

REsearch UPDATES

FOR THE LATEST IN WORLDWIDE INTEGRATED CANCER CARE

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IN THIS ISSUE: Since summer is finally here, people will probably start thinking a bit more about their diets and exercise routines. In keeping with that theme, this month's issue provides some evidence of the benefits of a good diet and regular exercise. For instance, Richman et al. found that brisk walking may prevent or delay prostate cancer progression. Sanchez-Zamorano and colleagues found that a healthy lifestyle that incorporates things such as a good diet, exercise, and limiting alcohol and tobacco can prevent breast cancer. Boyle and associates found that long-term sedentary work was associated with an increased risk of colorectal cancer. Couto et al. found evidence to support the conclusion that a Mediterranean diet can reduce the risk of cancer in general. In our study of the month, George et al. found that women with breast cancer improved their prognosis by adopting a better quality diet and more exercise.

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PROSTATE CANCER

Richman, EL, S. A. Kenfield, M. J. Stampfer, et al.

Physical Activity After Diagnosis and Risk of Prostate Cancer Progression: Data from the Cancer of the Prostate Strategic Urologic Research Endeavor.

Cancer Res. 2011 May 24;7111:1-7.

BACKGROUND: Vigorous activity after diagnosis was recently reported to be inversely associated with prostate cancer-specific mortality. However, men with metastatic disease may decrease their activity due to their disease; thus, a causal interpretation is uncertain. **METHODS:** We therefore prospectively examined vigorous activity and brisk walking after diagnosis in relation to risk of prostate cancer progression, an outcome less susceptible to reverse causation, among 1,455 men diagnosed with clinically localized prostate cancer. Cox proportional hazards regression was used to examine vigorous activity, nonvigorous activity, walking duration, and walking pace after diagnosis and risk of prostate cancer progression.

RESULTS: We observed 117 events (45 biochemical recurrences, 66 secondary treatments, 3 bone metastases, 3 prostate cancer deaths) during 2,750 person-years. Walking accounted for nearly half of all activity. Men who walked briskly for 3 h/wk or more had a 57% lower rate of progression than men who walked at an easy pace for less than 3 h/wk (HR = 0.43; 95% CI: 0.21-0.91; P = 0.03). Walking pace was associated with decreased risk of progression independent of duration (HR brisk vs. easy pace = 0.52; 95% CI: 0.29-0.91; P_{trend} = 0.01). Few men engaged in vigorous activity, but there was a suggestive inverse association (HR ≥3 h/wk vs. none = 0.63; 95% CI: 0.32-1.23; P_{trend} = 0.17). Walking duration and total nonvigorous activity were not associated with risk of progression independent of pace or vigorous activity, respectively.

CONCLUSION: Brisk walking after diagnosis may inhibit or delay prostate cancer progression among men diagnosed with clinically localized prostate cancer.



BREAST CANCER



Sanchez-Zamorano, LM, L. Flores-Luna, A. Angeles-Llerenas, et al.

Healthy Lifestyle on the Risk of Breast Cancer.

Cancer Epidemiology Biomarkers and Prevention. 2011 May 2011; 205: 912-922.

BACKGROUND: Many studies have analyzed the effect of behavioral risk factors such as common lifestyle patterns on the risk of disease. The aim of this study was to assess the effect of a healthy lifestyle index on the risk of breast cancer. **METHODS:** A population-based case-control study was conducted in Mexico from 2004 to 2007. One thousand incident cases and 1,074 controls, matched to cases by 5-year age category, region, and health institution, participated in the study. A healthy lifestyle index was developed by means of principal components by using dietary pattern, physical activity, alcohol consumption, and tobacco smoking. A conditional logistic regression model was used to assess this association.

RESULTS: The healthy lifestyle index was defined as the combined effect of moderate and/or vigorous-intensity physical activity, low consumption of fat, processed foods, refined cereals, complex sugars, and the avoidance of tobacco smoking and alcohol consumption. Results showed a protective effect on both pre- (OR = 0.50, 95% CI: 0.29-0.84) and postmenopausal women (OR = 0.20, 95% CI: 0.11-0.37) when highest versus lowest index quintiles were compared.

CONCLUSIONS: Healthy lifestyle was associated with a reduction in the odds of having breast cancer. Primary prevention of this disease should be promoted in an integrated manner. Effective strategies need to be identified to engage women in healthy lifestyles.

IMPACT: This study is the first to assess a healthy lifestyle index in relation to the risk of breast cancer.

Bertram, LAC, M. L. Stefanick, N. Saquib, et al.

Physical Activity, Additional Breast Cancer Events, and Mortality among Early-Stage Breast Cancer Survivors: Findings from the WHEL Study.

Cancer Causes and Control. 2011 March 2011; 223: 427-435.

OBJECTIVE: Research suggests that physical activity is associated with improved breast cancer survival, yet no studies have examined the association between post-diagnosis changes in physical activity and breast cancer outcomes. The aim of this study was to determine whether baseline activity and 1-year change in activity are associated with breast cancer events or mortality. **METHODS:** A total of 2,361 post-treatment breast cancer survivors (Stage I-III) enrolled in a randomized controlled trial of dietary change completed physical activity measures at baseline and one year. Physical activity variables (total, moderate-vigorous, and adherence to guidelines) were calculated for each time point. Median follow-up was 7.1 years. Outcomes were invasive breast cancer events and all-cause mortality.

RESULTS: Those who were most active at baseline had a 53% lower mortality risk compared to the least active women (HR = 0.47; 95% CI: 0.26, 0.84; $p = .01$). Adherence to activity guidelines was associated with a 35% lower mortality risk (HR = 0.65, 95% CI: 0.47, 0.91; $p < .01$). Neither baseline nor 1-year change in activity was associated with additional breast cancer events.

CONCLUSIONS: Higher baseline (post-treatment) physical activity was associated with improved survival. However, change in activity over the following year was not associated with outcomes. These data suggest that long-term physical activity levels are important for breast cancer prognosis.

GLIOBLASTOMA

Baglietto, L, G. G. Giles, D. R. English, et al.

Alcohol Consumption and Risk of Glioblastoma; Evidence from the Melbourne Collaborative Cohort Study.

International Journal of Cancer. 2011 15 Apr 2011; 1288: 1929-1934.

BACKGROUND: Despite the brain being highly susceptible to the action of alcohol and, therefore, potentially susceptible to its carcinogenic effects, it is not clear whether alcohol consumption is associated with risk of glioblastoma. **METHODS:** We analyzed data from 39,766 participants of the Melbourne



Collaborative Cohort Study recruited in 1990-1994 and followed to the end of 2008 for an average of 15 years. Incidence of glioblastoma of the brain was ascertained via linkage to the Victorian and other State cancer registries in Australia. During a structured face-to-face interview at baseline we elicited each participant's history of alcoholic beverage consumption during the current decade at baseline. We used Cox regression models with age as the time metric, adjusted for country of birth, sex, total energy intake, educational attainment and coffee consumption to estimate hazard ratios (HR) and corresponding 95% confidence intervals (CI).

RESULTS: A total of 67 glioblastomas was diagnosed in the cohort during follow-up. The HRs associated with each additional 10 grams per day of alcohol intake was 1.16 (95% CI, 1.05 to 1.29; p for linear trend = 0.007). Compared to lifetime abstainer, the HR for glioblastoma associated with alcohol consumption were 1.07 (0.55 to 2.10) for 1 to 19 g/day, 1.79 (0.81 to 3.95) for 20 to 39 g/day, 3.07 (1.26 to 7.47) for 40 to 59 g/day and 2.54 (0.92 to 7.00) for 60 or more g/day.

CONCLUSION: Alcohol consumption at baseline was associated with the risk of glioblastoma in a dose-response relationship.

COLORECTAL CANCER

Boyle, T, L. Fritschi, J. Heyworth and F. Bull.

Long-Term Sedentary Work and the Risk of Subsite-Specific Colorectal Cancer.

Am J Epidemiol. 2011 15 May 2011; 17310: 1183-1191.

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BACKGROUND: Research suggests that sedentary behavior may increase the risk of some chronic diseases. **OBJECTIVE:** The aims of the study were to examine whether sedentary work is associated with colorectal cancer and to determine whether the association differs by subsite. **SUBJECTS:** A total of 918 cases and 1,021 controls participated in a population-based case-control study of colorectal cancer in Western Australia in 2005-2007. **METHODS:** Data were collected on lifestyle, physical activity, and lifetime job history. The estimated effects of sedentary work on the risk of cancers of the proximal colon, distal colon, and rectum were analyzed by using multinomial logistic regression.

RESULTS: Compared with participants who did not spend any time in sedentary work, participants who spent 10 or more years in sedentary work had almost twice the risk of distal colon cancer (adjusted odds ratio = 1.94, 95% confidence interval: 1.28, 2.93) and a 44% increased risk of rectal cancer (adjusted odds ratio = 1.44, 95% confidence interval: 0.96, 2.18). This association was independent of recreational physical activity and was seen even among the most recreationally active participants. Sedentary work was not associated with the risk of proximal colon cancer.

CONCLUSION: These results suggest that long-term sedentary work may increase the risk of distal colon cancer and rectal cancer.

Loh, YH, P. Jakszyn, R. N. Luben, et al.

N-Nitroso Compounds and Cancer Incidence: The European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk Study.

Am J Clin Nutr. 2011 01 May 2011; 935: 1053-1061.

BACKGROUND: Humans are exposed to preformed N-nitroso compounds (NOCs) and endogenous NOCs. Several NOCs are potential human carcinogens, including N-nifrosodimefhyamine (NDMA), but evidence from population studies is inconsistent. **OBJECTIVE:** We examined the relation between dietary NOCs (NDMA), the endogenous NOC index, and dietary nitrite and cancer incidence in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk, United Kingdom, study. **DESIGN:** This was a prospective study of 23,363 men and women, aged 40-79 y, who were recruited in 1993-1997 and followed up to 2008. The baseline diet was assessed with food-frequency questionnaires.

RESULTS: There were 3268 incident cancers after a mean follow-up of 11.4 y. Dietary NDMA intake was significantly associated with increased cancer risk in men and women [hazard ratio (HR): 1.14; 95% CI: 1.03, 1.27; P for trend = 0.03] and in men (HR: 1.24; 95% CI: 1.07, 1.44; P for trend = 0.005) when the highest



quartile was compared with the lowest quartile in age- and sex-adjusted analyses but not in multivariate analyses (HR: 1.10; 95% CI: 0.97, 1.24; HR for men: 1.18; 95% CI: 1.00, 1.40; P for trend > 0.05). When continuously analyzed, NDMA was associated with increased risk of gastrointestinal cancers (HR: 1.13; 95% CI: 1.00, 1.28), specifically of rectal cancer (HR: 1.46; 95% CI: 1.16, 1.84) per 1-SD increase after adjustment for age, sex, body mass index, cigarette smoking status, alcohol intake, energy intake, physical activity, education, and menopausal status (in women). The endogenous NOC index and dietary nitrite were not significantly associated with cancer risk. There was a significant interaction between plasma vitamin C concentrations and dietary NDMA intake on cancer incidence (P for interaction < 0.0001).

CONCLUSIONS: Dietary NOC (NDMA) was associated with a higher gastrointestinal cancer incidence, specifically of rectal cancer. Plasma vitamin C may modify the relation between NDMA exposure and cancer risk.

BLADDER CANCER

Choi, H, S. H. Kang, D. K. Yoon, et al.

Chewing Gum has a Stimulatory Effect on Bowel Motility in Patients After Open Or Robotic Radical Cystectomy for Bladder Cancer: A Prospective Randomized Comparative Study.

Urology. 2011 April 2011; 774: 884-890.

OBJECTIVES: To determine whether chewing gum during the postoperative period facilitates the recovery of bowel function and has different efficacy according to operative method used in patients with radical cystectomy. **METHODS:** From July 2007 to September 2009, we randomized open radical cystectomy (ORC) patients into Group AI (ORC without gum chewing) and Group AII (ORC with gum chewing). Robot-assisted radical cystectomy (RARC) patients were randomized into Group BI (RARC without gum chewing) and Group BII (RARC with gum chewing).

RESULTS: A total of 32 ORC (17 Group AI and 15 Group AII) and 28 RARC (13 Group BI and 15 Group BII) patients were completed. The patient's perioperative data between the control (AI + BI) and chewing gum (AII + BII) group showed no differences. The median time to flatus and to bowel movement were significantly reduced in chewing gum group compared with the control patients: 57.1 vs. 69.5 hours 76.7 vs. 93.3 hours. In the ORC patients, decrease in time to flatus and bowel movement were observed in gum chewing (AII) group than control (AI) group: 64.3 vs. 80.3 hours 83.8 vs. 104.2 hours. In RARC patients, decrease in time to flatus and bowel movement were found in gum chewing (BII) group than control (BI) group: 48.8 vs. 60.3 hours 69.1 vs. 84.6 hours. No adverse effects were observed with chewing gum.

CONCLUSIONS: Chewing gum had stimulatory effects on bowel motility after cystectomy and urinary diversion. Chewing gum was safe and could be used for postoperative ileus regardless of the operative method (ORC or RARC).

MEDITERRANEAN DIET

Couto, E, P. Boffetta, P. Lagiou, et al.

Mediterranean Dietary Pattern and Cancer Risk in the EPIC Cohort.

Br J Cancer. 2011 26 Apr 2011; 1049: 1493-1499.

BACKGROUND: Although several studies have investigated the association of the Mediterranean diet with overall mortality or risk of specific cancers, data on overall cancer risk are sparse. **METHODS:** We examined the association between adherence to Mediterranean dietary pattern and overall cancer risk using data from the European Prospective Investigation Into Cancer and nutrition, a multi-centre prospective cohort study including 142 605 men and 335 873 [women]. Adherence to Mediterranean diet was examined using a score (range: 0-9) considering the combined intake of fruits and nuts, vegetables, legumes, cereals, lipids, fish, dairy products, meat products, and alcohol. Association with cancer incidence was assessed through Cox regression modelling, controlling for potential confounders.

RESULTS: In all, 9669 incident cancers in men and 21 062 in women were identified. A lower overall cancer risk was found among individuals with greater adherence to Mediterranean diet (hazard ratio 0.96, 95% CI



0.95-0.98) for a two-point increment of the Mediterranean diet score. The apparent inverse association was stronger for smoking-related cancers than for cancers not known to be related to tobacco (P (heterogeneity) 0.008). In all, 4.7% of cancers among men and 2.4% in women would be avoided in this population if study subjects had a greater adherence to Mediterranean dietary pattern.

CONCLUSION: Greater adherence to a Mediterranean dietary pattern could reduce overall cancer risk.

ACUPUNCTURE

Simcock, R, L. Fallowfield and V. Jenkins.

Group Acupuncture to Relieve Radiation Induced Xerostomia: A Feasibility Study.

Acupuncture in Medicine. 2009 Sep; 273: 109-113.

BACKGROUND: a distressing complication of radiotherapy treatment for head and neck cancer is xerostomia (chronic oral dryness). Xerostomia is difficult to treat conventionally but there are reports that acupuncture can help. We conducted a feasibility study to examine the acceptability of a standardised group acupuncture technique and adherence to group sessions, together with acceptability of the objective and subjective measurements of xerostomia. **METHODS:** 12 males with established radiation induced xerostomia were treated in three groups of four. Each received eight weekly sessions of acupuncture using four bilateral acupuncture points (Salivary Gland 2; Modified Point Zero; Shen Men and one point in the distal radial aspect of each index finger (LI1)). Sialometry and quality of life assessments were performed at baseline and at the end of treatment. A semi-structured interview was conducted a week after completing the intervention.

RESULTS: adherence to and acceptability of the treatment and assessments was 100%. There were objective increases in the amounts of saliva produced for 6/12 patients post intervention and the majority also reported subjective improvements. Mean quality of life scores for domains related to salivation and xerostomia also showed improvement. At baseline 92% (11/12) patients reported experiencing a dry mouth "quite a bit/very much" as compared to 42% (5/12) after the treatment. Qualitative data revealed that the patients enjoyed the sessions.

CONCLUSION: the pilot study shows that a standardised group technique is deliverable and effective. The tools for objective and subjective assessment are appropriate and acceptable. Further examination in a randomised trial is now warranted.

STUDY OF THE MONTH

George, SM, M. L. Irwin, A. W. Smith, et al.

Postdiagnosis Diet Quality, the Combination of Diet Quality and Recreational Physical Activity, and Prognosis After Early-Stage Breast Cancer.

Cancer Causes and Control. 2011 April 2011; 224: 589-598.

OBJECTIVE: To investigate, among women with breast cancer, how postdiagnosis diet quality and the combination of diet quality and recreational physical activity are associated with prognosis. **METHODS:** This multiethnic, prospective observational cohort included 670 women diagnosed with local or regional breast cancer. Thirty months after diagnosis, women completed self-report assessments on diet and physical activity and were followed for 6 years. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals for death from any cause and breast cancer death.

RESULTS: Women consuming better-quality diets, as defined by higher Healthy Eating Index-2005 scores, had a 60% reduced risk of death from any cause (HR_{q4;q1}:0.40, 95%CI: 0.17, 0.94) and an 88% reduced risk of death from breast cancer (HR_{q4;q1}:0.12, 95% CI: 0.02, 0.99). Compared with inactive survivors consuming poor-quality diets, survivors engaging in any recreational physical activity and consuming better-quality diets had an 89% reduced risk of death from any cause (HR: 0.11, 95% CI: 0.04, 0.36) and a 91% reduced risk of death from breast cancer (HR: 0.09, 95% CI: 0.01, 0.89). Associations observed were independent of obesity status.

CONCLUSION: Women diagnosed with localized or regional breast cancer may improve prognosis by adopting better-quality dietary patterns and regular recreational physical activity. Lifestyle interventions emphasizing postdiagnosis behavior changes are advisable in breast cancer survivors.



ELECTRONIC RESEARCH UPDATES - BONUS ABSTRACTS

PROSTATE CANCER

Bourke, L, H. Doll, H. Crank, A. et al.

Lifestyle Intervention in Men with Advanced Prostate Cancer Receiving Androgen Suppression Therapy: A Feasibility Study.

Cancer Epidemiology Biomarkers and Prevention. 2011 April 2011; 204: 647-657.

BACKGROUND: Healthy lifestyle behaviors could have a role in ameliorating some of the adverse effects of androgen suppression therapy (AST) in men with prostate cancer. The primary aim of this study was to assess the feasibility of a tapered supervised exercise program in combination with dietary advice in men with advanced prostate cancer receiving AST. **METHODS:** Advanced prostate cancer patients receiving AST for a minimum of 6 months were randomized to a 12-week lifestyle program comprising aerobic and resistance exercise, plus dietary advice (n = 25), or standard care (n = 25). Exercise behavior, dietary macronutrient intake, quality of life, fatigue, functional fitness, and biomarkers associated with disease progression were assessed at baseline, after the intervention, and at 6 months.

RESULTS: The lifestyle group showed improvements in exercise behavior (P < 0.001), dietary fat intake (P = 0.001), total energy intake (P = 0.005), fatigue (P = 0.002), aerobic exercise tolerance (P < 0.001), and muscle strength (P = 0.033) compared with standard care controls. Although a high rate of attrition (44%) was observed at 6 months, the improvements in key health outcomes were sustained. No effects on clinical prostate cancer disease markers were observed.

CONCLUSIONS: This preliminary evidence suggests that pragmatic lifestyle interventions have potential to evoke improvements in exercise and dietary behavior, in addition to other important health outcomes in men with advanced prostate cancer receiving AST. Impact: This study shows for the first time that pragmatic lifestyle interventions are feasible and could have a positive impact on health behaviors and other key outcomes in men with advanced prostate cancer receiving AST.



KIDNEY CANCER

Trinh, L, R. C. Plotnikoff, R. E. Rhodes, et al.

Associations between Physical Activity and Quality of Life in a Population-Based Sample of Kidney Cancer Survivors.

Cancer Epidemiology Biomarkers and Prevention. 2011 May 2011; 205: 859-868.

BACKGROUND: Physical activity (PA) improves quality of life (QoL) in several cancer survivor groups, but no study to date has focused on kidney cancer survivors (KCS). The purpose of this study was to estimate the prevalence of PA in KCS and determine any associations with QoL. **METHODS:** All 1,985 KCS diagnosed between 1996 and 2010 identified through a Canadian provincial Registry were mailed a survey that consisted of the Godin Leisure Time Exercise Questionnaire and several Functional Assessment of Cancer Therapy QoL scales. Standard demographic and medical variables were also reported.

RESULTS: Completed surveys were received from 703 (43%) of the 1,654 KCS that received the survey. Over half (56.3%) were completely sedentary (CS), 17.6% were insufficiently active, 11.9% were active within public health guidelines, and 14.1% exceeded public health guidelines. After adjustment for key demographic and medical covariates, analyses of covariance indicated a dose - response association between PA and most QoL outcomes from CS to within guidelines (WG) with no further improvements for exceeding guidelines. For the primary QoL outcome of patient-reported physical functioning, the overall difference between CS and WG was 8.6 points (95% CI: 4.2-12.9, P < 0.001) which exceeds the minimally important difference of 5.0 points for this scale. Few associations were moderated by demographic or medical variables.

CONCLUSION: Over half of KCS are CS; however, even some PA may be beneficial for QoL. Impact: PA is a modifiable lifestyle factor that may have implications for QoL and disease outcomes in KCS.

COLORECTAL CANCER

Jefford, M, K. Lotfi-Jam, C. Baravelli, et al.

Development and Pilot Testing of a Nurse-Led Posttreatment Support Package for Bowel Cancer Survivors.

Cancer Nurs. 2011 May-June 2011; 343: E1-E10.

BACKGROUND: Colorectal cancer (CRC) is the most common cancer affecting both men and women in Australia. The illness and related treatments can cause distressing adverse effects, impact on emotional and psychological well-being, and adversely affect social, occupational, and relationship functioning. Current models of follow-up fail to address the complex needs arising after treatment completion. Strategies to better prepare and support survivors are urgently required. **OBJECTIVES:** This study aimed to develop and pilot test an innovative supportive care program for people with potentially curative CRC. **METHODS:** The SurvivorCare intervention was developed by a multidisciplinary team using 3 key principles: (1) promote patient involvement and engagement; (2) address the specific needs of individual patients, and (3) use evidence-based strategies to promote well-being and reduce treatment sequelae. It also addressed 4 essential components of survivorship planning, defined by the US Institute of Medicine. Ten survivors completed questionnaires and satisfaction interviews before and after receiving the intervention.

RESULTS: SurvivorCare comprises survivorship educational materials (booklet, DVD, and question prompt list), a tailored survivorship care plan, a tailored nurse-led end-of-treatment consultation, and 3 follow-up telephone calls. Pilot data demonstrated that survivors considered the intervention appropriate, relevant, and useful.

CONCLUSIONS: SurvivorCare is a well-received, comprehensive intervention that will now be evaluated in a randomized controlled trial aiming to reduce distress and unmet needs and improve quality of life in CRC survivors. **Implications For Practice:** If SurvivorCare is shown to be effective, it will be possible to quickly and broadly disseminate this model of care.



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