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The Dangers of a Broken Heart: Collaborating on Cardiomyopathy

Dr. Lisk:

You're listening to *NeuroFrontiers* on ReachMD. Today, we have Dr. Ilan Wittstein, Director of the Advanced Heart Failure Fellowship and Assistant Professor of Medicine at Johns Hopkins School of Medicine. When you hear of broken heart syndrome, you may think of a tragic breakup relationship or a loss of a spouse, but broken heart syndrome is a stress-induced cardiomyopathy that can happen with any type of event whether be emotional or physical. And Dr. Wittstein, today, is here to enlighten us on these problems of the heart.

To start off, Dr. Wittstein, can you explain what stress cardiomyopathy is?

#### Dr. Wittstein:

So stress cardiomyopathy is a unique syndrome that's well recognized now, and it really entails three things. Number one, it's an acute heart failure syndrome where there is sudden heart muscle dysfunction. The second component of it is that it's precipitated by some type of stressful event, in the majority of cases, up to about 70 to 80% of cases are precipitated by acute stress. And the third, I think, major component of it is that if you're not familiar with the syndrome, it can look like a heart attack, but once you become more aware of this condition, you realize that it has very unique clinical features and a pathophysiology that's completely different from an acute heart attack. So when we think about stress cardiomyopathy now, in the modern era, we're thinking about a stress-induced heart failure and cardiomyopathy syndrome.

# Dr. Lisk:

You make me think back, which every physician knows that when we're seeing patients in the clinic, you'll hear family members say that the spouse passed away two years later. And they always say that it had something to do with the other spouse's death. This could be probably related to that, as well right?

### Dr. Wittstein:

Well, I think it's along the spectrum, you know, when you hear about people who die a year after their spouse dies, there's clearly a connection there, but there can be a lot of reasons for something like that. For instance, you know, the wife may die and now the husband, who had relied previously on the wife to fill the medications and to drive him to the doctor, etc., is no longer there, so there can be multiple reasons why a spouse dies shortly after a spouse. But I think there are some physiologic reasons too, and I would say the condition you just described falls along the spectrum of this topic, where stress and grief and emotional trauma can precipitate cardiac events. I think with stress cardiomyopathy, the event is quite acute, so the stress occurs and we're talking about within minutes, often of that event developing heart failure and heart muscle dysfunction.

#### Dr. Lisk:

Well, how do stress cardiomyopathy patients typically present, and what are some of the complications of having stress cardiomyopathy and how they vary from patient to patient?

# Dr. Wittstein:

When we talk about stress cardiomyopathy, we have to be careful not to lump all patients into the same category. And some researchers in Switzerland have actually developed a nomenclature where they describe stress cardiomyopathy as either type 1 or type 2.

Type 1 refers to patients who are out in the community and who develop usually some type of emotional stress. It could be, you know, anger, it could be heartbreak, it could be sadness, it could be arguing with a colleague at work, but you're out in the community and then you present to the hospital with your symptoms. Type 1 patients often present with symptoms that are indistinguishable from a heart

attack. So the most common symptoms are chest pain and shortness of breath, sometimes diaphoresis, sometimes they'll come in with hypotension, so it can look from a symptom standpoint, almost exactly like a heart attack.

Then there's the type 2 patient. The type 2 patient tends to be a patient who is already in the hospital and who is dealing with some type of medical illness or who is undergoing some type of procedure. And we now know that there are numerous medical conditions, whether it's pneumonia or hypoglycemia or blood loss, or some type of neurologic event, like a stroke or a seizure, numerous medical conditions can precipitate stress cardiomyopathy.

The other thing that's common in the hospital are procedures, people who get anesthesia, who get intubated, who undergo surgery, these are frequently patients who come out of surgery or out of their procedures and who develop stress cardiomyopathy. Now of course, because these patients are often sedated or they may be intubated, they may not complain of the kind of symptoms that type 1 patients have, and sometimes it has to be tests that doctors do in the hospital to actually know that this is going on.

# Dr. Lisk:

And so the type 1 patients, are those the patients with the elevated troponins that are not having the heart attack?

# Dr. Wittstein:

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Yeah. So they all actually fall under that category. Type 1 patients will come in after their emotional stressor out in the community and they'll have chest pain and shortness of breath, they will have elevated troponins. But so will type 2, but you'll only detect it in the type 2 patients if you know to look for it. So for instance, if the patient is intubated and sedated, and they're not complaining of chest pain, you may not get a history that tells you that I better look for troponin elevation. But if doctors know to look for it, and if they, for instance, see an EKG abnormality, or if the blood pressure is abnormal or if for some reason, they get an echocardiogram that's abnormal, then they can look for the troponins, also. But 90% of patients in both type 1 and type 2 will present with an elevated troponin.

### Dr. Lisk:

Who are the people most likely to develop stress cardiomyopathy? Let's go into that and then we're gonna go talk about the mechanism of action.

### Dr. Wittstein:

Yeah, so it was apparent, very early on, when we started seeing patients with this, that there is one very specific group that seems to be the ones to get this condition. And that is older, post-menopausal women. Women make up 90% of the reported cases of stress cardiomyopathy. The average age, if you look at sort of all the studies is about 65 and the risk of developing stress cardiomyopathy increases five times after the age of 55. Now, that doesn't mean that men can't get it; about 10% of the reported cases are men, and we have seen younger people get it. People in their 20s and 30s and 40s can also get it. But no question that the vast majority are older, post-menopausal women.

#### Dr. Lisk:

For those tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Jerome Lisk, and I'm speaking with Dr. Ilan Wittstein about stress-induced cardiomyopathy, also called "broken heart syndrome." So, now that we've explained the cardio-neuro connection, let's talk about the mechanism of the event and treating our patients.

What is the proposed mechanism of action for stress cardiomyopathy?

# Dr. Wittstein:

So if you talk to experts in this around the world, I think most people would tell you the same things but they would also say we don't know exactly that that's the mechanism, but we have strong suspicions. And what I would say, most of the literature points to now, including what we published back in 2005, is that this seems to be mediated by a sudden burst of catecholamines. So an increase in the sympathetic tone that occurs in response to stress. Now, we've known for decades and decades that high catecholamine levels, like epinephrine and norepinephrine, can be toxic to the heart in high quantities. So, the theory is that, after an acute stressor, whether it's a physical one or an emotional one, there is a surge of catecholamines and those catecholamines can cause injury to the heart. Now, the exact mechanism in which catecholamines injure the heart is not totally known, but we believe it's one of two mechanisms or a combination that catecholamines either injure the cardiac myocytes directly, by binding to beta receptors and causing intracellular changes, and/or they also cause microvascular dysfunction and ischemia. So, we believe that unlike a major heart attack that involves one of the major epicardial coronary arteries, the problem in stress cardiomyopathy is catecholamines-mediated microvascular injury. And it's the microvascular injury that gives you these unique characteristics and probably also leads to a level of ischemia and stunning that isn't permanent and doesn't cause permanent injury.

# Dr. Lisk:

Yeah, that would explain the diffuse process, too. And you've mentioned that cardiologists do not need fancy diagnostic testing. They

have all the basic diagnostic testing they need, ultrasound, EKG, troponins, etc. How do you treat stress cardiomyopathy both acutely and chronically, and what are the short- and long-term prognoses?

# Dr. Wittstein:

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So there is no question that the acute treatment of this condition revolves around supportive care. If a person comes in with congestive heart failure, they should receive diuretics to relieve the congestion; if they're hypotensive and they have low cardiac output, a wide variety of things have been used to support them including intra-aortic balloon pumps, even mechanical pumps that can be put in percutaneously and sometimes, even the same types of medications that we commonly used in intensive care units to support the blood pressure, all of those things are done with the expectation that if we can get the patient through the acute period, the heart muscle will start to recover. And what you often see is that even the sickest patients who are in the ICU within a few days will start to make a very rapid and dramatic recovery. I've seen people who are critically ill on a Monday, who are ready to go home by Thursday or Friday, and that's something that you just don't see with most heart conditions, that cause you to be critically ill.

In a longer term, more chronic basis, that's a bit more difficult in terms of getting consensus. I think nobody really knows the best way to treat this condition long term. Certainly most of the medications that we use for other types of heart muscle problems we'll frequently use, so things like ACE inhibitors and beta blockers or angiotensin receptor blockers. Patients are often sent out of the hospital on these medications because doctors are used to using them for people who have heart muscle weakness.

Truth is, though, we don't really know once the heart muscle fully recovers, if these medicines are helpful at all. So I'll frequently stop medications after the heart fully recovers and I won't leave people on, you know, four or five different heart medications if they've gained completely normal heart function. There are some data out there that people who get ACE inhibitors in the first year have a better one-year survival, so that's a medicine that you'll frequently see people using. But to be honest, there is no established or agreed upon long-term treatment for this condition and we do not know of any medicines that can help prevent a repeat episode.

# Dr. Lisk:

So what is the recurrence rate of stress cardiomyopathy?

### Dr. Wittstein:

It depends on who you ask, but there have been different registries out there around the world. The biggest registry is out of Switzerland, it's called the InterTAK registry, which stands for the International Takotsubo registry. And in their registry, they found that the recurrence rate was about 1.8% per patient year. That could range anywhere from a recurrence at twenty-five days and a recurrent up to nine years after the original event.

There was a German and Italian registry that found the recurrence rate to be about 4% overall. So, what we can say is that, while this can recur, the recurrence rate is relatively low. So, this is not something where half the people are getting it a second time, or 75% of the people are getting it again. This is something where about 4 to 5% of people will have a recurrent episode, so it's relatively low overall.

### Dr. Lisk:

Dr. Wittstein, I'm so happy to have you on the program today to share your expertise in stress-induced cardiomyopathy, also called "broken heart syndrome," and I feel, as a neurologist that you have made me a better physician today, and I'm sure you've made many physicians listening to this more knowledgeable and more capable of recognizing this condition and more confident on the outcome and prognosis to discuss with family members. It was great having you on the program. We hope to have you again.

Dr. Wittstein: Thank you very much.