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**MIND, BODY & SOUL Part II:
Innovations in Prevention, Treatment, and Sustainability**

The Link Between Cancer and Cardiovascular Disease

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Ron Winslow:

Hello, I'm Ron Winslow. I'm delighted to be here with Dr. Laurie Glimcher from the Dana-Farber Cancer Institute and Dr. Michael Farkouh of University of Toronto. And we're here to talk about the link between cardiovascular disease and cancer. Most of us think these two major killers are entirely separate diseases. So, Dr. Glimcher could you start by giving us a little insight into how they are linked?

Laurie H. Glimcher, MD:

Well, I'd say there's a number of similarities between cancer and cardiovascular disease. For one thing, they are the two leading causes of death. So they've touched the lives of almost all of us. And as a public health challenge, we have to keep working toward better treatments for both of these terrible diseases.

But there are a number of similar risk factors. For example, obesity and diabetes, both are risk factors for cancer and cardiovascular disease. And the microbiome, and a general environment of inflammation also clearly plays a role in how both diseases develop.

I would say finally that these diseases are also connected by the critical importance of scientific medical research and huge gains were made in treating cardiovascular disease up sort of 30 years ago. And now cancer is in the midst of revolutionary research that is helping us to treat many more patients with cancer successfully.

Ron Winslow:

Dr. Farkouh any thoughts about these links?

Michael E. Farkouh, MD:

Oh, I agree completely with Dr. Glimcher. The link in terms of the traditional risk factors that we have for cardiovascular disease and cancer are very common. And so we can expect that if the patient has cardiovascular disease risk or cancer, that they're more at risk for the other disease. And I think we have large bodies of epidemiologic data suggesting it.

We actually came to the table because our patients who were treated for cancer often had complications that were cardiovascular-related, related to impairment of the muscle, increased incidents of atherothrombotic events, and venous thrombotic events. And so we really came to the table as a complication of cancer therapy. But it's so much more than that. And that's what we've uncovered in the last, I would say three to five years.

Ron Winslow:

One of the interesting links, if you will, is that more and more people have been diagnosed with both of these diseases. And I think my initial thought was, well, primary prevention in cardiovascular disease has been very good and there's some side effects for instance, of some breast cancer drugs and other drugs that are not good for the heart. But this link, maybe there's some biology there. And also, maybe this is a good reason to make sure we're using sort of a comprehensive treatment for patients with both of these conditions.

Michael E. Farkouh, MD:

Absolutely. We have seen [crosstalk]. Go ahead.

Laurie H. Glimcher, MD:

I think that one clear link between the two is inflammation. If you look at the tumor microenvironment, you have your tumor and it's surrounded by a very hypoxic, low pH nutrient-deprived tumor microenvironment. And the tumor is secreting inflammatory substances. And the immune cells that surround the tumor are secreting inflammatory substances. And so that clearly is a risk factor for cancer.

It's also a risk factor as Michael will say for cardiovascular disease, because that's what happens in coronary arteries, right? You get a lot of inflammation and you get migration of cells like macrophages, inflammatory macrophages, into the site of the plaque. So in that sense, they're rather similar because they both depend on a pro-inflammatory environment.

Michael E. Farkouh, MD:

No question. We believe that link is extremely well substantiated. We've learned about this through different therapies. My colleagues, Drs. Ridker and Libby in Boston have studied some very potent anti-inflammatory drugs, and they've not only reduced the incidence of

cardiovascular disease, but also reduced the incidence of, for example, lung cancer, in the CANTOS trial, which was a very large-scale trial of a very potent anti-inflammatory drug.

The other association that we've seen is with genetics and there is an entity called Clonal hematopoiesis. It's a big term, but really these are hematopoietic stem cells for which genetic mutations in the cells develop in a whole body of cells, develop with this mutation, which is different from the healthy blood cells. And there's an association between this entity and blood cancers, as well as with cardiovascular disease. So we actually have a pathway that's well-described that links cancer with heart disease through the genetic-[crosstalk].

Laurie H. Glimcher, MD:

I would love to expand on that because Clonal hematopoiesis was discovered by Dr. Ben Ebert at Dana Farber Cancer Institute. And it's a novel driver, as Michael said, of cancer and cardiovascular disease. It's an age associated disorder and it's marked by expansion of these little hematopoietic clones that carry somatic mutations. So, what the surprise is that Ben found, was that not only do patients with clonal haematopoiesis have a higher risk of hematologic malignancies and mortality, but they also have excess cardiovascular disease.

So, that, as Michael pointed out, it is a unifying factor, clonal hematopoiesis has about an 0.5% to 1% absolute annual risk of developing a malignancy, a hematopoietic malignancy, but it has a two- to four-fold higher risk of coronary artery disease, stroke, and cardiovascular disease deaths. So, I think that's a very interesting and provocative link between the two. And it's been postulated that inflammation might be a potential mechanism.

Ron Winslow:

So, what are these links say about how patients with these diseases should be treated? Is there insights that we can gain here for tailoring treatment or for coming up with new strategies for making these patients have better lives?

Laurie H. Glimcher, MD:

I think this is all about early detection of cancer, and the earliest detection would be something like a diagnostic test that looks for the presence of these little hematologic clones. And they increase as you get older. So, they're rare if you're under 40, but by the time you're 90, 15 to 20% of older individuals do have clonal hematopoiesis.

So, we need to really focus on early detection of cancer and identify those individuals who are at higher risk for cancer because of lifestyle or because they have inherited cancer, or because they have lifestyles like obesity or tobacco that put them at very high risk. And, cancer incidence I have to say is rising. Two out of every five Americans are going to develop some form of cancer in their lifetime. And what really alarms me the most is that studies are now showing that more cancers are rising in incidence in younger people.

We have established the center for young adult onset colorectal cancer, because we were seeing so many people in their 30s and 40s who presented to us with metastatic colorectal

cancer. And that led to a change in the rules for when you should get a colonoscopy. The age now is 45, not 50. So, we don't understand why that's happening. And, it's true in other cancers as well. In endometrial cancer, in breast cancer for women most recently in lung cancer, especially for young women who are non-smokers.

So, this is why you need academic medical centers, because we need to understand the fundamental science behind why this is happening. I think there are a number of factors at play here, including the ones that we've already touched on. So, at Dana-Farber, we've been taking a very multidisciplinary approach to support our patients.

And, we actually have a cardio oncology program that collaborates with our affiliate Brigham and Women's Hospital, Heart and Vascular Center. I think this is one of the few programs in the country that brings together expert oncologists and cardiologists, so that we can provide optimal cardiovascular care. As Michael pointed out, chemotherapy, radiation of the left breast, for example, could lead to cardiac toxicity.

Ron Winslow:

Dr. Farkouh tell me in the early detection of heart diseases [crosstalk]

Michael E. Farkouh, MD:

Well, I think there is another flip of the coin on the risk of cardiovascular disease, there's a study just published a few weeks ago showing that the incidence of cancer is related to atherosclerotic risk, based on traditional risk factors, which were on multivariate analysis, where sex, age and smoking were the big three that emerged, obesity did not emerge, but we know it's associated.

Michael E. Farkouh, MD:

And then the other thing that emerged was the atherosclerotic risk, your risk of developing atherosclerotic disease in a predictive model that we've used for years based initially on the Framingham study that shows that that is also a predictor of incidents [of] cancer, developing cancer. So, as Dr. Glimcher points out, either you detect the cancer, but I think if you detect the heart disease risk early as well, we may also get on top of this. So it goes on...

Ron Winslow:

Is there some commonality? Both of those suggest some cellular processes that are out of control.

Michael E. Farkouh, MD:

That's right. And we all believe that inflammation may be a control, maybe an issue in Clonal hematopoiesis and other factors that are environmental as well, that could be playing a role. So the idea here is how do we work together? Should someone who has heart disease be screened more aggressively for cancer and should a cancer patient be screened more effectively for heart disease?

And that's something that these combined clinics, I think are great advances. Certainly, the one at Dana-Farber with the Brigham, we have the same with the Peter Munk Centre in Toronto with the Princess Margaret [Cancer Centre], a very similar operation where we're actually doing combined clinics together, not just about cardiotoxicity of cancer therapy, but also about actually clonal hematopoiesis program. That is more fulsome than just clonal hematopoiesis, but as a screening clinic for cancer and heart disease.

Laurie H. Glimcher, MD:

You know, one thing that has puzzled me, is the question, why does cancer rarely develop in the heart in cardiac muscle? We do get an occasional rhabdomyosarcoma, and there are cancers like melanomas, which can metastasize and spread to the heart. Breast cancers, lung cancers can, can cause fluid to collect around the heart in a pericardial effusion, which is very dangerous, but it's very rare to develop cancer in cardiac muscle. And it's not that we don't develop cancer in other muscles because we do, a lot of sarcomas arise in muscle. So why not in cardiac muscle? And I have no answer to that question, but it's so...

Michael E. Farkouh, MD:

Often I've wondered the same thing Dr. Glimcher. The issue was that, why is it so rare? In fact, we have a registry worldwide of cardiac tumors. It takes almost all the countries in the world to come together just to understand primary cardiac tumors, which are, as you say, often sarcomas. So, it is a challenge and it raises the question of the association.

Ron Winslow:

One other way these two diseases are linked is that people of color, people of minority status, people of low socioeconomic status seem to be at higher risk for both of them. A conundrum that has certainly faced the U.S. health care system and probably global health systems for a long time. We have a little time left, is there a way to use this link or at least, is there a way to help? How do we get to making improvements in this particular area?

Laurie H. Glimcher, MD:

Well, I think this is a really complex program. It stems from a whole range of factors. There's no question that socioeconomic factors do link to cancer incidence and at the Dana-Farber Harvard Cancer Center, which is a consortium of seven Harvard affiliated institutions, we're really focusing on this, trying to understand the social determinants of health, cancer prevention and cancer screening, because it should not matter what zip code a patient is from.

We should be delivering equitable cancer care for all of our patients. They do have shared risk factors, cancer and cardiovascular disease, and that contributes to many other diseases as well. But I think this is where a collaboration amongst experts could go a long way to support our communities and our patients. And the other issue is clinical trials.

We don't have adequate representation of underrepresented communities in clinical trials. And I don't know how you can approve a drug and say, it's safe for everybody. If you

haven't had a clinical trial that is very diverse. And so, we're doing a number of things at Dana-Farber to lower the barriers for patients that come from underrepresented communities to come to Dana-Farber and be part of our clinical trials.

Ron Winslow:

Dr. Farkouh, do you have any thoughts about this?

Michael E. Farkouh, MD:

No, I agree completely that we need to have a total evaluation of the health care system. Focusing more on health, cardiovascular health prevention will take us to where we need to go. If we're just treating disease, I think that we're going to not be able to make it from a fiscal point of view and we're not going to meet the needs of society. So I think the social determinants of health are all part of a great prevention program. And that's something that goes beyond our academic centers and into the community.

Ron Winslow:

Well, I think that's a good way to wrap it up. Thank you very much, Dr. Glimcher and Dr. Farkouh, for a great conversation.

Laurie H. Glimcher, MD:

Thank you. It was a pleasure.

Michael E. Farkouh, MD:

Great pleasure. Thanks.