REsearch UPDATES

For the latest in worldwide integrated cancer care

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InspireHealth
INTEGRATED CANCER CARE

Research Updates is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

Breast

Lengacher, CA, M. P. Bennett, L. Gonzalez, et al. **Immune Responses to Guided Imagery during Breast Cancer Treatment**. *Biol Res Nurs*. 2008 Jan; 93: 205-214. BACKGROUND: The use of relaxation and guided imagery to reduce stress and improve immune function has great potential benefits for patients with breast cancer. METHODS: This pilot study used a pretest-posttest experimental design with 28 breast cancer patients, aged 25 to 75 years, with the diagnosis of stage 0, 1, or 2 breast cancer. The experimental group received a relaxation and guided imagery intervention and the control group received standard care. The effects of the intervention on immune function were measured by natural killer (NK) cell cytotoxicity and IL-2-activated NK cell activity prior to surgery and 4 weeks postsurgery. NK cell activity was measured using a 15-hr incubation chromium release assay. Cytotoxicity of NK cells was measured against chromium-labeled K-562 target cells. IL-2 was used to enhance reactivity of NK cells against tumor cells. After incubation for 15 hr, cytotoxicity was measured through the release of radioactive chromium. RESULTS: Significant differences between groups were found at 4 weeks postsurgery. T-tests showed increased NK cell cytotoxicity for the intervention group at 100:1, 50:1, and 25:1 effector cell: target cell ratios (E:T) ($p < .01$ to $p < .05$) and increased activation for IL-2 at 100:1, 50:1, 25:1, and 12.5:1 (E:T) ($p < .01$ to $p < .05$) for the intervention group as compared to the control group. DISCUSSION: These findings suggest that a relaxation intervention such as guided imagery could have an effect on NK cell cytotoxicity and NK cell cytotoxicity after activation with IL-2 in patients undergoing surgery for breast cancer.

Chunlestskul, K, L. E. Carlson, J. P. Koopmans and M. Angen. **Lived Experiences of Canadian Women with Metastatic Breast Cancer in Preparation for their Death: A Qualitative Study.** *J Palliat Care.* 2008 241: 5-15.
Part I--Preparations and Consequences. OBJECTIVES: This study aimed to detail the tasks of death preparation and the consequences of such preparation for women with metastatic breast cancer. METHODS: A phenomenological qualitative approach was used. Five women with metastatic breast cancer were interviewed on two occasions. Themes were analyzed, described, and validated, until saturation was met. Outcomes of thematic analysis related to the impetus, process, and consequences of preparing for one's own death. FINDINGS: The women prepared for their death by: acknowledging their grief; preparing mentally; seeking information and support; preparing the family; and preparing for the end of life. They also engaged in creating life projects that enhanced their connections with loved ones, and lived full and joyful lives. These activities helped increased their readiness to die in peace. CONCLUSIONS: Preparing for their own death can help women with incurable cancer live full, satisfying lives, and be prepared to face their own death with peace. Helping women express their feelings around their own death and their preparation for death should be a key interdisciplinary psychosocial nursing intervention.

Part II--Enabling and Inhibiting Factors; the Paradox of Death Preparation OBJECTIVES: This study examined the essence of lived experiences of a sample of women with metastatic breast cancer in preparing themselves for their own death, with the goal of informing health provider interventions that support an acceptance of and preparation for death. METHODS: A phenomenological qualitative approach was used. Five women with metastatic breast cancer were interviewed on two occasions. Themes were analyzed, described, and validated, until saturation was met. Qualitative outcomes of the thematic analysis related to the enabling and inhibiting factors involved in preparing for one's own death. RESULTS: Factors that enabled and inhibited death preparation tasks in these women included: personal past death experiences; the availability of time and a place to think, learn, and work on death preparation activities; a chance to connect with others in similar situations; and personal and cultural attitudes towards death. Gaps and unmet needs within the health care system were identified. Finally, the paradoxical nature of various aspects of death preparation was highlighted. CONCLUSIONS: Death preparation can be accomplished through enhancing supportive care from health care professionals, with beneficial outcomes for patients and families.

Nurses should be conscious of the paradoxical nature of death preparation, and help women to confront and manage these.

Prostate

Allen, NE, T. J. Key, P. N. Appleby, et al. **Animal Foods, Protein, Calcium and Prostate Cancer Risk: The European Prospective Investigation into Cancer and Nutrition**. *Br J Cancer*. 2008 May 6; 989: 1574-1581. We examined consumption of animal foods, protein and calcium in relation to risk of prostate cancer among 142 251 men in the European Prospective Investigation into Cancer and Nutrition. Associations were examined using Cox regression, stratified by recruitment centre and adjusted for height, weight, education, marital status and energy intake. After an average of 8.7 years of follow-up, there were 2727 incident cases of prostate cancer, of which 1131 were known to be localized and 541 advanced-stage disease. A high intake of dairy protein was associated with an increased risk, with a hazard ratio for the top versus the bottom fifth of intake of 1.22 (95% confidence interval (CI): 1.07-1.41, P(trend)=0.02). After calibration to allow for measurement error, we estimated that a 35-g day(-1) increase in consumption of dairy protein was associated with an increase in the risk of prostate cancer of 32% (95% CI: 1-72%, P(trend)=0.04). Calcium from dairy products was also positively associated with risk, but not calcium from other foods. The results support the hypothesis that a high intake of protein or calcium from dairy products may increase the risk for prostate cancer.

Renal

Hu, J, Y. Chen, Y. Mao, M. DesMeules and L. Mery**. Alcohol Drinking and Renal Cell Carcinoma in Canadian Men and Women.** *Cancer Detect Prev.* 2008 321: 7-14. Background: Epidemiologic studies have reported that moderate alcohol consumption is inversely associated with the risk of renal cell carcinoma (RCC), but sex-specific results are inconsistent. The present study examines the association between alcohol intake and the risk of RCC among men and women. Methods: Mailed questionnaires were completed by 1138 newly diagnosed, histologically confirmed RCC cases and 5039 population controls between 1994 and 1997 in eight Canadian provinces. A food frequency questionnaire provided data on eating habits and alcohol consumption 2 years before data collection. Other information included socio-economic status, lifestyle habits, alcohol use, and diet. Odds ratios (ORs) and 95% confidence intervals (CIs) were derived through unconditional logistic regression. Results: Total alcohol intake was inversely associated with RCC in men and in women; the OR for the highest intake group ([greater-than or equal to]22.3 g/day among men and [greater-than or equal to]7.9 g/day among women) versus the non-drinkers was 0.7 (95% CI, 0.5-0.9) for both sexes. Analysis of menopausal status produced ORs for the highest intake group versus the non-drinkers of 1.2 (95% CI, 0.7-2.1) among premenopausal women and 0.6 (95% CI, 0.4-0.9) among postmenopausal women. Smoking and obesity were not important effect modifiers. Conclusion: Moderate alcohol consumption may be associated with a decreased risk of RCC in men and in women (mainly postmenopausal women).

Lung

Chao, C **Associations between Beer, Wine, and Liquor Consumption and Lung Cancer Risk: A Meta-Analysis**. *Cancer Epidemiology, Biomarkers & Prevention.* 2007 Nov; 1611: 2436-2447.

OBJECTIVE: Epidemiologic studies suggest that the effect on lung cancer risk may be different for beer, wine, and liquor. We conducted dose-specific meta-analyses and dose-response meta-regression to summarize findings from the current literature on the association between consumption of beer, wine, or liquor and lung cancer risk. RESULTS: Average beer consumption of one drink or greater per day was associated with an increased risk of lung cancer [relative risk (RR), 1.23; 95% confidence interval (95% CI), 1.06-1.41]. This association was observed in both men and women, although it was only significant in men. A J-shaped dose-response curve was suggested for beer intake. An inverse association was observed for both average wine consumption of less than one drink per day (RR, 0.77; 95% CI, 0.59-1.00) and one drink or greater per day (RR, 0.78; 95% CI, 0.60-1.02) in the drinking range incurred in the source studies. Average liquor consumption of one drink or greater per day was found to be associated with increased risk in men (RR, 1.33; 95% CI, 1.10-1.62). No association was observed for liquor drinking in women. The presence of heterogeneity between studies was detected. Study design, country, gender, adjustment factors, and lung cancer histologic type were not significant predictors of the heterogeneity. CONCLUSIONS: The results from this meta-analysis suggest that high consumption of beer and liquors may be associated with increased lung cancer risk, whereas modest wine consumption may be inversely associated with risk. More research with improved control of confounding is needed to confirm these findings and to establish the dose-response relationship, particularly risk at high consumption levels.

Ovarian

Barrett, SV, J. Paul, A. Hay, P. A. Vasey, S. B. Kaye and R. M. Glasspool. **Does Body Mass Index Affect Progression-Free Or overall Survival in Patients with Ovarian Cancer? Results from SCOTROC I Trial.** *Annals of Oncology.* 2008 May; 195: 898-902. Background: Previous studies have indicated an association between obesity and poor survival in several tumour types, including ovarian cancer. We sought to test the hypothesis that obesity reduces survival in a large, well-characterised and relatively homogeneous cohort of ovarian cancer patients. Patients and methods: The relationship between body mass index (BMI) and overall survival (OS) and progression-free survival (PFS) in 1067 patients participating in the Scottish Randomised Trial in Ovarian Cancer I trial was assessed. All patients received first-line carboplatin/taxane chemotherapy. The dose of carboplatin was determined by a measured glomerular filtration rate (GFR), ensuring accurate dosing in all categories of BMI and the dose of taxane was not capped. Patients were assigned to one of four categories: Underweight (BMI < 18.5), ideal weight (BMI 18.5-24.9), overweight (BMI 25-29.9) or obese (BMI [greater-than or equal to] 30). Results: There were neither statistically significant differences in PFS or OS between these four groups nor were there any differences in taxane or carboplatin dose intensity. Furthermore, there was no association between BMI and tumour stage or grade at presentation, or completeness of debulking surgery. Conclusions: Obese patients with epithelial ovarian cancer do not have a poorer prognosis, provided that they receive optimal doses of chemotherapy based on measured GFR and actual body weight. copyright The Author 2008. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved.

Lifestyle

Blanchard, CM, K. S. Courneya, K. Stein and S. C. S. -I I. American Cancer Society's. **Cancer Survivors' Adherence to Lifestyle Behavior Recommendations and Associations with Health-Related Quality of Life: Results from the American Cancer Society's SCS-II.** *Journal of Clinical Oncology.* 2008 May 1; 2613: 2198-2204.

PURPOSE: To examine the prevalence and clustering of physical activity (PA), fruit and vegetable consumption (5-A-Day), and smoking across six major cancer survivor groups and to identify any associations with health-related quality of life (HRQoL). METHODS: A total of 9,105 survivors of six different cancers completed a national cross-sectional survey that included the lifestyle behavior questions and the RAND-36 Health Status Inventory. RESULTS: Only a minority of cancer survivors were meeting the 5-A-Day (14.8% to 19.1%) or PA (29.6% to 47.3%) recommendations, whereas most were meeting the smoking recommendation (82.6% to 91.6%). In terms of the lifestyle behavior clusters, only 5% of cancer survivors were meeting all three recommendations. Analyses of covariance generally showed higher HRQoL in survivors who were meeting versus not meeting each lifestyle behavior recommendation with the strongest associations emerging for PA. Trend analyses showed a steep positive association between the number of lifestyle behavior recommendations being met and HRQoL for breast ($P < .001$), prostate ($P < .001$), colorectal ($P < .001$), bladder ($P < .001$), uterine ($P < .001$), and skin melanoma ($P < .001$) cancer survivors. CONCLUSION: Few cancer survivors are meeting the PA or 5-A-Day recommendations, and even fewer are meeting all three lifestyle recommendations. The association between the current lifestyle recommendations and HRQoL in cancer survivors appears to be cumulative. Interventions to increase PA and fruit and vegetable consumption and reduce smoking are warranted and may have additive effects on the HRQoL of cancer survivors.

Antioxidants

Saiko, P, A. Szakmary, W. Jaeger and T. Szekeres. **Resveratrol and its Analogs: Defense Against Cancer, Coronary Disease and Neurodegenerative Maladies Or just a Fad?** *Mutat Res.* 2008 Jan-Feb; 6581-2: 68-94. Resveratrol (3,5,4'-trihydroxy-trans-stilbene; RV), a dietary constituent found in grapes and wine, exerts a wide variety of pharmacological activities. Because the grape skins are not fermented in the production process of white wines, only red wines contain considerable amounts of this compound. RV is metabolized into sulfated and glucuronidated forms within approximately 15min of entering the bloodstream, and moderate consumption of red wine results in serum levels of RV that barely reach the micromolar concentrations. In contrast, its metabolites, which may be the active principle, circulate in serum for up to 9h. RV has been identified as an effective candidate for cancer chemoprevention due its ability to block each step in the carcinogenesis process by inhibiting several molecular targets such as kinases, cyclooxygenases, ribonucleotide reductase, and DNA polymerases. In addition, RV protects the cardiovascular system by a large number of mechanisms, including defense against ischemic-reperfusion injury, promotion of vasorelaxation, protection and maintenance of intact endothelium, anti-atherosclerotic properties, inhibition of low-density lipoprotein oxidation, and suppression of platelet aggregation, thereby strongly supporting its role in the prevention of coronary disease. Promising data within the use of RV have also been obtained regarding progressive neurodegenerative maladies such as Alzheimer's, Huntington's, and Parkinson's diseases. Because neurotoxicity is often related to mitochondrial dysfunction and may be ameliorated through the inclusion of metabolic modifiers and/or antioxidants, RV may provide an alternative (and early) intervention approach that could prevent further damage. RV induces a multitude of effects that depend on the cell type (e.g., NF-kappaB modulation in cancer cells vs. neural cells), cellular condition (normal, stressed, or malignant), and concentration (proliferative vs. growth arrest), and it can have opposing activities. RV affects whole pathways and sets of intracellular events rather than a single enzyme and, therefore, may be an effective therapy to restore homoestasis. Nonetheless, the question of whether RV or its metabolites can accumulate to bioactive levels in target organs remains to be addressed.

Yoga

Raghavendra, RM, R. Nagarathna, H. R. Nagendra, et al. **Effects of an Integrated Yoga Programme on Chemotherapy-Induced Nausea and Emesis in Breast Cancer Patients**. *European Journal of Cancer Care*. 2007 Nov; 166: 462-474. This study examined the effect of an integrated yoga programme on chemotherapy-related nausea and emesis in early operable breast cancer outpatients. Sixty-two subjects were randomly allocated to receive yoga (n = 28) or supportive therapy intervention (n = 34) during the course of their chemotherapy. Both groups had similar socio-demographic and medical characteristics. Intervention consisted of both supervised and home practice of yoga sessions lasting for 60 min daily, while the control group received supportive therapy and coping preparation during their hospital visits over a complete course of chemotherapy. The primary outcome measure was the Morrow Assessment of Nausea and Emesis (MANE) assessed after the fourth cycle of chemotherapy. Secondary outcomes included measures for anxiety, depression, quality of life, distressful symptoms and treatment-related toxicity assessed before and during the course of chemotherapy. Following yoga, there was a significant decrease in post-chemotherapy-induced nausea frequency (P = 0.01) and nausea intensity (P = 0.01), and intensity of anticipatory nausea (P = 0.01) and anticipatory vomiting (P = 0.05) as compared with the control group. There was a significant positive correlation between MANE scores and anxiety, depression and distressful symptoms. In conclusion, the results suggest a possible use for stress reduction interventions such as yoga in complementing conventional antiemetics to manage chemotherapy-related nausea and emesis.

Diet & Nutrition

Ghosh, C, J. A. Baker, K. B. Moysich, R. Rivera, J. R. Brasure and S. E. McCann. **Dietary Intakes of Selected Nutrients and Food Groups and Risk of Cervical Cancer**. *Nutr Cancer*. 2008 May; 603: 331-341.
We investigated the relationships between intakes of selected dietary nutrients and food groups and risk of cervical cancer in a hospital-based, case-control study including 239 cases diagnosed with squamous cell carcinoma of the cervix and 979 hospital patients with nonneoplastic diagnoses who completed a self-administered questionnaire between 1982 and 1998 at Roswell Park Cancer Institute. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by unconditional logistic regression adjusting for age, education, smoking status, use of oral contraceptives, barrier contraceptives and spermicides, family history of cervical cancer, year questionnaire completed, and energy intake. Significant reductions in risk of approximately 40-60% were observed for women in the highest vs. lowest tertiles of dietary fiber (OR = 0.59, 95% CI = 0.37-0.94), vitamin C (OR = 0.52, 95% CI = 0.33-0.80), vitamin E (OR = 0.44, 95% CI = 0.27-0.72), vitamin A (OR = 0.47, 95% CI = 0.30-0.73), alpha-carotene (OR = 0.41, 95% CI = 0.27-0.63), beta-carotene (OR = 0.44, 95% CI = 0.29-0.68), lutein (OR = 0.51, 95% CI = 0.33-0.79), folate (OR = 0.55, 95% CI = 0.34-0.88), and total fruit and vegetable intake (OR = 0.52, 95% CI = 0.34-0.77). Our findings suggest that a diet rich in plant-based nutrients may be important in reducing the risk of cervical cancer.

Colomer, R, R. Lupu, A. Papadimitropoulou, et al. Giacomo Castelvetro's Salads. **Anti-HER2 Oncogene Nutraceuticals since the 17th Century?** *Clinical & Translational Oncology: Official Publication of the Federation of Spanish Oncology Societes & of the National Cancer Institute of Mexico*. 2008 Jan; 101: 30-34. We are accumulating evidence to suggest that 17(th) century Renaissance foodways -largely based on the old "Mediterranean dietary traditions"- may provide new nutraceutical management strategies against HER2-positive breast cancer disease in the 21st

century. Epidemiological and experimental studies begin to support the notion that "The Sacred Law of Salads" (i.e., "raw vegetables... plenty of generous (olive) oil") -originally proposed in 1614 by Giacomo Castelvetro in its book The Fruit, Herbs & Vegetables of Italy- might be considered the first (unintended) example of customised diets for breast cancer prevention based on individual genetic make-up (i.e., nutraceuticals against human breast carcinomas bearing HER2 oncogene amplification/overexpression). First, the so-called salad vegetables dietary pattern (i.e., a high consumption of raw vegetables and olive oil) appears to exert a protective effect mostly confined to the HER2-positive breast cancer subtype, with no significant influence on the occurrence of HER2-negative breast cancers. Second, all the main olive oil constituents (i.e., the omega-9 monounsaturated fatty acid oleic acid and polyphenolic compounds such as the secoiridoid oleuropein or the lignan 1-[+]-acetoxypinoresinol) dramatically reduce HER2 expression and specifically induce apoptotic cell death in cultured HER2- positive breast cancer cells, with marginal effects against HER2-negative cells. Third, an olive oil-rich diet negatively influences experimental mammary tumorigenesis in rats likewise decreasing HER2 expression levels. If early 1600s Castelvetro's salads can be used as dietary protocols capable to protecting women against biologically aggressive HER2-positive breast cancer subtypes is an intriguing prospect that warrants to be evaluated in human pilot studies in the future. Here, at least, we would like to recognise Giacomo Castelvetro as the father of modern nutritional genomics in oncology.

Hu, J, C. La Vecchia, M. DesMeules, et al. **Meat and Fish Consumption and Cancer in Canada**. *Nutr Cancer.* 2008 May; 603: 313-324.
In this study, we examined the association between meat and fish intake and the risk of various cancers. Mailed questionnaires were completed by 19,732 incident, histologically confirmed cases of cancer of the stomach, colon, rectum, pancreas, lung, breast, ovary, prostate, testis, kidney, bladder, brain, non-Hodgkin's lymphomas (NHL), and leukemia and 5,039 population controls between 1994 and 1997 in 8 Canadian provinces. Measurement included information on socioeconomic status, lifestyle habits, and diet. A 69-item food frequency questionnaire provided data on eating habits 2 yr before data collection. Odds ratios and 95% confidence intervals were derived through unconditional logistic regression. Total meat and processed meat were directly related to the risk of stomach, colon, rectum, pancreas, lung, breast (mainly postmenopausal), prostate, testis, kidney, bladder, and leukemia. Red meat was significantly associated with colon, lung (mainly in men), and bladder cancer. No relation was observed for cancer of the ovary, brain, and NHL. No consistent excess risk emerged for fish and poultry, which were inversely related to the risk of a number of cancer sites. These findings add further evidence that meat, specifically red and processed meat, plays an unfavorable role in the risk of several cancers. Fish and poultry appear to be favorable diet indicators.

Exercise

Courneya, KS, D. C. McKenzie, R. D. Reid, et al**. Barriers to Supervised Exercise Training in a Randomized Controlled Trial of Breast Cancer Patients Receiving Chemotherapy.** *Annals of Behavioral Medicine.* 2008 Feb; 351: 116-122.
Background: Exercise adherence is a challenge for breast cancer patients receiving chemotherapy but few studies have identified the key barriers. Purpose: In this paper, we report the barriers to supervised exercise in breast cancer patients participating in a randomized controlled trial. Methods: Breast cancer patients initiating adjuvant chemotherapy (N=242) were randomly assigned to usual care (n=82) or supervised resistance (n=82) or aerobic (n=78) exercise. Participants randomized to the two exercise groups (n=160) were asked to provide a reason for each missed exercise session. Results: The two exercise groups attended 70.2% (5,495/7,829) of their supervised exercise sessions and provided a reason for missing 89.5% (2,090/2,334) of their unattended sessions. The 2,090 reasons represented 36 different barriers. Feeling sick (12%), fatigue (11%), loss of interest (9%), vacation (7%), and nausea/vomiting (5%) accounted for the most missed exercise sessions. Disease/treatment-related barriers (19 of the 36 barriers) accounted for 53% (1,102/2,090) of all missed exercise sessions. Demographic and medical variables did not predict the types of exercise barriers reported. Conclusions: Barriers to supervised exercise in breast cancer patients receiving chemotherapy are varied but over half can be directly attributed to the disease and its treatments. Behavioral support programs need to focus on strategies to maintain exercise in the face of difficult treatment side effects. copyright 2008 The Society of Behavioral Medicine.

CAM of the Month

He, X and Jingchuan Fan. **The Effect of a Complex Healing Treatment on 2-Year Survival Rate of Patients with Malignant Tumors.** *Integrative Cancer Therapies.* 2008 Mar; 71: 18-23. PURPOSE: The purpose of this study is to discuss the effect of an intervention measure combining oncology, psychology, and sociomedicine on survival and quality of life in cancer patients. METHODS: 639 cases of malignant tumor were divided into intervention and control groups. Follow-up was completed on 254 cases in the intervention group (93.38%) and 330 cases in the control group (89.91%). The intervention consisted of systematic mass anticancer education and rehabilitation activities guided by specialists over the period of 2 years, while the control group was in a state of self-rehabilitation. Differences between groups in survival status and survival rate for different disease stages were reviewed after 2 years. Survival status was evaluated by the Cox proportional hazards model. RESULTS: Statistical analysis of survival was controlled for sociological variables such as marriage and age. The 2-year survival in stage 2 patients was 94.84% (108/114) in the intervention group and 80.67% (121/150) in the control group. There was a striking and significant (P < .01) difference in 2-year survival rates. Further analysis disclosed that 2-year survival rate for early- and medium-stage patients was 88.03% (163/177) in the intervention group and 82.8% (184/222) in the control group. CONCLUSION: An intervention including oncology, psychology, and sociomedicine improved 2-year survival rate in early and middle stages of malignant tumor.