RE*search* UPDATES

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IN*side*

IN THIS ISSUE: Fang et al. reported that men with prostate cancer with higher levels of vitamin D had a better prognosis than those with lower levels of vitamin D. Kristal and colleagues found that lycopene did not prevent prostate cancer. Gall and associates discussed spiritual growth in relation to coping with breast cancer. Li et al. found that a high daily intake of coffee was associated with a decreased risk of ER-negative breast cancer in postmenopausal women. Lim and colleagues found that fish consumption may protect against lung cancer in never smokers. Helpman and associates reported about CAM use by women with ovarian cancer in Canada and the UK. Lai et al. found that aroma massage helped to relieve constipation in advanced cancer patients. Ando and associates found mindfulness meditation useful for coping. In our study of the month, Van Duijnhoven and colleagues reported about the association between colon cancer and cholesterol.

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PROSTATE CANCER

Fang, F, J. L. Kasperzyk, I. Shui, et al.

Prediagnostic Plasma Vitamin D Metabolites and Mortality among Patients with Prostate Cancer.

PloS one. 2011; 64: e18625.

Laboratory evidence suggests that vitamin D might influence prostate cancer prognosis. We examined the associations between prediagnostic plasma levels of 25(OH) vitamin D [25(OH)D] and 1,25(OH)(2) vitamin D [1,25 (OH)(2)D] and mortality among 1822 participants of the Health Professionals Follow-up Study and Physicians' Health Study who were diagnosed with prostate cancer. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of total mortality (n= 595) and lethal prostate cancer (death from prostate cancer or development of bone metastases; n=202). In models adjusted for age at diagnosis, BMI, physical activity, and smoking, we observed a HR of 1.22 (95% CI: 0.97, 1.54) for total mortality, comparing men in the lowest to the highest quartile of 25(OH)D. There was no association between 1,25(OH)(2)D and total mortality. Men with the lowest 25(OH)D quartile were more likely to die of their cancer (HR: 1.59; 95% CI: 1.06, 2.39) compared to those in the highest quartile ($P_{(trend)}$ = 0.006). This association was largely explained by the association between low 25(OH)D levels and advanced cancer stage and higher Gleason score, suggesting that these variables may mediate the influence of 25(OH)D on prognosis. The association also tended to be stronger among patients with samples collected within five years of cancer diagnosis. 1,25(OH)(2)D levels were not associated with lethal prostate cancer.

Although potential bias of less advanced disease due to more screening activity among men with high 25(OH)D levels cannot be ruled out, higher prediagnostic plasma 25(OH)D might be associated with improved prostate cancer prognosis.

Kristal, AR, C. Till, E. A. Platz, et al.

Serum Lycopene Concentration and Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial.

Cancer Epidemiology, Biomarkers & Prevention. 2011 Apr; 204: 638-646.

BACKGROUND: Lycopene has been promoted for prostate cancer prevention, despite the inconsistency of scientific evidence. **METHODS:** This nested case-control study examined whether serum lycopene was associated with prostate cancer risk among participants in the Prostate Cancer Prevention Trial, a placebo-controlled trial of finasteride for prostate cancer prevention. Presence or absence of cancer was determined by prostate biopsy, recommended during the trial due to elevated prostate specific antigen (PSA) level or abnormal digital rectal examination (DRE) and offered to all men at the trial end. There were 1,683 cases (461 Gleason score >= 7, 125 Gleason score >= 8) and 1,751 controls.

RESULTS: There were no associations of lycopene with prostate cancer risk. The odds ratios for a linear increase in lycopene (per 10 mug/dL) were 0.99 (95% CI: 0.94-1.04), 1.01 (0.94-1.08), and 1.02 (0.90-1.15) for Gleason 2 to 6, 7 to 10, and 8 to 10, respectively. In the placebo arm, a 10 mug/dL increase in lycopene was associated with a 7% (95% CI: 14-0) reduced risk of cancer diagnosed following an elevated PSA or abnormal DRE, which are cancers that best match those detected in screened populations. However, a 10 mug/dL increase in lycopene was also associated with an 8% (95% CI: 1-16) increased risk of cancer diagnosed without a biopsy prompt, which are cancers generally not detected. These findings were similar for low- and high-grade cancer.

CONCLUSION: This study does not support a role for lycopene in prostate cancer prevention.

IMPACT: Scientists and the public should understand that early studies supporting an association of dietary lycopene with reduced prostate cancer risk have not been replicated in studies using serum biomarkers of lycopene intake. Recommend-ations of professional societies to the public should be modified to reflect the likelihood that increasing lycopene intake will not affect prostate cancer risk.

BREAST CANCER

Gall, TL, C. Charbonneau and P. Florack.

The Relationship between religious/spiritual Factors and Perceived Growth Following a Diagnosis of Breast Cancer.

Psychol Health. 2011 Mar; 263: 287-305.

This study investigates the role of religious salience, God image and religious coping in relation to perceived growth following a diagnosis of breast cancer. Eighty-seven breast cancer patients were followed from pre-diagnosis up to 24 months post-surgery. The findings of this study provided limited support for the role of positive aspects of spirituality in relation to perceived growth. Religious involvement at pre-diagnosis was predictive of less growth at 24 months post-surgery while a positive image of God had no association with growth. While some forms of positive religious coping demonstrated positive associations, others evidenced no relationship or negative relationships with growth. Negative aspects of spirituality were more consistently related to growth with the nature of the association again depending on the type of negative spirituality being assessed. For example, passive deferral coping was related to less growth while spiritual discontent coping was related to greater growth across time.

Such findings underscore the need to attend to negative aspects of spirituality from early on in the process of cancer adjustment as such expressions may have implications for women's ability to develop and maintain a positive perspective in their coping over the long-term.

Li, J, P. Seibold, J. Chang-Claude, et al.

Coffee Consumption Modifies Risk of Estrogen-Receptor Negative Breast Cancer.

Breast Cancer Res. 2011, 13, R49

INTRODUCTION: Breast cancer is a complex disease and may be sub-divided into hormone-responsive (estrogen receptor (ER) positive) and non-hormone-responsive subtypes (ER-negative). Some evidence

suggests that heterogeneity exists in the associations between coffee consumption and breast cancer risk, according to different estrogen receptor subtypes. We assessed the association between coffee consumption and postmenopausal breast cancer risk in a large population-based study (2,818 cases and 3,111 controls), overall, and stratified by ER tumour subtypes. **METHODS:** Odds ratios (OR) and corresponding 95% confidence intervals (CI) were estimated using the multivariate logistic regression models fitted to examine breast cancer risk in a stratified case-control analysis. Heterogeneity among ER subtypes was evaluated in a case-only analysis, by fitting binary logistic regression models, treating ER status as a dependent variable, with coffee consumption included as a covariate.

RESULTS: In the Swedish study, coffee consumption was associated with a modest decrease in overall breast cancer risk in the age-adjusted model (OR> 5 cups/day compared to OR: 0.80, 95% CI: 0.64, 0.99, P trend = 0.028). In the stratified case-control analyses, a significant reduction in the risk of ER-negative breast cancer was observed in heavy coffee drinkers (OR> 5 cups/day compared to OR: 0.43, 95% CI: 0.25, 0.72, P trend = 0.0003) in a multivariate-adjusted model. The breast cancer risk reduction associated with higher coffee consumption was significantly higher for ER-negative compared to ER-positive tumours (P heterogeneity (age-adjusted) = 0.004).

CONCLUSIONS: A high daily intake of coffee was found to be associated with a statistically significant decrease in ER-negative breast cancer among postmenopausal women.

LUNG CANCER

Lim, W-, K. L. Chuah, P. Eng, et al.

Meat Consumption and Risk of Lung Cancer among Never-Smoking Women.

Nutr Cancer. 2011 August 2011; 636: 850-859.

The relationship between diet and lung cancer, apart from the protective effect of fruit and vegetables, is poorly understood. Reports on the role of dietary components such as meat are inconsistent, and few studies include sufficient numbers of nonsmokers. We examined the relationship between meat consumption and never-smoking lung cancer in a hospital-based case-control study of Singapore Chinese women, a population with low smoking prevalence. Three hundred and ninety-nine cases and 815 controls were recruited, of whom 258 cases and 712 controls were never smokers. A standardized questionnaire (which included a food frequency questionnaire module) was administered by trained interviewers. Among these never smokers, fruit and vegetable intake were inversely associated with lung cancer risk. Seventy-two percent of meat consumed was white meat (chicken or fish). Meat consumption overall was inversely associated with lung cancer [adjusted odds ratio (OR), 0.88, 0.59 for second, third tertiles, Ptrend =.012]. An inverse relationship between fish consumption and lung cancer (adjusted OR, 0.81, 0.47 for 2nd, 3rd tertiles, Ptrend .001) was observed.

No association was seen between consumption of processed meats and lung cancer, nor between dietary heterocyclic amines and lung cancer. Our data suggest that fish consumption may be protective against lung cancer in never smokers.

CAM USE IN OVARIAN CANCER

Helpman, L, S. E. Ferguson, M. Mackean, et al.

Complementary and Alternative Medicine use among Women Receiving Chemotherapy for Ovarian Cancer in 2 Patient Populations.

International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2011 Apr 2011; 213: 587-593.

The authors evaluated attitudes toward complementary and alternative medicine (CAM) use in 2 populations of women receiving chemotherapy for epithelial ovarian cancer (EOC). Women with EOC currently being treated with chemotherapy at 2 tertiary cancer centers, in Canada and the United Kingdom, completed a self-administered questionnaire on attitudes and perceptions of CAM and types of CAM used within the previous month. One hundred ninety-two patients (94 from Canada, 98 from United Kingdom) completed the questionnaire. Overall, 85 women (44%) were identified as CAM users. Complementary and alternative medicine use was more common among Canadian women (52%) compared with women from

the United Kingdom (37%), P = 0.02. Participants used 71 different types of CAM, the majority (61%) taking multiple CAM. The frequency of CAM use was the same in primary compared with recurrent disease. Eighty-nine percent of CAM users considered it important for their oncologist to be aware of CAM use. Canadian women, however, were less likely to inform their physician (Canada: 50%; United Kingdom: 81%), P = 0.02. Motivations for CAM use were the same in both populations including assist healing (60%), boost the immune system (57%), improve quality of life (48%), and relieve symptoms (45%). Thirteen percent thought CAM could cure cancer, whereas 17% thought it would prevent recurrence.

Complementary and alternative medicine use is common in women receiving chemotherapy for EOC. Increasingly, interactions between CAM and prescribed medication are being identified. Oncologists should be aware and actively inquire about CAM use. Although patterns of CAM use differed, the motivation for starting CAM was similar, highlighting the need to address supportive care in all patients.

MASSAGE

Lai, TKT, M. C. Cheung, C. K. Lo, et al.

Effectiveness of Aroma Massage on Advanced Cancer Patients with Constipation: A Pilot Study.

Complementary Therapies in Clinical Practice. 2011 February 2011; 171: 37-43.

PURPOSE: The purpose of this study was to verify the effect of aroma massage on constipation in advanced cancer patients. **METHODS:** This study employed a randomized control group pre- and post test design and included an aroma massage group, plain massage group, and control group. To evaluate the effect of aromatherapy, the degree of constipation was measured using a constipation assessment scale, severity level of constipation and the frequency of bowel movements. Data was analyzed by repeated measures of Mann-Whitney U test, Wilcoxon signed ranks test, Spearman's rho and ANOVA using SPSS program.

RESULTS: The score of the constipation assessment scale of the aroma massage group was significantly lower than the control group. Apart from the improvement in bowel movements, the results showed significantly improved quality of life in physical and support domains of the aroma massage group.

CONCLUSION: The findings of this study suggest aroma massage can help to relieve constipation in patients with advanced cancer.

MEDITATION

Ando, M, T. Morita, T. Akechi and Y. Ifuku.

A Qualitative Study of Mindfulness-Based Meditation Therapy in Japanese Cancer Patients.

Supportive Care in Cancer. 2011 July 2011; 197: 929-933.

PURPOSE: The primary objective of the study was to examine mindfulness-based meditation therapy qualitatively. A secondary goal was to examine the differences in themes selected by Japanese and Western patients receiving this therapy. **METHODS:** The subjects were 28 patients who were undergoing anti-cancer treatment. The subjects participated in two sessions of mindfulness-based meditation therapy, including breathing, yoga movement, and meditation. Each patient was taught the program in the first session, then exercised at home with a CD, and subsequently met the interviewer in a second session after 2 weeks. Primary physicians recruited the patients and interviews were conducted individually by nurses or psychologists with training in the program. Patients provided answers to pre- and post-intervention interviews about the meaning of their illness.

RESULTS: Narrative data from the semi-structured interview were analyzed qualitatively. Pre-intervention, themes such as "Effort to cope," "Looking back," "Spirituality," "Personal growth," and "Suffering" were often chosen. Post-intervention, themes such as "Adapted coping," "Personal growth," "Positive meaning," "Spirituality," and "Negative recognition" were more commonly chosen.

CONCLUSIONS: Mindfulness-based med-itation therapy may be effective for producing adapted coping, including positive recognition and changes for an adapted lifestyle. There were some common aspects and some differences in the themes selected by patients in this study and Western patients received mindfulness therapy in other studies.

CALCIUM AND VITAMIN D

Brunner, RL, J. Wactawski-Wende, B. J. Caan, et al.

The Effect of Calcium Plus Vitamin D on Risk for Invasive Cancer: Results of the Women's Health Initiative (WHI) Calcium Plus Vitamin D Randomized Clinical Trial.

Nutr Cancer. 2011 August 2011; 636: 827-841.

In the Women's Health Initiative (WHI) trial of calcium plus vitamin D (CaD), we examined the treatment effect on incidence and mortality for all invasive cancers. Postmenopausal women (N = 36,282) were randomized to 1,000 mg of elemental calcium with 400 IU vitamin D3 or placebo. Cox models estimated risk of cancer incidence and mortality. After 7.0 yr, 1,306 invasive cancers were diagnosed in the supplement and 1,333 in the placebo group [hazard ratio (HR) = 0.98; CI = 0.90, 1.05, unweighted P = 0.54]. Mortality did not differ between supplement (315, annualized% = .26) and placebo [(347, 0.28%; P = 0.17; HR = 0.90 (0.77, 1.05)]. Significant treatment interactions on incident cancer were found for family history of cancer, personal total intake of vitamin D, smoking, and WHI dietary trial randomized group. Calcium/vitamin D supplementation did not reduce invasive cancer incidence or mortality.

Supplementation lowered cancer risk in the WHI healthy diet trial arm and in women without a first-degree relative with cancer. The interactions are only suggestive given multiple testing considerations.

The low vitamin D dose provided, limited adherence, and lack of serum 25(OH)D values should be considered when interpreting these findings.

STUDY OF THE MONTH

Van Duijnhoven, FJB, H. B. Bueno-De-Mesquita, M. Calligaro, et al.

Blood Lipid and Lipoprotein Concentrations and Colorectal Cancer Risk in the European Prospective Investigation into Cancer and Nutrition.

Gut. 2011 August 2011; 608: 1094-1102.

OBJECTIVE: To examine the association between serum concentrations of total cholesterol, high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol, triglycerides, apolipoprotein A-I (apoA), apolipoprotein B and the incidence of colorectal cancer (CRC). **DESIGN:** Nested case-control study. **SETTING:** The study was conducted within the European Prospective Investigation into Cancer and Nutrition (EPIC), a cohort of more than 520 000 participants from 10 western European countries. Participants: 1238 cases of incident CRC, which developed after enrolment into the cohort, were matched with 1238 controls for age, sex, centre, followup time, time of blood collection and fasting status. **MAIN OUTCOME MEASURES:** Serum concen-trations were quantitatively determined by colorimetric and turbidimetric methods. Dietary and lifestyle data were obtained from questionnaires. Conditional logistic regression models were used to estimate incidence rate ratios (RRs) and 95% CIs which were adjusted for height, weight, smoking habits, physical activity, education, consumption of fruit, vegetables, meat, fish, alcohol, fibre and energy.

RESULTS: After adjustments, the concentrations of HDL and apoA were inversely associated with the risk of colon cancer (RR for 1 SD increase of 16.6 mg/dl in HDL and 32.0 mg/dl in apoA of 0.78 (95% CI 0.68 to 0.89) and 0.82 (95% CI 0.72 to 0.94), respectively). No association was observed with the risk of rectal cancer. Additional adjustment for biomarkers of systemic inflammation, insulin resistance and oxidative stress or exclusion of the first 2 years of follow-up did not influence the association between HDL and risk of colon cancer.

CONCLUSIONS: These findings show that high concentrations of serum HDL are associated with a decreased risk of colon cancer. The mechanism behind this association needs further elucidation.

ELECTRONIC RESEARCH UPDATES - BONUS ABSTRACTS

PROSTATE CANCER

Lazarevic, B, G. Boezelijn, L. M. Diep, et al.

Efficacy and Safety of Short-Term Genistein Intervention in Patients with Localized Prostate Cancer Prior to Radical Prostatectomy: A Randomized, Placebo-Controlled, Double-Blind Phase 2 Clinical Trial.

Nutr Cancer. 2011 August 2011; 636: 889-898.

We conducted a placebo-controlled, block-randomized double-blind Phase 2 study to examine the effect of 30 mg synthetic genistein daily on serum and tissue biomarkers in patients with localized prostate cancer (CaP). Fifty-four study subjects were recruited and randomized to treatment with genistein (n = 23) or placebo (n = 24) for 3 to 6 wk prior to prostatectomy. Seven study subjects were noncompliant to the study protocol. Adverse events were few and mild. Serum prostate specific antigen (PSA) decreased by 7.8% in the genistein arm and increased by 4.4% in the placebo arm (P= 0.051). The PSA level was reduced in tumor tissue compared to normal tissue in the placebo arm. In the genistein arm, the PSA level in tumor and normal tissue was comparable. Total cholesterol was significantly lower in the genistein arm (P = 0.013). There were no significant effects on thyroid or sex hormones. Plasma concentrations of total genistein were on average 100-fold higher in the genistein arm after treatment (P < 0.001).

Genistein at a dose that can be easily obtained from a diet rich in soy reduced the level of serum PSA in patients with localized CaP, without any effects on hormones. It was well tolerated and had a beneficial effect on blood cholesterol.

BREAST CANCER

Franca, CA, C. R. Nogueira, A. Ramalho, et al.

Serum Levels of Selenium in Patients with Breast Cancer before and After Treatment of External Beam Radiotherapy.

Annals of Oncology. 2011 May; 225: 1109-1112.

BACKGROUND: To evaluate the influence of radiotherapy on the selenium serum levels of breast cancer patients. **PATIENTS AND METHODS:** This prospective study includes 209 breast cancer patients treated by external beam radiotherapy from December 2007 until August 2008. Plasma selenium concentrations were determined before and at the end of the radiotherapeutic treatment. Age, clinical stage, prior chemotherapy, body mass index (BMI) and personal habits (smoking and alcoholism) were recorded for each patient.

RESULTS: The mean age was 61 years; the mean BMI was 28.7. One hundred and seventy-four patients (83.3%) were nonsmokers. One hundred and eighty-nine patients (90.4%) showed no drinking habits and 110 (52.6%) have no prior chemotherapy. Sixty patients (28.7%) were in clinical stage I, 141 (67.5%) in clinical stage II and 8 (3.8%) in clinical stage III. At the beginning of radiotherapy, the mean selenium value for all patients was 86.4 mug/l and after radiation this value dropped to 47.8 mug/l. Multivariate analysis showed statistically significant difference in the plasma selenium concentration before and after radiotherapy for age (P > 0.001), BMI (P > 0.001), smoking (P > 0.001), alcoholism (P > 0.001), chemotherapy (P > 0.001) and clinical stage (P > 0.001).

CONCLUSIONS: Significant reduction in plasma levels of selenium is recorded in patients undergoing radiotherapy, suggesting attention to the nutritional status of this micronutrient and other antioxidant agents.

Vignes, S, R. Porcher, M. Arrault and A. Dupuy.

Factors Influencing Breast Cancer-Related Lymphedema Volume After Intensive Decongestive Physiotherapy.

Supportive Care in Cancer. 2011 July 2011; 197: 935-940.

BACKGROUND: Lymphedema treatment is based on an intensive decongestive physiotherapy phase of

volume reduction followed by a long-term maintenance phase. Factors influencing the morbid lymphedema volume increase during maintenance were analyzed. **MATERIALS AND METHODS:** Among 867 consecutive women recruited and followed in a single lymphology unit, 682 were analyzed. The other 185 were not analyzed because of an initial lymphedema volume =50% of the total reduction obtained during the intensive phase.

RESULTS: Median lymphedema volume was 936 ml before and 335 ml after intensive decongestive physiotherapy (P< 0.0001). Median follow-up was 28 months. During the maintenance phase, the risk of treatment failure at 1, 2, and 4 years was estimated to be 38.1%, 53.1%, and 64.8%, respectively. Wearing an elastic sleeve during the day and an overnight multilayer low-stretch bandage (median, four nights per week; interquartile range, 2-6) significantly decreased the risk of treatment failure [hazard ratio, 0.53, (0.34-0.82), P=0.004], whereas manual lymph drainage adjunction to those therapeutic components did not. The risk of treatment failure was also associated with weight and body mass index at inclusion.

CONCLUSION: Risk of maintenance-therapy failure after intensive decongestive physiotherapy was associated with patients characteristics (younger age, higher weight, and body mass index), while elastic sleeve and bandage were associated with better maintenance results. Paradoxical effect of manual lymph drainage is likely to be related to indication bias.

LUNG CANCER

Ganesh, B, S. Sushama, S. Monika and P. Suvarna.

A Case-Control Study of Risk Factors for Lung Cancer in Mumbai, India.

Asian Pacific Journal of Cancer Prevention: *Apjcp*. 2011 122: 357-362.

In the year 2010, it is estimated that nearly 1.35 million new cases and 1.18 million deaths with lung cancer occurred. In India, among males, lung cancer rates vary across the country which has encouraged us to conduct a case-control study to study the risk factors. The present unmatched hospital-based case-control study conducted at Tata Memorial Hospital included subjects registered between the years 1997-99. There were 408 lung 'cancer cases' and 1383 'normal controls'. Data on age, tobacco habits, occupational history, dietary factors, tea, coffee were collected by the social investigators. Univariate and regression analysis were applied for obtaining the odds ratio for risk factors. In the study, cigarette smoking (OR=5.2) and bidi smoking (OR=8.3), as well as alcohol consumption (OR=1.8), demonstrated dose-response relationships with lung cancer risk.

Among the dietary items, only red-meat consumption showed 2.2-fold significant excess risk. Consumption of milk showed a 60% reduction in risk; while coffee showed a 2-fold excess risk for lung cancer. In addition, exposure to use of pesticides showed a 2.5-fold significant excess risk for lung cancer.

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