BARBARA A. PISANI: Good morning, and thank you for coming. I hope that this will be a somewhat enlightening lecture for you. Sadly, it's a beautiful day outside, and you guys are stuck in here with me. So I'm going to talk a little bit about management of heart failure. And I'm not going to go over the basic general heart failure management, but I'm going to talk a little bit more about some of the advanced issues related to heart failure, both in terms of transplant, mechanical circulatory support, and in terms of how to troubleshoot sometimes when you see patients who are really sick in the hospital.

So I'm going to start with a case study. CS was a 57-year-old woman who came as a transfer to a hospital that I was at previously. And the patient had a history of hypertrophic cardiomyopathy. And there was a rumor that she had had a septal myomectomy 20 years prior. She had called the local hospital because she was having palpitations and dyspnea, and promptly had of a ventricular fibrillation arrest. And she'd been complaining of palpitations for a week before she had arrived.

By the time she was resuscitated she had respiratory failure. Unfortunately she aspirated during her intubation. After the arrest, she was in complete heart block. She was taken to the cath lab. She was found to have normal coronary arteries. A transvenous pacemaker was done. And a bedside echo showed that her ejection fraction was 20%. And she had severe mitral regurgitation. She was stabilized after her arrest. And she was actually transferred to our organization for extracorporeal membrane oxygenation. On arrival she was intubated. She was on Dobutamine, Levophed, Dopamine, Vasopressin, and Amiodarone.

And on physical exam at that time with all those agents, she was actually hypertensive. She was not obese. Her oxygen saturation was 100%. And you can see that she was on 100% FIO2. She was on a fair amount of PEEP at that time. She was sedated. She had the typical post-code physical exam with coarse breath sounds and a paced rhythm, and arms and legs. But that was about all we got from the person who wrote the history and the physical.

She was hyponatremic. She was acidotic. She was in acute renal failure. Her blood sugar was 149. Despite the severity of her illness her cortisol level was over 40. She had shock liver. She was coagulopathic. She was anemic. She was also, despite this, not terribly with a severe lactic acidosis, although she had a significant metabolic acidosis. Her EKG showed a left bundle branch block. And she was in sinus bradycardia. She underwent emergent ECMO placement.

Her hospital course was not without events.

She developed a compartment syndrome and had a fasciotomy. She developed acute renal failure. She was on CVVH. She developed supraventricular, and actually ventricular arrhythmias. She developed atrial fib. At one point in time we thought she might be comatose, but her CAT scan was negative. She developed a radial artery occlusion.

And ultimately, despite all of these things she was able to be weaned off ECMO about two weeks later. She underwent a tracheotomy. She ultimately underwent a AV node ablation, and placement of a bi-ventricular pacemaker for a left bundle branch block. She developed profound diarrhea, which was treated as c-diff. She had hearing loss related to the prolonged intubation. She had ERCP and sphincterotomy for gallstone pancreatitis.

And finally, about a month after she had arrived to us, she was deemed stable to be transferred to a rehab facility. And she spent about a month in a rehab facility. She came to see me in clinic.

She had a foot drop. She still had leg swelling as a result of her fasciotomy. She couldn't walk on a treadmill or ride a bike. She was doing some housework. She had poor energy. She did not remember anything related to the cardiac arrest.

She still had draining from the fasciotomy. She couldn't hear well, because of all the antibiotics. She was going to need hearing aids. She had chronic diarrhea due to the antibiotics, although her PEG tube and her trach were closed.

And I explained to her what had happened to her. And she and her husband were enormously grateful that we had saved her life. Her son had told me that after her cardiac arrest, he went over to her and said, mom, do you want us to keep doing this? And she had squeezed his hand and that was the reason why she was transferred to our hospital, because her son believed that she was still there, and that he wanted all this stuff done.

So when we talk about heart failure, we know that there are about six million people in the United States with heart failure. By the year 2030, they'll be almost 18 million people with heart failure. This is the only type of heart failure that's increasing in frequency.

And that's because we survive cardiac arrest. We survive hypertension and strokes. And now we survive our MIs and sudden death because we have defibrillators.

So if you're over 40, and I'm going to guess one or two of us in the room are over 40, we have a one in five chance of developing heart failure. There are almost a million cases each year that are new to diagnosis. And it's a contributor or direct cause of death in about 300,000 people. One in nine death certificates mentions the words heart failure on it. There are over a million heart failure hospitalizations each year.

And if you just think about the mortality, the one-year mortality, if you get admitted to the hospital is 23%, which means you have an 80% one-year year survival just with one hospitalization. And think of how many cancers give that outcome survival. There are almost a million ambulatory visits. And at five years the mortality is around 50%. This is the number one reason why patients are admitted to the hospital if they're over 65-years-old.

And if you combine all of the cost of all the cancers together, heart failures still cost the government more money. It is the largest federal Medicare and Veterans Administration expenditure. And by the year 2030 we expect that the government will spend almost $70 million on heart failure.

And where does that money go? Most of the money goes towards hospitalizations. And you can see a fair amount of it also goes toward nursing home care. So heart failure is really a pretty big problem. And when we think about heart failure, we oftentimes think of this person, bloated, swollen, with PND and orthopneia. But heart failure presents in many other ways. And oftentimes it's not picked up appropriately. The patient who has VF or VT is very easy to detect.

But I would say that when I worked in organizations that had liver transplant programs, probably twice a year we would see a patient who would come to us via the liver transplant program, because the patient had an extensive liver work up and was diagnosed with cirrhosis, only for somebody to go back and look at the chest x-ray and the echo, and say, oh my god, guess what this guy has? And you can see that not everyone with heart failure has a low EF. You can see some patients have preserved EF. Most of the information I'm giving you is related to patients with reduced EF. Patients get LV thrombi. They have strokes. So heart failure really can present in more than just the volume overload state.

How do we define heart failure? Most of us think of heart failure as high output, low output, forward failure, backward failure, right heart failure, left heart failure. But the American Heart Association really has pretty clear definitions. They say patients with a reduced EF, have any EF less than 40%. Patients with a preserved EF, have an EF over 50%. And then borderline patients 41% to 49%.

And now they've recently added this classification of patients that had a low EF, maybe they've recovered from their MI, maybe they've recovered for myocarditis or postpartum cardiomyopathy. Their EF has improved. So this would be heart failure with preserved EF that has improved.

When we look at an older definition, we can see that heart failure is a family of syndromes characterized by new or worsening symptoms of heart failure that either lead to hospitalization or unscheduled medical care. There's a gradual or rapid change in heart failure signs and symptoms that result in the need for urgent therapy. So it doesn't mean you need to be in the hospital, but it does mean that you usually are requiring some therapy.

And when we look at patients that have advanced heart failure, these are not just your run of the mill patients with a low EF on an ACE inhibitor and a beta blocker. These are patients that are requiring other procedures. They're requiring CRT. They're requiring mechanical circulatory support, continuous infusions, innovative therapies.

And these are people that are symptomatic and have functional class three to four symptoms. They can do their activities of daily living. Don't ask your patient if they're short of breath.

Ask your patient what can you do? Because if the patient says, I'm not short of breath. And all they do is sit over here with a channel changer watching television, they're not going to be short of breath. But if you ask them, can you take a shower? Can you walk up a flight of stairs? Can you do the laundry? This will really give you a better clue as to how sick your patient is.

These are patients that have abnormalities on echo-cardiogram. They have low EF. They have abnormal hemodynamics. And they are unable to exercise. Their peak oxygen consumptions are low. And they can not walk more than 300 meters, which is about 900 feet, without being short of breath. These are people that have a history of repeated hospitalizations. And these are people that despite doing all the right things, just do not get better, and some of them even get worse.

When we look at how we identify these people, and these are people in your mind you should be thinking, I have the patient on the right medicines, do I need to do something else. They repeatedly hospitalized. They have worsening renal function, despite the fact that they're not getting any increase in diuretics. They're losing weight. They have cardiac cachexia. They cannot tolerate ACE inhibitors or beta blockers without being hypotensive. They have persistent symptom. They are unable to walk flat on the ground.

And this is very important, these are patients that are on high doses of diuretics. And when we talk about high doses, this is over 160 milligrams of lasix a day, which means if your patients on more than 80 milligrams of lasix twice a day, that person is in this high risk category, or someone that you need to use Metolazone or Diuril on These are people that are hyponatremic. And they're people that are getting recurrent ICD shocks. So this is a separate class of people. This is not the person going to their primary care doctor every six months and is doing well and is back at work.

And when we look at these patients that are repeatedly hospitalized you can see that with just one single hospitalization, how the survival changes for these patients. So each hospitalization leads to a worsening one-year survival. And if you look at patients who come into the hospital, a very easy way to determine how high risk they are for mortality, this is the ADHERE registry. This looked at 33,000 patients who were admitted to the hospital.

And if you just look at patients that have a BUN that's over 43, their systolic blood pressure is less than 115, and they have creatinine of over 2.75, these patients have an almost 22% in hospital mortality. Think about how many patients you see on the floor on a single day like this. They came in. They got some extra diuretics. They're hypotensive, because we decide to titrate up their meds. They're in-hospital mortality is almost 22%.

And when you look at patients who come into the hospital, if their creatinine limit increases by over 0.3, you can see that the mortality increases significantly. And with each successive mortality, we're changing creatinine. You can see that this survival curve changes. So this is a very, very dramatic difference in survival.

And you can see that this survival is at 90 days. This is not years and years after you come into the hospital. When you look at patients that have persistent renal failure after their hospitalization, their mortality is much, much worse than the patients that at least recover their renal function. So renal insufficiency in these patients that get admitted to the hospital is a very significant thing.

Now we're talking about patients with reduced EF, but when we talk about patients that have preserved EF, while the in-hospital mortality is better, you need to keep in mind that patients that have a preserved EF-- and a lot of this data comes out of the Mayo Clinic-- these patients have the same one-year mortality as patients with reduced EF.

So many times patients tell me, oh, I want to know my number. I want to know what my EF. Is it 50%? And I tell them, just because your EF is 50, if you have a clinical heart failure, it does not mean that your survival will be better. So patients need to understand that whether you have a reduced EF or preserved ER, having heart failure is not a very good thing.

And you can see, as patients develop heart failure, this plateau here of this clinical course for some patients could last years and years and years. A patient with hypertension who suddenly stops taking their medicine, as opposed to a person who has an acute myocardial infarction, and then has a progressive decline. And there's this magic window over here where we identify these patients, and try and make sure that we can get them advanced heart failure therapies to ensure that we can prolong their survival.

So when we look at this group of end-stage heart failure patients, one definition is looking at patients that have a one-year survival that's less than 40%, or two-year survival that's less than 25%. And this is some data from Maryland by Freudenberger. And he looked at 100 patients who were referred to his organization for transplant evaluation. Most of them were referred by cardiologists. And when you look at these patients, these are patients who were referred by cardiologists-- 33% of the patients were deemed by their cardiologist to well to be listed for transplant.

But when you look at this group of patients, 10% of them died, and 6% of them were functional class three. And when we looked at some of these patients, just with titrating their medications in a heart failure program, 84% of them were still alive and well. So you can see that oftentimes even patients manage by cardiologists, particularly if they don't have a good feel for heart failure, do not have their medications optimally maximized. And also many patients referred to us are referred to us when it's too late to really do anything for them, because they really are too sick for transplant, or even for mechanical circulatory support.

So when we're looking at these patients, what we really need to look at when we're talking about heart failure, and VADs or transplant, or advance therapies, what we really need to do is look at the risk-benefit ratio here, because when we look at mortality data, we look at population data. So that if we say the one-year survival with transplant is 92%, which means 8% of the people will not survive.

If you happen to be the person who dies, it's 100%. So when we're looking at how to decide which of these patients are end stage, which patients need inotropes, which patients need mechanical circulatory support, which patients need transplant, we really need to ensure that the patient is not so sick that we really don't do them any benefit and they might be better off getting palliative care or that we're not doing it soon enough, versus we've waited too long.

So when we look at ways to determine how we can tell if a patient is too sick, we can use the heart failure survival score, or we can also use the Seattle Heart Failure Model. This is a very nice thing that you can download on your iPhone. You can plug-in all this information. It gives you clinical data with respect to patient age, what the cause of their disease is, medications, and it'll give you a curve as to what the patient's expected survival is, putting what you plan to do for the patient.

Start on inotropes, put a ICD in them. And then it will give you a second curve. And it will show you what your predicted outcome is for that patient. So these are different ways to determine if a patient is truly sick enough to need some of these advanced therapies.

And when you look at this data, you can see if you combine the data, patients that are high risk with the heart failure survival score and the Seattle Heart Failure Model have a very, very, very poor outcome. So these are easy ways to help you better risk stratify your patients.

And when you look at heart failure patients, most of us would never think that heart failure would have a worse survival than most of these diseases. So patients, I think, do not appreciate how serious a disease heart failure is. I had a little fluid on my lung, does not translate into a five-year mortality of 75%. So when we talk about guideline directed medical therapy, ACE inhibitors, beta blockers, aldosterone antagonists, CRT for patients that have bundle branch blocks, or intraventricular conduction delays, defibrillators, all of those things are very, very important.

And when patients come into the hospital, we want to make sure we continue those therapies. We should not stop the ACE inhibitor. We should not stop the beta blocker. We should continue those when the patient is admitted to the hospital, unless they are hemodynamically unstable. If the patient is not on a beta blocker, we used to say it was OK to start a beta blocker when the patient is in the hospital. But now the American Heart Association recommends that we do not start the beta blocker until the patient is successfully diuresed, is off IV vasodilators, and IV inotropes.

And we want to start them on a low dose. We don't need to put them on the target dose the first day they get there. But we do want to make sure that the patient has the beta blocker initiated in the hospital.

When we look at patients that have fluid overload, when the patient gets into the emergency room, is when the patient should get the diuretic. And the diuretic dose should equal or exceed the daily dose. If you don't feel comfortable given 80 of Lasix, don't give 80 of Lasix, ask someone else to give 80 of Lasix. Because if someone's on 8 of Lasix, and you give them 20, you really have not done anything good for them.

And then go back and see the patient. How much urine output did they actually have after that, because if you gave them 80 of Lasix and nothing came out, then maybe they need other therapies. And when their other therapies occur, sometimes higher doses, sometimes we consider Lasix drips, or Bumex drips, whatever your particular hospital uses, or sometimes we'll add a thiazide diuretic like Matolozone or IV Diuril.

Also recommended, which we did not use very frequently in more current times, the American Heart Association also recommends low dose dopamine in addition to loop diuretics to facilitate diuresis. And the reason why the dosing of the drugs is so important is you can see this is the normal curve for the fractional excretion of sodium. And when you look at patients with heart failure, this curve is shifted to the right.

So patients really require higher doses of that drug. And there's many reasons for that. They get diuretic resistance. They get tubular hypertrophy. So there's many reasons why they don't respond. But if you don't give them an adequate dose, they're not going to do better. And I think of this as like IV vancomycin. We check vancomycin levels, and we would never say, well, this guy's got normal creatinine and his vanco level is two, but the standard dose is 1,000, so we're only going to give him 1,000 BID. We would change the dose of vancomysin.

And when we look at diuretic dosing, you can see that the higher your diuretic dose requirement, the worse your mortality. So again, when patients are on over 160 milligrams of IV furosemide, this just tells you that that is a really sick patient, and that that patient may need more advanced therapy.

So when we look at diuretics, how do we know whether we should use a diuretic as a bolus or whether we should give a drip? The dose study, which I will go over pretty quickly for you, randomized patients into high or low dose diuretics. And all of these slides are in there. It's not my intent to go over every single slide, because there are a lot of slides in there.

But mainly as a reference for you, you can see that patients were either randomized to low dose, which was one times their home dose, either as a drip or bolus, or two and 1/2 times that dose. And when they looked at these patients, you can see what they found here was that there was better improvement with the Lasix drip as opposed to the bolus. There was also a greater fluid loss.

But that came at the expense of renal insufficiency. So nothing in this world is for free. So getting more water off sometimes just means that you're just going to get acute renal failure. And it is possible to conduct these studies. They are somewhat difficult to conduct when we randomize in this manner.

But there really is no advantage to infusion therapy over bolus therapy. I'm not sure what the cost is, because it may actually be cheaper to have an infusion if you have to consider nursing time to push a bolus, et cetera, and the pharmacy to make that. There are greater degrees of decongestion, but there's no long term benefit to that.

If they don't respond to diabetics, you can certainly consider ultrafiltration. I don't know how many people use this particular product. This is a product that's usually done on the floor. It requires only a 20 gauge IV, or it has its own catheter. You attach this. It really is just like an IMED pump.

And you can literally ultrafilter off the water, as opposed to the way we use with the renal dialysis machine. And this can be done at the bedside by the bedside nurse. So this is another way to remove fluid if the patients are not responding to diuretics. And there are some advantages to ultra filtration-- better functional capacity, less activation of the neurohormonal cascade, and greater improvement in lung water content.

When we look at the data comparing these-- and these data are different. These are patients coming in acutely with heart failure-- 200 patients with acute decompensated heart failure. What they found for this group of patients was there was greater weight loss, greater improvement in symptoms, and lower re-admissions.

However, when you look at a group of patients that are in the hospital, that develop worsening renal insufficiency while they're in the hospital with heart failure, you can see that ultrafiltration actually was worse. So if you start ultrafiltration too late, you're actually going to have worse outcomes. And that's why, again, if you upfront think about how sick your patient is, you won't be moving toward these directions too late. And you can see that a higher percentage of the patients within this group had adverse events when compared to the patients that were not treated with ultrafiltration.

Other therapies you can use depends on your hospital. Not every hospital will allow IV nitroglycerin on the floor. Most people don't use IV nitroprusside because you have to put them in a unit, and need an arterial line. And some people still use nesiritide, although that did get a bad rap for a while. If patients are hyponatremic, arginine vasopressin antagonists like Tolvaptan, Conivaptan. This is for patients with symptomatic hyponatremia that are related to heart failure. This has never been shown to make people live longer, or feel better, but it does help keep people symptomatic.

So what about inotropes? When we look at people that are in shock, like my patient was, patients with cardiogenic shock may require temporary inotropic support, as we ensure that we maintain systemic perfusion. So put the patient on an inotrope, put the patient on a presser, if they get better, move them on to something else. Or if they don't get better, talk about other things, hospice or palliative care.

We can use these inotropes as a bridge in patients that are really sick, so that we can titrate up guideline directed medical therapy. Try and start the ACE inhibitor, after load, reduce the patients. And then certainly patients that are on continuous inotropes, sometimes if they have severe LV dysfunction, they're hypertensive, they have severely depressed blood pressure, sometimes we'll also start them on inotropes to help maintain blood pressure and cardiac output.

But when you look at people that require inotropes, long term you can see that this therapy is really not a good therapy. This is data looking at Novacore, which is just a particular brand that makes VAD devices. This was looking at Novacore versus inotropic therapy. And you can see that those patients had less than 10% survival.

When we talk about what can we do at the bedside in the average hospital, we've gone through the guideline therapy. We've gone through inotropes. The patient is still not better. I don't have hi-tech stuff. Remember, we can sometimes use balloon pumps. These can be placed in the bedside or in the cath lab.

The problem with balloon pumps is they really do not augment significantly. Most of the data shows that if we use a balloon pump, particularly in patients who are post MI, that there really is no survival advantage. But every now and again, we do get patients who do well. Remember, balloon pumps increase diastolic pressure. As such, they increase coronary perfusion pressure. They lower systolic blood pressure. So they improve cardiac output and lower systemic vascular resistance.

If you don't have that option, but have options for more advanced therapies, mechanical circulatory support is certainly an option. And I'm going to spend a little time talking about mechanical support. So when we talk about mechanical devices, we talk about short term devices-- devices that are only going to be in place for less than 30 days.

We talk about patients that will be on prolonged support, like a patient who has a bridge to transplant, or a person who will be on a permanent device, like destination therapy for the rest of their life. These devices could be outside your body. These devices can be outside your body. They can be inside your body. Hard to believe somebody put one of these buggers in their body.

So devices can be immediately outside the body. This is what we would call a paracorporeal corporeal device. Or we can have a device that's totally away from our body. Or we can have one that's inside. And that's an intracorporeal device.

When we look at these devices, we use them as bridge to recovery. I had an acute MI, I had mycarditis. Bridge to a bridge-- my patient, she was put on ECMO. She was bridged to something better or something different.

Bridge to a decision. I'm a cocaine addict. I might be a good person, but I just had a bad predilection to things. I'm going to get a device, if I stop taking drugs, you might list me for transplant. Destination therapy-- I'm not a transplant candidate. Bridge to transplant-- I am a transplant candidate. I'm going to have a device put in place while I wait for transplant.

So when we look at some of these things, and I'm not going to talk about these extensively, but this is putting in in the cath lab. This is a catheter that has an impeller. It's like a little propeller, like see on a ship. And it's inside here. This goes retrograde up the aorta, across the aortic valve, sucks blood in an attempt to improve cardiac output. It only puts out about two and 1/2 to five liters, depending on what kind of device you have.

The randomized trials with this device have not shown a survival advantage, but most of these devices, when you look at the data, were put in people were having CPR as they were put in. So the fact that the patients didn't survive might be a reflection of the fact that they really were not destined to survive.

This is a different type of device. This is a tandem heart. So this is a centrifugal pump that is outside the body. This device circulates the blood perpendicular to the body, so that here we have a catheter that goes up the IVC. And you can see it crosses the interatrial septum, stays in the left atrium, and it sucks blood out of the left atrium, brings it back through the device so that it can circulate the blood through your heart. It can put out up to 10 liters of blood.

And then these are what we call the extracorporeal devices. These are somebody who had cardiogenic shock in the cath lab, had cardiogenic shock in the OR. This device is put in quickly in an attempt to try and resuscitate the patient so that they can recover, their myocardial can recover from the pump run, the myocarditis, the code, whatever happened to the patient.

And then ECMO, which is what my patient had. These are canulas that are put in through the femoral artery and the femoral vein for patients that are on ECMO for H1N1 or whatever pulmonary process they have. Those are vino vino cannulas. So these are ways to support the circulation so that we can oxygenate the patient, maintain organ perfusion, and hopefully help the patient to survive.

Now none of these is a free ride, because all of them have side effects. And I'm not going to go over this specifically, but this is one of the big side effects that ECMO has. So these cannulas go into the femoral artery. They can cause great gangrene. These are older ways of doing things.

Nowadays we put in what we call a profusion catheter. So we pass a little catheter from the femoral artery down to the peroneal artery, so that we maintain profusion to the foot. But if you don't think about this in advance, you can certainly cause harm to the patient.

And when we look at patients, you can see that these are very, very sick patients. So it's kind of hard to figure out did the patient died because of the protoplasm we had, or did the patient die because the device was not effective. But you can see that when you look at these patients, the way that you can best determine if they will survive is if they're lactic acidosis resolves. So patients that are on extracorporeal membrane oxygenation, if they remain acidotic, they still have lactate, you have probably not cleared the problem. And they're not apt to do well. And those are the patients that are not going to survive.

And that's because cardiogenic shock is not just a low EF. Cardiogenic shock is multiorgan system dysfunction. I always wonder when somebody says, oh my god, the person has a white count and a fever. I think they have sepsis. And it just so happens they have a low EF.

Well, think about what happens when you have shock. Your catecholamines go up. Your cortisol goes up. All of those things make your white blood cells go up. You have low tissue perfusion. You have translocation of bacteria.

So not uncommonly, these patients go into the unit, in the ICU, in the medical ICU. No one knows they have a low EF. They just know the patient has a systemic inflammatory response syndrome. And then the following day, after a SIRS protocol has been followed, or an ARDSNet protocol has been followed, they've gotten 10 liters of fluid, and somebody realizes, oh my gosh, this patient had heart failure, and this is really heart failure with cardiogenic shock, and sepsis, or multiorgan system failure, as opposed to the other way around.

When we look at these devices, we use them for patients that have low EF, because if the person has LVH the cavity to the heart is very small, and the device can't suck the blood into it. We use non-durable devices as a bridge to recovery or bridge to decision. And then we use durable devices for patients that we think are not transplant candidates, and might be candidates for destination therapy.

And while you're saying, wow, that's pretty spiffy. They're doing all that stuff, the first case reported here was done in 1978. This was done by Doug Norman and Denton Cooley. And this patient went on to get a transplant, but only survived 15 days post-transplant, because at that time, we had no way of treating gram-negative sepsis. So the patient's heart showed no allograft rejection. He died from gram-negative sepsis.

So when we're looking at these patients, you may be saying, well, what kind of decrepit person gets a VAD. This person is a young woman who decided to get pregnant while she had a VAD and had her baby in spite of that. So when we look at these patients, patients who are HIV are living longer. These are patients that would have previously never considered doing device therapy.

And if you're a Republican, you might feel very strongly about this. You might feel equally strongly if you're a Democrat. But also we have people on our political agenda.

So when we decide about transplanting patients, or transplanting with bridge to transplant or destination therapy, we have to figure out which of the patients are too well, which of the patients are too sick, because if you look right here, patients that are high risk for a VAD do no better than patients that get medical therapy. So you want to make sure that the patient is an acceptable operative risk.

And we determine that by looking at the INTERMACS score, because that score will help us determine where on this curve we are. Are we in this window where the survival will be better or are we all the way over here, where the best option for the patient actually is palliative care. And some ways to help you determine this is when we see patients, we look to see if they're a transplant candidate.

If they are, we list them for transplant and we put a device in them. If we say they're not a transplant candidate, or we're not sure if they're a transplant candidate-- maybe they are somebody who's got some illness we're hoping they'll recover from. I had a patient who underwent bypass surgery. And during the bypass operation he failed to come off pump. He underwent a VAD as what we thought was going to be a bridge to transplant. Well as it turned out, the guy had not had a colonoscopy. And after he had colonoscopy he was found to have colon cancer. So five years on that device. He was pretty lucky because the device failed just about the time his cancer was cured. And then he ultimately went on to get a transplant.

So many people do not realize how many people out in the community this really does affect, because if you're getting chemo, we can't let you survive your cancer, because of the chemo side effects. And at the same time you're not eligible for transplant.

And when we look at this, you can see that this very high risk people with a very high mortality with medical therapy, with our early outcomes with VADs were not very good. They were better than medical therapy, because 100% of the people were dead at one year. But 50% survival at two years was really not a whole lot better. And now you can see we're almost to 85% one-year survival with devices for patients that are appropriately selected. And that's true for anything. If we don't appropriately select patients for the right antibiotics, we get multidrug resistant bugs.

And you can see that this is probably the most commonly used device. This is called a Heartmate II. This was the Model T. This was the first VAD that was FDA approved as a bridge to transplant and destination therapy. A person who had a BMI of less than 1.6 could not get this. The driveline would come out of s skin. It was a big driveline.

This transitioned into this device, which is a much smaller device. Even a little person could get this. And then now we have much, much smaller devices. This is a hardware device, which goes into the pericardial space. So the devices have become much, much smaller. And they all have different profiles. You like a Cadillac. I like a Mercedes. Somebody else likes an Audi. They're all very, very good devices as bridge to transplant.

This one is FDA approved as bridge to transplant and destination therapy. This one was FDA approved for bridge to transplant. It's off the market now. The company was sold to somebody else. And then this is a new device, the little one I just showed you. This one is FDA approved as bridge to transplant, but not destination therapy yet.

So for these patients, if you think your patient is not a candidate for a transplant, could not get these devices. And there are very specific criteria for these devices. And you can see this is the older device that I showed you. These are the paracorporeal devices. These used to be the only devices we had available for small people, because we couldn't fit them inside. And these can be used for right ventricular support, left ventricular, support or both, if the patient needs it.

You can see here these are the Berlin Heart. And if you ever go online to Berlin Heart, you'll see these little hearts. You can see they come in all different size, like going to the shoe store for your kid. As the child grows, you get a bigger Berlin Heart. But you can see these devices-- children cannot go home with these devices-- or at least at this age. This has a portable driver, so you can see this young kid is at home.

This is a total artificial heart. This was a patient of mine in Milwaukee. You can see he was a big dude. And he was a guy who we could not get a defibrillator in. He had a vest. And after he had multiple, multiple vest shocks. He was the guy that everybody knew in the shopping mall. And when he went to the ground, they better know CPR, until finally we had to put in a total artificial heart.

At the time he had this device put in, this was the only way we could power the device. So he would go on a 30 minute walk around the hospital until the battery wore down, the air tank went down, and then he would replug in. Now there's a freedom driver. Patients can actually go home with this device now. So these are used only as bridge to transplant.

And when we look at patients who are being evaluated for transplant, when we look at the history of transplant, early on they really did not have a very good survival. This was probably a shocking paper. Most of the good or bad news you get in the world comes out of *Life Magazine*, or *Look,* or the *New York Times*. And these patients all died at less than a year out from transplant. And now when we look, the longest surviving transplant is 31 years post-transplant. So better anesthesia, better immunosuppressants, better antibiotics, better selection of candidates, have all translated into better survival for patients with transplant.

However, I've already told you, there are millions of people out there with heart failure. There's only 4,000 transplants a year. So this is not going to solve the heart failure dilemma that we face. And that's because we have really a true organ shortage. And that's true not just for hearts. That's true for kidneys, liver, pancreas.

You can see the number of people who get a transplant versus the number of people who are waiting for a transplant. And a lot of this has really translated into some of the donors that we use. It used to be we got young spiffy donors, but we have helmet laws, seat belt laws, speed limit laws. And so a lot of those people that sadly had traumatic deaths no longer have that. So we see an older patients and so we can't just select anybody as a transplant donor. And what has that translated into is that a lot more people get VADs as bridge to transplant, because in order for them to survive they really do need some other support.

When we look at the indications for transplant it would be patients with irreversible cardiogenic shock with reversible end-organ damage, stage D heart failure, people who have chronic intractable angina. I had a patient of mine who had a bazillion stents. And she kept coming in, angina, angina, angina, until one day she had an MI. She got a balloon pump. She got listed for transplant. And it was transplanted like two days later.

People with primary cardiac tumors, people with recurrent ICD shocks. How are they going to survive if they can't stop getting shocks, or people that are hypertrophic or restrictive, sometimes these people need total artificial heart. Or people who have had transplants, and develop transplant vascular apathy, or coronary artery disease.

The way that we determine whether patients need a transplant is based on cardiopulmonary stress testing. So if you're a metabolic, your peak oxygen consumption is over [INAUDIBLE] keep on with your medical therapy. Less than 10-- consider transplant. In between there we're going back to that heart failure survival score. Should the patient be transplanted? Should they not be transplanted? Let's look at that heart failure survival score, and see if the patient actually is sick enough to need transplant.

And if not, repeat the stress test in six months. Repeat the stress test in three months. See if you can titrate the medications. See if you can get the patient better.

Because when we look at patients with transplant, or who are transplanted, you can see very, very few of those patients have functional limitations. And that's because they are so carefully screened and selected. And when we look at patients we see that many of the patients are able to work. Some of them don't work because they lose their insurance benefits.

But patients are quite functional after transplant. I've had transplant patients go back to work as doctors, veterinarians, nurses, teachers, construction workers. I've had people post-transplant get pregnant and have children. So really can certainly improve someone's life. And when we look at transplant-- transplants not a free ride either, because patients get rejection. Patients get infections. Patients can die from malignancies. They can go on to develop coronary artery disease. But they do have a good quality of life for those that are appropriately selected.

What is destination therapy? This is a very specific s definition based on CMS guidelines. These are people who are not candidates for transplant. They're functional IIIB to IV, low life expectancy, on optimal medical therapy, who either have these criteria or have a balloon pump, inotropes, low EF, and low functional capacity. And again, the only device that's currently FDA approved for destination therapy is the Heartmate II, which is this device. And this device also has a driveline that comes out of the abdominal wall. It's a little bit smaller.

Who gets destination therapy? These are people who are sometimes older, obese, hopefully in the hopes of helping them lose weight so that they can move on to something better. Diabetics who are not candidates for transplant. People that have organ dysfunction in attempt to sometimes improve the organ dysfunction. Patients with recent malignancy, as I told you, like my patient. Or people who we think have fixed pulmonary hypertension. We put a VAD in them. And what we thought was fixed pulmonary hypertension was actually reversible, because we actually gave them a better heart failure therapy.

People with PAD or sometimes people who get a VAD as bridge to transplant get transfused, and become highly sensitized. Sometimes we're unable to find donors for those patients, and they ultimately stay as destination therapy. I've had some patients who have told me I don't want to get a transplant. I had a young guy who was misdiagnosed and mismanaged for his heart failure for many years. Ultimately got a VAD, almost died before he got his VAD. And he had the VAD, he's like, I'm too afraid to have another surgery. I'd rather just keep my VAD. And is back to college.

So when we look at mechanical support versus medical therapy, this was the original rematch data here. This is the INTrEPID data I showed you. You can see that as we have progressed with these smaller, newer devices, you can see that the survival outcomes for these patients are much, much better. And when we look at these patients you can see even with devices the percentage of patients prior to implant who perceive themselves as having severe problems is markedly reduced when they have device therapy completed.

And this is really important, because these devices that we use now days are continuous flow pumps. They're nonpulsatile pumps. And we thought, as we developed these devices, that we wouldn't have as good of outcomes, but in actuality the outcomes are quite comparable to the older big model. And this is important because these devices are also not without complications. Patients can bleed. Patients can have strokes. Patients can have embolic events. The device can get infected. But nonetheless, patients can still do well. And I think the longest surviving Heartmate II, the small one-- I think the longest surviving patient with this is seven years out now, with the same device.

So when we're looking at these devices, and I've shown you some of the older stuff, this is some of the newer stuff. And this device, you can see is a circulate. These are devices that will only provide partial support. So maybe a person doesn't need 10 liters of cardiac output. Maybe they need five liters of cardiac output.

And this device-- this is a CircuLite Device, which is not on the market. It's still in study. This is the size of a AA battery. And then when we look at this device, looks like, wow, this is humongous. But everything is internal. So there's no driveline. Everything here is within. There's transcutaneous transfer of energy, because this hopefully, or this type of device will hopefully allow for the elimination of the driveline and the infection that is associated with these devices.

So as our technology gets better, certainly these devices will get smaller. When I think about when I was in high school, I had a calculator that big, and all I could do was add and subtract. And now I have a calculator, a phone, a computer, a scale, and everything else on my handheld. So I think the technology will progress. It's just how quickly the technology is able to go through the FDA regulatory process also.

So when we look at patients, sadly my little realm of the world is at the end of the road here. But if you're taking good care of patients, you're looking for at risk patients, stage A patients with heart failure, making sure they're on appropriate anti-hypertensive, diabetic control, cholesterol control, et cetera. And then once they develop reduced EF, symptomatic heart failure, make sure they're on guideline directed medical therapy, ACE inhibitor, beta blocker, aldosterone antagonists.

Do they need a defibrillator as primary prevention or secondary prevention? Are they a candidate for CRT, for biventricular pacing? Are they candidates for bypass surgery, high-risk bypass surgery or high-risk valve surgery? Are they a candidate for hospice therapy? Not everybody with heart failure needs to have a device. Some patients are best served by saying, there really is nothing to help you with, because in my opinion, more is not always better. Sometimes more is just more. And you really need to know when more is right and when more is wrong.

So when we look at patients that have this type of heart failure, you see patients. You are not able to manage them. You see them slipping and sliding, coming in and out of the hospital, do they need a heart failure disease management program? Because sometimes when you send someone to see a heart failure specialist, it's not really the doctor that makes them better.

It's the nurse who answers the phone call, who they feel comfortable telling that they're there cheating on their diet, they're not taking their medicines. Sometimes the social worker who can help them get the money or the resources to get their medication. Or sometimes it's the financial person who goes through drug studies, and involves people in management of the finance piece. So sometimes the heart failure team provides more than just a doctor. And that's what's really important.

And when you discharge the patient from the hospital, if they've been readmitted frequently, you know they're non-compliant, you know they don't have money, you know they don't have somebody to take them back and forth to the hospital, try and get them in early, get visiting nursing services out there. Get home visiting doctors if you have that in your area. Or if nothing else, call them up. Did you take your medicine? Did you even pick them up from the pharmacy? Because if you don't even have them in the house, you certainly can take those medications.

So when we think about patients that have advanced heart failure, remember they've been admitted to the hospital multiple times. They're BUN and creatinine are going up. They're losing weight, and it's not because they're on a diet. They cannot tolerate ACE inhibitors or beta blockers. They're hypotensive. They are symptomatic with functional class three symptoms. They can't do their activities of daily living.

Ask the person, can you take a shower? Can you take a shower and stand up and not have to sit on the commode? That is a sure sign the patient is a functional class 3. Do I need to go up on their diuretics? Do I need to add metolazone? Are they hyponatremic? Or are they getting frequent ICD shocks? All of these things should make you consider getting a heart failure evaluation. And if you ever need a heart failure evaluation here in Winston-Salem, this is my cell phone. I gave it to you guys in case you have any questions or concerns.

What happened to my patient? So her diarrhea got better. If she eats too much, she still gets nausea and vomiting. Her hearing's bad. She doesn't have to listen to her husband quite as closely. She has sinus issues. She can walk three flights of stairs when I last saw her. And she did not want to go to cardiac rehab. She moved to Arizona with her husband. And sadly her husband was diagnosed with colon cancer. So now she has to care for her husband. And she is currently listed for transplant in Arizona.

So consider evaluation by a heart failure team. Be cautious in selecting candidates for transplant who are not sick enough. Cautious in patients who are too sick, that won't benefit from either device therapy or transplants. And then close follow up in collaboration, not just with the doctor, but with the advanced practice nurse, palliative care, general cardiologist, and input from the patient. Because telling the patient they need a transplant, when the patient says I don't want that, means the patient does not want that. No means no. And I'd be happy to answer any questions if I can. Thank you.