JAE K. OH: Hi, I am Jae Oh of Mayo Clinic, Rochester, Minnesota. I'm very pleased to have this opportunity to discuss diastolic exercise echocardiography with you. There is topic during the-- one of our Grand Rounds earlier this year. The-- in 1979, Dr. Feigenbaum's group reported this very groundbreaking data that the echocardiography was able to demonstrate myocardial ischemia with exercise.

On your left, you can see resting wall motion in this patient with the significant coronary disease in the left anterior descending coronary artery. And with exercise, on your right, you can see that the regional wall motion abnormality on the apex-- apex, and also the anterior wall. And we need to do the same for patients with diastolic dysfunction. And this graph shows you the cardiac index and pulmonary capillary wedge pressure in normal subject, and also subjects with the diastolic dysfunction.

And yet, as you can see, their resting chemodynamics, cardiac index, and pulmonary capillary wedge pressure are quite similar. But with exercise in normal individual, the cardiac index goes up with a very minimal increase in pulmonary capillary wedge pressure so that there is no dyspnea with exertion. But the individuals with a diastolic dysfunction, they are able to increase the cardiac index, but at the great expense of the increasing filling pressure so that they are short of breath.

So we need to really evaluate the chemodynamics, not only in resting stage, but with the-- also exercise, especially in patients with the exertional symptoms of dyspnea. And this slide shows a very characteristic pressure tracing in the cardiac catheterization laboratory in such a patients. And filling pressure is a 12 millimeter mercury at rest, but with a very moderate exercise, that filling pressure, pulmonary capillary wedge pressure, increased to about 40 millimeter mercury, and explains patients dyspnea. And then we can do the same with the-- using Doppler and to the echocardio evaluation.

We use two parameters. This is animation showing the contraction and relaxation of the left ventricle. And the left atrium in the ventricle generates a pressure, as you see over there. And that transmitral pressure gradient can be detected by mitral inflow velocity by Doppler echocardiography. As you see, you have early filling E velocity and late filling A velocity, as you see, and we measure E and A velocity, and also deceleration time.

Another important parameter we use for estimation of filling pressure is mitral annulus velocity. And this animation shows you the contraction and relaxation of the left ventricle. As you can see, the-- when the calcium enters a cell, as you see the yellow round thing bound to the troponin, see, that's what initiates the contraction of the myocardium and diastole relaxation is precisely controlled when the cell leaves-- the calcium leaves the cell. And that contraction relaxation happens every cardiac cycle, as you can see. And echocardiography can measure the status of relaxation. As you can see in your echocardiogram, good relaxation, the annulus really moves back and forth from the base to the apex very nicely.

But patients with impaired relaxation, there's a very minimal change in the movement of the mitral annulus. And we can measure that-- the velocity of the annulus by Tissue Doppler. And you can see over here where the simple volume at the mitral annulus, you can see early diastolic velocity is more than 10 centimeter per second for normal relaxation. But someone with impaired relaxation, E prime velocity is only five or six centimeter per second, as you see.

And that-- the E prime velocity we considered as a noninvasive tau and reflecting the status of the myocardio relaxation. That E prime velocity, it turned out that it changes quite significantly with the increase in transmitral gradient and pressure gradient in individuals with a normal relaxation. That's how we actually improves our filling with the exercise and tachycardia.

But in individuals with a diastolic dysfunction, as you see with the abnormal relaxation, the E prime velocity, early diastolic velocity of the mitral annulus, really does not change much at all. So that we now then use these two parameters. One is a mitral inflow velocity, which is very sensitive to the preload, so that the E velocity increase gradually with the worsening of diastolic function, and increase filling pressure. So as you see over here, and the deceleration time gets very shortened, but the mitral annulus velocity is relatively independent or insensitive to the filling pressure and is reduced in all stages of the diastolic dysfunction as you see.

So if you combine those two parameters with the increased filling pressures, E velocity increases and annulus E prime velocity decreases, so that the EOA prime ratio remains-- EOA prime ratio increases with an increase filling pressure. So this is the data from doctors here now away from Houston, and also from our group. Dr. Steve Amens, many years ago, showing that the EOA prime ratio, if it is more than 15, the most of times the pulmonary capillary wedge pressure is graded in 20 millimeter mercury. And also if-- eight or lower, the filling pressure is usually normal body. But between 8 and 15, the filling pressure is a mildly elevated, as you see in this graph.

So we hypothesize, I think it's about 10 years ago now, that in normal individuals, the EOA prime ratio, this is a noninvasive estimate of filling pressure, remains same with exercise since both E velocity and E prime velocity increases with exercise. But in individuals with the diastolic dysfunction, especially someone with the exertional dyspnea with the increased filling pressure, we see the EOA prime ratio increases with exercise since E velocity, mitral E velocity increases, but the E prime velocity does not change much at all.

So this is how we utilize the mitral inflow and mitral annulus, the E prime velocity, to estimate filling pressure at resting, and also with the exercise. So this is our diastolic exercise protocol. You can do this with a supine bike or a treadmill. And then with a gradual increase with exercise, you can measure the-- those parameters each stage, or you can wait until the completion of the exercise where they develop symptoms.

And then we obtain the systolic function at baseline, also with the exercise, to make sure that the patient does not have myocardial ischemia looking at the wall motion abnormalities, and also the four diastolic assessment, we measure mitral inflow velocity, and the mitral annulus velocity by Tissue Doppler imaging, and we can calculate EOA prime ratio at resting stage, and also with exercise.

And also is very important that we try to measure tricuspid regurgitation velocity. Because the tricuspid regurgitation velocity, with reflecting the RV systolic, or pulmonary arteries systolic pressure, usually increases with increase in filling pressures on the left side.

So, this is our initial report of the normal values in the healthy individuals. E velocity, as we expected increases about 25% from 73 to 90 centimeter per second. And the deceleration time decreases slightly. And E prime velocity also increases about 25%. So from 12 to 15. So that the ratio of the EOA prime, the velocity ratio, remains about the same at 6.7 and 6.6 and upward normal be around a nine or a 10 in this healthy individuals.

So this is our initial feasibility study in patient groups. And when patients have the normal filling pressure at rest, with exercise about 2/3 of them remain having normal filling pressure so that EOA prime ratio did not increase. And then one-third of them with normal filling pressure increase their filling pressure with the exercise. But if someone has increased filling pressure at resting, meaning, EOA prime ratio is already 12 or 15, or greater, and then they continue to have a high filling pressure with the exercise, as you see over here.

And the other interesting aspect of this is that when you look at their exercise duration, whether you have the normal filling pressure or increased filling pressure resting, if they have the increased filling pressure with exercise, their exercise duration is quite limited compared to the individuals with the normal filling pressure at the resting, and also with the exercise.

So this is an example of-- a normal example after a patient was having exertional dyspnea, the E velocity is reduced at resting, but the-- with exercise continue to increase. And also the E prime velocity, as you see, is a slightly reduced, but increase accordingly with exercise and this patient turned out to have the exertional asthma-- exercise induced asthma, rather than cardiac diastolic dysfunction. And, in comparison, this is a 73-year-old women with hypertension and significant dyspnea exertion this year, and multiple evaluation showed, including coronary angiography, showed there is no evidence of coronary disease. And the resting stage shows the reduced E prime velocity, meaning there's a relaxation abnormality of the heart.

But the EOA prime ratio was only seven, indicating normal filling pressure. So with exercise, however, with a very moderate exercise, E velocity increased from 50 to 85 and looks very, very restrictive. As you see, the pattern looks very restrictive with very short deceleration time. And then E prime velocity, however, the relaxation of heart of the patient, really did not change much at all at 7 and 7. And then, therefore, the EOA prime ratio, the noninvasive estimate of filling pressure change from 7 to 12. And, more importantly-- more importantly, the TR velocity, the-- reflecting the RAP systolic pressure, or PA systolic pressure, that velocity increased from 2.4 to 3.8 miter per second. So the TR-- the systolic pressure RAB systolic pressure went from about 30 to about 60, 65 millimeter mercury, explaining patients exertional dyspnea.

So this is, again, a hemodynamic cath, a finding of the normal filling pressures to the high filling pressure with exercise. And we can do the same thing with the echocardiography showing the relaxation abnormality with the normal filling pressure with-- to the increased filling pressure with relatively restrictive physiology as you see with the exercise.

And there is a good amount of-- good documents now, multiple laboratories, including our own. This is that they are coming from Australia showing good correlation between the EOA prime ratio by echocardiography, with the simultaneously-- simultaneously obtained the mean LV diastolic pressure at rest, a triangle with exercise on this yellow circle, as you see over here.

And also they've shown that the-- that response was very prognostic. If someone has ischemia, or motion abnormality, plus increased filling pressure, had the worst prognosis with the mortality and hospitalization, compared to the patient with the normally EOA prime and no ischemia, and then if you have one of those two, ischemia or increased filling pressure, their outcome was middle of those patients as you saw-- see in this graph.

This is our initial experience. Now, at Mayo Clinic, we incorporated this diastolic component to the-- both exercise and [INAUDIBLE] stress, and this initial evaluation show that if someone presents to us with the exercise limiting dyspnea, which is actually the most common referred diagnosis, or indication for exercise testing nowadays. And if you're just looking at the ischemia, that abnormality was only 27%. But if you look at the-- or include the pulmonary hypertension, and also increased filling pressure, or hemodynamic parameters for our evaluation over exercise tests, that the yield was doubled to 54% as you see here.

If you look at the patients with-- with age of 60 years or older, elderly patients, who has a more dyspnea dysfunction and more heart failure with the preserve ejection fraction HFpEF or diastolic heart failure, that yield even greater with the ischemia was at 32% or so, and then the increase filling pressure and pulmonary hypertension, that actually doubled the yield of the exercise stress test, you know, experience.

So, again, in our practice, now, we have incorporated this diastolic stress test in our stress testing practice. Let me just show you a few examples and-- and finish. And this is an example of patients with the exertional dyspnea, and showing the ischemia at the anterior wall again, and then just resting. Doppler studies shows the grade one diastolic dysfunction with relatively normal filling pressure. But with exercise, with ischemia, has a significant increase in E velocity 200 from the no significant change in E prime velocity. So the EOA prime ratio is higher than 15.

So the patient has ischemia and exertional dyspnea related to the-- to ischemia. And this next patient, though, patient has the exertional dyspnea, but there's no evidence of ischemia, right? There's no-- one motion changes with exercise and resting, but the, again, E velocity increases from 100 centimeter per second to 150 centimeter per second with minimal change in the E prime velocity. This is a purely diastolic dysfunction, and I think early stages of the heart failure with the preserve ejection fraction.

Another example, here is patient with hypertrophic cardiomyopathy, has several fresh pulmonary edema. The resting echocardiogram shows, again, mild diastolic dysfunction with the-- no increase in filling pressure with some mitral valve regurgitation not able to explain patient's fresh pulmonary edema. But with exercise, as you can see into the next slide, the-- with the mild degree of exercise, as you see, a little bit more mitral regurgitation becomes very restrictive in mitral inflow velocity with no significant change in E prime velocity. And now a little bit more exercise here the mitral regurgitation gets even more, and then becomes quite restrictive in Stage 4. And that really explains why these patients goes into a pulmonary edema with a relatively normal filling pressure resting. But with some stress, the patient develop significant increase in filling pressure, and also a mitral valve regurgitation.

And this is the same patient that want to cut a cath, and there were three demonstrating that the relatively normal filling pressure at rest, but with exercise, you can see goes up almost to 40 millimeter mercury with this type of allergy on echocardiopathy.

So, I'd like to give you a few take home points. I think that if patients, the main symptom is exertional, we just cannot look at resting study alone, just like what we do with the microischemia, we exercise. And we have to do exercise if somebody has a shortness of breath, especially with exertion, and I mentioned to you that the E prime velocity by Tissue Doppler really reflects the myocardial relaxation, and it does not really change much with exercise, if the relaxation has already reduced.

And, therefore, we use the EOA E prime ratio as the noninvasive estimate of the LV filling pressure and resting, and also with the exercise and we feel that the diastolic stress test really provides a prognostic and diagnostic information.

So, evaluation of the diastolic function really should be an essential part of the all exercise in echocardiography. And what we do here is the main indication of the diastolic stress test now is exertional dyspnea, and we obtain mitral inflow, Tissue Doppler imaging of the mitral annulus, and tricuspid regurgitation at baseline, and also with the exercise.

And then we do either a supine bite, but most of the time, the treadmill exercise test, then you obtain the wall motion analysis first, or take about minute or a minute and a half. And then when the heart rate returns to the baseline or mitral inflow E and A velocities separates so we can measure them, and you can obtain those measurements, and also tricuspid regurgitation velocity.

I think that if you do that in patients with the exertional dyspnea, the yield of the exercise echocardiography is much higher, in our experience almost doubled, and you will be able to identify patients with very early stages of the diastolic dysfunction, or heart failure with the preserved ejection fraction.

Thank you very much you're listening. I hope that this presentation is helpful for your evaluation of the patients with the exertional dyspnea.

Thank you.