Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This week, doctors Foss and Chagpar welcome Dr. Kerry Russell and Jessica Coviello for a conversation about cardiac side effects of cancer treatment. Dr. Russell is an Associate Professor of Medicine in Cardiology and Jessica is an Associate Professor at the Yale School of Nursing focusing on cardiovascular disease prevention and management. Here is Dr. Francine Foss.

Foss Could we start off by having each one of you give us a little introduction about your background and how you came to Smilow Cancer Hospital?

Russell I am Kerry Russell, and I came from a background of doing a combined MD, PhD where my PhD training was actually in oncology, particularly in molecular oncology, and then I later did my residency and fellowship training at Yale and ended up specializing in cardiology. I particularly developed an interest in the cardiotoxicity that is associated with Herceptin, which is a drug that is used to treat breast cancer.

Coviello I am Jessica Coviello and my interest has risen from about 30 years in cardiology practice as a nurse practitioner in a private cardiology practice, and we noticed, in patients with whom I was taking care of for heart failure, a larger number of women returning with problems after cancer chemotherapy, so I was very interested in what brought them to the table for their cardiac problems and started to look at cardiovascular risk in women as they went through breast cancer chemotherapy. It was that along with working with Dr. Maysa Abu-Khalaf and Tish Knobf that I started to work on my doctorate nursing practice dissertation, looking at cardiovascular risk in women at baseline before starting chemotherapy, at six months, and at one year. With the excitement over that study and then meeting Dr. Kerry Russell and her husband Dr. Raymond Russell, both cardio-oncologists at Yale, I have been able to join that particular group and we will be looking at cardiovascular risks in cancer patients prior to starting therapy.

Foss I just want to say for the audience that we actually have a cardio-oncology program now at Smilow Cancer Hospital in one of our practice areas and it has been really remarkable for us to have your program there because we are able to directly access you and many more of our patients benefit from

the services. And Anees, I know in your area of breast cancer it has been an important aspect.

Chagpar Tell us a little about cardiac toxicities in cancer patients, as I am certain that many people who are in the audience listening are thinking about cancer and oftentimes heart failure is not the first thing that pops into their head. Tell us a little bit about the incidence of heart failure with various treatment modalities associated with cancer and what exactly a cardio-oncologist does?

Russell This field came about because of the widespread use of a group of drugs that are called 4:00 into mp3 file http://yalecancercenter.org/podcasts/2013%200317%20YCC%20Answer%20Cardiac%20Side%20Effects.mp3 anthracyclines, and these are very-very potent and effective drugs used to treat cancer, but unfortunately they also happen to be somewhat toxic to the heart. Oncologists have done a wonderful job over the years trying to figure out the best way to administer those drugs and the safest way to administer those drugs while still allowing for their potent anticancer effects and so I think that the side effects from the poster child, or initial cardiotoxic chemotherapeutic agent to be used are relatively low, but it is still something that we do see and there are ways to screen and protect against the toxicity from those drugs. Since that time a whole new generation of drugs have been developed and I alluded to one of them in my opening statement, which is Herceptin, and many times although those drugs are targeting very important parts of the way that cancer grows and survives, they also can accidently target the growth and survival of cardiovascular tissues, blood vessels, and the heart muscle, so part of our job is to make sure that those drugs can be given safely to treat cancer while protecting the heart and blood vessels.

Foss Other than chemotherapy many of our patients are also getting radiotherapy, and I know that there have been some issues with Hodgkin's patients and radiation to the chest. To what degree does radiotherapy contribute to cardiac toxicity?

Russell This is another area that radiation oncologists have studied very well, which is the way in which radiation therapy is given, in particular to the chest, and that has been significantly modified in the last 10 or 20 years so that they are very careful about how it is given to reduce the amount of radiation that the heart receives, but nevertheless, it is impossible to radiate the chest for example, in breast patients, in particular those with a left-sided cancer, without having some radiation that spills over onto the heart and the effects of that are actually pretty well known and can lead to accelerated development of

blood vessel disease, the kind of blood vessel disease that contributes to heart attacks. So it is very important that we monitor and treat any other concomitant cardiac risk factors that patients have, and that is where Jessica's program comes in. So both before chemotherapy and before radiation therapy, and even before surgery because sometimes people undergo very extensive surgeries, it is important to make sure that the patient has their cardiovascular system in the best shape possible so that they can come through all those treatments and come out of their cancer without having damaged their cardiovascular system and that is the main role of the program.

Chagpar Let's talk a little bit about that. Should every patient undergoing chemotherapy and radiation be seen by a cardiologist or a cardio-oncologist prior to starting treatment?

Coviello Ideally in this country all of us should have a comprehensive cardiovascular assessment at the age of 20 and one of the things that we found in the study that I had done for my doctorate is that the majority of the women that we saw had never had that comprehensive cardiovascular assessment. I think it is really important to take a look at what the patients bring to the table as far as cardiovascular risks before they start therapy. That is one of the reasons why we began to look at this particular study and looked at whether people came to treatment with hypertension or high blood pressure, if their glucose was already elevated, if their waist circumference was already 7:59 into mp3 file http://yalecancercenter.org/podcasts/2013%200317%20YCC%20Answers%20-%20Cardiac%20Side%20Effects.mp3 elevated, if they had a strong family history, if they already had disease, those are patients that we would earmark more at risk and we would follow them more closely. If they needed therapy before they started cancer treatment, then we would start them on therapy to protect their heart. So, our job would be to see what risk they came in with and to follow them through treatment so that we can protect them as they went along.

Foss Those risk factors that you are screening for, could you just outline them for the audience again?

Coviello Absolutely, it is high blood pressure, a family history particularly of early heart disease so for men that would be under the age of 50 and for women under the age of 60, we would look at weight, we would look at waist circumference, we would look at cholesterol levels like high density lipoprotein, protective cholesterol, LDL, and triglycerides. We would look at what glucose levels were before people started, and whether they had a tendency to develop high levels of glucose. A history of pregnancy for instance might be important,

did they have high glucose during pregnancy? Did they have high blood pressure during pregnancy? So, we really go back and evaluate all those factors and determine whether they are at risk.

Chagpar Let's suppose that you have somebody and they have not had this complete cardiovascular panel, as I suspect many of us in the audience may not have had at the age of 20, and many of us in the studio may not have had at the age of 20, but let us say that they have been diagnosed with cancer and they are about to start a cardiotoxic regimen, maybe an anthracycline, maybe even with Herceptin, if they happen to be a patient of mine, and you do this panel, how reversible or preventable are some of these cardiac toxicities, in other words, what can you do about it?

Russell This is a very active area of research in this country and in other countries to try to understand how you can decide who is at risk, who might benefit from closer follow-up, and who might benefit potentially from the addition of cardioprotective drugs? We do know that right now we follow patients usually using cardiac ultrasound, or echocardiography, serially to monitor their cardiac function and we know that there are certain markers with that that would allow us to detect early changes in heart function, and we know that there are some drugs out there, some of which are also used to treat other cardiac conditions, that can protect the heart against injury in response especially to anthracyclines. I think though that we need a lot more information to be gathered in this area. There has been no particular specialty drug developed that can protect against all chemotherapy. There has been at least one main drug that has been shown to be protective against the anthracycline injury, and so deciding which patients will benefit from that is also something that our program is involved in. I guess the real answer is that right now, this has to be done on an individual patient level, and that is why understanding what your risks are is really important. We would not want to give a cardioprotective drug to a patient who had very low risk, because even the cardioprotective drugs could have side effects, so that is what we are doing.

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Foss Kerry, how often during say a six-month treatment period would you have the ultrasounds, and the echocardiograms done? And does that information feed back to their treating oncologist in a way where they actually make modifications of the treatment program?

Russell It depends on which particular drugs they are getting. Each drug has its own sort of follow-up depending on the dose that is being used, and what other drugs are being given with it at the same time. Let's say someone is getting a drug and six months follow up. For anthracyclines there is no real mandate to follow-up that closely. For Herceptin on the other hand we do monitor about every three months. I think that close follow-up is important because we know that if there are changes in cardiac function, early treatment can prevent further declines in cardiac function and one of the things our program seeks to do is to make that follow-up more organized. So careful serial visits, asking dedicated questions, looking for signs or symptoms of heart failure, and monitoring blood pressure. A number of new drugs that are being developed have profound effects on blood pressure, which can obviously have adverse outcomes over the long term. We are here to help the oncologists with feedback and communication, you mentioned that we are actually physically located in the cancer center, which is extremely important and does not always happen if you are not in that close working environment. We really do make efforts to give feedback to the oncologist so that they can modify their regimen and the patient gets the best overall outcome.

Chagpar That is fantastic. We are going to pick up a little more on cardioprotective treatments for patients undergoing cancer treatment, but first we are going to take a break for a medical minute. Please stay tuned to learn more information about the cardiac side effects of cancer treatment with Dr. Kerry Russell and Jessica Coviello.

Medical

Minute This year over two hundred thousand Americans will be diagnosed with lung cancer and in Connecticut alone there will be over two thousand new cases. More than 85% of lung cancer diagnoses are related to smoking, and quitting, even after decades of use can significantly reduce your risk of developing lung cancer. Each day patients with lung cancer are surviving thanks to increased access to advanced therapies and specialized care. New treatments options and surgical techniques are giving lung cancer survivors more hope than they ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatment for lung cancer. An option for lung cancer patient in need of surgery is a video-assisted thoracoscopic surgery also known as VATS procedure, which is a minimally invasive technique. This has been a medical minute and more information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my co-host Dr. Francine Foss. In addition, we have two guests with us, Dr. Kerry Russell and Jessica Coviello, both of whom are very interested in the heart and cardioprotection when it comes

15:20 into mp3 file http://yalecancercenter.org/podcasts/2013%200317%20YCC%20Answers%20-%20Cardiac%20Side%20Effects.mp3 to cancer treatments. Before the break we were talking about some of the cancer treatments that we offer and how those can affect the heart, whether it is with drugs like anthracyclines and Herceptin, or radiation, and it was mentioned that we can follow these patients closely, but one of the things that I wanted to pick up on was the fact that there may be ways that you can protect the heart or prevent it from having a downward spiral despite cancer treatments. Can you tell us a little bit more about cardioprotective regimens or treatments that you use that can obviate some of the side effects of these cancer treatments?

Russell There has been some very interesting research that has been done in this area. We still need a lot more, but it demonstrated that if you are able to detect early injury to the heart, whether that be by imaging cardiac function or by doing blood testing to look for markers of cardiac injury, if you can pick that up early and put people on medication similar to what is used to treat hypertension and heart failure, that will protect those patients against going on to have more serious negative changes in their heart function. That is the reason why it is important to engage in this level of monitoring. If there was nothing we could do about it, then who cares, but in fact there are lots of thing that we can do about it and in cardiology there has been a revolution in the treatment of heart failure and what we have learned from all the years of treating patients who had big heart attacks and ended up with heart failure after that, is that there is a whole set of different bodily pathways that we can target that will prevent progressive changes in cardiac function and many of those can also be used to prevent cardiac changes in patients undergoing chemotherapy or radiation therapy. So, there are good reasons to look, and we find a lot of things that we can do.

Foss We talked a little about follow-up, but how long after chemotherapy do we need to be worried? Can you focus a little bit on the pediatric population? There are lots of kids out there that were treated and are living normal lives now, so at what point do we have to worry or stop worrying about those kids?

Russell Survivorship programs are very important both for pediatric cancer survivors and for adult cancer survivors. Obviously the adults who were treated as children, many of them did get things like anthracycline and we know from those patients that you can have cardiac issues many-many years after you receive the treatment and we do not know how much that is going to apply to adults, but I would say if you received those types of drugs or radiation, you

should be actively involved in a Survivorship Program. The heart is not the only organ that can be inadvertently targeted by the treatments that we give for cancer and so it is important for maintenance of your health to be enrolled in a program that understands the long term effects of these drugs.

Chagpar Picking up on that, let's suppose you are a pediatric patient and you were treated with an anthracycline and now you are an adult and you are living a long and healthy life, because that's what kids with cancer can do these days thanks to research and lots of physicians and nurses who do tremendous work, and you do end up having a heart attack or high blood pressure or other

19:18 into mp3 file http://yalecancercenter.org/podcasts/2013%200317%20YCC%20Answers%20-%20Cardiac%20Side%20Effects.mp3 cardiac issues, how much of that can be related to the cancer and the cancer treatment? How much of that is just due to the fact that heart disease remains the number one killer of Americans these days?

Coviello I think the point is that first of all we have to look to see if people develop those things, so you have to maintain good monitoring after people leave treatment and we would recommend the same thing for the general public, we need to look and find hypertension early and treat it aggressively so that people do not end up with heart disease. The same will be true for survivors, we would want to make sure that the cardiovascular risks was diminished, that risks are picked up early and treated aggressively so that you can have a long and healthy life. We would recommend a heart healthy diet and also exercise. We would recommend maintaining weight. I think what the long term effects of cardiotoxic therapies might mean is that we need to take a longer and harder look at monitoring to make sure that the heart muscles stay strong and healthy and if we see any early changes, we act upon them early. I think that monitoring is very important and I think that monitoring for a long time out is very important as well.

Foss When we think about prevention in that group of folks, is there anything special that should be done for prevention, for instance exercise programs or other things that would be helpful in preventing perhaps late occurrence of congestive heart failure and cardiomyopathies?

Russell We have an active research program that is looking into that a little bit. I would say in general as a cardiologist, we have not found anything that did not help, so get out of the chair, get off the couch, these patients who had chemotherapy have been shown during and even within the following year

of having received these agents, to have a significantly diminished efficiency of their bodies use of oxygen. So, we know that the more inactive we are that inefficiency is already bad and then you compounded it with receiving these medications. In many type of cancer, especially breast in particular, patients tend to actually gain weight, paradoxically, we think of people as losing weight, but many times they do not and that inefficiency of oxygen use, that decreased activity of folks that are undergoing therapy are all contributing to increased cardiovascular risk, and so I think it is really important that patients maintain their activity. One patient I have was treated for lymphoma and he was a very active man before this. He said to me afterwards that he wished somebody had told him that he should have at least kept up some level of exercise through the whole thing because he said that now he feels that not only is he recovering from the cancer, but he allowed himself to become deconditioned and he said he felt like he had a deeper pit to dig out of. I believe that is really true, if people can stay active, we already know it is good for your cardiovascular health, but I think it is particularly important when you are going through this type of therapy.

Coviello I think that an observation in the Heart Strong study, the study that we did with breast cancer patients was that women felt better at the end of treatment if they continued to walk 10 to 20

minutes a day even on the days when they did not feel particularly great after chemo. Even if they divided the walking into 10-minute or 5-minute sessions, if they got up and moved around, at the end they felt a lot less fatigue and in better condition.

Chagpar Do you think that some patients may still be under the misperception that if you are on chemotherapy it means that you should not walk, you should not exercise, you should not work, you should not live your life? How do you think that plays into their overall cardiac health?

Coviello What we found was that people fared better if they saw themselves as generally well other than the cancer and had a greater awareness to cardiovascular risk, so maybe they changed their diet and adapted to something that was a little bit more healthy. They moved around. They exercised. They maintained their normal lifestyle as much as possible. Those people just felt better. So, if you adopt a sick role, looking at it as the cup half empty, then

people didn't fare as well as far as feeling strong and healthy at the end of chemo.

Foss I have a question for Kerry, and that is, what if a patient is unlucky enough to actually have a cardiac event during chemotherapy, what happens then? Does the patient need to stop their chemotherapy? How do you manage that?

Russell This is also one of the beauties of having a specific set of cardiologists that deal with these patients because most of the time we can deliver good cardiac care without interrupting their cancer treatment and I think my colleagues at MD Anderson, which is where I actually did a bit of my training, have really pioneered this. I was at a meeting there last fall and they were talking about patients uninterrupted, unfortunately they have a heart attack, but no problem they can have heart cauterization and sometimes we have to modify specifically what we do, but working together they were able to still deliver the best cardiac care and still treat with chemotherapy, and I think we all can learn from that. We do not have to derail treatment of the cancer, if there are other bumps along the road that involve the heart, there are lots of ways that we can work together to deliver good care to the whole patient.

Chagpar The other place where cardiac events can happen in a cancer patient is postoperatively. In that circumstance, how would you manage that? Do you see those patients and is your management of their heart attack different when they are fresh post-op, they just had a massive operation for pancreatic cancer? How does that effect their treatment in terms of their heart attack?

Russell This is another area where it is very important for the cardiologist that is treating that patient to have a good concept of what is going to come next for the cancer aspect of this patient's treatment, because there are different ways that we can treat heart attacks and some treatments might not be optimal if you have to have additional surgeries, we have certain stents we can put in where patients have to remain on super aspirin, type of blood thinner for a long period of time. So, we then might modify what we are going to do to avoid something like that where we know they 27:03 into mp3 file http://yalecancercenter.org/podcasts/2013%200317%20YCC%20Answers%20-%20Cardiac%20Side%20Effects.mp3 would needed additional surgery. So, having communication between the oncologist and the cardiologist allows us to optimally treat whatever cardiac event there is without making it so that the treatment of their cancer is problematic later on.

Foss One of the things that we run into is chest pain, and obviously there are lots of reasons for chest pain in a cancer patient and they are not all cardiac, so how you do you sort that out? Patients obviously are very concerned whenever they get left-sided pain that it is a cardiac event. How do you sort that out with patients?

Russell Luckily cardiology has made quite a career of diagnosing cardiac chest pain. So there are lots of different things that we can do besides just taking a good history and doing a good physical exam that really are no different then what we would do for anyone else that had chest pain. It is a particular problem though because people can have metastatic disease or those kinds of things that could also cause chest pain and so our role is to help decide which aspects of potential cardiac problems would be life threatening, or cause long term damage, and evaluate for those right away and then we can go down the list of what other possibilities there are that might be related to the cancer or might have nothing to do with either of those things.

Dr. Kerry Russell is an Associate Professor of Medicine in Cardiology at Yale School of Medicine and Jessica Coviello is an Associate Professor at the Yale School of Nursing focusing on cardiovascular disease prevention and management. If you have questions or would like to add your comments, visit yalecancercenter.org where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.