

Title: Cardio-oncology A-Z: Breast Cancer Treatment Related Cardiotoxicity Participants: Dr Anne Blaes (University of Minnesota, Minneapolis, MN, US)

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- My name is Dr. Anne Blaes. I'm a Medical Oncologist and Associate professor at the University of Minnesota in Minneapolis, Minnesota, where I'm also the Director of Cancer Survivorship Services and Translational Research for the Masonic Cancer Centre.

What are the main cancer treatments that cause this problem?

Dr Blaes: When I see patients with breast cancer, there are a number of things that can cause cardiac issues or heart complications after their therapies or during their treatment. Some we think of as chemotherapies, such as anthracyclines or trastuzumab, otherwise known as Herceptin. The anthracycline for our breast cancer patients, these are your medications like AC or EC. These are the anthracyclines that can disrupt microtubules in the cardiac myocytes of the heart itself and cause heart failure like symptoms. Trastuzumab or Herceptin can cause cardiac dysfunction in a different mechanism and is oftentimes reversible when we stop that medication. Other types of therapies, some of the medications that are used can cause hypertension or hypercholesterolemia. When patients receive breast cancer treatments such as radiation, there's a slight increased risk of cardiac ischemic disease or higher rates of cardiovascular disease in individuals who have left-sided breast radiation compared to right-sided breast radiation. And then some of our newer medications like immunotherapy that are now being used in triple negative breast cancer have rare complications where they can affect inflammation in and around the heart. This is a rare complication, but something that can happen with those treatments.

Are there risk factors which predispose patients to this problem?

Dr Blaes: Typically, I tell patients, you want to know the treatments that you've received. So you want to know the names of the chemotherapy drugs, whether or not you receive radiation, how much you had as well as the antiestrogen therapy that you might be receiving.



There are traditional cardiac risk factors, such as things like hypertension, hypercholesterolemia, diabetes. These can all augment or increase the toxicity or the potential for somebody to have heart complications after their breast cancer treatment. So typically, when I see patients, I'll talk to them about those risk factors upfront.

Are we working with a primary care provider to optimise those risk factors such as, is your blood pressure under good control? Has your cholesterol or blood sugars been checked recently? But we also talk about those things during the course of treatment and in the survivorship period. When blood pressures are elevated in our breast cancer survivors, they can augment or increase the risk for later complications after their treatment.

How common is this issue?

Dr Blaes: When I think about heart risk in individuals who've gone through breast cancer treatment, it's important to know how much of particular drugs they've received as well as the types of treatments. So really having a treatment summary can impact sort of what that risk is. For example, a patient who received anthracycline such Doxorubicin, their risk of cardiac dysfunction may be on the order of 3 to 4%. This is dose related, so it all depends on how much somebody received. If you received, for example, four cycles of AC as part of your breast cancer treatment, you received a total of 240 milligrammes per metre squared of doxorubicin, giving you an ultimate risk of heart complications of approximately 1 to 2%. This risk increases significantly if somebody had larger amounts of the medication and can go up into the order of 10 to 12% and sometimes even higher.

As oncologists, when we prescribe these medications, we take very good histories about whether or not somebody might have received that. For example, if someone had a prior lymphoma and they might have received chemotherapy and now has breast cancer, this might increase that risk of cardiovascular complications. So as oncologists, we oftentimes will ask, can I give a different treatment and get the same outcome?

For other medications like trastuzumab or Herceptin, the risk of cardiac issues is a few percent. I think what's not always recognised though, is the fact that many of our breast cancer patients are getting older, and as they age, they are also at higher risk for things like high blood pressure, high cholesterol.



There was a recent publication in JACC Cardio-oncology looking at our older breast cancer patients. And as women get farther out, seven to eight years after their breast cancer diagnosis, their cardiovascular risk surpasses that of a breast cancer recurrence. So thinking about ways to reduce that risk is really important.

Should it be screened before treatment or monitored during or after treatment for this?

Dr Blaes: And so, when I think about somebody and their heart risk, and they're sitting in front of me with a new breast cancer diagnosis, it's important actually to think about heart risk throughout the course of their treatment. So, at the time somebody originally presents with breast cancer and I'm making a prescription on how to treat their breast cancer, we should be thinking about those risk factors at the very get-go, asking ourselves, do they have other risk factors? Are they an older individual? Do they have some of the risk factors that I mentioned such as high blood pressure, high cholesterol? Am I prescribing one of these medications, such as an anthracycline? Will they need radiation such as left-sided breast radiation, which can slightly increase the risk of heart complications, and do they have prior heart disease or prior history of heart failure? If they have any of those risk factors and part of their treatment requires me to use some of these medications that can affect heart function, I would recommend that they see a cardio-oncologist and have a baseline assessment.

That baseline assessment can include looking at blood biomarkers such as a proBNP or a troponin. It may also include using a heart ultrasound or an echocardiogram to really look at the way that the heart pumps. As people go through their cancer treatment then and are on treatment, we typically will follow their cardiac function, particularly if they're receiving medications like anthracyclines or trastuzumab-based therapies.

For trastuzumab-based therapies, these are typically heart ultrasounds, are recommended every three months during the course of their treatment. This can sometimes be modified for patients that are in the metastatic setting and are receiving these types of treatments for many years, particularly if they've had no complications. And then for individuals in the survivorship period where they may be done with their treatment and their cancer has been cured, we also talk about cardiovascular risk and risk reduction.

As I mentioned, there are several cohort studies emphasising the fact that our older breast cancer patients are at higher risk for cardiovascular disease than the general population.



And as a result, it's important we work with primary care doctors to optimise their risk factors such as blood pressure cholesterol, helping to make sure that they're avoiding tobacco use, and all my patients in clinic will hear me say, keep moving. So I think it's really important that individuals are exercising regularly. That may be moderate intensity walking, 30 minutes most days of the week, five to six days a week. We know that that helps to prevent recurrence and can help prevent cardiovascular complications.

How can it best be managed?

Dr Blaes: This is a good question. So, I'm going to break your question down into kind of two pieces. How do we best manage this? Well, if you have breast cancer and you have some other risk factors for cardiac complications, I would first say, are there things I can do to help prevent this? We can't make our breast cancer go away without treating it, but we can be proactive about how to reduce risk factors for potential complications.

This might include meeting with a cardiologist or primary care doctor to ask, what about using blood biomarkers or preventative medications like ACE inhibitors or beta blockers to help prevent any of these cardiac issues.

If it's a patient who's in the metastatic setting and they're living with their breast cancer, it's important to work with cardiology and oncology about how to optimise breast cancer outcomes while keeping the heart well.

What do I mean by that? So, for individuals, for example, on trastuzumab, this can vastly improve breast cancer outcomes, helping these patients live for many, many years. If they have their heart monitored regularly and there is a decline in the way that their heart pumps, there are medications such as ACE inhibitors or beta blockers that can help stabilise the cardiac function.

These medications can be continued through their treatment, and oftentimes it's close collaboration between cardiology and oncology in helping patients stay on their breast cancer treatment while keeping their heart healthy. And in the survivorship period, as I mentioned, you know, I always tell patients, keep moving, avoid tobacco use, and keep an eye on your blood pressure and cholesterol and blood sugars. All these things can contribute to heart disease and can accelerate the risk of cardiac issues in breast cancer patients.