Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.comhttps://cme.pace-cme.org/programs/cme/hcm-and-heart-failure-your-patient-risk/16265/

Released: 07/26/2023
Valid until: 07/26/2025
Time needed to complete: 42m

ReachMD

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

HCM and heart failure: is your patient at risk?

Today, we will be discussing the presence of heart failure in hypertrophic cardiomyopathy. Is your patient at risk? Here are my disclosures.

We will be discussing the following topics. Is it common? Should we care? What are these risk factors?

Intuitively, with hypertrophic cardiomyopathy, people do not think about heart failure, but in effect it is a very important complication of hypertrophic cardiomyopathy. Here, in the simplified cartoon, you see there's basically two pathways, so to speak. There's an obstructive root, and there is a non-obstructive root. Either way, this may lead to severe heart failure. We'll dive a little bit deeper into that just now.

This is a very busy slide. In the second column, you see your archetypical heart failure, non-HCM heart failure with an annual mortality of about 10%, with 50% preserved but also 50% reduced ejection fraction. With pump failure, lots of people suffer from that. Hospitalization, comorbidities are very common. In the middle column and the right column, you see obstructive and non-obstructive hypertrophic cardiomyopathy, and the metrics are completely different. This is very atypical heart failure.

Let's look into that. What are the data from registries? Here you see the HCM SHARE consortium. Over 4,500 patients with hypertrophic cardiomyopathy. They're also divided into patients who are genotyped, so SARC- meaning having no sarcomeric mutation, or SARC+ having a sarcomeric mutation or a variation of unknown significance. What you will appreciate if that, overall, the family history is important, it's important whether or not there is a family proband. In any ways, in patients who have a sarcomeric mutation, the likelihood of developing heart failure is much higher.

Here's another way of plotting that same groups, and you see across the board. Here, you see the metrics, over 4,500 patients. A mean follow-up was over five years. Between 20% and 25% of all patients with HCM will develop a heart failure composite, so either full-blown heart failure complaints, etc. A sizable proportion develops heart failure, so yes, it is important.

It's furthermore important to realize that-- Here, you see in the lower left panel heart failure composite, that it's far more common in patients with an early diagnosis. Patients in their 20s have about 60% chance of developing heart failure, whereas patients who are diagnosed at the age of 60 have only 10% chance.

Here are a few more risk factors that are identified from this consortium. The sarcomeric proteins we have been talking about, but also female sex is associated with a higher likelihood of developing heart failure.

Well, you may ask yourself, "Should we care?" because in the end, we know some diseases are very lethal, like lung cancer, or all cancer, or dilated cardiomyopathy. Here at the very bottom is hypertrophic cardiomyopathy, so it appears to be a benign condition, but here's the trick. If congestive heart failure complicates hypertrophic cardiomyopathy, it is no longer benign.

HCM is an oversimplification. We know there's many diseases hidden within this phenotype. There may be genetic diseases, storage diseases, neuromuscular or mitochondrial disorders, or other rare syndromes.

This is important, in this paper by Rosmini and colleagues, it was shown that rare phenocopies, so mitochondrial diseases, Friedreich

ataxia, and so forth, were rare, but were very important with regard to heart failure development.

That is shown here. The overall cohort is shown. Idiopathic or sarcomeric HCM, of course, presents the large majority, and the rare phenocopies about 400 of them. This is associated with a higher likelihood of complaints. It is associated with a lower ejection fraction.

This is what it looks graphically. The cumulative incidence of all-cause mortality on the left, or heart failure on the right, is far more common in these rare forms, rare phenocopies. This is important to look out for. It's a risk factor.

What about LVEF? These are data from a very large Korean registry. Patients with HCM were categorized as a normal preserved LVFF 60% or above, low to normal 50% to 60%, or reduced below 50%. As you can appreciate, patients with a reduced EF below 50% have a far high likelihood of developing a heart failure or being hospitalized for it.

Again, this is what it looks like graphically. Already a moderately decreased LVEF is associated with an increased likelihood of heart failure.
I think it's also important to realize that heart failure in HCM may present as HFrEF, or also HFpEF. Here, you see two typical trajectories of patients, but it's very much similar. Some hearts seems to dilate and then HFrEF develops, whereas other hearts seem to stiffen and then HFpEF develops.

The severity of obstruction, of course, always important in HCM. Here, you see data showing that non-obstructive cardiomyopathy is associated with New York Heart Association class III to IV in about 10% of the cases. If there is a provocable obstruction, this doubles to 20%. If there's rest production, it quadruples. Almost 40% of those patients are highly symptomatic. Obstruction is very important, it's a risk factor.

What about imaging? This is an interesting study showing the value of global longitudinal strain. Well, you know the typical maps. This is about 500 patients or so that underwent echo. You see that some echo parameters were associated with heart failure endpoints, LV and systolic volume, but also GLS, Global Longitudinal Strain. This was predictive also on top of very common-to-do risk factors such as age, previous atrial fibrillation, end systolic volume, or E/E'. This is what it looked like. Patients with GLS below 15%, which is a substantial reduction, are at risk of developing heart failure.

Well, another very important imaging modality obviously is MRI. This allows to visualize fibrosis by late gadolinium enhancement. Again, on the right is the flow chart of the study. About 450 patients with HCM were scanned with an MRI. There's a long list of factors that are univariably associated with heart failure development, but there's really a short list of factors that are multi-variably associated with heart failure development. Here, LGE per 10%, so late gadolinium enhancement, is the most strongest predictor. As you see here plotted, it's about as strong as left ventricular and systolic volume index, as age or as mitral regurgitation, so it's a very strong predictor of heart failure.

Well, finally, biomarkers. Cross-sectionally, NT-proBNP and high sensitivity troponin I are associated with left atrial diameter, with left ventricular wall thickness, and with E/E'.

In this recent meta-analysis, the predictive value of cardiac troponin I or NT-proBNP for mortality are weak at best, and it has to do with the quality of the studies. I think here's work to do. I think there is a weak association between biomarkers and incident heart failure.

To sum up, yes, heart failure often complicates hypertrophic cardiomyopathy. There's an easy rule in HCM. Prognosis is good without heart failure, but is poor with heart failure. There is the importance of etiology, remember these rare phenocopies, and there's a long list of risk factors. Sarcomere mutations, female sex, age of onset, LVEF below 50%, GLS below 18%, late gadolinium enhancement, rest obstruction, more important than provocable obstruction, more important than no obstruction, and I think biomarkers are somewhat in the gray zone. With that, I'd like to end, and I'd like to thank you for your attention.