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Cardio-Oncology: An Emerging Field to Improve Cardiovascular Care for Cancer Patients

Announcer:

Welcome to ReachMD. This special program titled, *Exploring the Origins & Future of Cardio-Oncology*, is brought to you by Mayo Clinic.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:

Continuing advances to cancer treatments are steadily, if not dramatically increasing survival rates for patients across a broad range of tumor types, but as the numbers of cancer survivors grow nationwide, so do the long-term impacts of cancer treatments. Among these impacts, cardiovascular disease is an area of particular concern, which has played a small role on the emergence of a new field of cardio-oncology. That field, and the people who are helping bring it into prominence will be the focus of our discussion today. Welcome to Advanced Treatments and Innovations from the Mayo Clinic on ReachMD. I'm your host, Dr. Jennifer Caudle. And joining me are Drs. Kathryn Ruddy and Joerg Herrmann. Dr. Ruddy is medical oncologist and co-lead of the Population Sciences Program for Mayo Clinic Cancer Center. And Dr. Herrmann is a cardiologist at the Mayo Clinic. Doctors, welcome to you both.

Dr. Ruddy:

Thanks for having us.

Dr. Herrmann:

Thank you, Jennifer, I appreciate it.

Dr. Caudle:

Absolutely. Well, I'm excited to have you both here. And to start us off, Dr. Ruddy, can you tell us more about this field of cardio-oncology?

Dr. Ruddy:

This is really a field devoted to improving cardiovascular health, both during and after cancer therapy. As an oncologist, I spend a lot of time thinking about whether or not the side effects of a given treatment could outweigh the benefits. You know, mostly we think about benefits in terms of cancer control, and side effects can include cardiovascular complications. These are particularly important because in some in some severe cases they can be fatal and, more often, they can impair quality of life over the long term.

Dr. Caudle:

Interesting. And – and what about you, Dr. Herrmann? What are your thoughts on this field and how you became involved in it?

Dr. Herrmann:

Yeah. I became involved about 15 years ago, so quite some time ago when we were doing experimental studies on ischemic heart disease with a proteasome inhibitor. That's a therapy that's used in patients with multiple myeloma. And contrary to our expectations, we saw more, not less, disease. And at that time, we realized that cancer therapies can worsen or cause cardiovascular disease with significant impact. And this really shaped what is now the core goal of cardio-oncology; and that is to uncouple cancer-cancer therapy from cardiovascular disease risk so that patients receive the best possible cancer therapy at the lowest possible rate of cardiovascular complications.

Dr. Caudle:

You know, that makes a lot of sense. And keeping that core, goal in mind, Dr. Herrmann, what types of cancer treatments are known to cause or exacerbate cardiovascular disease?

Dr. Herrmann:

This is, this, Jennifer, is really a broad spectrum, but the most important are, I would say, number one: reduction in heart function and heart failure. Number two: acute vascular events such as myocardial infarction. And then number three: arrhythmias. And so, going back to number one, for reduction in heart function and heart failure, the classic example for this is anthracycline therapy. These types of drugs are used still currently widely to treat breast cancer, leukemia, lymphoma, and sarcoma. And it's been well recognized for many years that they can permanently harm heart function. Other therapies can also carry a risk to reduce the heart function and may even lead to heart failure include trastuzumab, Herceptin is the brand name. And this has been used to treat certain types of breast cancer, and even gastric cancer. And the decline in heart function we see with this type of drug, trastuzumab, occurs mainly during therapy, but some recent data indicated it may persist afterwards, just as what we've seen with the anthracyclines. And then more recently too, we've seen inflammation of the heart with immune checkpoint inhibitors, and that's becoming an increasingly important topic just based on the fact that these immune checkpoint inhibitors are now more and more used in the ever-expanding arsenal. So then for the number two aspect, which as mentioned, are vascular events and may even include heart attacks; this can be due to various processes. And one is acute clot formation in the heart vessels because of the damage to the inner lining of the heart vessels and the predisposition to clot formation in cancer patients. Cancer patients, as we know for many years, are predisposed to venous thrombus development, pulmonary embolism, but we feel we can see the same even in the arteries. So that's an important aspect that has emerged. And there's always the vascular activity that some of the vessels spasm down, so to speak, with certain types of therapies. And then we've also learned that some – some medications may actually accelerate the narrowing of heart vessels and other vessels in the body and this is particularly seen with VEG-F inhibitors. These are another type of designer drugs used in renal cell carcinoma patients, but also in GI malignancies and with older style therapies like cisplatin and then the last category where we've seen these kind of accelerated atherosclerosis, the narrowing of the vessels, that is something of particular interest in patients with CML, chronic myeloid leukemia. And then to round it up, item number three, which are the arrhythmias, there are changes in the ECG that we can see and recognize that may predispose to potentially life-threatening rhythm problems. And that's something that's really emerged with the newer agents. We always thought the older chemotherapies are the most risky types of interventions here, but paradoxically, in a way, these newer drugs we have now, particularly since the turn of the millennium, have been found to be associated with various rhythm abnormalities of a certain interval in the ECG, and so this is something to bear in mind in a variety, so of cardiovascular problems can be seen in these kind of medical therapies, but in also we – I just want to briefly mention, shouldn't forget about radiation therapy, because even though there's been significant improvements in reducing exposure, being as preventive as we can be, still there can be risk with radiation therapy and then finally with bone marrow transplantation, there can also be some very important long-term implications. And, as I said in the beginning, Jennifer, this is really a broad spectrum, and we don't have enough time to cover it today, but I think those are the highlights.

Dr. Caudle:

You certainly sort of touched on, or given us a good idea of how broad spectrum this is, even though those are only the highlights. You know, now that we have a better idea of just how serious the effects of cancer treatments can be on a patient's cardiovascular health, how do you both work together to improve cardio-oncology care at Mayo? So, Dr. Ruddy, let's go back to you. Let's hear your perspective first.

Dr. Ruddy:

Well, this is really something that we work hard on to optimize. Dr. Herrmann and his colleagues in the cardio-oncology clinic provide truly exceptional care. I treat only breast cancer. I'm a medical oncologist, so I'm giving sometimes chemotherapy for breast cancer, and I'm often referring patients to cardio-oncology at the start of their treatment. So if they're about to start potentially cardiotoxic treatment, I want to assure that a patient's cardiac medications and doses will be optimized first. And sometimes I'm also trying to make sure that the plan I've devised for cancer treatment really makes sense in light of the patient's overall cardiovascular health. And that's where Dr. Herrmann and his colleagues really play a very critical role.

Dr. Caudle:

That's excellent. And what does this collaborative care look like from your vantage point, Dr. Herrmann?

Dr. Herrmann:

Yeah. I think it's really important that we come out of our silos, as a medical community we tend to, and given the wealth of information, the developments at such an accelerated pace, and it's hard – it's very easy to lose track. And it's hard for that reason to remain focused, and so we might try even harder to do that, but then it keeps us separate. So what we've been trying, Dr. Ruddy and I, as well as, I mean, across cardiology-oncology, is really a team approach to work together. And I would emphasize that communication is key.

And it's a moving target. We continue – we will continue to see different toxicities, new toxicities, so it's not static. And I mean, really the reason we need to have this on an ongoing basis, which we do. So we often discuss topics as they arise. And we look at cancer patients across the continuum of care and this starts even before they receive any cancer therapy. So right there, Dr. Ruddy and I then often have a discussion as what the cardiovascular risk would be and how this might impact the planned cancer therapy. If it's during that therapy that complications arise, then we're always available to discuss further. And if we know ahead of time, thus the importance of this pre-therapy evaluation, we continue to see the patient and follow this. Also goes for - for survivorship. And, um, this is another very important aspect that Dr. Ruddy and I are very passionate about, because I do feel that we need to bring it across the finish line. It's to bring patients through the therapy; that is important, but I think also long-term for them to have a great quality of life, have a great perspective for many years after cancer therapy I think is a really, really important goal.

Dr. Caudle:

For those of you who are just joining us, this is advanced treatments and innovations from the Mayo Clinic on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with oncologist, Dr. Kathryn Ruddy, and cardiologist, Dr. Joerg Herrmann, about the emerging field of cardio-oncology. So, we've been talking about this field's origins in improving cardiovascular care for cancer patients, but let's now focus on the research being done to advance that cause. And I understand you're both pretty active in that arena. So Dr. Herrmann, can you share the research you're currently working on in – in this field?

Dr. Herrmann:

Yeah. So Dr. Ruddy and I, we're currently running a large randomized trial to understand how to best prevent drop in heart function, heart failure in particular, symptomatic heart failure in patients on, a particular type of therapy called trastuzumab in breast cancer patients. And we're looking at echocardiograms. We're looking at certain biomarkers. We have an ECG component to this, looking at some elements of artificial intelligence and machine learning, how we can utilize this. And, also moving forward, how this could be of asset when patients are being followed after the cancer therapy "remotely." And then we're also doing experimental studies in this area, focusing on anthracyclines, um, the ones that, historically, have been associated with the greatest, cardiotoxicity risk. And that spans from basic signs to clinical signs. So it's a little bit of a portfolio.

Dr. Caudle:

That's excellent, and really quite interesting. How about your research efforts, Dr. Ruddy?

Dr. Ruddy:

Well, in addition to the study Dr. Herrmann mentioned, the TACTIC trial, we're also working on using specimens from a variety of different resources. Actually, Mayo Clinic has some tremendous registries to which patients have contributed both tissue and blood and survey data, and that's an incredible opportunity for us to learn more about cardiotoxicity and how best to protect patients from it. Currently, we are using samples from the 8,000 patient Mayo Clinic breast disease registry to look into biomarkers of cardiac compromise, and we're also able to use wonderful patient-reported survey data related to symptoms and side effects of treatment over time in this work.

Dr. Caudle:

Wonderful. And, let's stay with you just for another moment, Dr. Ruddy. You know, how do you say this field of cardio-oncology has changed or is changing as cancer treatments evolve?

Dr. Ruddy:

Well, one of the major changes recently has been the introduction of immunotherapeutic cancer care. This is really a huge advance for the treatment of so many cancers. In some cases, it allows patients to live much, much longer than would have ever been possible previously. But with immunotherapy comes the risk of overstimulating the immune system, and that comes with some cardiac risks, including myocarditis. This is a sudden and potentially fatal inflammation of the heart muscle. And similarly, we have development of a lot of other different targeted therapies, which we're just now trying to figure out the cardiovascular side effects of, and really more research is needed in this area.

Dr. Caudle:

And how do you see things in this field changing over time, Dr. Herrmann?

Dr. Herrmann:

Yeah. Similar to Dr. Ruddy, I do see the same; that these cardiovascular toxicities of cancer therapies are evolving, and there are over 700 drugs in the pipeline, and that's quite a solid number, and then the immune therapy revolution that Dr. Ruddy mentioned, and that includes the immune checkpoint inhibitors and CAR-T cell therapy, and really fascinating improvements and advances. And I think a key aspect to this then is the improved long-term outcomes. So with all these advances in therapies, this is what we've seen already since the 90s. It continues to decline in cancer-related mortality. And with this, an ever-increasing number of cancer survivors. And now this

needs to be coupled with the aging of the risk population. So this will add just another huge wave to this dynamic to this as age is a risk factor for both cancer and cardiovascular diseases. So I think then, more than ever before, we will see this kind of topic to be of significance. And we've, Dr. Ruddy and I, we've recently reviewed and commented on a study that was published in a leading cardiology journal, which looked at a particular database, the SEER database that's run by the National Cancer Institute, and looking over the decades now from the 70s into the current era, and looking at 28 different malignancies. And the key point was that there's already a third of these malignancies where, over time, cardiovascular disease mortality has – has overrun, has surpassed cancer-related mortality, another third of these malignancies are on their way to get there. They're getting really close, cancer and cardiovascular disease mortality. And then another third that included malignancies such as lung cancer, I think is a moving target with the immune checkpoint inhibitors that Dr. Ruddy mentioned. That, in a few years, might also change completely, so I think what we are going to see is a changing dynamic in every increasing significance too of cardiovascular diseases and outcomes in cancer patients. It's the fascinating evolution here that we see that number of cancer patients no longer die from their malignancy but live with their malignancy. Our oncology colleagues have really succeeded so much in their effort, that they turned this into a chronic disease condition. And that's just something new and of significance for many, many years to come.

Dr. Caudle:

Those are both great takeaways for us to think on as we come to the end of today's program. And with that, I'd like to thank my guests, Dr. Kathryn Ruddy and Dr. Joerg Herrmann, for joining me to explore the origins and future directions for the field of cardio-oncology. Doctors, it was great having you both on the program.

Dr. Ruddy:

Thanks for inviting us.

Dr. Herrmann:

Thank you so much, Jennifer. It was a huge honor, and we really welcome and appreciate this opportunity very deeply.

Announcer:

This was a special program titled: Exploring the Origins & Future of Cardio-Oncology is brought to you by Mayo Clinic. To access other episodes of this series, visit reachmd.com/MayoClinicInnovations. Thank you for listening to Reach MD, where you can be part of the knowledge.