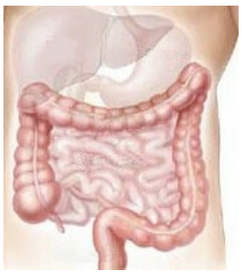
Colorectal Cancer Association of Canada

COLORECTAL CANCER RESEARCH UPDATES

Month Ending June 10, 2016



The following colorectal cancer research update extends from April 16th, – June 10th, 2016 inclusive and is intended for informational purposes only.

CONTENT

22. Fat-rich, low fibre diet may up colorectal cancer risk (May 23/16)

DRUGS / SYSTEMIC THERAPIES

1. USPSTF Backs Aspirin for Primary Prevention (Apr 11/16)

In a finalized update of guidelines regarding aspirin use in the primary prevention of cardiovascular disease and colorectal cancer, the U.S. Preventive Services Task Force (USPSTF) now recommends that individuals between the ages of 50-59 who are at an increased risk for cardiovascular disease (10% or greater 10-year risk) and do not have an elevated risk of bleeding should consider aspirin as primary prevention. Their recommendation did not extend to adults between the ages of 60-69. While aspirin is widely accepted for secondary prevention in patients with existing cardiovascular disease, its use in primary prevention has been greatly contested over the years. The 2009 USPSTF recommendations for aspirin use in the primary prevention of cardiovascular disease suggested its usefulness in a wider age range (45-79) in both men and women, while earlier guidelines discouraged aspirin and nonsteroidal anti-inflammatory drugs (NSAIDS) in the prevention of colorectal cancer at all. Low-dose daily aspirin can aid in the prevention of cardiovascular disease and colorectal cancer, but it has also been linked to gastrointestinal bleeding and haemorrhagic strokes. Despite the updated USPSTF recommendations, some healthcare professionals still believe that current data with aspirin in primary prevention are inconclusive, given that a large part of the data comes from trials among low-risk individuals. Several well-designed trials in higher-risk individuals without cardiovascular disease, such as the elderly or people with diabetes among other risk factors, are currently underway with results expected in the next five years.

http://www.medpagetoday.com/Cardiology/CardioBrief/57299

2. Vitamin C may kill cancer cells in KRAS-mutant colorectal cancer (Apr 19/16)

A recent study examined the effect of high doses of vitamin C in inducing cell death among KRAS-mutant colorectal cancers. It was observed that the doses of vitamin C required to induce cell death are far higher than what is normally attainable through traditional diets or supplements, indicating that intravenous administration would be necessary. Trials are currently being designed to test this potential treatment in human patients with KRAS-mutant colorectal cancers.

http://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/online/%7B49c88d85-8e50-451f-993e-3b452047ba9d%7D/video-vitamin-c-may-kill-cancer-cells-in-kras-mutant-colorectal-cancer

3. Trastuzumab Plus Lapatinib Active in Refractory HER2+ Metastatic Colorectal Cancer (Apr 21/16)

A recent study demonstrated that among patients with refractory human epidermal growth factor 2 (HER2) – positive metastatic colorectal cancer, the combination of trastuzumab (Herceptin) and the kinase inhibitor lapatinib (Tyverb/Tykerb) was active and well-tolerated. Both drugs are indicated in the treatment of HER2-overexpressing breast cancer, and trastuzumab is approved in the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma. Previous research has demonstrated that the blockade of HER2 with both trastuzumab and lapatinib inhibited tumour growth, which led researchers to investigate the antitumour activity of the drug combination in patients with HER2-positive colorectal cancer. The study included 27 adult patients with KRAS exon 2 wild-type and HER2-positive metastatic colorectal cancer, all of whom were non-respondents to standard of care treatment including cetuximab (erbitux) or panitumumab (vectibix). Results demonstrated that within a median follow-up of 94 weeks, 30% of the 27 patients achieved an objective response, with 1 patient having achieved a complete response and 26% a partial response. 12 patients achieved stable disease. 22% of patients experienced grade 3 adverse events, including fatigue, rash and elevated bilirubin concentration.

Sartore-Bianchi A, Trusolino L, Martino C, et al. Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial [published online ahead of print April 20, 2016]. Lancet Oncol. doi: 10.1016/S1470-2045(16)00150-9.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-mcrc-trastuzumab-lapatinib-treatment-risk/article/491437/

4. Numerous Frontline CRC Options Allow Individualized Approach (Apr 23/16)

According to MD Wells Messersmith, clarifying the goals of therapy in frontline colorectal cancer (CRC) care is essential in order to effectively navigate and benefit from the numerous treatment options available. In cases where the patient might be cured, an “all-in” approach with a cytotoxic (FOLFOXIRI) base combined with a targeted agent in highly symptomatic patients might be used in

order to achieve a high response. In other patients, such as elderly patients or asymptomatic/unresectable patients, where a frontline response is irrelevant because the patient is not likely to be cured, a 5-FU plus bevacizumab (Avastin) treatment is used to stabilize the cancer and keep symptoms at bay. In terms of which chemotherapy regimen is preferred for frontline CRC treatment, FOLFOXIRI in the phase III TRIBE trial demonstrated the highest response rate, a result confirmed by the phase II STEAM trial. With respect to treatments using VEGF and EGFR inhibitors, despite inconsistent results comparing VEGF and EGFR inhibitors in the frontline setting for patients with KRAS wild-type CRC, Messersmith believes that both drugs remain valid options in frontline treatment. Immunotherapy is yet another frontline treatment option emerging onto the CRC scene, with the FDA having granted a breakthrough therapy designation to the anti-PD-1 agent pembrolizumab (Keytruda) as a potential therapy for patients with microsatellite instability-high (MSI-H) metastatic CRC. An ongoing phase II study demonstrated high response rates with Keytruda among patients with pre-treated CRC with mismatch repair deficiency, a pre-condition to MSI. Lastly, the importance of tumour location was stressed by Messersmith – the prognosis and outcomes for CRC patients may be impacted depending on the location of the tumour (right-sided or left-sided).

http://global.onclive.com/conference-coverage/SOGO-2016/numerous-frontline-crc-options-allow-individualized-approach?p=2

5. Taking low-dose aspirin during cancer treatment cuts deaths (May 11/16)

Researchers suggest that **low-dose aspirin** may be a beneficial addition to cancer treatment. Through a literature review including 5 randomised trials and 42 observational studies in colorectal, breast and prostate cancer, it was observed that low-dose aspirin taken during routine cancer treatment reduced the risk of mortality by 24% in colorectal cancer, particularly among patients with mutations in the PIK3CA gene. Low-dose aspirin reduced the risk of mortality by 13% and 11% in breast and prostate cancer, respectively. Further research is required to examine the drug's effects on cancer survival and its relationship with biomarkers.

Elwood PC, Morgan G, Pickering JE* et al. *Aspirin in the treatment of cancer: reductions in metastatic spread and in mortality: a systematic review and meta-analyses of published studies.* PLoS One *2016;11:e0152402. doi: 10.1371/journal.pone.0152402

http://www.pharmaceutical-journal.com/news-and-analysis/research-briefing/taking-low-dose-aspirin-during-cancer-treatment-cuts-deaths/20201122.article

6. Blood marker determines who will respond to colorectal cancer drug (May 13/16)

Researchers discovered the blood marker FCGR2A identifies a subgroup of patients that will benefit from taking cetuximab in the treatment of colorectal cancer (CRC). An international clinical trial that began 10 years ago suggested that among refractory metastatic CRC patients, cetuximab is the most effective in a subset of patients with tumours carrying a RAS mutation. This treatment, however, did not work consistently well across the patient group. The most recent research analysed archived tumour and normal tissue samples from some of the patients enrolled in this previous trial, refining and defining another subset of patients who carried the blood marker ***FCG2A*** and who experienced a positive response to cetuximab. Thus through examining heritable genetic variations that are presented in the blood and normal tissues, cancer treatments may become more targeted and more effective. In this way, a personalized treatment strategy avoids undesirable side effects and unnecessary costs.

G. Liu, D. Tu, M. Lewis, D. Cheng, L. A. Sullivan, Z. Chen, E. Morgen, J. Simes, T. J. Price, N. C. Tebbutt, J. D. Shapiro, G. M. Jeffery, J. D. Mellor, T. Mikeska, S. Virk, L. E. Shepherd, D. J. Jonker, C. J. O'Callaghan, J. R. Zalcberg, C. S. Karapetis, A. Dobrovic. *Fc- Receptor Polymorphisms, Cetuximab Therapy, and Survival in the NCIC CTG CO.17 Trial of Colorectal Cancer.* **Clinical Cancer Research*, 2016; 22 (10): 2435 DOI: 10.1158/1078-0432.CCR-15-0414***

https://www.sciencedaily.com/releases/2016/05/160513083118.htm

http://www.eurekalert.org/pub_releases/2016-05/uhn-rfb051016.php

7. Location of primary tumour predicts colorectal cancer survival outcomes (May 18/16)

Results from a retrospective analysis demonstrated that patients with metastatic colorectal cancer (mCRC) with a left-sided primary tumour achieved a greater overall survival (OS) and progression-free survival (PFS) compared with patients with a right-sided primary tumour. Over time, a better understanding of tumour mutations such as RAS and BRAF has predicted whether drug therapies will work or not, and such mutations are not distributed randomly throughout the colon. Based on genetic patterns, many subtypes of CRC have been identified and these variants of the disease are located in different parts of the colon. The CALGB/SWOG 80504 study demonstrated no difference in overall survival (OS) or progression-free survival (PFS) with bevacizumab or cetuximab addition to first-line FOLFOX or FOLFIRI chemotherapy treatment in mCRC patients. Researchers examined data from the CALGB/SWOG 80504 study to determine the effects of tumour location on survival

outcomes. Among 1025 patients with KRAS wild-type CRC, 293 had a right-sided primary tumour (cecum to hepatic flexure) and 732 had a left-sided primary tumour (splenic flexure to rectum). Given that these regions are discrete and develop differentially in the embryo, it follows that they are different tissues and thus behave differently. Patients with left-sided primary tumours achieved a significantly longer median OS than right-sided primary tumour patients – 33.3 months and 19.4 months, respectively. This prolonged OS was observed regardless of whether cetuximab or bevacizumab treatment was administered. Patients with left-sided primary tumours also achieved longer median PFS overall, and in the cetuximab and bevacizumab arms. Among patients with right-sided primary tumours, those who received bevacizumab achieved a greater OS compared to those who received cetuximab. Furthermore, researchers evaluated data from a subset of patients in the CALGB/SWOG 80504 study with KRAS mutations. Among this subset of patients, patients with left-sided primary tumours also achieved longer OS compared to those with right-sided primary tumours. Further research is being conducted to determine whether tumour location can be used as a biomarker for the difference in treatment outcomes. Nonetheless, findings suggest that right-sided colon cancers should be treated differently than left-sided cancers, and that patients with right-sided primary tumours get little to no benefit from cetuximab.

Venook AP, et al. Abstract 3504. Presented at: ASCO Annual Meeting; June 3-7, 2016; Chicago.

http://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/online/%7B71735b87-5788-4cb8-a1da-820828585e35%7D/location-of-primary-tumor-predicts-colorectal-cancer-survival-outcomes

8. Will Bristol-Myers Squibb checkmate colorectal cancer now? (Jun 3/16)

Bristol-Myers Squibb is a leading proponent in the rapidly emerging field of immunotherapy in the treatment of cancer. CheckMate 142 is a phase I/II study aimed at assessing the efficacy of nivolumab alone and nivolumab in combination with ipilimumab for the treatment of colorectal cancer. Nivolumab is an anti-PD-1 monoclonal antibody that works to block the signal that prevents activated T cells from attacking the cancer, thereby allowing the immune system to better target the malignant cells. Ipilimumab is a monoclonal antibody that works to stimulate the immune system by targeting CTLA-4 protein receptor, which is responsible for downregulating the immune response. Patients included in this study also carried a biomarker called microsatellite instability, a genetic aberration that increases the rate of mutations and results in poorer prognoses. This aberration occurs in 15-20% of sporadic cases of CRC. 27% of patients in the nivolumab arm and 15% in the combination arm achieved a response. 24% and 67% in the nivolumab and combination arms, respectively, achieved stable disease status at the time of analysis. The four-month progression-free survival rate was 55% and 80% for the nivolumab and combination arms, respectively. The five-month overall survival was 75% and 100%, respectively.

http://seekingalpha.com/article/3979766-will-bristol-myers-squibb-checkmate-colorectal-cancer-now

SCREENING

9. FDA approves first blood test for colorectal cancer (Apr 13/16)

The Epi proColon blood-based screening test has been approved by the FDA for use in the early detection of colorectal cancer (CRC). The approval is based on safety and efficacy data from three clinical studies, as well as the demonstrated potential to increase CRC screening rates. This test detects methylated Septin9 DNA, a biomarker that is found specifically hypermethylated in colorectal cancer and not in normal colon tissue. Hypermethylated Septin9 tumour DNA released into the bloodstream exhibits a unique methylation pattern that can then be detected in plasma by real-time PCR. This CRC screening test has been indicated for average-risk individuals who choose not to undergo colonoscopy or stool-based fecal immunochemical testing. Without dietary restrictions or changes in medications, the test requires only a blood sample to be analyzed at a diagnostic laboratory. The test will become available in the U.S. under joint commercialization agreement between Epigenomics and Polymedco, while Epigenomics is scheduled to begin a post-approval study of the long-term benefits of the test.

http://www.healio.com/gastroenterology/oncology/news/online/%7B72080fea-1472-4445-b5a3-408a0147f2fd%7D/fda-approves-first-blood-test-for-colorectal-cancer

RADIATION THERAPIES/INTERVENTIONAL

10. Researchers discover liver metastases have different radiation sensitivities based on primary tumour histology (Apr 12/16)

While radiation is commonly used to treat liver metastases with the majority of tumours maintained under control after one year, some patients do not respond well to radiation treatment. The factors which impact patient response to radiation remain unclear. Recent findings from the Moffitt Cancer Center have reported that liver metastases have different sensitivities to radiation therapy based on the primary tumour location. Moffitt researchers have used a radiosensitivity index (RSI) that examines the expression of 10 different genes to predict how well tumours will respond to radiation therapy. Through an analysis of 372 different metastatic liver lesions from the Total Cancer Care Database for radiosensitivity using the RSI, researchers found that liver metastases originating from gastrointestinal stromal tumours were the most resistant of all analyzed tumours. In a separate set of 33 patients with liver metastases treated with radiation therapy, among whom the primary tumours were colorectal cancer, breast adenocarcinoma, anal squamous cell cancer and lung adenocarcinoma, it was found that ***liver metastases originating from colorectal cancers were far more resistant to radiation than liver metastases originating from non-colorectal cancers***. The study indicates that analysis of primary histology is crucial in determining how liver metastases should be managed, and that this data should be taken into account by radiation oncologists when determining radiation dosage.

Kamran A. Ahmed et al. Radiosensitivity differences between liver metastases based on primary histology suggest implications for clinical outcomes following SBRT, International Journal of Radiation Oncology*Biology*Physics (2016).DOI: 10.1016/j.ijrobp.2016.03.050

http://medicalxpress.com/news/2016-04-liver-metastases-sensitivities-based-primary.html

PSYCHOSOCIAL

11. Depression makes recovery from cancer tough: study (May 14/16)

Findings have shown that individuals with depression are far less likely to recover well after colorectal cancer treatment compared to those without depression. Findings demonstrate that one in five colorectal cancer patients suffer from depression at the time of diagnosis. Such individuals are seven times more likely to have “very poor health”, which may include severe difficulty walking or being confined to bed two years post-treatment compared to those without depression. They are also thirteen times more likely to have “very poor quality of life”, including problems with thinking and memory or sexual functioning. Findings demonstrate that self-reported depression prior to cancer treatment predicts quality of life and health status during treatment and up to two years post-treatment; this suggests the importance of taking psychological factors into consideration when determining the best means of supporting patients who have recently been diagnosed with colorectal cancer.

http://www.ndtv.com/health/depression-makes-recovery-from-cancer-tough-study-1406144

12. Confidence levels may affect recovery from surgery for colorectal cancer (Jun 1/16)

A recent study revealed that colorectal cancer (CRC) patients with higher levels of self-efficacy or personal confidence that they can manage illness-related problems were found to recover better compared to patients with depression and anxiety. Findings were based on results from a questionnaire from 857 patients awaiting initial surgery to cure their colorectal cancer. The questionnaires were given before surgery, and at 3, 9, 15 and 24 months later to assess the patient’s quality of life (QOL), health status and well being, and included evaluation of the patient’s depression, anxiety and self-efficacy. Researchers categorized the patients into four distinct groups depending on their recovery from colorectal cancer. Groups 1 and 2 recovered well with QoL, health status and wellbeing above or within the normal range, group 3 experienced some decreases across the three indicators, while group 4 experienced consistently poor on all three indicators. About 20% of participants were depressed at the start of the study. Of these patients, 21% were in group 4 having the worst health two years post treatment, compared to 2.9% of patients without depression. 18.4% of patients were in the group with the worst quality of life two years post-treatment, compared to 1.4% of patients without depression. From a clinical standpoint, these findings suggest that initial assessment of patients’ self-efficacy from the time of diagnosis is important in determining which patients are more likely to experience a poorer recovery. Patients identified to have depression and anxiety have the opportunity to receive the necessary psychological and emotional support, thereby improving their chances at a more positive recovery.

Foster C, Haviland J, Winter J, et al. Pre-surgery depression and confidence to manage problems predict recovery trajectories of health and wellbeing in the first two years following colorectal cancer: results from the CREW cohort study. PLOS One. 2016 May 12;11(5):e0155434.

http://www.curetoday.com/articles/confidence-levels-may-affect-recovery-from-surgery-for-colorectal-cancer

OTHER

13. Some colon polyps pose greater cancer risk (Apr 14/16)

Findings from a recent study suggest that flat adenomas or precancerous polyps in the colon that do not have a typical appearance can indicate the presence of larger adenomas with a higher risk of being cancerous. Researchers have suggested that greater surveillance is necessary when flat adenomas are found due to more frequent occurrence of large, advanced adenomas appearing simultaneously. While the removal of adenomas significantly decreases the risk for colon cancer, polyp type is highly variable among patients. Higher risk indicators, such as the appearance of flat adenomas, must be screened for regularly. In an analysis of data from three clinical trials where patients had colonoscopies for screening or surveillance purposes, of 1911 adenomas removed, 15.3% were flat while 84.7% were polypoid. Findings demonstrated that patients who had at least one flat adenoma were more likely to also have a large adenoma or three or more adenomas overall, suggesting that the presence of flat adenomas can be a good indicator of cancer risk. Further research is required to investigate the relationship between flat adenomas and higher-risk polyps, evaluating whether shorter surveillance intervals after a flat adenoma has been found would be beneficial.

http://www.upi.com/Health_News/2016/04/14/Some-colon-polyps-pose-greater-cancer-risk/3081460636266/

14. Specific gene in the tumour determines the effectiveness of cancer treatment (Apr 14/16)

Findings from a large study conducted among colorectal cancer patients demonstrated that the effectiveness of standard chemotherapy depended on the presence of mutations in the TP53 gene in the tumour. Researchers from the p53Research research group at MedUni Vienna have studied over 1000 cancer patients with varying cancer types such as lung cancer, liver metastases and colorectal cancer. They found that several commonly used chemotherapies were effective only when the TP53 gene was normal and not mutated in the tumour. Conversely, certain drug therapies were only effective when the TP53 gene was mutated. Thus in cases where the prescribed chemotherapy was coordinated to the TP53 gene status of the targeted tumour, patients experienced greater survival rates compared to cases where chemotherapy was not coordinated to TP53 gene status, wherein such treatments could even be unfavourable to patients' survival rates. A highly sensitive test developed by the Viennese research group, MARK53, has made it possible to predict the effect of therapy on patient outcomes. The large-scale clinical study examined the MARK53 result on the effectiveness of standard chemotherapy treatment using fluorouracil (5-FU). It was observed that when the MARK53 result was normal (i.e. TP53 gene is not mutated), patients survived significantly longer than expected for patients with equivalent-sized tumours. When the MARK53 result was mutated, patient survival was significantly reduced. Researchers noted that the MARK53 test is exclusively predictive of the effect of a therapy. In cases where no treatment or ineffective treatment is administered, no effect will be predicted. Many standard chemotherapy drugs, including fluorouracil, function by destroying the DNA of cancer cells. DNA damage triggers the TP53 gene, which works to protect human genetic information. In cases of irreparable DNA damage, the gene will trigger a cascade of activity leading to programmed cell death. In cancer, the TP53 gene is often mutated, occurring with varying frequency in almost all types of cancer. Clinical use of the TP53 gene as a biomarker provides a promising method to improve efficiency of cancer treatment and minimize risks to patients by increasing personalization of chemotherapy.

Medical University of Vienna. "Specific gene in the tumor determines the effectiveness of cancer treatment." ScienceDaily. ScienceDaily, 14 April 2016. <www.sciencedaily.com/releases/2016/04/160414082124.htm>.

https://www.sciencedaily.com/releases/2016/04/160414082124.htm

15. Hormones responsible for some men's long legs may up their colorectal cancer risk (Apr 22/16)

Findings from a recent study suggest that men with longer legs have 42% greater risk of developing colorectal cancer than men with shorter legs. It was found that men with the longest legs (an average of 35.4 inches) have a 91% greater risk of developing colorectal cancer than men with the shortest legs (average of 31.1 inches). No statistically significant difference in cancer risk was observed between women with the tallest and shortest legs. Data was collected from the Atherosclerosis Risk in Communities (ARIC) study, which included 14,605 men and women followed from the late 1980s through the year 2006. Researchers used estimates of leg length calculated from standing height minus sitting height and compared these numbers to colorectal cancer incidence among the group. Throughout the ARIC study, 344 participants were diagnosed with cancer affecting the colon or rectum. Data was adjusted for demographic factors as well as considering for hormone replacement therapy and smoking status. Through statistical analysis based on quartiles of height and leg length, male participants in the highest quartile of leg length were associated with a 42% increased risk of colorectal cancer compared to the lowest quartile, an association that did not hold true for female participants. The highest quartiles of total height and

sitting height also demonstrated a greater risk of cancer compared to the lowest quartiles, but the association was far less significant. Researchers hypothesize that the link between leg length and colorectal cancer risk could be due to taller men having a greater number of colonic cells, thereby increasing the probability of some cells becoming malignant. They believe, however, that the increased risk may be more likely caused by greater exposure to insulin-like growth factor-1 during puberty. The National Cancer Institute has linked high levels of this naturally occurring hormone (it is produced by the liver to regulate bone length development) to colorectal cancer in men and women.

Onyeaghala GC, Lutsey PL, Demerath EW, et al. Associations of leg length with increased colorectal cancer incidence in the atherosclerosis risk in communities (ARIC) study. AACR Annual Meeting, 2016.

http://www.medicaldaily.com/men-long- legs-colorectal- cancer-383030

16. Chronic HBV treatment linked to increased rates of colorectal and cervical cancer (May 2/16)

A recent study revealed a potential link between long-term oral treatment for chronic hepatitis B virus (HBV) with nucleos(t)ide analogues and an elevated risk for colorectal and cervical cancers. For some patients with chronic HBV, prolonged treatment with nucleos(t)ide analogues is used to inhibit viral reproduction – a treatment that has raised questions regarding its long-term safety. Data on 45,299 patients with chronic HBV were analysed, among whom 7323 patients had undergone nucleos(t)ide analogue treatment. At a median follow-up of 4.4 years, cancers occurred in 538 of the untreated patients and 274 patients who had received nucleos(t)ide analogue therapy. Among those who had received therapy, patients were found to have higher risk of developing colorectal cancer and cervical cancer. It was found that the risk among patients treated and untreated with nucleos(t)ide analogues was similar for developing lung, breast and renal cancers. This study suggests that patients undergoing nucleos(t)ide analogue treatment for chronic HBV may require a different approach to colorectal and cervical cancer surveillance.

Wong G. Incidences of all malignancies in patients with chronic hepatitis B receiving long-term oral nucelos(t)ide analogue treatment – a study of 45,299 subjects. Presentation at: The International Liver Congress; April 13 - 17, 2016; Barcelona, Spain. Abstract PS052.

http://www.oncologynurseadvisor.com/colorectal-cancer/chronic-hbv-treatment-linked-to-increased-rates-of-colorectal-and-cervical-cancer/article/493401/

17. Colorectal cancer rate rising among young people (May 24/16)

Findings from a new study demonstrate that despite a decline in the overall rate of colorectal cancer (CRC) in recent years, CRC incidence has been increasing in individuals under the age of 50. While a great deal of attention has been given by the healthcare system to address rates of the disease in individuals over 50 years old, such as increased patient awareness and screening programs, findings demonstrate that such attention is lacking and much needed among the under 50 age group. In an age group not normally considered at risk, the rate of CRC has been on the rise and a higher percentage of individuals were diagnosed with the disease at later stages of cancer (stage 3 or 4). Over a 10-year period, the incidence of young individuals diagnosed with CRC increased by 11.4%, while the incidence in individuals over 50 fell by 2.5%. The younger group experienced a greater incidence of diagnosis at an advanced stage compared to the older group, with 30.6% vs. 25.1% diagnosed with stage 3 cancer, and 25.6% vs. 18.2% diagnosed with stage 4 cancer. It was also shown that the incidence of young-onset CRC cases were more prevalent in non-white individuals compared to the incidence of older-onset CRC. Despite the increase in CRC incidence among younger individuals, it is still important to note that the bulk of incidences still occur in the over-50 age group. The study suggests that greater attention must be directed towards improving CRC awareness and screening among a wider population, regardless of age.

http://medicalxpress.com/news/2016-05-colorectal-cancer-younger-people.html

NUTRITION/HEALTHY LIFESTYLE

18. Yes, bacon has been linked to cancer again – here's how bad processed meats actually are for you (Apr 20/16)

Last October, a paper published by the World Health Organization stated that eating processed meats was linked to a higher risk of developing colorectal cancer. Experts concluded that each 50g portion of processed meat eaten daily, equal to one hot dog, increases the risk of colorectal cancer by 18%. A similar correlation was found by the American Institute for Cancer Research (AICR) and the World Cancer Research Fund (WCRF) between eating processed meat and developing cancer of the lower stomach. It was concluded that for every 50g of processed meat eaten per day, the risk of cancers of the lower stomach also increases by 18%. It is important to note, however, that it is

regular consumption of such meats that puts an individual at risk; a piece of bacon now and then is not going to cause cancer. To put these statistics further into perspective, the Global Burden of Disease project estimates that about 34,000 cancer deaths per year across the globe can be linked to diets high in processed meats like bacon. About 29 times that amount or 1 million people die each year from cancer related to smoking, 600,000 from cancer related to alcohol consumption and 200,000 form cancer related to air pollution.

http://www.businessinsider.com/does-bacon-cause-cancer-2016-4

19. Higher vitamin D levels lower risk of cancer in women (Apr 22/16)

High blood serum levels of 25-hydroxyvitaminD (25(OH)D) have been shown to be linked to a reduced risk of cancer in women. Research from a 1980 study suggested a relationship between the development of some colorectal cancers and vitamin D deficiency. Populations at higher latitudes with less sunlight experienced higher rates of 25(OH)D deficiency and higher rates of colorectal cancer. Further research demonstrated correlations between 25(OH)D deficiency and risk of breast, lung and bladder cancers. For the present study, data from two previous studies was collected and analyzed. The Lappe study was a randomized clinical trial of 1169 women with a median blood serum level of 25(OH)D of 30ng/mL. The GrassrootsHealth prospective cohort was a prospective cohort study of 1135 women with a median blood serum level of 25(OH)D of 48ng/mL. It was observed that as 25(OH)D serum levels increased, cancer incidence decreased. Women with serum levels of 25(OH)D greater than 40ng/mL had a 67% reduced risk of cancer compared to women with serum levels less than 20ng/mL. These findings suggest an inverse relationship between 25(OH)D serum levels and risk of cancer. For cancer prevention, these findings emphasize the importance of maintaining blood serum concentrations above 20ng/mL which is also the recommended concentration for maintaining bone health.

McDonnell SL, Baggerly C, French CB, et al. Serum 25-hydroxyvitamin D concentrations ≥40 ng/ml are associated with >65% lower cancer risk: pooled analysis of randomized trial and prospective cohort study

http://www.oncologynurseadvisor.com/colorectal-cancer/vitamin-d-and-cancer-higher-levels-lower-risk-in-women/article/491569/

20. The impact of lifestyle on colorectal cancer (Apr 29/16)

The Centers for Disease Control and Prevention (CDC) cites colorectal cancer (CRC) as the third most common cancer and the second most common cause of cancer death in American men and women. In recent years, the link between CRC incidence and lifestyle has been a topic of great interest, suggesting the modern American diet and way of life as an important causal factor in CRC incidence and outcomes. While the most commonly cited risk factors for CRC incidence are age, family history, inflammatory bowel disease, and genetic syndromes, lifestyle factors such as diets poor in fibre, vegetables and fruit and high in fat, minimal physical activity and obesity have been increasingly studied and correlated to disease incidence. Individuals with a baseline BMI greater than 35kg/m^2 were exposed to a higher risk of recurrence of CRC or other primary cancers. A meta-analysis of 56 studies with over 7 million participants found that for each increase in body mass index by 5kg/m^2, CRC risk increased by 18%. This link was more evident among men and for CRC compared to rectal cancer.

A higher risk of CRC recurrence and mortality has been linked to a greater consumption of the Western diet high in processed foods, fat and red meat. High fibre consumption in a diet rich in grains, fruit and vegetables is associated with shorter intestinal transit time and higher production of short-chain fatty acids related to an increase in bacterial fermentation, a process that improves nutrient availability to the body and promotes prompt elimination of wastes toxins from the body. The observational European Prospective Investigation into Cancer and Nutrition (EPIC) study examined more than 500,000 participants, concluding that a doubling of dietary fibre intake by populations with a low intake could reduce CRC risk by 40%. The Adventist Health Study 2 was a prospective, cohort study of more than 90,000 Seventh-Day Adventists who are vegetarians. Participants were followed for an average of 7.3 years using validated food questionnaires. 100 cases of rectal and 380 cases of CRC were observed. A lower risk for all CRC in vegetarians was observed compared to non-vegetarians and a lower risk among pesco-vegetarians (vegetarians who consume fish) was also observed compared to non-vegetarians.

An inverse relationship for physical activity and CRC risk has also been supported. A self-report of 6 or more hours of physical activity weekly was linked to a reduction in CRC recurrence and improved survival. Suggested mechanisms include reduction in fat tissue and body mass, decreased inflammation and insulin levels and increased insulin sensitivity. The American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention recommends 75 minutes of vigorous or 150 minutes of moderate intensity physical activity weekly. Their recommendations also suggest limiting sedentary behaviour such as “screen-based entertainment”.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal- cancer-lifestyle- impact-risk/article/493215/

21. Body mass index associated with colorectal cancer mortality risk (May 23/16)

A recent study demonstrated that body mass index (BMI) at the time of diagnosis and post-diagnosis is associated with risk of death in colorectal cancer (CRC) patients. The retrospective observational study analyzed data from 3408 patients diagnosed with stage I to III CRC who had also undergone surgery. Results showed that BMI at the time of cancer diagnosis was linked to all-cause mortality, with patients who were underweight and patients who were class 2 or 3 obese demonstrating increased risk of death compared to patients who were low-normal weight. It was also observed that patients who were high-normal weight, low-overweight, and high-overweight experienced lower mortality risk than patients who were low-normal weight. No difference in mortality risk between patients who were class 1 obese and those who were low-normal weight was observed. Study findings highlighted that the risks for CRC-specific mortality were similar to the risks of all-cause mortality, though patients who were class 1 obese experienced significantly lower all-cause and cancer-specific mortality risks. This suggests that recommending weight loss may not be justified in the immediate period after cancer diagnosis in overweight patients.

Kroenke CH, Neugebauer R, Meyerhardt J, et al. Analysis of body mass index and mortality in patients with colorectal cancer using causal diagrams [published online ahead of print May 19, 2016]. JAMA Oncol.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-bmi-body-mass-higher-mortality-risk/article/498099/

22. Fat-rich, low fibre diet may up colorectal cancer risk (May 23/16)

A recent study suggests that a Western diet high in fat and low in fibre, vitamin D and folate may increase the risk of developing colorectal cancer (CRC). The development of CRC is the result of complex interactions between genetic and environmental factors such as diet. Understanding the early changes in normal colonic mucosa that could aid in the prevention of CRC development remains a challenge in the CRC community. Researchers from the University of Helsinki used a mouse model of Lynch syndrome, the most common form of inherited CRC, to conduct a long-term diet experiment. Mice with Lynch syndrome carry a mutation in MIh1, one of the main susceptibility genes in the disease that is responsible for correcting errors that occur during DNA replication. When cells divide, DNA must replicate itself. During the process, errors may occur which lead to instabilities in the genome and sometimes cancer. Carriers of Lynch syndrome have one healthy and one mutated mismatch repair gene, thereby bearing an 80% risk of developing cancer. Researchers aimed to detect the earliest changes in the colon mucosa before tumours developed by using such mutation carriers requiring just a single mutation for cancer development to occur. In this way, researchers hoped to observe changes in the colon mucosa prior to any malignant transformation and distinguish these from changes that may occur later in cancer development. Results demonstrated that gene expression patterns of normal mucosa in mice that developed CRC were significantly different from those of mice that did not develop CRC. The Western diet appeared to be a significant risk factor, with 80% of cancers detected occurring in Western-diet fed mice. While MIh1 gene expression was observed to have severely decreased in the mucosa, no lack of MIh1 protein or microsatellite instability (consequences of decreased MIh1 gene expression) were detected. This suggests that the decrease in the MIh1 gene expression may suffice in inducing the development of tumours, even where the DNA mismatch repair mechanism that corrects errors in DNA replications is still functioning normally.

http://www.financialexpress.com/article/lifestyle/health/fat-rich-low-fibre-diet-may-up-colorectal-cancer-risk/263440/