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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Recognizing and diagnosing heart failure in patients with HCM

Dr. Linhart:
Ladies and gentlemen, I'm Aleš Linhart. I will review today the topic of heart failure and hypertrophic cardiomyopathy. I'm a cardiologist working in Prague. These are my disclosures.

And I will start right away by showing the problem we have with heart failure and hypertrophic cardiomyopathy. As you can see, those gray bars are representing the rate of death, or transplant, for patients who are having hypertrophic cardiomyopathy. As you can see, of course, the cause of death is very often the sudden cardiac death in the early age of patients. But later on, heart failure starts to dominate, and it remains a problem for our patients who are advanced age. So heart failure is of interest, and we can also appreciate that patients with hypertrophic cardiomyopathy, whenever they start to have an increased NT-proBNP, and the bar was set very close to the definition we are using today for the general practice, 135 picograms per liter. Here, you can see that straight after that, they are increasing the rate of developing severe heart failure and its complications.

So if we look on hypertrophic cardiomyopathy from the broader perspective, we have several issues. Of course, we are talking about hypertrophy, that's the definition. That's the hallmark of the disease. But we should keep in mind that fibrosis is developing perivascular and replacement fibrosis, left ventricular obstruction is an issue, and mitral regurgitations come to that, and also pulmonary hypertension, atrial fibrillation, systolic dysfunction. And I will try to review very briefly all those issues with you to get the picture of heart failure in patients with hypertrophic cardiomyopathy.

So the typical picture of hypertrophic cardiomyopathy includes obstruction of the outflow tract. And here we can see the picture of the SAM systolic anterior movement of the mitral valve and the obstructive gradient. About 1/3 of patients are having that at rest. But if we stress our patients on a bicycle, then we can see that there is another proportion of patients having an obstructive gradient, like the case from our center, where you can see a very mild obstruction at rest, but up in exercise, up to 100 the patient was developing quite a significant obstructive gradient. So those patients are obviously at high danger for developing heart failure, especially those having the obstruction at rest.

But if you see, the picture of the progression rate of heart failure in patients with inducible obstruction, this is also different as compared to patients with nonobstructive hypertrophic cardiomyopathy. So obstruction is definitely representing a risk for our patients. And, of course, the solution could be that septal reduction therapies, either alcohol septal ablation or septal myectomy would be the solution. And if we look on the data from Mayo Clinic, it looks like patients who underwent a successful septal myectomy, they are behaving roughly the same as those with nonobstructive hypertrophic cardiomyopathy.

But who are those who were non-operated? What patients are in this very large group of patients? So if we look on the picture of patients after septal myectomy, if myectomy is successful, those patients are doing really very good. Their quality of life is impressively increasing, but so does the quality of life after alcohol ablation. Again, an example from our center where you can see the dark area is actually the difference between the aortic pressure and the left ventricular systolic pressure, and you can see the gradient. And we are always focusing on the gradient, but look very carefully at what's happening to diastolic pressures immediately after the procedure; they are dropping substantially, and this is exactly what's causing the shortness of breath of our patients with hypertrophic cardiomyopathy.

So septal reduction therapies are working very nicely, but if we look on the data from Europe, we are disappointed. Why are we disappointed? Well, a lot of patients included in this large European registry, most of them symptomatic, but septal myectomy was used in less than 5%, and alcohol septal ablation only in 4% of patients. So there is a gap in the treatment of our patients. The need is much bigger than the reality and the daily clinical practice. And we should keep in mind those were relatively large expert centers, so it might be even worse when we are going and dealing with general clinical practice.

So why are we having those gaps in clinical care? So first of all, let's have a look on Mayo Clinic data again. And here you see the group of non-operated patients. Who are those patients? On one hand, you can say, well, they are not so symptomatic. Many of them were in NYHA II class, as compared to patients who had septal myectomy, who mostly were in NYHA III class. But in the same time, they were older, and it's legitimate to suppose that they were also having lot of comorbidities, so probably preventing them to go to septal myectomy. And if you remember the Kaplan-Meier curve, they were not doing so well. Their prognosis for developing heart failure was really good. So another reason why not to get the appropriate treatment is the treatment risk. So again, large volume centers are having excellent results.

We can look on Mayo Clinic data, on big centers data, and the mortality is very acceptable, but it goes much higher for medium-volume centers or low-volume centers. And in some low-volume centers, the mortality was reaching 100% and that's not acceptable, and that's probably why not so many patients are undergoing septal reduction therapy in clinical practice.

Another issue could be mitral valve in hypertrophic cardiomyopathy. Here we can see an example of functional mitral regurgitation, an eccentric jet propagating to the left atrium below the posterior mitral leaflet. but some patients may have organic mitral regurgitation, and this could be an issue. And again, looking on surgical data from different large centers, it’s testifying about heterogeneity of approach of cardiac surgeons to this problem. And some centers, the numbers are very low; patients are not getting an intervention at the level of the mitral valve. In the others, it's very high, and of course, it might be of advantage, because fixing the mitral valve may also reduce the obstructive gradient. So the approach is not systematically even, and we don't know what is the real need for patients having mitral valve surgery.

One important chapter shouldn't go overlooked, and that's fibrosis of the myocardium. Another example from our center, extensive fibrotic replacement not only in the hinge points between the right and left ventricle, where fibrosis can occur, but this is the replacement fibrosis in most thick areas of the myocardium.

And if we look on histological picture, the fibrosis is not only the replacement fibrosis, but also perivascular fibrosis and interstitial fibrosis. So that might be an important issue in hypertrophic cardiomyopathy. Again, discussing mitral regurgitation and fibrosis, are they predicting development of heart failure? The answer is yes, both those features are actually associated with increased risk of developing severe heart failure in our patients.

Now, some features should be discussed also. One of them is pulmonary hypertension. We look on patients, about half of the patients are developing pulmonary hypertension. Most of them are having postcapillary hypertension. But you can see on hemodynamic data that some reactive changes are occurring in some patients. Even hemodynamics was compatible with pulmonary arterial hypertension. So the question is, how much of this is reversible after fixing, for example, obstructive flow gradient.

The other issue is, of course, atrial fibrillation. Logically, we would think that presence of atrial fibrillation would be associated with a problem for our patients not having the atrial contribution to the left ventricular filling, logically, should decrease the capacity of our patients to exercise. But it seems that it's not so much true. this large series of patients from the United States is actually showing that it didn't matter whether the cardiomyopathy was obstructive or nonobstructive, and that the difference of patient between patients having atrial fibrillation and not having it was not statistically significant. Then it's not surprising that other data are actually supporting this finding by showing that ablation of atrial fibrillation was not preventing clinical complications in patients with hypertrophic cardiomyopathy. Of course, this should be confirmed, but it seems that atrial fibrillation is rather a bystander than the causal thing for developing heart failure.

Now let's move to the last thing, and last chapter, end-stage hypertrophic cardiomyopathy. And we can obviously discuss other issues, like, for example, non-LVOT obstruction, but let's move to this end-stage left ventricular cardiomyopathy, where we can see systolic dysfunction developing progressively in those patients.

So those patients were, of course, analyzed, and they are not representing a large proportion of patients. About 5% of patients with hypertrophic cardiomyopathy are actually developing this end-stage appearance. But their destiny is not very good. You can see they are having lots of different complications compared to patients who are not having this systolic dysfunction.

We should look on data from magnetic resonance. A subset of patients from this cohort had MRI. And MRI was confirming that there is a

replacement fibrosis. So fibrosis may be the cause of developing this end-stage left ventricular systolic dysfunction.

So let's sum it up. What do we know? We have obstructive and nonobstructive hypertrophic cardiomyopathy. The obstructive is actually developing systolic dysfunction. Very rarely, they are having mostly the diastolic pressures elevated, and they may be alleviated by either septal myectomy or alcohol septal ablation. But in the future, we are hoping that myosin inhibitors may help in that and may alleviate the symptoms of heart failure in those patients.

On the right side, we have this nonobstructive cardiomyopathy, which is often leading to systolic dysfunction at the end of the course, and this is associated with fibrosis. And for those patients, actually, we don't have a simple solution. The problem in hypertrophic cardiomyopathy heart failure is that those patients are not responding so well to the current treatments for heart failure, so we should do as much as possible to prevent heart failure in those patients.

The patients, of course, are with left ventricular outflow tract are having most problems, and we should focus on them, and myosin inhibitors may help with that. Heart failure is usually caused by elevated filling pressures that may be elevated by septal reduction therapy, but we have seen that there is a gap in the treatment, availability for those patients.

At the end-stage hypertrophic cardiomyopathy, often associated with fibrosis, has so far no solution. We should keep in mind that mitral regurgitation may be a problem and it should be fixed in those patients, especially with but also the functional regurgitation deserves our attention. And last but not least, atrial fibrillation may be symptomatic, but it seems it doesn't contribute so much for development of heart failure.

With this, I would like to thank you for your attention.