Cardio-oncology A-Z: Radiation Induced Heart Disease

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1. Types of Radiation Induced Heart Disease

Radiation-induced heart disease really is a collection of different issues that can come from radiation to the heart and vasculature.
Radiation can affect any part of the cardiac structure or sub-structure that's within the radiation field. I think it's also important to realise that radiation can affect the vasculature outside the radiation field, including the great vessels, such as subclavian stenosis, or other areas of vasculature.
I have a couple of pictures to show you. One is from the "Polish Heart Journal," which is due for publication just this next month led by postgraduate Dr. Pederson and Dr. Bergom of Radiation Oncology, and it shows you the many ways that radiation can affect the cells, the vasculature, the heart, the pericardium, and leads to pericardial disease, valvular disease, myocardial fibrosis, coronary artery disease, as well as peripheral vascular disease.
And here, I also have a slide from our recent international Cardio-Oncology Society Guidelines that shows that radiation can affect any part of the vasculature that's within the radiation field.
We often typically think of radiation heart disease and think of the heart itself, but we also really need to think more broadly as far as the vasculature that's within the radiation field.
And sometimes, too, we think of the radiation as the mean heart dose or the mean amount of radiation delivered to the heart, but really, we have to think of the amount of radiation delivered to each substructure, and so here, we also have a picture of the heart, as well as the evidence that shows that radiation to any part of the heart, the cardiac substructure, can lead to disease in this area.

2. RIHD Risk Factors

The risk factors for radiation-induced heart disease or radiation-induced cardiovascular disease really come from a few different areas. The first are treatment-related risk factors. Those treatment-related risk factors can be broken down to the radiation itself, how much radiation is delivered to the heart or the vasculature, and in what manner, as well as two, concomitant therapies.

If a patient's treated with anthracyclines, for instance, the risk of heart failure goes dramatically up. Other than the treatment-related risk factors are the patient-related risk factors. And so, does the patient have pre-existing cardiovascular disease? Do they have underlying cardiovascular risk factors, such as hypertension or hyperlipidemia?

We know from childhood cohorts, from St. Jude's and Dr. Armstrong's group, that these cardiovascular risk factors in addition to the radiation dose itself dramatically increase the patient's risk for radiation-induced heart disease, hypertension chief among them.

If it develops in the patient, even in survivorship, dramatically increases that patient's risk for cardiomyopathy, coronary artery disease, or valvular disease.

We also know with emerging research that, beyond these traditional cardiovascular risk factors, if we see evidence of coronary artery calcium on the radiation planning scan, or other screening CT scans, that's evidence of underlying coronary artery disease itself, and finding coronary calcium, or CAC, on these baseline CT scans can be even more predictive than the ASCVD risk score or other risk scores that are derived from traditional risk factors.

And so when we're looking for the risk of disease, we're really focusing on number one, the radiation dose to the heart itself, or cardiac or vasculature substructure, number two, what other therapies they may be on, and number three, what are their underlying cardiovascular risk factors or cardiovascular disease to include coronary artery calcium?

3. How common is RIHD?

The prevalence of radiation heart disease completely depends on the cohort in question. So if you're looking at a cohort of patients that were treated with high dose radiation to the heart with mantle radiation, for instance, their risk of radiation heart disease is going to be much higher than a cohort of patients that has relatively small dose of radiation to the heart.

However, we also know that there is no dose of radiation to the heart below which is safe. So any dose of radiation to the heart causes issues down the line.

I have here a couple of graphs to help illustrate what the prevalence of radiation-induced heart disease. On the left side of the screen, you can see the risk of radiation heart disease in a group of lymphoma, leukaemia, and sarcoma patients in the childhood cohort from St Jude's.

And in blue, you can see the risk of these diseases in a radiation cohort versus patients with cancer who do not receive radiation or match siblings, and the risk of coronary artery disease approaches 10%, 20-plus years after radiation.

You can see the risk of valve disease, or arrhythmia, and heart failure. And what you can appreciate from this graph is that this risk continues to increase further out from radiation. A lot of the risk for radiation heart disease is many years after the radiation dose, and it's important not to lose these survivors, to follow up.

We also see on the right-hand of the screen data from the recent WECARE study that was published in "JACC:CardioOncology," and this compared patients with left-sided radiation to the breast versus right breast cancer, and you see that we have a significantly increased risk for coronary artery disease after the radiation dose to the breast and to the heart. And you can also see that this generally develops 10, 15 years after the radiation dose.

That all being said, in certain cancers, such as lung cancer or esophageal cancer, especially with higher doses of radiation to the heart, we can see issues with radiation-induced heart disease soon after that radiation treatment.

And so, it's important to be aware of these patients' risk for heart disease, screen them for their risk factors, optimise them, follow them closely early on, but also continue to follow them in screening for many years to decades afterwards.

4. When to Monitor or Screen Patients?

It is recommended that any patient who's undergoing radiation with the heart in the radiation field, undergoes baseline cardiovascular screening and optimization. We are especially more concerned with patients with higher doses of radiation to the heart or who

have other risk factors, such as underlying cardiovascular risk factors or receiving concomitant therapy, such as anthracyclines.

We see here the International Cardio-Oncology Society Expert Consensus Guidelines for screening of patients undergoing radiation in general, and this particular guideline doesn't just focus on radiation-induced heart disease, but really radiation-induced cardiovascular disease, whether that be in the head and neck region, thoracic region, or abdominal and pelvic region. And it's recommended that all patients undergoing radiation or cardiotoxic cancer therapy should receive a baseline comprehensive cardiovascular history and physical exam.

We really want to identify those cardiovascular risk factors that can be optimised at baseline and throughout treatment.

There are no recommendations in particular where if someone has hypertension, et cetera, that they should not receive the same dose of radiation or the same treatment, but these patients should be optimised to reduce the risk of heart disease down the line.

It's also recommended that when those same patients receive a radiation planning CT, that that CT is reviewed for any baseline coronary artery calcium.

Here you see evidence of coronary artery calcium on a screening CT in the top right of your screen from a patient on their baseline exam for prostate cancer. In identifying this coronary artery calcium, which really is reflective of underlying coronary artery disease, is paramount to optimising their risk factors and they're reducing their risk for future CV events.

It's been shown, and in certain cohorts, that presence of coronary artery calcium on the baseline CT scan is more important than the mean heart dose. And so this is really an important factor to look for.

Once those cardiovascular risk factors are optimised, and you can consider whether a patient needs an echocardiogram, for instance, if they're at higher risk for sure, or an ECG, then those patients should be continued to be followed over time. So patients with radiation with the heart in the radiation field should then undergo an annual CV history and physical exam to, again, identify any risk factors that may have developed and optimise the ones already present, and then be on the lookout for other types of things that may develop, such as subclavian stenosis, and looking at blood pressures in both arms, or signs of superior vena cava obstruction that can also develop.

And really most of your evaluation is just focused on the history exam. In asymptomatic patients, then you would want to consider whether they would benefit from an echocardiogram at six to 12 months. These are patients that have higher doses of radiation in the heart, or have concomitant therapy, such as anthracyclines, or underlying risk factors. And then you should consider whether to get an echo at five-year intervals, as well as a potential ischemic evaluation. In the IC-OS Expert Recommendations, Expert Consensus Recommendations, we really focused on prevention.

And so we shift the focus a little bit further away from the fact that we are just looking at stress echocardiograms, for instance, that look for obstructive disease rather than non-obstructive disease, and look for opportunities to use CT scans, or other tests that are already available, where we can identify non-obstructive coronary disease, such as coronary calcium and start preventative therapy. Because really this preventive therapy is key.

5. Methods to minimise radiation to the heart

Modern radiation therapy has developed a lot of techniques to try and reduce the radiation dose to the heart while still delivering radiation to the tumour itself. And this is best shown in breast cancer where using prone radiation or deep inspiratory breath-hold is able to focus that radiation on the mass itself, the tumour itself, while minimising delivery to the heart. And we have seen a drastic reduction in radiation dose to the heart over several years with the development of this technology.

I do always want to give the caveat that, number one, these radiation techniques are not available for every patient, either because of the patient themselves or because they may be being treated in a community centre that may not have the availability of the most modern techniques.

And two, that even with these techniques, we still can get radiation doses to cardiac substructures.

So here on this slide, you can see several different techniques to minimise radiation dose to the heart, including the deep inspiratory breath-hold, use of prone radiation, or even use of proton therapy. But on the right side of the screen, you can see that even with the most

modern techniques, on the top we have conformal radiation therapy and deep inspiratory breath-hold.

We have focusing of the radiation to the chest wall, but we still see that the heart is involved to a lesser degree in certain substructures more than others. And with volumetric modified arc therapy on the bottom right, we again see that the delivery of the radiation is focused to the tumour and chest wall, but we still see some heart involvement.

And so even with these techniques, we still need to screen for disease. In the WECARE study, which patients were given radiation through approximately 2008, these are relatively recent patients that are still developing coronary artery disease.

We still have to screen for these patients, but it is amazing what we're able to do now to limit the radiation dose to the heart with current techniques.

6. How can RIHD best managed?

In general, if someone develops radiation-induced heart disease or radiation-induced cardiovascular disease, it is going to be managed in a similar manner as the general population, so using preexisting guidelines from either European guidelines, or the American guidelines, targeted at that particular radiation-induced heart disease, whether it be coronary artery disease or valvular disease.

So many of the recommendations that we talked about today are really for screening, but if we diagnose aortic stenosis, for instance, then we would start to follow the guidelines for aortic stenosis for further evaluation down the line and treatment.

There are a few caveats, however. Patients who've had radiation to the chest will have subsequent fibrosis and scarring of their chest wall and tissues, and in general, their risk of surgical mortality is significantly higher. These patients can undergo surgical valve replacement or other types of surgical procedures if it's really necessary for their overall care, but there should be consideration for percutaneous techniques. With retrospective data, we have seen that TAVR over SAVR has improved 30-day mortality, for instance, in patients with previous radiation-induced heart disease undergoing aortic valve replacement. And so we certainly have seen a trend where these patients are at much higher risk for

surgical treatment because of their previous scarring and fibrosis and may benefit from percutaneous techniques.

Other important considerations for the management of these patients is in patients that present with diastolic heart failure. It's important to consider restrictive cardiomyopathy from the radiation to the muscle, as well as constrictive pericarditis from radiation to the pericardium.

These other disorders can mimic each other, and it's important to consider all of them when encountering a patient with diastolic heart failure in deciding on their future management.