

Support for Yale Cancer Answers is provided by AstraZeneca, a science-led biopharmaceutical company dedicated to partnering with leading scientific companies, organizations and the community to improve outcomes for advanced cancer patients. More at astrazeneca-us.com. Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about cardio-oncology with Dr. Lauren Baldassarre. Dr. Baldassarre is the Director of the Smilow Cancer Hospital Cardio-Oncology Program, and Dr. Gore is a Professor of Internal Medicine in Hematology at Yale School of Medicine and Director of Hematologic Malignancies at Smilow.

Gore Cardio-oncology, is that cancer of the heart?

Baldassarre The field of cardio-oncology is a relatively new field. It was started to address the concerns of some potentially harmful effects of some cancer chemotherapy and other therapeutics as far as effects that they may have on the heart in some patients. Originally, the field was started specifically with concern for some of the agents used in breast cancer and that is how the field initially started to grow, but now, it actually encompasses a large variety of cancer patients looking at not only side effects that patients may have from some of the therapeutics they received to treat their cancer, but also we help to treat patients who have complex cardiac disease alongside with their concomitant cancer as well.

Gore How did you become interested in this particular area of cardiology?

Baldassarre I always had an interest in prevention within cardiology as well as cardiac imaging. And from my perspective, these 2 interests are actually very well related to cardio-oncology as the approach for cardio-oncology is a preventative one where we hope to be able to risk stratify patients and also to help with diagnosing any potential problems early on and then help with management of those problems in order to get the patients through the care of their cancer.

Gore But most patients I imagine who get to you, excluding the ones who have prior cardiac history and we need you to help manage them, are patients in whom there has already been a problem right? And that is why they are referred to you in the first place?

Baldassarre Absolutely. Sometimes, that is the case. But we also do have a preventative approach with a fair amount of patients, specifically with some of the breast cancer patients where we actually see them early on to help with risk stratification as far as cardiovascular risks, help to decide any extra imaging they may need or any medications that may be helpful at the beginning of the treatment for their cancer rather than waiting to see if there is a problem.

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Gore Do you screen all breast cancer patients about to get chemotherapy?

Baldassarre At this time, we do not screen all patients. We tend to screen those who have at least one or more cardiovascular risk factor like high blood pressure, diabetes, high cholesterol, family history of cardiac disease, but also really any patient who wants to discuss and get more information about the potential side effects of their therapy, they are more than welcome to be seen by one of us and have those discussions prior to beginning the treatment.

Gore But it is up to the primary treating oncologist in general to suggest that maybe they should see you, is that right?

Baldassarre It is primarily up to the general oncologist, but the patients also sometimes come to us on their own.

Gore What kind of preventative strategies are available?

Baldassarre One of the big approaches we have with these patients is advanced cardiac imaging to help get more information either at the beginning of their treatment or throughout, and sometimes afterwards. And these could be techniques such as echocardiography, which is ultrasound of the heart where we apply some advanced imaging techniques, where we try to detect problems early on if they occur before they become clinically apparent. Other techniques that we use would be something called cardiac MRI and that is another way to look at the structure and function of the heart and to get some additional information about potentially early changes before we would see any real clinical harmful effects.

Gore If you start to detect some changes, are there options besides changing the drugs or reducing the dose, is there anything that one can administer prophylactically or is it really a question of early detection?

Baldassarre Yes, if we see any concern early on, we will put the patient on medications to ideally prevent any further effects and to help strengthen the heart muscle moving forward. Our goal really in the end is to help support the patient so that they can receive the treatment that they need for their cancer and to carry them through this therapy and then also to help monitor and take care of them afterwards. Although sometimes we do have a scenario where if there is a lot of concern, we will recommend a change in the treatment of their cancer such as stopping one drug and starting another instead or potentially reducing the dose, but to be honest, that is relatively uncommon. We try to not do that unless it is absolutely necessary.

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Gore I know that there is a classic class of drugs which we know to potentially influence heart function if you get too much of them, the drugs that we call anthracyclines and related drugs, but how do we find out about other drugs that we do not know, there are so many new drugs coming out nowadays, how

are they vetted for potential cardiac toxicity, is it all animal models, somebody gets heart failure when they are on a clinical trial, how do we follow up on that? How does one sort that out?

Baldassarre That is a great question. It actually is a challenge in the field because as you mentioned, there are a lot of different agents used to treat a variety of cancers, and there are a few that are sort of top of the list that we are concerned about such as the anthracycline group, but there are many other therapeutics that can potentially cause harmful effects on the heart, and it is really our job to know what those are and to be aware of those effects and be able to recognize them if they do pop up. Unlike the breast cancer patients, there are not a lot of other strict guidelines as far as monitoring these patients for example with serial imaging, with echocardiography as we do in the breast cancer patients. Those guidelines are pretty clear for us, but with the other agents, we really have to manage the patient on a case-by-case basis as far as deciding what type of monitoring to do for them.

Gore And in breast cancer, why is there so much success there? Is it because so many patients are treated in order to prevent recurrence in the future, so that a lot of people have gotten these drugs and are not expected to relapse, or is that just what people are thinking about or is it the breast cancer population which is so active?

Baldassarre From my perspective, I think the main reason is just that we have more data in those patients. We have been using those agents for longer. The data about the cardiac effects of the anthracycline-based therapy dates back to the late 70s or early 80s actually where that was discovered here at Yale where they used nuclear imaging to detect these early changes and that was really how the field began. I just think we have more data in that patient population and therefore that data is able to shape guidelines and certainly it has actually made a lot of sense as that data has come out, we have seen that as breast cancer treatment has progressed, the patient survival from breast cancer is significantly improved compared to what it was decades prior, and these patients are living a lot longer which is great, but actually what the data has shown us is that after they survive their breast cancer, their risk of cardiovascular disease is significantly increased compared to those who have not been treated for breast cancer. So, we have that long-term data that is helping to shape those guidelines for us.

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Gore And is there a finite time period after the chemotherapy where the risk is no longer increased or is it something that just increases with time as long as the patient survives?

Baldassarre These are effects that we can see both in the short term and in the long term actually, so that is why we recommend the monitoring early on, baseline assessment before treatment, assessment during treatment and assessment

after, and usually for the breast cancer population, we will see them and if everything went smoothly, there were no cardiac issues during their therapy, we will see them after completion at about 6 months, then another 6 months and then we will start to space it out to follow up every year and sometimes eventually every 2 years if there really are not any concerns. But we do not know that there is really a time point where that risk is actually gone. So, what we recommend is that all survivors of cancer have regular follow-up with either a survivorship clinic or potentially with cardiology, ideally cardio-oncology long term, in that you check in at least ideally once a year, so we can assess how things are going and potentially get an imaging study, that is our recommendation right now.

Gore So, annual imaging studies even in the absence of symptoms?

Baldassarre Correct.

Gore Wow. That is a lot and that could be a lot of patients for you guys right? I mean, you saw all these breast cancer patients in Connecticut, you are going to be a pretty busy clinic.

Baldassarre Right.

Gore It is also one of those things where you be careful what you wish for because as cardiologists, I imagine outside of prevention, you also like to do some treatment, but you certainly do not wish any badness for the patients but if it is all prevention, that would limit your scope of practice a little bit.

Baldassarre Correct. We would like to have a preventative approach, but of course, even with prevention, we are still going to have patients that have effects of these therapies.

Gore It is just inevitable. Some of these drugs are also used in pediatric cancers, for which there are many cures, for example, some of the pediatric leukemias, and when these kids age into adults, is there a role for them to be monitored by cardio-oncology or is there a pediatric practice of cardio-oncology?

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Baldassarre There is absolutely a role, and often these patients ideally would be plugged into a survivorship clinic where they tend to do the screening that is necessary for them, which often does include some cardiac screening, usually with echocardiography that is spaced out more like every 2-5 years depending upon what their exposure was to the agents. And what we usually would do in that case is then the survivorship clinic will send the patient to see us if there are any concerns of symptoms or if there is any abnormality in any of their screening tests, such as the echo, but any patient that is not being seen in a survivorship clinic is of course welcome to come and see us directly for assessment as well.

Gore Great. I would like to follow up on that a little bit after our break. Right now, we are going to take a short break for a medical minute. Please stay tuned to learn more about cardio-oncology with Dr. Lauren Baldassarre.

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Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest, Dr. Lauren Baldassarre. We have been discussing cardio-oncology. Lauren, just before the break we were talking a little bit about kids treated for leukemia and other diseases with some of these potentially cardiotoxic drugs who are likely to be long-term survivors. I am wondering does it matter what age you are as a kid when you get these drugs? I know kids sometimes have better regenerative powers in their organs than adults, but I do not know how it is in the heart or do we know?

Baldassarre I do not think we know the exact answer to that question, but we do have slightly different recommendations based on the age at the time the treatment was administered as well as the amount of treatment, and that will dictate for us how often we will be screening those patients if they were very early at exposure with a lot of

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exposure that was not only chemotherapy but radiation and that could potentially put them at a higher risk and require some more frequent monitoring than those who were exposed potentially at a later age with less exposure.

Gore I seem to remember from earlier in my career that there was a big concern, particularly with lymphoma patients who had gotten chest irradiation, and Hodgkin's disease, for example, as well as breast cancer, there were people having some risks for heart failure, but actually they were developing coronary disease, is that still a problem?

Baldassarre Yes, that is still a concern, and we do regular screening for symptoms and in some patients, we do some extra cardiac imaging not to look at the function like with echocardiography, but actually sometimes we do look directly at the coronary arteries, and often what we do in that case is something that is called a coronary CT angiogram and that looks directly at the coronary arteries to screen for that type of coronary disease that can sometimes be seen in these patients which is often a more proximal coronary disease, a little bit different than what you would see in sort of regular atherosclerosis that we see in older patients that develops overtime.

Gore Proximal means, closer to the origin of the arteries?

Baldassarre Correct. And the cause is different. The cause is more from the damage from the radiation.

Gore How fascinating. Hopefully, the radiation oncologists are also I am sure are paying close attention to some of the newer techniques that are so specific in terms of where they are aiming their beams.

Baldassarre Yes, absolutely. There have been newer techniques that limit as much as possible the direct exposure to the coronary arteries and also to the valves, which is another concern with radiation exposure to cause some thickening of the valves, which could eventually over time lead to some valve disease that either causes a leaky valve or a tight valve.

Gore Wow. Lots to worry about. You think you are done with cancer right? You mentioned cardiac MRIs a few times and this is something that is pretty new to me and what I think of is patients are always complaining when they go for an MRI that they are supposed to lay absolutely still for so long, but the heart is beating. How do you take an MRI of a beating heart?

Baldassarre The way that works is a couple different ways because as you mentioned we are trying to take a picture of something that is constantly moving. We use two techniques – one

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we use is an EKG and EKG gating so that we can capture the image at certain parts of the cardiac cycle when the heart is more still so that helps us to image that moving object, and then we also will do breath holds or gated to the respiratory breathing in order to account for the motion that can be caused with breathing as well, and by doing those 2 things, we actually get some very nice clear images of the heart that look at not only the overall structure and function but also can look a little bit closer at the cardiac muscle itself to pick up more subtle changes like inflammation or fibrosis or scar that could be there.

Gore Wow, fascinating. I probably need to spend some time with you, I do not know if it was you that I was chatting with or one of your colleagues last week in clinic about how in my old career we used to not infrequently do a lot of biopsies of heart muscle, when we were considering whether there was damage from chemotherapy, but it seems that is not done very much, at least not in your practice?

Baldassarre That is not done routinely much anymore because we do have such great imaging techniques to give us that information that we need, we will reserve that for a more difficult or extreme case when we are thinking about effects of agents from breast cancer, there are some newer agents where there is concern for a more acute inflammatory process with some of the new immunotherapy

agents and in that case, a biopsy actually often is indicated in that more acute setting we do still utilize that procedure actually.

Gore And why is that?

Baldassarre That is because some of these immunotherapy agents which actually are really revolutionizing cancer right now, many, many different cancers - having increased response rate and survival in patients, what these agents do is they actually utilize the patient's own immune system to help fight the cancer and help fight the tumor, which can work very well, but it does this in a manner that sort of unleashes or augments that immune system and some of the side effects of this are that you can have an exaggerated inflammatory response in multiple different organs of the body. One of those organs is the heart. It is a less common organ to be affected than say the colon or the lung, which can be affected more frequently, but it still can happen and when it happens, it can be pretty significant. And so, in that case, if we have concern for inflammation of the heart which is called myocarditis or inflammation of lining of the heart, which is called pericarditis, in those circumstances we really need to get the information pretty quickly and make some decisions about what to do for that patient and in that case a biopsy actually gives us that information that we need as well as some advanced imaging, usually with cardiac MRI and with echocardiography.

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Gore But the MRI may not be enough or may not have changes early enough, is that what is going on?

Baldassarre Sometimes it does and we do not always have to go for a biopsy, but this is an area where again because this therapy is so new, we just do not have all the data that is needed to really answer that question quite yet. And that is something we are working on.

Gore I can imagine without biopsies you cannot really know at the cellular level what is going on, I am guessing unless MRI has gotten really crazy sophisticated. So, I would think if you have had a new drug or a new kind of drug with these immunotherapies, there has really got to be some advantage to getting some tissue to look at and say, what is going on here so that we can understand how to treat it?

Baldassarre Right. It kind of again is sort of a case by case basis, sometimes it is very clear to us based on the lab values and the imaging, sometimes the cardiac MRI shows very clearly a myocarditis picture and we may not need to go to that next step of the biopsy, but if it is not 100% clear and the clinical picture is not 100% clear, which unfortunately sometimes it is not because often these patients on these agents are sick and have other symptoms that are very difficult sometimes to tease out the cardiac symptoms from the other symptoms and in that case, we often do need some more information by getting the tissue.

Gore It sounds really scary and even dangerous to biopsy the heart, is it?

Baldassarre It does sound scary, I understand that, but actually for us it is a relatively straightforward and simple procedure where we go in with a catheter onto the right side of the heart and use tiny little forceps to just take a couple little bits of the heart tissue there to take a look at under the microscope with pathology and it is actually a pretty safe procedure with a very low complication rate.

Gore Amazing.

Baldassarre You know every procedure that you do has some risks, of course we do not do it when it is not completely indicated, but if it is indicated, the risks are pretty low and we think that the benefits will outweigh those even low risks in order to get the information to help the patient.

Gore And does your practice actually perform those tests or do you send them to people who are full-time catheter people?

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Baldassarre We do not perform them. We send them to specialists, interventional cardiologists, who do these types of invasive procedures all day in and out.

Gore Sure, it makes sense. And I know that there is kind of an old story of cancer-related heart problem where protein gets accumulated in the heart and people with myeloma and such that can cause heart problems. I guess it is called amyloidosis. Do you guys deal with that as well?

Baldassarre We do. We see patients with concern for amyloid, either patients to help make that diagnosis or patients that already have that diagnosis to help manage that cardiac problem. And the diagnosis of that is a diagnosis that is made with a combination of different lab tests and also with cardiac imaging. And in that case, we normally start with echocardiography and then we utilize cardiac MRI as well to help look at that tissue closer to see if we can see actually evidence of those deposits within the heart muscle, which we are able to image and then sometimes depending upon the type of amyloid that it is, we also get nuclear imaging studies as well to help get more information.

Gore Wow. That sounds cool. Using an antibody or something that is labeled, is that how it works?

Baldassarre It is a little bit different than that. What it does is it is a radiotracer, it helps to distinguish between the different types of amyloid.

Gore Oh! I see. I feel like back in the old days, maybe some of those patients got biopsied, but I may be remembering wrong.

Baldassarre Some of those patients do still get biopsied, but in that case if the imaging is clear which often it is because we do have a fair amount of data as

far as cardiac MRI and nuclear studies in diagnosing amyloid and those studies did compare those imaging to the gold standard of biopsy as you mentioned showing that it is very good. So, once we have a truly positive imaging study, it is not always necessary to go for biopsy, but we actually have specialists within each of those subspecialties, not just cardiology, also GI, pulmonary, nephrology, the list goes on and on, and there is at least one specialist in each of those and we all meet and work together about how to help manage these patients as a whole and to diagnose and manage these potential side effects of these agents which are truly helpful agents and really patients are responding well, but we do have to also address the effects of them.

Dr. Lauren Baldassarre is Director of the Smilow Cancer Hospital Cardio-Oncology Program. If you have questions, the address is cancer-answers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.