[MUSIC PLAYING]

SAUL SILVER: So what I'm going to talk to you a little bit about today is the cardio-oncology consult. And I just came off service, and I was just talking to my partners about how crazy it is. And I want to talk about bread and butter medicine, the stuff that we see every day. Because the unique stuff and the imaging, you're going to hear a lot about.

I don't have any conflicts. The only conflict I have is I got a free pen when I walked in.

[LAUGHTER]

And I just want to make sure everybody knows that. Does this work? So as Dr. Durand told us, more and more people are living with cancer.

And I really want to point out that the age group that's really living with cancer right now is the group that's over 85 and the group that's 75 to 84. So we're almost doing geriatric oncology and cardio-oncology as well, because we're seeing an older population that's living. It works now? OK, thank you.

So we're seeing an older population that's living. And by the year 2040, we're going to have about 26 million cancer survivors. Right now, around 2020, we're about at 15 to 16 million cancer survivors. So look how these curves are going and the direction that they're going.

Now, cancer survivors, as we've told you, experience serious cardiovascular complications. In fact, 30% of all cancer survivors do die because of therapeutic-related cardio toxicity. Cardiovascular events are the second common cause of death and morbidity among cancer survivors. And we, as cardiologists and internists, need a better understanding of the diagnosis, the drugs, and the potential complications. And it's really being a complete physician that we need to do.

The most important thing is to be a complete physician. And sometimes I'm looking at a patient from head to toe, and taking a full history, and physical exam. I care if they're hyperthyroid, because I'll tell you in a minute, I see a lot of atrial fibrillation. So all these things we need to do.

And we need to treat the risk factors, which you've heard about, and aggressively. As Rob told you, you've got to treat that premenopausal woman with hyperlipidemia that's had chemotherapy for her lipids. Because these are the risk factors that we have to address, and we have to more aggressively address them in the cancer patient.

Smoking-- you've got to worry about coronary disease. Activity, very important, which Rob pointed out as well. And what I'm going to talk to you about today is the acute concept, the stuff I see in the hospital more so than the maintenance therapy that we do in our office every day.

I'm going to talk about three things-- atrial fibrillation. Another common consult I get is, what should I do about the QT interval? We have to give some chemotherapy.

And then I'm just going to point out some of the vascular toxicities of some of the novel agents. Dr. Durand did a great job of that. We've talked a little bit about that as well from Matt, who mentioned it. But I'm just going to give you a quick overview. So let's talk about AFib first.

It's the most common arrhythmia that I see. In fact, of the consults I had this week coming off this service, I probably saw half my patients had atrial fibrillation. Now, thrombocytopenia in the cancer patient is a common problem. And what do we do?

And you've got to remember, even if you have thrombocytopenia, it does not protect you against venous thrombosis or an arterial stroke. It does not protect you at all. And as Dr. Durand told us, maybe some of these platelets in the thrombocytopenic patients may be overactive, and I thought that was a good point as well. So maybe that's another reason why it doesn't protect you.

So decisions about anticoagulation in patients with thrombocytopenia have to weigh the risks of thrombosis against the risks of bleeding. And so that's what we really need to do. And what are some of the bleeding risk factors that I look for when I see a patient?

I look for platelet dysfunction. We really use 50,000 as a cutoff for platelet where we don't want to give any anticoagulation. If somebody is having a stem cell transplant, they're going to be dropping their platelet count. So I probably don't want to give them any.

Liver disease, recent major bleed-- those are the kinds of things. Old age-- things that are in the HAS-BLED score. I mean, those are the things that we have to worry about.

And for individuals with venous thromboembolism, or AFib, who do not have one of these risk factors, in general, we would probably anticoagulate if the platelet count is over 50,000. We'll probably hold anticoagulation if the platelet count is under 50,000. In general, what we're doing for atrial fibrillation when we see these patients is we're doing rate control.

I'm not a fan of Cardizem, and I'll tell you about that in a second. And I mostly use beta blockers. And we use amiodarone quite a bit for rate control and cardioversion as well.

In these cancer patients, I'm seeing potassium at 2.9, magnesiums that are 1.3. So we really need to correct the electrolytes as well. And cardioversion is used only if I have an unstable patient.

We get baseline echo, baseline thyroid function, and don't forget pulmonary embolism. These patients do get PEs. They're probably hypercoagulable, and so you've got to think about that.

And don't forget, in the cancer patient, you get pericardial infusions. And so you can see atrial fibrillation from that. So doing that full evaluation is important. And for people that are rapid rates with atrial fibrillation, look at the EKG and look for ischemia, because ischemia is a prominent part as well.

I try to avoid calcium blockers for a few reasons. First of all, I don't like them with cardiomyopathy. Second, Cardizem, especially because of the way it's metabolized, can increase the effects of apixaban, for example. Or it can increase the effects of doxorubicin or ibrutinib.

And so because of the way it's metabolized, I tend to avoid it. These patients come in, they get Cardizem in the ER even though their EF is 25%. It's probably the first drug I stop, and I try to go with beta blockers for rate control. And I use that amiodarone for rate control, especially if the patient's stable, and usually they are.

So in summary, for the atrial fibrillation patient, I control the rate. Judgment's needed about anticoagulation. We do shared decision-making with our oncology colleagues, and I avoid drug interactions. And that's what we're basically doing with atrial fibrillation.

I also am not worried about giving amiodarone for the period that this patient is being treated for their cancer. Yes, we monitor thyroid function. Yes, we worry about all those side effects that you see in the PDR with amiodarone, but it's probably the most common drug we use in maintaining sinus rhythm.

The next thing. I got a consult, this patient has a prolonged QT. Can I give a TKI inhibitor? Can I give a tyrosine kinase inhibitor? And that's not an uncommon consult.

So this is the normal QT interval. It starts from the beginning of the Q wave right to the end of the T wave. The normal QT interval is a little shorter in men than it is in women. Some people think it's because women may have-- sex hormones may affect the QT interval.

So men, top normal's 440. In women, it's 460. We usually start to worry about Torsades when the QT interval's over 500. Or if you have an abnormally short QT, you start to wonder as well.

But a rule of thumb is that a normal QT is less than half the preceding RR interval. It's a rule that we would look at. So remember also, that the QT changes with heart rate, right?

The faster the heart rate, the shorter the QT. The slower the heart rate, the longer the QT. It's pretty common to see.

Abnormally prolonged QT intervals are associated with an increased risk of ventricular arrhythmias and especially Torsades. And congenital short QT syndrome as well has been found to be associated with a risk of atrial ventricular fibrillation and sudden cardiac death. So what do we do with the oncologic patient that has a long QT and we now need to give a drug that might prolong the QT even further?

So we correct the QT interval, and we have a couple of ways of doing this. And the corrected QT is what the QT would be if you measured it with the heart rate being 60 beats a minute. So if you happen to have an EKG where the heart rate is exactly 60, just measure the QT, and that's what it is. But for all other heart rates, we have a couple of formulas that we could use to correct the QT.

One is the Bazette's formula. And I believe that most of the EKGs give you a QTc based on the Bazette's formula. And there's another formula called the Frederique formula. And you can see the Bazette's formula is the QT over the square root of the RR interval. Whereas, the Frederique is the corrected QT equals the QT over the cubed root of the RR.

Now, why is that important in the oncologic patient? And it's what I told you, is that if the heart rate's 60, just measure the QT. That's what it is.

It's important, because many chemotherapeutic drugs raise the QT interval. It's important, because the Frederique formula gives you probably a better correction, especially in our oncologic patients. And what happens is, there was a study looking at putting oncology patients into a clinical trial. And what was found was that, if you use the Bazett's formula, you had to eliminate 10.8% of patients from getting into a clinical trial.

Whereas, if you use the Frederique formula, only 3.9% of patients were eliminated with whatever the QT interval was that kept you out of that clinical trial. So people believe that it's a more appropriate way of measuring the QT. And it allows us to give therapy to patients that might otherwise be eliminated.

One thing you have to know, there are other things-- and I can't remember who mentioned them earlier. But we did talk about other things that prolong the QT interval-- female sex, electrolyte abnormalities, older age, you can have congenital issues, HIV. And there are drugs that we give that prolong the QT interval-- antiemetics especially, antihistamines. And yes, as cardio-oncologists, we're saying, hey, let's stop some of these drugs because they're prolonging the QT interval.

At least nine tyrosine kinase inhibitors either carry a standard black box warning or some other warning that you can't give it to patients if they have a prolonged QT. It's very interesting, because nilotinib, for example, which is a TKI that's used to treat Philadelphia chromosome positive CML, has made a major difference in life. I remember being in medical school, and I had a project back in whatever year it was-- I'm not going to tell you-- but I had a project on a CML patient. They lived for four years. They developed acute leukemia, and they died.

In fact, my project patient died during my medical school stay. And today, I am following some patients in my office that are eight, nine, 10 years out on Gleevec-- drugs that have just changed the realm for Philadelphia chormosome positive CML-- unbelievable. The problem is, though, that these drugs do prolong the QT interval.

And if you look at the instance of sudden cardiac death from any of these drugs, it's exceedingly low. I think Dr. Durand said it's less than 1%. Yet, there's this black box warning. So we can't use these drugs.

And so it's really important that we pick a formula to measure the QT interval that's going to allow us to at least get some of these patients in. Because when you've got a black box warning, you're sort of under the gun as an oncologist or a cardio-oncologist to recommend that. So here are my recommendations with the QT interval when you get that consult.

If you're starting therapy, you obviously get a baseline EKG. And then you check another EKG a couple weeks later. If the QT, using the Frederique formula is less than 480 and a patient's stable, then you could check an EKG every three to six months. And you're OK.

If the patients on, let's say, a TKI, and you change the dose, check another EKG in about three to five days. And don't worry about trying to do the cubed root, the QT over the cubed root. There are apps for this.

And so if you go to MDCalc, you can get an app that will measure your QT interval. And so you'll be able to do this. And when you're doing the consult, you can basically tell people that it's OK to go ahead and give the TKI. And that's a good thing to do.

So the last thing-- and really a lot of people touched base on this already-- is what are the vaster toxicities of the novel cancer therapeutic drugs? You've got to think about everything from head to toe. I could tell you on this diagram you've got to think of everything from mucositis to colitis and myocarditis in the middle. I mean, everything can happen to a cancer patient that's on immunotherapy.

And we talk about IRAEs, or Immune-Related Adverse Events, and they grade them actually from grade one to grade four. And grade one to grade two are mild. But grade three and grade four, where you can get myocarditis or you can get severe inflammatory diseases of the bowel, you've got to recognize this stuff real fast. And if you don't, you're going to get in trouble.

We talked about the PD-1 inhibitors. We talked about the CTLA inhibitors. If you give just one of those drugs, you've got about a 20% chance of an immune-related event. But if you combine a CTLA-4 with a PD-1 inhibitor, you could be up to about, what, 55% of immune-related adverse events. And it's very, very important for these immunomodulary agents that we recognize the toxicity right away.

I'm not going to go through any of the mechanisms. But to tell you that this is a diagram that I like, and I think Dr. Durand showed it as well. It turns out that the T cell has-- and I need to do this, because I'm a cardiologist, and I'm not an oncologist. And I have to keep reminding myself how this stuff works.

So it's interesting that the T cell has a PD-1 receptor on it, and the tumor cell has a PD-L1 receptor on it. And when those two hook up, the T cell's turned off. So when we're giving immunomodulatory agents, we're actually giving an antibody to the PD-1 or PD-L1.

When we block those receptors, it turns on the immune system. And all of a sudden, the lymphocytes start killing the tumor cell. And that's what's amazing.

The problem is, as has been pointed out, it starts hitting you all over your body. It's not just on the tumor. If it was just on the tumor, that would be great.

And I just want to end by reminding everybody-- these are, by the way, the PD-1 inhibitors that we have, the PD-L1 inhibitors, CTLA-4 4 inhibitors. These are the drugs that we have, but there are hundreds of drugs out there that we have to keep in mind. So what do we do about the immune-related adverse events?

You've got to be careful to think about everything, from skin, to GI, to lung, to endocrine. The endocrine's stuff is easy. Because if they're hypothyroid, just give the a little Synthroid. Hypoadrenal, you just get them a little cortisol. That that's how they manage them, right?

But for the other stuff, you've got to recognize it early. You've got to stop the drug. You may have to give steroids, and you have to be very, very aggressive.

So in conclusion, immune checkpoint inhibitors or targeted monoclonal antibodies have revolutionized cancer treatment. There's non-specific activation of the immune system, though, and it causes a lot of immune-related adverse events. You've got to educate your patient.

And this is what the oncologists do a great job on. And they have nurse practitioners that help with that as well, and nurses to tell patients what to look for. It's very important. Because if you recognize it early, you can treat it.

If you wait too long, your patient's screwed. And you have to have a multidisciplinary approach. I'm a cardiologist, but I depend on so many of my consultants and my colleagues as we're taking care of these patients. You've got to recognize, report, and manage these patients.

And they may be coming to me just to look at their QT interval. And I recognize that they may have some other kind of problem, I get on the phone and call the oncologist and say, hey, there's something else going on here. And really, just use evidence-based management for clinical decision-making.

And if you have a grade three or grade four immune-related adverse event, you've got to stop the drug, give high-dose steroids, and aggressively treat these patients. Don't think that just these new drugs are causing problems. 5-FU, which we've used for colon cancer forever, and FOLFOX, and every single drug that our oncology colleagues give cause problems. And of gemcitibine that we give for pancreatic cancer, look at what it can cause-- MI, Takotsubo disease, Raynaud's, angina, vasospasm. The TKIs, the monoclonal antibodies, the VEGF drugs, they all cause these problems.

And so we have to be totally vigilant as we do that consult. So my bottom line is, you got to be a complete doctor, unfortunately. You've got to treat the risk factors. You've got to get people to exercise.

You got to do all the things that you want to do to prolong life in a cancer patient. And be aware of the type of cancer and the type of chemotherapy. Do what Josh has taught me to do, look at some of the imaging and look for the potential complications.

Be aware that, if somebody had cancer 10 or 20 years ago and they got radiation, you've got to think about pericardial fusion, coronary disease, valvular heart disease. It can all be there. And so you've got to think of it all. And that's it, thank you.

[APPLAUSE]