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Trials and Tribulations of Treating PAH in Geriatric Patients

Dr. Shlobin:
Hi, I'm Dr. Oksana Shlobin, a medical director of the Inova Fairfax Hospital Pulmonary Hypertension Program, and an associate clinical professor at University of Virginia. I'm here today to speak about issues that the geriatric patients with pulmonary hypertension face and should be considered while treated for this disease. So let's begin.

There is a case of a patient, a geriatric patient that we saw in our clinic. RR is a 75-year-old female with idiopathic PAH. She was originally treated at the outside Hospital. You can see that her right heart catheterization in 2017 showed severe disease. At that time, her mean pulmonary pressure was 49 and the wedge pressure was 10. She was in right heart failure, with a right atrial pressure of 16. And her cardiac index was measured at 2.28. Pulmonary vascular resistance was calculated at 8.84 with units. A nitric oxide challenge was not done. We do not have a BNP, and the six-minute walk test distance was 463 meters. According to the records at that time, her functional class was two. The records also indicate that the echocardiogram showed the right ventricular systolic pressure of 85 millimeters of mercury, the right ventricular function was moderately decreased, and the report mentions flattened septum in systole and diastole. At that time, the patient was started on sildenafil and oral Treprostinil.

We met this patient a year later, when she came to our institution for a second opinion. She wasn't feeling too good, and her functional class was estimated at three. An echocardiogram showed right ventricular systolic pressure of 110, and the RV function was severely decreased. Again, the septum was flattened in systole and diastole, and the 3D parameters showed FAC of 11%, and the ejection fraction of 21%. TAPSE was estimated at 1.4.

You can see the echo images on the screen, and they indeed show that the right ventricle was very dilated. And on the parasternal short axis view, there is a pericardial effusion. BNP was estimated at 855.

She underwent right heart catheterization, and despite being on sildenafil and a low dose of oral Treprostinil, her mean pulmonary pressure was almost the same as it was at the 2017 right heart catheterization, meaning that there was no improvement with treatment. The right heart pressure was 15, again demonstrating decompensated RV function, and the nitric oxide challenge did not result in a decrease of mean pulmonary pressure. The wedge was 10 again, and the cardiac index at this point was measured at 1.9, with a calculated PVR of 11. PA set was 61%. At this point, her six month walk distance was very reduced, at 331 meters. In addition to that, it demonstrated that she desaturated with walking to 88%.

So if you calculate REVEAL score, one of the risk assessments scores that can be used, you can see that she really falls into the high-risk categories. And the particular parameters that put her in the high-risk categories, functional class. So functional class three gives you one point, the vital signs, systolic blood pressure, less than 110, and heart rate more than 96. The six-minute walk test distance actually gave her an advantage, but BNP added two points to the REVEAL score, and the pericardial fusion added another one. The very high-risk category equates to 12 months mortality over 12.5%. So at this point, the decision way was to escalate her therapy, and her oral Treprostinil was switched to Intravenous Epoprostenol.

So the patient actually did very well over the next couple of years. We added an ERA, and so she was on triple therapy for her disease. Her quality of life improved and did so ability to perform activities of daily living, and for her functional class was two. Six month walk test

was 420 meters, BNP went down to 250, and despite the fact that it did not go below 50, it did decrease substantially. She unfortunately did not tolerate further titration of Epoprostenol due to gastrointestinal side effects despite intensive management of those side effects. Her REVEAL score went down to six. At that time, she was diagnosed with local breast cancer, she underwent mastectomy, and because she had breast cancer, she was not a transplant candidate.

So couple of years later, the patient lost her patient assistance for macitentan. So her therapy became dual therapy just with a PDE5 inhibitor and Epoprostenol. She also started struggling with progressive osteoarthritis of her left knee, and received multiple steroid injections. And this is when COVID pandemic started. At that time, she felt very uncomfortable coming to the hospital for care, and we instead had several telemedicine visits. She stopped pulmonary rehab again, due to COVID, and appeared to feel okay with somewhat limited ability to really ambulate, or take care of the house. Although we did do some blood work, she could not get BNP due to limitations due to Medicare coverage. And because we could not assess her functional class very well, and did not have some of the other parameters that go into the REVEAL score, we really were unable to accurately assess REVEAL score, and so did not have good risk assessment.

She finally came for an in-person visit, and at that point really complained of increased dyspnea on exertion. Her functional class symptoms were three, and she could not perform her six minute walk test because of her knee problems. The BNP was 260, so just a little bit more elevated than the prior one, and her vital signs appeared to be stable.

So if we talk about pulmonary hypertension in geriatric patients, there are a lot of issues to consider. The first thing that I want to bring your attention to is that the age at which patients are diagnosed with pulmonary hypertension, has increased over the years, and it has increased over all of the groups of pulmonary hypertension. In this study of about 360 patients, you can see that although they expected the age group three and group two, which is over 65 to 70, is high, so is the age group one. So 65 years of age.

If you go back to the NIH and French registries, the age at which patients were diagnosed with pulmonary hypertension was much lower. So 36 for the NIH registry, and 50 for the French registry. REVEAL was a little bit older, 53. But if you look at the more recent registries such as COMPERA and the Swiss registries, you'll see that the patients now present at a much older age with the diagnosis of pulmonary hypertension.

If you look at the COMPERA database specifically, because it was a very large database and well categorized, and break it down further, you'd see that in that database of almost 10,000 patients, there were several clusters of patients. So what the authors did is that they tried to really categorize the patient cohorts very, very, very precisely. So they whittled out a lot of patients and at the end had about 841 patients to look at. And so they identified the sort of classic pulmonary hypertension cohort, young female predominant with no comorbidities, but only 12.5% of patients fell into that category. The rest of the patients were older, they had frequent comorbidities. They also showed that those patients had inadequate clinical response and worse clinical outcomes.

So a lot of registries demonstrated that the older patients have a much higher rate of comorbidities. And the comorbidities are listed here on the slide. Ischemic heart disease is one of them, hypertension, AFib, diabetes, obesity, renal disease, sleep apnea, thyroid dysfunction. But there are also comorbidities that registries really have not looked for, and those are like orthopedic complications, cancers, and then some of the psychosocial issues such as dementia, depression, and inadequate social support.

So if you look at the response to therapy in patients that are older, there are a lot of issues that can account for that. One of them is longer time to diagnosis. The other one is, it's really a mixed patient population. Even in very well characterized patients with group one PAH, other condition creep up. As people get older, they develop diastolic dysfunction, they develop lung disease, they develop chronic clots, maybe because they have a malignancy. The patients tend to present with a more advanced disease. They are more symptomatic, they're less mobile, and what we did find from registries, is that they're not being treated as aggressively as younger patients.

If you look at risk stratification in elderly, there is really not a lot of data. There is a recent publication that looked at improvement in risk stratification in different cohorts that by age, and what the graph here shows you is that the patients who were over 75 did not have any improvement in their risk stratification scores.

Now risk stratification scores are also probably not accurate in older patients. And there are Different reasons for that. As I said already, they don't walk as far, their functional class may not be really accurate because there are other comorbidities that may really result in shortness of breath, and then there are a lot of different comorbidities that contribute to mortality that are just not accounted for in different risk scores.

If you look at the survival in older patients, the data really comes from registries. COMPERA registries showed that the one, three, and five year survival in patients who were over 65 was really much worse, in comparison to patients who were younger. And the meta-analysis of six RCTs showed that the patients who were over 65 had significantly higher mortality. And you'll see here that the mortality

was almost 30% in patients who were that old, in comparison to 16.6% for patients who were less than 50.

So let's go back to our patient. So when she came in, we got a three dimensional echo, and there was a Parasternal Long Axis View and Short Axis View that's presented on this slide. And it actually shows that the right ventricle, although it's not perfect, it's not bad. The RV modified view and RV focused view did confirm that the RV was squeezing pretty well, so we knew that we had to look for other things.

We did try to direst her and uptitrate her Epoprostenol, and it really did not result in any significant change in her symptoms. She also had pulmonary function tests and the CAT scan, and we could not find any other reason for worsening symptoms. At that time, she underwent the left heart catheterization and was diagnosed with coronary artery disease. There was one vessel with flow-limiting lesion, so she underwent the PCI and also medical management. In about six months later, she felt much better.

So I hope that this case demonstrates that there are a lot of issues that need to be considered in older patients. We know that PAH is much more common in older patients than it used to be, mixed phenotypes are also more common in older patients with PAH, older patients experience longer time to diagnosis, they are managed less aggressively, and they have worse outcomes. They're also more likely to have noncardiopulmonary comorbidities that affect both how we assess them, and what kind of care we give them. Older patients with PAH may require very different set of tools to assess their disease. To evaluate them. And in the current state, they may not accurately capture their underlying condition. Thank you very much for your attention.