

Aspirin may improve survival in colon cancer via interaction with platelets

It has previously been established that colon cancer patients who take low doses of aspirin after diagnosis demonstrate an improved outcome. However, the specific action of the drug that confers this survival benefit to patients is not understood. New research presented this week at the 2013 European Cancer Congress in Amsterdam (The Netherlands) suggested a new theory with regard to how aspirin works to slow cancer progression.

Marlies Reimers and colleagues from Leiden University Medical Center (Leiden, The Netherlands) employed tissue microarray technology to examine protein expression in the tissue of 999 colon cancer patients who were known to have taken aspirin after diagnosis. DNA was also extracted from 663 tumor samples to determine the mutational status of the *PIK3CA* gene.

The team found that in patients who took 80 mg aspirin a day, a survival benefit was only seen in those with tumors expressing the HLA class I protein. This protein is expressed on the cell surface and is known to play a role in immune function. Risk of death from the disease was noted to be halved in patients with tumors expressing HLA class I who took aspirin, compared with those with HLA class I-positive tumors who did not take the drug. The positive effects of aspirin were not found in patients who had tumors lacking in HLA class I expression. It is postulated that HLA class I may serve as an accurate predictive biomarker in the selection of colon cancer patients who would benefit from treatment with aspirin.

The effectiveness of aspirin in colon cancer was previously believed to be

somewhat linked to the expression of the enzyme COX-2 and/or *PIK3CA* mutation in the tumor. "Our results showed that there was no difference in the effect of aspirin in relation to COX-2 expression and *PIK3CA* mutation. When we stratified our analyses for COX-2 expression and *PIK3CA* mutation status, we did not see differences in survival benefit. For example, patients with aspirin use after diagnosis with strong COX-2 expressing tumors had the same survival benefit as tumors with weak COX-2 expression," stated Reimers (Leiden University Medical Center), addressing this phenomenon.

The researchers conclude by suggesting that aspirin has a dual mode of action in colon cancer; first in the preventative setting through interaction with COX-2 and *PIK3CA* mutation and second, as revealed in their study, in the malignant setting where they suggest aspirin assists in the prevention of metastasis. "We think that platelets are involved in cancer spreading to other parts of the body by shielding tumor cells in the bloodstream so that they cannot be recognized by the immune system and can finally colonize distant organs. Aspirin could help to 'unmask' those tumor cells by attacking platelet formation, so that the immune cells can detect and eliminate them," explained Reimers.

The investigators acknowledge that further evidence gained from larger clinical trials is required to support their findings and to confirm the findings that aspirin is efficacious in colon cancer patients with HLA class I expression. As such, aspirin use in colorectal cancer is being investigated in larger randomized trials, for example the ASCOLT trial.

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"Risk of death from the disease was noted to be halved in patients with tumors expressing HLA class I who took aspirin, compared with those with HLA class I-positive tumors who did not take the drug."

“The idea that aspirin can enhance the effect of our immune system and that we might be able to identify those cancer patients who best benefit from it, is worth further studies. Ongoing placebo-controlled randomized trials evaluating

the effect of aspirin in colorectal cancer can hopefully strengthen the evidence that aspirin is useful in patients with HLA class I expression,” Peter Naredi of the European Cancer Organisation concluded.

– Written by Emily Brown

Source: European Cancer Congress press release: www.esmo.org/Conferences/European-Cancer-Congress-2013/News/ECC-2013-Press-Release-New-Research-shows-how-Aspirin-may-act-on-Blood-Platelets-to-Improve-Survival-in-Colon-Cancer-Patients

Meta-analysis demonstrates increased risk of breast and colorectal cancer for those with diabetes mellitus

Research presented by investigators from the Erasmus University Medical Center (Rotterdam, The Netherlands) on the 29th of September at the European Cancer Congress (Amsterdam), and published in the *British Journal of Surgery*, has provided more defined evidence regarding the relationship between diabetes mellitus and cancer development and prognosis. The meta-analysis concluded that diabetic individuals are not only at a higher risk of developing breast and colorectal cancers, but they also have an increased risk of mortality due to these conditions.

Kristin de Bruijn (Erasmus University Medical Center) and colleagues completed the analysis utilizing data from over 1.9 million patients involved in 20 prospective, pooled cohort and controlled trials completed between 2007 and 2012. The meta-analysis combined the incidence and mortality data regarding breast and colorectal cancer while excluding all other causes of death. This makes it the first study of its kind to provide further detail regarding the already known link between diabetes mellitus and risk of cancer development.

Diabetic individuals were shown to have a 26% increased risk of developing colorectal cancer and a 23% increased risk of developing breast cancer compared with nondiabetic individuals. Furthermore, diabetic patients were found to have a 30 and 28% increased risk cancer-specific mortality from colorectal and breast cancer, respectively, when compared with nondiabetic individuals. de Bruijn stated: “The results for breast and colon cancer incidence in patients with diabetes are consistent with other meta-analyses. Furthermore, this meta-analysis shows a higher risk and a stronger association between diabetes and death from breast and colon cancer than previously reported.”

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Professor Cornelis van de Velde, President of European Cancer Congress, commented: “With the increase in incidence of both diabetes and breast cancer, this is an

important update of the meta-analyses on this subject and an interesting addition to the literature as this study excluded other causes of death.”

Researchers involved in this work intend to further investigate the link between diabetes mellitus and cancer by considering other factors, such as insulin, duration of diabetes and antidiabetic medication. de Bruijn explained: “It is extremely important that prevention campaigns on obesity and diabetes are intensified and that they also focus on children, to prevent them from becoming obese and developing cancer later in life.”

The overriding conclusion from this data is that not only is diabetes mellitus a risk factor for breast and colorectal cancers, but also for cancer-specific mortality.

– Written by Elizabeth Webb

Sources: de Bruijn KM, Arends LR, Hansen BE, Leeftang S, Ruiter R, van Eijck CH. Systematic review and meta-analysis of the association between diabetes mellitus and incidence and mortality in breast and colorectal cancer. *Br. J. Surg.* 100(11), 1421–1429 (2013); The European Cancer Organisation press release via Alpha Galileo: www.alphagalileo.org/ViewItem.aspx?ItemId=134904&CultureCode=en

Colonoscopy screening every decade could prevent colorectal cancer

“Colonoscopy is the most commonly used screening test in the US but there was insufficient evidence on how much it

reduces the risk of proximal colon cancer and how often people should undergo the procedure,” reports Shuji Ogino (Harvard

School of Public Health, MA, USA), coauthor of a study demonstrating the efficacy of colonoscopy published recently in the

New England Journal of Medicine. “Our study provides strong evidence that colonoscopy is an effective technique for preventing cancers of both distal and proximal regions of the colorectum, while sigmoidoscopy alone is insufficient for preventing proximal cancer.”

“Results demonstrated that colonoscopy and sigmoidoscopy correlated with decreased risk of both incidence and mortality associated with colorectal cancer.”

In the USA, colorectal cancer is the second-leading cause of cancer mortality, with over 130,000 people being diagnosed in 2009 and over 50,000 dying from the disease that same year. Therefore, the uncertainty regarding the effectiveness of colonoscopy in reducing both mortality and incidence of colorectal cancer, needed to be addressed. The present study analyzed results from two long-term studies (the Nurses’ Health study and the Health Professionals Follow-up study) with data gathered from questionnaires from 88,902 participants completed every 2 years between 1988 and 2008. This provided 1815 colorectal cancer cases, information regarding both colonoscopy and sigmoidoscopy (which screens the distal and lower colorectum for tumors) and mortality rate from the disease (474 participants).

Results demonstrated that colonoscopy and sigmoidoscopy correlated with decreased risk of both incidence and mortality associated with colorectal cancer. Colonoscopy was also shown to be protective against cancers of the proximal colon, but to a lesser degree compared with its effect against distal colorectal cancers. This is suggested to be a result of the molecular differences in those cancers. The authors also conclude that if all the study participants had undergone colonoscopy, 40% of colorectal cancers would have been prevented.

“Each year, more than 1.2 million people are diagnosed with colorectal cancer worldwide. Our findings could help improve and strengthen the current guidelines for colorectal cancer screening,” comments lead author, Reiko Nishihara (Harvard School of Public Health).

This large and long-term investigation supports the existing recommendation of a 10-year screening interval for colonoscopy in those at an average risk of developing colorectal cancer, with varying frequency dependent on the individual patients’ history.

– Written by Elizabeth Webb

Source: Harvard School of Public Health
Press Release: www.hsph.harvard.edu/news/press-releases/colonoscopy-screening-every-ten-years-could-prevent-40-of-colorectal-cancers/

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Laparoscopic surgery for colon cancer demonstrates postoperative benefits in the elderly

Investigators from Dalhousie University (Nova Scotia, Canada) demonstrated that laparoscopic surgical treatment for colon cancer will increase the chance of elderly patients being discharged to their own home after the procedure. “There is evidence that laparoscopic surgical treatment for colon cancer is similar to an open operation in terms of outcomes from a cancer treatment point of view,” reports Richard Liu (Dalhousie University). “Our

study results show that patients who have the less invasive colon cancer operation are less likely to be discharged to a nursing home.”

The data presented at the 2013 American College of Surgeons Clinical Congress (6–10 October, DC, USA) were obtained from the Nationwide Inpatient Sample database. The researchers reviewed data from all patients over 70 years old who underwent colon cancer resection in

the US between 2009 and 2010. Data included 9416 elderly patients, of which 5704 patients had open surgical resection, and 3712 had laparoscopic resection. A total of 20% of those who underwent the open surgery were discharged to nursing facilities for assisted postoperative care. This was significantly lower among elderly patients who underwent laparoscopic procedures, with only 12.5% requiring discharge to a nursing home.

“...patients over the age of 70 were more likely to be discharged to their own home following laparoscopic resection, in comparison to those who underwent standard open resections.”

The risk of discharge to nursing facilities also varied between patient age groups. Patients at the lowest risk were between the ages of 70 and 75, with the risk doubling for patients between the ages of 75 and 80. This doubled again for those between the ages of 80 and 85, and again for those over 85 years of age. Other factors such as concomitant diseases, including diabetes and heart disease, also increased the risk of discharge to a nursing facility. Furthermore, the status of the colon cancer was demonstrated to affect the need for postoperative care. “Colon cancer that has advanced outside the colon and invaded other structures makes the operation more difficult, and with more difficult operations, there may be more in-hospital complications, a longer length of stay and

other factors that may require postoperative nursing home care,” commented Liu.

The authors conclude that patients over the age of 70 were more likely to be discharged to their own home following laparoscopic resection, in comparison to those who underwent standard open resections. These data demonstrate that not only is laparoscopic colon cancer resection an option for the elderly to prolong survival, but may also help to preserve the patient’s quality of life.

– Written by Elizabeth Webb

Source: American College of Surgeons, Clinical Congress 2013 Press Release: www.facs.org/clincon2013/press/liu.html

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