high vs low exercisers. Therefore, while this information is useful, it is not specific. The Canadian Physical Activity Guidelines recommend 150 minutes per week of aerobic activity as well as 2-3 sessions per week of strength based activity and regular stretching. With a cancer diagnosis, it is recommended to be as physically active as possible before, during, and after treatment and therefore personal PA goals may need to be adjusted. InspireHealth's patient members can make appointments with an Exercise Therapist to develop a PA plan. InspireHealth also offers weekly yoga and strength classes.

ANDROGEN DEPRIVATION THERAPY

Owen, P.J., Daly, R.M., Livingston, P.M., et al.

Lifestyle guidelines for managing adverse effects on bone health and body composition in men treated with androgen deprivation therapy to prostate cancer: an update

Prostate Cancer and Prostatic Diseases (2017), 00, 1-9, DOI:10.1038/pcan.2016.69

ABSTRACT | Background: Men treated with androgen deprivation therapy (ADT) for prostate cancer are prone to multiple treatment-induced adverse effects, particularly with regard to a deterioration in bone health and altered body composition including decreased lean tissue mass and increased fat mass. These alterations may partially explain the marked increased risk in osteoporosis, falls, fracture and cardiometabolic risk that has been observed in this population. **Methods:** A review was conducted that assessed standard clinical guidelines for the management of ADT-induced adverse effects on bone health and body composition in men with prostate cancer. **Results:** Currently, standard clinical guidelines exist for the management of various bone and metabolic ADT-induced adverse effects in men with prostate cancer. However, an evaluation of the effectiveness of these guidelines into routine practice revealed that men continued to experience increased central adiposity, and, unless pharmacotherapy was instituted, accelerated bone loss and worsening glycaemia occurred. **Conclusions:** This review discusses the current guidelines and some of the limitations, and proposes new recommendations based on emerging evidence regarding the efficacy of lifestyle interventions, particularly with regard to exercise and nutritional factors, to manage ADT-related adverse effects on bone health and body composition in men with prostate cancer.

INSPIREHEALTH INTERPRETATION: Androgen deprivation therapy (ADT) is a hormone therapy that is commonly prescribed to men with both metastatic and non-metastatic prostate cancer to help improve survival. There are often many side effects of ADT, including bone mineral density loss, emotional lability, and changes to body composition (mainly increased fat mass and loss of lean muscle mass). These side effects have their own risks including bone fractures, cardio-metabolic disorders, and inflammation. Optimizing bone health and body composition is of great relevance to men taking ADT and this review examines the currently suggested management guidelines. The authors recommend monitoring known risk factors, as well as considering pharmacotherapy (medication), and/or lifestyle interventions. To be able to monitor changes to bone health, initial bone mineral density and fracture risk should be assessed. Ensuring adequate calcium and vitamin D intake, mainly through diet, is important, though supplementation may be warranted (it is advised to speak to your physician to ensure that there are no contraindications to supplementation). Should fracture risk be high, anti-resorptive therapy (medication to improve bone health) may be warranted through physician prescription. Adequate intake of good quality protein (e.g. fish, pulses, nuts, lean grass-fed animal protein) is also recommended (again, the amount required is individual, and consultation with a Registered Dietitian would be advised).

Regular exercise is highlighted as an important way to mitigate side effects related to bone mineral density loss and changes in body composition. Exercise that involves aerobic (cardio) endurance, progressive resistance exercise, weight-bearing impact exercise, and balance training is recommended. Specifically, men undergoing ADT should aim to build up to at least 30 minutes of aerobic exercise five or more days per week at moderate intensity (able to carry on a conversation, but challenging to sing a song). For resistance (or strength-based) exercise, it is recommended to perform between two and three sets of 8-10 repetitions of exercises that target all of the body's major muscle groups. These strength-based workouts should be performed two to three days per week on non-consecutive days. Weight-bearing impact exercises (i.e. jumping, bounding, hopping, skipping, step-ups) are also recommended for bone health. Exercise has been found to have no effect on PSA or testosterone levels and thus is not considered a risk factor for prostate cancer growth. Other lifestyle factors such as smoking cessation and limiting alcohol consumption (less than two standard drinks per day) are recommended. The authors advise that men prescribed ADT find suitable practitioners to aid in the implementation of these guidelines.

ANTI-INFLAMMATORY DIET

Ricker, M.A. & Haas, W.C.

Anti-inflammatory diet in clinical practice: A review

Nutrition in Clinical Practice (2017), 32(3), 318-325

ABSTRACT | Recently, there has been an increase in the research regarding the impact of acute and chronic inflammation on health and disease. Specific foods are now known to exert strong effects on inflammatory pathways within the body. Carefully selecting foods that are anti-inflammatory in nature while avoiding foods that are proinflammatory is central to an anti-inflammatory diet plan. Ultimately, the plan models a pattern of eating that (1) focuses on eating whole, plant-based foods that are rich in healthy fats and phytonutrients and (2) maintains a stable glycemic response.

INSPIREHEALTH INTERPRETATION: There is a lot of interest in the concept of inflammation, particularly chronic inflammation, and its role in the development of diseases such as diabetes, cardiovascular disease, dementia and cancer. Acute inflammation is considered protective as it eliminates destructive agents, and then restores tissues to a healthy state. Chronic inflammation, on the other hand, occurs when a destructive agent (such as a virus or environmental toxin exposure) persists or the acute inflammatory response fails to resolve the issue. Chronic inflammation is more slowly progressive, and over time, may damage many different organs. Of course, inflammation is not the only factor driving these chronic diseases; it is but one factor. The role that diet might play in encouraging a so-called “anti-inflammatory” state is of great interest to researchers, because diet is a lifestyle intervention available to us all. This review outlines the key components of an anti-inflammatory diet plan, including the roles of carbohydrates, fats, proteins, vegetables and fruits, and overall caloric intake. Perhaps not surprisingly, refined carbohydrates (e.g. white flour/sugar/rice) with high glycemic loads are one of the main dietary factors affecting inflammation with pro-inflammatory effects. Glycemic load is the glycemic index (the rate at which a carbohydrate food is digested, absorbed and metabolized) multiplied by the actual amount of that carbohydrate. Regular ingestion of foods with a high glycemic load can lead to chronic hyperglycemia (high blood sugar) which in turn fosters the production of pro-inflammatory molecules. Fats, in particular, the omega-6 and omega-3 fatty acids also play roles in inflammation, with the ratio of omega-6 to omega-3 being the most important factor. Both fatty acids are essential nutrients, meaning that we must ingest them because our bodies cannot synthesize them. In general, however, omega-6 fatty acids are considered more pro-inflammatory while omega-3s are considered more anti-inflammatory.

Though researchers differ as to the optimal ratio of omega-6 to omega-3, it is generally believed to be less than 5:1. A ratio of greater than 10:1 is certainly considered to be pro-inflammatory. Western diets typically have ratios of greater than 20:1, which is very different from the 1:1 ratio of our ancestors. Foods rich in omega-3 fatty acids include ground flax seeds, walnuts, and especially fatty fish such as salmon and sardines. Foods high in omega-6 fatty acids include corn/sunflower/safflower oils, meats, dairy and eggs. Interestingly, beef from grass-fed cattle has a much healthier ratio of omega-6 to 3 compared to that in grain-fed animals (see June/July 2015 Research Update for more on this topic). Trans fats are also pro-inflammatory and can be easily avoided by reducing or eliminating processed foods, especially bakery goods. Fruits and vegetables are the dietary anti-inflammatory heavy hitters and recommendations are to have them contribute up to 2/3 of total daily food volume. Consuming vegetables and fruits at all meals and choosing a variety of colours will ensure optimal nutrition and anti-inflammatory effects. Have plant-based proteins such as beans, lentils, and tofu predominate over animal protein, and choose cold water fish over meat (and choose grass-fed meat over grain-fed), when consuming animal protein. Green, black and white teas also have anti-inflammatory properties. Though resveratrol (from grape skins) in red wine is known to be anti-inflammatory, alcohol intake should generally be reduced to less than one to two drinks per day. For some cancers, alcohol may be best avoided. Herbs and spices such as ginger, turmeric, garlic, cayenne and oregano all have anti-inflammatory properties and can be liberally added to many dishes.

In addition to specific nutrients, the authors also review the role of overall caloric intake. Excess calories can lead to increased adiposity (fat) which directly contributes to chronic inflammation. Calorie reduction with optimal nutrient intake is purported to have anti-inflammatory effects. Finally, the authors review the role of how we eat. They state that “Americans eat too much, too quickly and on the run”. They suggest that eating smaller portions, slowly and mindfully can also reduce the impact of chronic inflammation on the body.

YOGA THERAPY DURING TREATMENTS

Danhauer, S.C., Addinton, E.L., Sohl, S.J., et al.

Review of yoga therapy during cancer treatment

Supportive Care in Cancer (2017), 25:1357–1372

ABSTRACT | Purpose: Reviews of yoga research that distinguish results of trials conducted during (versus after) cancer treatment are needed to guide future research and clinical practice. We therefore conducted a review of non-randomized

studies and randomized controlled trials of yoga interventions for children and adults undergoing treatment for any cancer type.

Methods: Studies were identified via research databases and reference lists. Inclusion criteria were the following: (1) children or adults undergoing cancer treatment, (2) intervention stated as yoga or component of yoga, and (3) publication in English in peer-reviewed journals through October 2015. Exclusion criteria were the following: (1) samples receiving hormone therapy only, (2) interventions involving meditation only, and (3) yoga delivered within broader cancer recovery or mindfulness-based stress reduction programs. **Results:** Results of non-randomized (adult n = 8, pediatric n = 4) and randomized controlled trials (adult n = 13, pediatric n = 0) conducted during cancer treatment are summarized separately by age group. Findings most consistently support improvement in psychological outcomes (e.g., depression, distress, anxiety). Several studies also found that yoga enhanced quality of life, though further investigation is needed to clarify domain-specific efficacy (e.g., physical, social, cancer-specific). Regarding physical and biomedical outcomes, evidence increasingly suggests that yoga ameliorates sleep and fatigue; additional research is needed to advance preliminary findings for other treatment sequelae and stress/immunity biomarkers. **Conclusions:** Among adults undergoing cancer treatment, evidence supports recommending yoga for improving psychological outcomes, with potential for also improving physical symptoms. Evidence is insufficient to evaluate the efficacy of yoga in pediatric oncology. We describe suggestions for strengthening yoga research methodology to inform clinical practice guidelines.

INSPIREHEALTH INTERPRETATION: Yoga is quickly increasing its popularity as a mind-body practice. On top of its popularity, there is a growing body of research examining the multitude of positive impacts that yoga can provide in the physiological, psychological, and immunological domains of one's life, all contributing to a greater overall quality of life. Because of these benefits, yoga has been studied as a practice that may offer these benefits to cancer patients, both during and after treatment. Previous research has suggested benefit in decreasing inflammation, decreasing stress (and the associated biological changes), improving immune response, and helping to maintain telomere (protective "caps" on the ends of chromosomes) length, all of which may disrupt cancer biology.

This paper summarized studies that had conducted yoga interventions among both adult and pediatric cancer patients during treatment. Because there were very few studies of pediatric patients, this interpretation will focus on the adult populations. Nine non-randomized studies (155 total participants) and 23 randomized controlled trials (RCT) (1022 total participant: 504 assigned to a yoga intervention and 518 assigned to a control group) were reviewed. The non-randomized studies varied in age, sex, and diagnosis, whereas the RCTs were primarily done in women with breast cancer. Most studies used a combination of movement (asana; yoga postures), breathing (pranayama; yogic breathing), and meditation. Delivery varied from single sessions, to classes up to three times per week with home practice. Most studies had adherence rates averaging about 70%. Interestingly, adherence rates were higher in the studies that involved both the patient and the patient's support person.

The majority of studies found significant improvements in mental health (mood, distress, depression and anxiety), as well as improvements in overall quality of life. Multiple studies included measurements of treatment-related side effects such as poor sleep, fatigue, pain, and nausea and vomiting, all of which showed improvements in those engaging in yoga. Although measured only in two studies, participants engaging in yoga regularly had lower salivary cortisol (one of the body's stress hormones), improved immune response, as well as lessened DNA damage. Overall, this paper illustrates a number of benefits of engaging in yoga practices while undergoing cancer treatment. InspireHealth offers multiple yoga classes each week for our members and supporters.

INTO THE VAULT

Thomas, J., Beinhorn, C., Norton, D., et al.

Managing Radiation Therapy Side Effects with Complementary Medicine

Journal of the Society for Integrative Oncology, (2010), 8(2), 65–80

ABSTRACT | Over one-third of Americans use complementary and alternative medicine (CAM). The prevalence among cancer patients may even be higher. Complementary therapies may reduce possible symptom burdens caused by conventional cancer treatments. Integrating CAM therapies has become more common and more accepted in clinical oncology. However, little research is available on beneficial CAM therapies for radiation therapy patients. This article reviews potential CAM therapies that have been shown to be effective in decreasing the symptom burden related to radiation therapy treatments and includes clinical observations from CAM practitioners in a comprehensive cancer center.

INSPIREHEALTH INTERPRETATION: This paper reviews the research examining the use of complementary medicine to manage radiation therapy side effects. Approximately 60% of people diagnosed with cancer undergo radiation therapy and common side effects may include fatigue, nausea, and pain. Complementary or alternative medicine (CAM) takes a whole person approach and includes a variety of techniques targeting the mind and body. Research on several CAM methods is reported in this paper, however not all methods have sufficient scientific evidence to be recommended as an effective or safe

treatment. It is important to note that the authors do not state the criteria for including studies in this review and therefore the quality of research reported is unknown. From the studies reviewed in this paper, an average of 31% of patients who underwent radiation therapy used CAM. The main reasons reported for seeking CAM were to minimize symptoms of traditional treatment (radiation) and to support immune system function. For managing fatigue, strong evidence supports participating in regular physical activity. Fatigue related to lack of sleep may be improved by practicing relaxation techniques such as restorative yoga. To help with insomnia, strong evidence exists for cognitive behavior therapy (a practical approach to problem solving). In terms of psychological side effects of radiation therapy (anxiety, stress, depression) various relaxation therapies have been reviewed. Progressive muscle relaxation, guided imagery, and meditation are all reported to be effective in reducing psychological side effects of radiation therapy. Massage and yoga are also reported to be beneficial. Finally, dietary modification and taking a probiotic preparation are reported to aid in management of radiation therapy-related gastrointestinal complications.

This paper also reports on CAM methods that have been researched but cannot be recommended as a treatment either because the evidence is not strong enough or because results do not report the same findings. These include valerian root for treating insomnia, herbs and supplements for addressing psychological effects, and various remedies for treating skin irritation and mouth sores. The research on energy therapies such as reiki and healing touch reports positive outcomes for managing fatigue however more research is required to understand the effectiveness of these techniques. Similarly, more research is needed to determine the effects of music therapy related to managing radiation therapy side effects. CAM therapies are relatively inexpensive and offer many options and therefore can be tailored to an individual's needs. CAM may also provide patients with a sense of empowerment as they take a role in their own health.

This review reports that certain CAM therapies can reduce radiation therapy related side effects, both physical and psychological, and improve overall quality of life. Perhaps the most important message from this paper is that caution must always be practiced when interpreting research results. Important considerations include the number of studies conducted on a certain topic, whether studies on the same topic report the same results, and most importantly, the quality of the study.

InspireHealth offers several evidence-based CAM programs such as meditation, acupuncture, relaxation and visualization. The BC Cancer Agency has curated a webpage of Complementary/Alternative Therapies Websites that are reputable and evidence-based (<http://www.bccancer.bc.ca/health-info/coping-with-cancer/complementary-alternative-therapies>).

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, and Terry Heidt, M.Sc. For more information, email library@inspirehealth.ca

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