[MUSIC PLAYING]

MATTHEW HARINSTEIN: I'm Dr. Matthew Harinstein. I'm an Associate Professor of Medicine at the UPMC Heart Vascular Institute and University of Pittsburgh School of Medicine and a Senior Vice President for UPMC International. And I'm going to be talking about cardio-oncology and screening and surveillance. I have no disclosures for this presentation.

So a cardio oncology program, why do we need it? There's many known and unknown cardiotoxicities that are related to chemotherapeutic agents. Years ago, we only knew of a couple. And now there are a multitude.

Treatment of hypertension has become a critical issue related to patients' ability to tolerate regimens. Patients may often not obtain recommended schedule of cardiac imaging assessment. So it's our job to make sure that they're properly assessed so that they're not surprised when they have a cardiac problem years later that could have been diagnosed substantially time before. Newer imaging techniques and suggested algorithms exist, which may be helpful in identifying a cardiomyopathy or what we call now CTRCD, which is Cancer Therapeutics-Related Cardiac Dysfunction. And a collaborative approach between cardiology and oncology is always best for patient care.

So CTRCD, what is it? It's a decline in the ejection fraction from baseline of greater than 10% change to a value that is a less than 53% ejection fraction. It can be symptomatic or asymptomatic and reversible or irreversible. So when we talk about this cardiomyopathy, or CTRCD, there's two types.

Type 1 is the prototype being doxorubicin or the anthracycline medications. And these are cumulative dose-dependent and irreversible types of cardiomyopathies. So these are typically cardiomyopathies that we don't anticipate, even with treatment, will improve substantially-- and, again, anthracyclines being the classical medication.

For type 2, the prototype is trastuzumab or Herceptin. Others are listed there. These are considered to be not cumulative dose-dependent.

For many of you who know, this is a common medication that might be used for HER2-positive breast cancer. These are mostly reversible types of left ventricular dysfunction, and there's no changes on the biopsy. So for the type 2 agents, we hope that with stopping the agent that the cardiomyopathy may actually resolve.

This, I show, is just a list to show you all of the different types of medications, and there are even more chemotherapeutic agents that may be associated with cardiomyopathy. So it's not just your classical doxorubicin and trastuzumab anymore. There's many other medications that have been implicated to various degrees.

So in terms of the anthracyclines, the mechanism of action, they inhibit DNA and RNA synthesis by intercalating between base pairs, preventing replication of cancer cells. They also inhibit topoisomerase II, and they can generate free oxygen radicals, damaging the DNA and the cell membranes. Commonly, they're used to treat leukemias, lymphomas, breast cancer, stomach, uterine, ovarian, bladder, and lung cancers.

So you can see that they're a very common type of medication-- excuse me-- chemotherapy agent that is used. And oftentimes, you'll see that survivors of childhood cancer have received anthracyclines. And so it's important to be aware of that and the total dose that they received, so you know how to monitor them and provide surveillance years later.

In terms of some of the risk factors associated with this type of CTRCD, cumulative dose oftentimes report is greater than 240 milligrams per meter squared. If it's given as an IV bolus administration, higher single doses, if there's a concomitant history of radiation therapy, concomitant use of other chemotherapy agents that are known to cause cardiotoxicity, female gender, underlying cardiovascular disease, uncontrolled hypertension, age, and increased biomarkers.

What are some of the prevention measures? So serial imaging-- very important that we monitor patients who are receiving these regimens. Make sure we understand what the doses they're receiving are, what the cumulative dose is, so we know how frequently to image them. Anecdotally, I think this is just so important because where I tend to see patients who have cardiomyopathies is they received these types of medications years ago.

Now, all of a sudden, they get an echo and find out that they have a cardiomyopathy or heart failure. And they never had this serial imaging in between. And one has to wonder, if we could have caught it sooner, at least we could have stopped the medication. So even if it didn't resolve, it potentially didn't get worse, and so on, and so forth.

Dexrazoxane is a cardioprotective drug that can be used. It reduces the risk of CTRCD by about one third. This chelates iron and reduces the number of metal ions complexed with the anthracycline, thus decreasing the number of superoxide radicals-- so another agent that we can use to try to limit risk. Liposomal formulations are less toxic to cardiac tissue, and longer infusion rates may also reduce plasma level.

So there are a series of cardio-oncology-related statements and guidelines that have come out now over the years. Before, there really wasn't much. But increasingly, year over year, we're seeing more and more literature coming out. And of course, medical journals are now devoted solely to cardio-oncology. So it's really a budding field.

In terms of the expert consensus statement on imaging from the*Journal of the American Society of Echocardiography* recommended cardio-oncology echocardiogram protocol is listed here. Certainly, a standard transthoracic echo in accordance with guidelines, 2D screen imaging acquisition, as well as screen imaging analysis-- we'll go into that a little bit more-- trying to use 3D image acquisition, if possible, to assess LV volumes and ejection fraction more precisely. As we mentioned, in terms of the diagnosis, the more precise you can be with an ejection fraction number, the better because we're looking at a change of greater than 10% to an ejection fraction of less than 53%.

So if you're off by 5% to 10%, obviously, sometimes, that can make a big difference. So trying to use the same technique, the same machine, the same sonographer can be very valuable. And then, of course, reporting as we normally would.

In terms of strain imaging, I show you that there are differences here based on age and gender-- certainly, as well, based on the type of machine that's used, whether it's GE versus Philips or Toshiba, for example. But this is another technique that we can utilize to understand everything subclinical left ventricular dysfunction. We use two standard deviations below the mean-- so about negative 17, so if it's more positive than negative 17. So if it's somewhere-- negative 16, negative 15, that is considered to be an abnormal strain. And if it's more negative or less than negative 17-- so into the negative 20 range, and so on, and so forth-- that would be better.

Just an example here of what we look at with this strain imaging. We look at the global longitudinal strain. And here's an example at baseline in the panel A, negative 20.6%.

This would be considered to be normal. And then three months post trastuzumab therapy, you have it less than-- or excuse me-- negative 14.4% global longitudinal strain, which demonstrates two things. Number one, that the strain is now in the abnormal range. And number two, that the difference between the baseline and the new strain is a greater than 15% change from the baseline.

So when we use strain, how do we use it? What we do is we'll start with-- excuse me-- when we use the echocardiogram, how do we use it? We start with the assessment of the left ventricular ejection fraction. And we also will try to use the 3D echo if possible and 2D echo with contrast, if needed, for left ventricle classification. If the ejection fraction is less than 53% and your global longitudinal strain is less than the lower limit of normal with positive troponin, certainly want to consider cardiology consultation. If your ejection fraction is normal and the strain is OK, you'll just want to follow along with your recommended algorithm.

With trastuzumab, again, same situation. If you have any reduction to the ejection fraction and development of CTRCD, you want to consider cardiology consultation. And the same would be in patients with a type 1 toxicity.

In terms of strain, how do we use it? So it's a reduction in global longitudinal strain of greater than 15% from baseline means that subclinical LV dysfunction is likely. So a patient can still have an ejection fraction that is normal or has not changed by greater than 10%. But if their global longitudinal strain has changed such that it is reduced by a factor of greater than 15%, this may be a warning sign of LV dysfunction is to come.

And so exactly how to tailor your therapy is still being studied and up for debate. But many people will think about using other regimens, if possible. Certainly, if that regimen is, by far and away, the best regimen to treat the patient's cancer, oftentimes, we'll just follow it even more closely. But if there's an alternative regimen that may be equally useful, we'll recommend that we switch the regimen and also consider starting medications that we commonly use for cardiomyopathy, such as beta blockers like carvedilol, or ACE inhibitors, such as lisinopril.

If the reduction in global longitudinal strain is less than 8%, then we consider that to be no evidence of LV dysfunction. So following this algorithm here, if you have a drop of 10 points to less than 53%, you have made the diagnosis. If the answer is no or yes, then-- excuse me-- if the answer is no, we still will look at the global longitudinal strain. And if the difference is less than 8%, there's no evidence of subclinical LV dysfunction. If it's greater than 15%, there is.

So it's important when you're doing your global longitudinal strain and looking for the subclinical LV dysfunction, that you try to use the same vendor ultrasound machine and, ideally, the same sonographer, if possible, and if it is identified that a cardiology consult is sought. And again, as I mentioned, no clear evidence-based management strategies at this point.

In terms of the ESC position paper on cancer treatments, this is a very valuable document that I recommend taking a look at with recommendations for cardiac cardiovascular toxicity related to these treatments. So what are some of the baseline risk factors for cardiotoxicity that you should be aware of? Many of the things that you would think of-- so previous cardiac history, so history of heart failure, if you already have asymptomatic LV dysfunction. And this gets into another discussion about when should you start treatment.

And oftentimes, you want to have an ejection fraction of at least 40%, but that's certainly where the cardiology consultation comes in and a discussion between the doctors. If you have a history of evidence, it can be a history of coronary artery disease. If you have valvular heart disease, hypertensive heart disease with LV hypertrophy, hypertrophic cardiomyopathy, dilated or restrictive cardiomyopathy, sarcoidosis, or significant arrhythmias.

Again, also, risk factors for cardiac toxicity include previous anthracycline use-- so particularly, in patients who might have been childhood cancer survivors-- or if you have a history of radiotherapy to the chest in the past. Other risk factors include age, family history, history of hypertension, diabetes, high cholesterol, smoking, alcohol intake, obesity, and sedentary lifestyle. So again, many of the risk factors you would typically think of for cardiovascular disease, again, are relevant here.

What are some of the factors associated with a risk of higher toxicity following treatment with anthracyclines? So again, we touched on this a bit before-- cumulative dose, female gender, age over 65 or the pediatric population, kidney problems, radiation therapy, concomitant chemotherapy, or pre-existing conditions.

Some of the factors associated following anti-HER2 compounds and VEGF inhibitors. So these are the trastuzumab that we talked about earlier for the top panel here and very similar. So previous or concomitant anthracycline use, age, obesity, LV dysfunction, hypertension, radiation therapy, and similar for VEGF inhibitors as well.

One of the other things we want to think about is VTE. So what are some of the risk factors for cancer-associated VTE? So things you should be aware in terms of screening and surveillance for patients. You want to think about cancer-related factors-- so primary site of the cancer, mostly in the pancreas, brain, stomach, kidney, and the lung, lymphoma, or myeloma, the histology, especially adenocarcinoma, metastatic disease, and an initial period right after the diagnosis of cancer.

Some of the patient-related factors include older age, again, female gender, African ethnicity, comorbid conditions, a history of venous thromboembolism in the past, or inherited thrombophilia, low performance status. And then some of the treatment-related factors include major surgery, as one would expect, hospitalization, as we know, is always a risk factor, chemotherapy, and antiangiogenic agents, hormonal therapy, transfusions, and central venous catheters.

How about some of the surveillance modalities that we should be aware of for CTRCD detection? So we talked about echocardiography as well nuclear cardiac imaging with MUGA, so certainly very common in the past to use as the assessment of ejection fraction. We still do use MUGA, but we also use now a resting spec studies as another way to do this. One could also use cardiac magnetic resonance, although maybe a bit less practical from an availability standpoint and a lot longer to obtain the ejection fraction.

And certainly, as it relates to nuclear imaging techniques, particularly in resting spec studies, with some of the newer technologies, like the solid state or CCT cameras, the radiation dose can be lowered quite a bit now, and the study can be done much more quickly. So it may be more practical as well to get that specific number and try to have reproducibility of the data. As well, other surveillance modalities that we use would be troponins and BNP for biomarkers.

What are some of the strategies to reduce chemotherapy-induced cardiotoxicity? So you want to identify, of course, and treat the risk factors. So everything you can do to make the patient otherwise healthier beyond their cancer is always beneficial. You want to treat those co-morbidities, minimize any radiation exposure to the chest or to the heart, if possible.

You want to always limit the anthracycline dose as much as possible. So the lower, the better, of course. You want to alter the delivery systems, as we talked about, the liposomal formulation or longer infusion times. Consider use of dexrazoxane. And potentially, there may be roles for medications like ACE inhibitors and beta blockers in both anthracycline and trastuzumab use.

So just as a summary for strategies to prevent CTRCD, if you have the use of tumor-targeting formulations and liposomal doxorubicin, that's better. Try to consider the use of the dexrazoxane therapy. You want to identify the risk factors prior to administration of chemotherapy. You want to identify the patients where anthracycline should be avoided.

A patient should be monitored regularly on completion of the therapeutic regimen. So I think one of the things that we'll go in is as I show you our strategy for monitoring patients is it's important to remember, even when patients are nearing therapy or have concluded therapy, that you make sure to continue to follow up those patients to make sure that you're not missing anything because the doses have been higher at that point in time. You want regular follow-up with patients for detecting long-term cardiotoxicities and the appropriate use of cardioprotective drugs when essential.

So in terms of our proposed imaging algorithms, these are based on guidelines from the American Society Echo, the ESC, and ASCO. So for type 1 agents, these are the anthracyclines that typically cause the more dose-dependent, irreversible cardiomyopathy. You want to get an echo or assessment of the ejection fraction at baseline. If the cumulative dose is higher than 240 milligrams per meter squared or equivalent, you want to then image prior to each additional 50-milligram per meter squared dose.

You then want to image again at the conclusion of therapy. So even if a patient has gotten their last dose, they're done, they're not getting any more, you want to still get an echo because you just completed a course. And then, again, there is still a risk of cardiomyopathy appearing in that next six-month period. And so six months post-therapy, you also want to get an imaging study. And I think that's very important to remember.

Where the type 2 agents, like the trastuzumab, that can cause the more reversible type of CTRCD or cardiomyopathy, you want to image at baseline. Then you want to image every three months during therapy-- so very important to remember-- at completion of therapy. and then six months post-therapy-- so very similar to the type 1.

In terms of radiation-induced heart dysfunction, in terms of screening and surveillance, what are some of the things that we want to drive home? Well, when you think about this, what are patients at risk for? Patients can develop early coronary artery disease, dysfunctional valves, microvascular disease, myocardial ischemia, myocardial fibrosis, conduction abnormalities, or even be susceptible to pericarditis-- so many risks that we need to think about.

So you want to make sure that for these patients, you pay attention to their traditional cardiovascular risk factors, their age at the time of radiation therapy. If they have any pre-existing cardiovascular disease, it should be treated. You want to screen for the risk factors and symptoms annually, perform an annual electrocardiogram because the chance of conduction abnormalities. Functional stress test and echo following radiation therapy and then every five years. And then you want to pay attention to all of those risk factors and associated variables that we know of for cardiovascular disease, like the blood pressure, lipid management, hemoglobin A1C if diabetic, and make sure that they're taking the appropriate lifestyle modifications.

So what are some of the strategies specifically to reduce the risk of radiotherapy complications? You want to think about heart-sparing techniques. So the less radiation that can be applied directly to the heart, the better. So you want to think about the ALARA principle-- As Low As Reasonably Achievable. You want to reduce the field in the cardiac volume. You want to deep inspiration breath hold technique or respiratory gating, and planning of radiotherapy to minimize the distance between the cardiac contour and the posterior tangential field edges.

So now I'm going to take you through a little bit of a tour here of the ASCO clinical practice guideline and, again, another document that I would refer you to and recommend to take a look at. So there are about five primary recommendations that came out of this document. And there was an overarching number of clinical questions that were addressed in this document. So one was, which cancer patients are at increased risk for developing cardiac dysfunction?

So that was related to recommendation 1. Recommendation 2 is related to which preventative strategies minimize risk before initiation of therapy. For 3, what strategies minimize risk during potentially cardiotoxic therapy? For 4, what are the preferred surveillance and monitoring approaches during treatment in patients at risk for cardiac dysfunction? For 5, what are the preferred surveillance monitoring approaches after treatment in patients at risk for cardiac dysfunction?

So in terms of the summary of recommendations, clinical question 1 was, which cancer patient are at increased risk for developing cardiac dysfunction? I think we've already addressed that overall here in this presentation. But again, you want to think about the high anthracycline dose, high radiotherapy dose. And even if patients have lower anthracycline does, you want to think about things like if they're in combination with radiotherapy.

As well, you want to be cautious and considerable cardiac risk factors, like older age at cancer treatment, multiple cardiovascular risk factors, including smoking, hypertension, diabetes, and so forth, and a compromised cardiac function at any time prior to or during treatment.

Clinical question 2-- which preventive strategies minimize risk prior to initiation of therapy? So for the 2.1, you want to make sure you avoid or minimize the use of potentially cardiotoxic therapies. And established alternatives exist that would not compromise cancer-specific outcomes. So I think this is an important point in where a cardiology consultation is very important.

Again, as cardiologists, I think one of my experience has been that we are very concerned about having cancer, and we want to make sure we do everything to treat the cancer. Whereas you'll find that oncologists know how to treat the cancer, and they're very concerned about the cardiac problems. And so this is why working together is so, so important to make decisions for patients. And if there is a specific cancer treatment regimen that is just so superior, we want to do everything possible we can to try to get that patient through that. Now, having said that, if they're having severely compromised cardiac function, then we need to think about changing the regimen.

On the other hand, if we look at something and we say, yeah, there are alternatives, they're pretty close, there's not a big difference, then it's probably reasonable to switch to that new regimen to prevent the cardiac complication or to limit some of the effect that we're already seeing. And so this is where having that great relationship between cardio-oncology-- cardiology and oncology is so important.

In terms of highlights of a clinical question 3, which preventive strategies are effective in minimizing risk during the administration of potentially cardiotoxic cancer therapy? Clinicians should screen for an actively managed modifiable cardiovascular risk factors in all patients receiving potentially cardiotoxic treatments. And clinicians may incorporate a number of strategies, including the use of the cardioprotectant dexrazoxane, continuous infusion, liposomal formulation of the anthracyclines, as we discussed before-- so all of those recommendations that we had touched on previously in this presentation. Also important that you should select a lower radiation dose when clinically appropriate, and use more precise or tailored radiation fields with exclusion of as much of the heart as possible.

Clinical question 4-- what are the preferred surveillance monitoring approaches during treatment in patients at risk for cardiac dysfunction? We touched on that earlier. We go into in this recommendation, the use of echocardiograms, cardiac MRI, MUGA scans, biomarkers, and so forth that we discussed earlier. But very important to follow a regimen.

And I can't stress that enough, is I think when we see complications, it's because patients didn't receive this. And I think, again, that's why it's so important to have a cardio-oncology program because the oncologist can work with the cardiologist who is aware. And that's their job is to focus on the heart, and the oncologist can focus on the cancer, and everybody works together. So having that coordinated clinic is just really beneficial. Again, routine surveillance and so forth.

In terms of clinical question 5, what are the preferred surveillance monitoring approaches after treatment in patients at risk for cardiac dysfunction? Clinicians should complete a careful history and physical exam in cancer survivors previously treated with potentially cardiotoxic therapies. Also important to remember, as I mentioned to you, at the conclusion of therapy and at six months post-therapy, continued to monitor the ejection fraction. And we'll focus mostly on adults in this presentation but also important to think about patients who have been survivors of cancer, particularly those in childhood, and to continue in follow-up after their cancer therapy, even those who are in remission or who have been cured, to continue to monitor them for the effects of those potentially cardiotoxic medications.

So I want to also touch base on hypertension screening in terms of Vascular Endothelial Growth Factor inhibitors, the VEGF inhibitors. These are some of the medications that you might have heard of, like bevacizumab, sunitinib, or sorafenib as examples. They're typically used to treat solid organ tumors. The mechanism is such that they affect normal homeostasis by interfering with production of nitric oxide, leading to vasoconstriction and, ultimately, decreased blood flow to the tumor.

This can lead to increased systemic vascular resistance, which leads to increased systemic hypertension. Typically, when we see this, oftentimes, it'll occur within the first month, but it can occur later as well. And important for weekly blood pressure monitoring the first cycle and surveillance that follow-up visits. And again, I think this is anecdotally another thing that we see in the cardio-oncology clinic, where patients come to us from physicians who might not be aware of some of these effects or accustomed to treating such substantial hypertension.

We can see patients with very significant hypertension who had normal blood pressure before they started treatment. And now, all of a sudden, the blood pressure is in the 160s, 170s, or 180s, and require even two agents to treat. And so this gets to, oftentimes, be out of the expertise or comfort level of some of the treating physicians and, again, why cardiology follow-up can be so important. And again, the sooner we can treat this, the better so that patients aren't subjected to potentially some of the side effects related to the significant hypertension.

Just touching briefly on childhood cancer survivor cardiomyopathy risk-- so again, we could do a whole other presentation on this topic alone. But I think it's important to recognize that you may have patients who received anthracycline therapy as a child, were treated when they were five to 10 years old and now have been, quote/unquote, cured. But now they're in their 20s, or 30s, or 40s, and how do we continue to monitor them? What are some of the key risk factors that we think about?

So things that increase your risk in particular-- those who have a higher cumulative anthracycline dose that they received, a higher radiation dose that they received, the lower the age at greater toxic exposure, and if they developed cardiac comorbidities, like hypertension, hyperlipidemia, and diabetes.

Things that reduce the risk are the typical things that you would think about-- exercise, normal body weight, pharmacologic intervention, diet, and aggressive management of cardiac comorbidities. So when we look at a number of different variables, what are some of the different things that we can utilize in clinical practice in terms of cancer survivors at risk for cardiotoxicity, should they need treatment? Again, a lot of the same features that we discussed before. But one of the things I want to highlight is on the panel recommended frequency of echocardiogram that we have here on the slide is you might have patients, again, who had cancer, no longer have it.

And you might not know that they need to continue to be imaged, but it's really important that they are. So you can see here, we look at the age of treatment, as well, whether or not they had radiation therapy, what their cumulative anthracycline does, and what the recommended frequency was. So let's say, for example, you had a patient who had age at treatment that was greater than or equal to five years old, and they had radiation with potential impact to the heart. And then the anthracycline dose, for example, was less than 300 milligrams per meter squared. You would want to image them actually every two years to monitor them for cardiac dysfunction.

On the flip side, if it was greater than 300, you want to monitor them every year. And if that differs from if you look below, if they did not have radiation exposure and less than 200, it would be every five years. So somewhere between every year to every five years, you want to continue to screen patients and look for cardiac dysfunction.

And certainly, if you see any sign of it, you want to evaluate it as you ordinarily would because, of course, patients, even if they had cancer, can still be susceptible to all of the other variables that they can develop over time, like diabetes, and obesity, and so forth, and could have coronary artery disease just like any other patient would. So it's important to do a stress test or whatever modality you feel is appropriate to assess that patient and put them on therapy for their cardiomyopathy. But , important to be mindful of the fact that they did have a childhood cancer and to get as much data as possible on the cumulative doses, what the regimens were, and then make a determination of how often that you want to image them or refer them, of course, to a cardio-oncologist.

Getting back to where we started, we said, what's the importance of a cardio-oncology program? And I think we highlighted here in this presentation a lot of the different variables you want to think about when screening patients and then providing surveillance for patients who are getting ongoing therapy with either chemotherapy, radiation, or otherwise. And so what are some of the referrals that you might see in a cardio-oncology practice or clinic?

And those might be for things like cardiac mass or tumor evaluation, pericardial disease or effusion evaluation, preoperative cardiac risk assessment, cardiac amyloidosis evaluation, congestive heart failure or cardiomyopathy evaluation, cardiovascular risk assessment before stem cell transplant, a vascular disease evaluation, including TKI or radiation induced, for ischemic heart disease evaluation, for cardiovascular risk assessment before radiation to the chest, head, and neck, and so forth, for treatment-associated hypertension, as we touched on recently with the VEGF inhibitors, for patients who might have arrhythmias, or syncope, or autonomic dysfunction that they might develop from the treatments, and for cardiovascular risk assessment before chemotherapy-targeted therapy, and, of course, now immunotherapy as well.

In terms of referrals, what's the timeline that we're thinking about? This is just some suggestions, but things that might be more urgent would be a new referral for active cancer therapy pending or ongoing. And I think this is important to think about because, oftentimes, patients might not have much wrong with them in terms of the cardiovascular issue or might not have a history of cardiovascular disease. And yet, they're calling to say, we need to be seen right away. And this is why it's important to have that good communication between the cardiology office and the oncology office because it's important to remember that when a patient has been diagnosed with cancer, in many cases, they may need to be treated ASAP.

And if that's the case, we want to make sure that whatever is needed to get them screened and cleared to get their therapy and to make sure that the appropriate precautions are taken, we do right away. So we might need to get a patient in within the next day. They might need to be sent down. They might have gone upstairs, and we got a call saying, can we send them down to your office to be seen or to get an echocardiogram? So again, that can be an urgent referral, even if someone doesn't have a significant cardiac problem. But I think it highlights the importance that good communication and the overall cardio-oncology program and concept.

And progressive heart failure as well, new or worsening angina, uncontrolled arrhythmias-- excuse me-- and post-hospitalization heart failure. Something that might be more semi-urgent-- new diagnosis of compensated heart failure or class II to III heart failure symptoms. And something that's more routine might be a new referral with stable cardiovascular disease but no active cancer therapy. It's not needing to be done right away or just follow-up care.

So what are some of the summary recommendations to take home? You want to determine patients who are at increased risk for CTRCD. You want to consider preventive strategies to minimize risk. You want to think about surveillance strategies during and after conclusion of therapy-- so remember, at the conclusion and then post-therapy as well, and then, of course, management strategies.

You want to evaluate patients for risk factors prior to treatment. You want to review side effects of treatments in addition to type 1 and type 2 agents. You want to monitor patients during and after treatment. Think about development of type 1 CTRCD.

If they have that, no further treatment with the offending agent at that point is recommended. And if they develop type 2 CTRCD, you want to stop the trastuzumab. And if the LVEF returns to normal, you can attempt to restart therapy and, of course, at that point, refer to a cardio-oncology clinic for further management at that stage.

And I want to thank you very much for your attention and for allowing me to present this presentation about cardio-oncology screening and surveillance. Thank you.