

Duke Cardio-Oncology

news

A joint publication of the Duke Cancer Institute
and the Duke Division of Cardiology

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Welcome to the latest edition of our Cardio-oncology newsletter.

We hope these newsletters help to inform you of the latest scientific findings that support the connection between cardiology and cancer care, with Duke leading the way in this field.

We had an excellent turnout for our First Annual Cardio-Oncology Symposium on March 5th featuring national and international experts as keynote speakers. Thank you to Dr. Susan Dent, Medical Oncologist at The Ottawa Hospital Cancer Centre and Associate Professor in the Department of Medicine at the

University of Ottawa, and Dr. Gregory Hundley, Professor in the Cardiology Comprehensive Cancer Center Wake Forrester Baptist Health, for sharing their insights with our attendees. Plans are underway for our second symposium, so stay tuned for more details.

Meanwhile, continue reading to learn more about the newest findings in cardio-oncology.



Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults

Moore SC et al. *JAMA Internal Medicine* [[E pub May 16, 2016](#)]

Summarized by: Michael R. Harrison, MD (Duke Genitourinary, Medical Oncology)

Multiple studies have reported on the association between physical activity and cancer. For example, reductions in risk have been shown in breast, colon, and endometrial cancers, when those with high levels of physical activity are compared with those with low levels. Overall, studies have been limited by small numbers, varied types of physical activity (i.e., leisure vs. occupational), and in the comparisons assessed (i.e., highest quartile vs. lowest quartile). It does appear that physical activity may be an important cancer reduction strategy; however, the influences of body size and smoking status are unresolved. The objective of this study was to determine the association of

leisure time physical activity with the risk of 26 cancers considering body mass index (BMI) and/or smoking habit.

Data were pooled from 12 U.S. and European cohorts, resulting in a cohort size of 1.44 million participants. Physical activity was self-reported and harmonized by conversion to cohort-specific percentiles. Cancer ascertainment was excellent, with 99% of cases confirmed by medical records or pathology reports. Comparison of cancer risk at the 90th vs. 10th percentiles of physical activity was the basis for computation of hazard ratios for high vs. low levels of physical activity. Models included covariates selected based on known associations with cancer; multiplicative effect modification was assessed.

Compared with a low level of physical activity, a higher level of physical activity was associated with a significantly lower risk

for 13 cancers. Seven cancers had a strong inverse association (>20% risk reduction): esophageal adenocarcinoma; cancers of the liver, lung, kidney, gastric cardia, and endometrium; and myeloid leukemia. A moderate inverse association (10-20% risk reduction) was observed for the remaining six cancers: myeloma, colon, head and neck, rectal, bladder, and breast cancers. Ten of the 13 associations retained statistical significance after adjustment for BMI. Of note, smoking history modified the association in lung cancer. Interestingly, high level of physical activity was positively correlated with risk of prostate cancer and melanoma. On deeper examination, high physical activity was associated with increased risk of non-advanced, but not advanced, prostate cancer. In areas of the U.S. with higher levels of solar radiation, the positive physical activity association

[continued on page 3](#)

Leisure-time physical and risk of cancer

(from page 2)

with melanoma was statistically significant; however, it was not in regions with lower levels of solar radiation.

These results suggest that physical activity could be associated with reduced risk of a broader range of cancers than previously reported. Strengths of this study include the size (largest study ever conducted) and consistent methodological approach (minimizing heterogeneity and maximizing

statistical power). Limitations include the inability to exclude residual confounding and use of self-reported data (leading to possible recall bias). Future work will examine the type (modality), intensity, and amount of physical activity necessary to reduce cancer risk by subtype. Timing of physical activity (i.e., at what point in life) and mechanism(s) (i.e., to strengthen biological plausibility) underlying the association also

need to be thoroughly assessed. Overall the results appear to be widely generalizable. These important findings suggest that physical activity is an important public health strategy to reduce the burden of cancer both in the U.S. and around the world.

ASCO 2016 Scientific Sessions

An Extended Education session titled “Heart to Heart: How to Protect the Heart During Cancer Therapy” was held at the 2016 ASCO Annual meeting in early June. This session was chaired by FDA representative Laleh Amiri-Kordestani, MD, who presented her thoughts on the FDA’s perspective regarding cardiovascular safety monitoring in drug development. Learning objectives of this session included a review of the various

cardiovascular toxicities that are associated with anthracyclines, anti-HER2 therapies, VEGF Signaling Pathway Inhibitors, and tyrosine kinase inhibitors, and an examination of the emerging cardiovascular toxicities with the use of tyrosine kinase inhibitors. The session also included a description of the implementation of imaging modalities for the prevention and diagnosis of cardiovascular toxicities as well as a discussion of the optimal

use of blood biomarkers for early detection of cardiovascular toxicities, how to stratify patients for risk of cardiovascular toxicities, and the role of cardio-protective strategies prior to, during, and after radiation therapies.

ASCO members and/or meeting attendees can view videos of this session at the following link:

<http://iplanner.asco.org/am2016/#/session/11149>

Venous thromboembolism and cancer

Venous thromboembolism (VTE) includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). Patients with cancer have a 4- to 7-fold greater risk of VTE when compared with patients without cancer. The increased risk does not appear to be constant over the course of the disease, it is acutely increased after surgery, and varies also by the type of surgery. In addition, risk is higher during the course of chemotherapy and during the initial months after cancer diagnosis. The type of cancer plays a role as well, with pancreatic cancer being associated with the highest rate of VTE. As a result of the increased risk, VTE is the leading cause of death in hospitalized patients with cancer, second only to death from cancer alone. Cancer affects each component of the Virchow triad: venous stasis, blood components, and vessel damage. Anticoagulant treatment is the “go to” choice for prevention and treatment of VTE.

Low molecular weight heparin (LMWH) has been shown to be more effective and equally safe

to conventional anticoagulation. LMWH are actually recommended over anticoagulation with vitamin K antagonist for the treatment of VTE in patients with cancer.

New oral anticoagulants have been recently introduced in clinical practice to overcome the limitation of conventional anticoagulation therapy (such as cost of drug, feasibility of long-term parenteral administration, need for laboratory monitoring, and dose adjustment). Factor X-a inhibitors (rivaroxaban, apixaban, edoxaban) and factor-II inhibitor/thrombin (dabigatran) have a predictable anticoagulant effect, can be administered at fixed doses, they do not need dose adjustment.

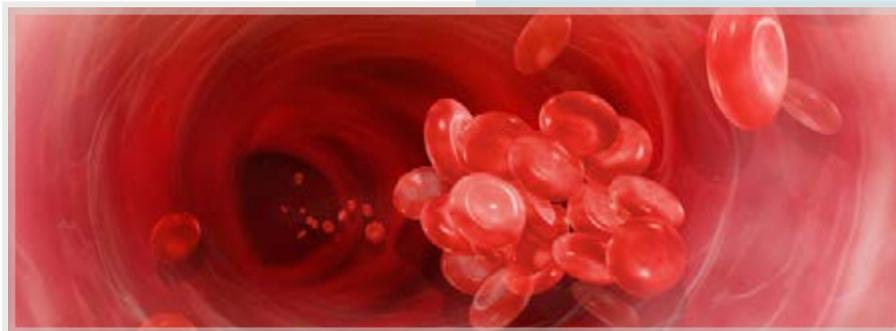
[continued on page 5](#)

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Venous thromboembolism and cancer

(from page 4)

Six trials have evaluated their use for initial and long-term treatment of patients with VTE and were shown to be non-inferior to conventional anticoagulation. Overall, fewer than 10 percent of the patients enrolled in these studies had cancer. A meta-analysis of these randomized clinical studies assessed the safety and efficacy of direct oral anticoagulant in patients with VTE and cancer. VTE occurred in 3.9 percent of cancer patients treated with novel oral anticoagulant compared with 6.9 percent of cancer patients treated with conventional therapy (OR 0.63; 95 percent CI 0.37–1.10). Major bleeding occurred in 3.2 percent versus 4.2 percent, respectively. Although preliminary analysis from these studies seem to demonstrate that the new oral anticoagulants are as effective and safe as conventional therapy, there is still limited evidence to provide any recommendation for the use of new anticoagulant agents in patients with cancer-associated VTE.

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Recent publications

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Save the date

**Global Cardio-Oncology Summit 2016,
September 29–30, 2016**

Hyatt Regency Vancouver, 655 Burrard
Street, Vancouver, BC, Canada V6C 2R7

Registration now open— register today!

The Global Cardio-Oncology Summit 2016 is co-hosted the Canadian Cardiac Oncology Network and the International CardiOncology Society. This year's summit will be co-chaired by Dr. Sean Virani, cardiologist at the Vancouver General Hospital, and Dr. Christine Simmons, medical oncologist at the BC Cancer Agency, in Vancouver, British Columbia, Canada.

This summit models a leading-edge interdisciplinary approach to preventative and targeted medicine in cardio-oncology. This important field of study, aimed at understanding cardiac complications of oncology treatments, has gained a growing interest from a number of healthcare providers including oncologists, cardiologists, radiologists, nurses, pharmacists, and basic scientists.

The Global Cardio-Oncology Summit will feature the latest research and clinical guidelines in the multidisciplinary field of cardio-oncology. We invite abstract submissions for the Global Cardio-Oncology Summit on the prevention, management, and treatment of cardiac complications related to oncology therapy.

Useful links

cardiooncologyjournal.biomedcentral.com, a new open access cardio-oncology journal

icosna.org, International Cardioncology Society, North America

cardiaconology.ca, Canadian Cardiac Oncology Network (CCON)

[MD Anderson cancer lecture series](#) on the practice of onco-cardiology discussing important topics relevant to cancer patients with heart disease and cardiotoxicity



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