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Epidemiology and clinical features of HCM

Dr. Elliott:
Welcome to this presentation on the epidemiology and clinical features of hypertrophic cardiomyopathy. These are my declarations of interest.

So let's begin by considering: What is hypertrophic cardiomyopathy? The term cardiomyopathy was first coined by this cardiologist, Wallace Brigden, in the 1950s when he invented the term to describe a family of heart muscle diseases that were not explained by current disease or hypertension. Since that time, we have classified heart muscle diseases according to the morphology and the function of the heart, and this has persisted to the present day. So you see here in the 2023 guidelines from the European Society of Cardiology, the approach to describing the morphology and function of the left and right ventricle, whether there be hypertrophy, dilatation, or motion abnormalities or systolic or diastolic dysfunction.

The only difference in the 2023 guideline is that there is now a focus on tissue characterization for some particular types of cardiomyopathy, including non-dilated left ventricular cardiomyopathy.

How common is hypertrophic cardiomyopathy? Well, if we define it in this very simple way of unexplained left ventricular thickening, then the estimates for this in the general population are around 1 in 500 adults. From our best estimates, it seems to be much less common amongst children, of the order of 3 per 100,000. The data that you see on this slide are derived from a number of very different studies using different methodologies and different populations, screening with echocardiography and ECG, using population cohorts or, indeed, registry studies. The most recent example of this is from the UK Biobank, where you can see in this population study, we see an estimate of maybe 1 in 1,000 people who fulfill diagnostic criteria. Although you can see here an important difference between men and women, in that 1 in 500 men met what we would regard as being conventional criteria for the disease, whereas only 1 in 2,500 women met that criteria. And what this may represent is the fact that we perhaps should be using a less stringent criteria in women.

The data of 1 in 500 and 1 in 1,000, of course, come from populations of people who are largely asymptomatic. If we look at the prevalence in hospital populations as here from the UK electronic health record, you can see the prevalence of hypertrophic cardiomyopathy is of the order of 3 to 4 per 10,000. Interestingly, however, if you look at the prevalence of coding within this database, the prevalence of HCM is increased by 59%, reflecting probably better reporting.

Now, if we define this disease by a morphology, left ventricular hypertrophy, that in essence is not a true diagnosis. It's simply a description of a phenotype. So the classical phenotype of hypertrophic cardiomyopathy is, as shown on this slide, with asymmetric hypertrophy, myocyte disarray, extensive fibrosis, and often, outflow tract obstruction. For this phenotype, the majority of individuals have mutations in the genes in coding the proteins of the cardiac sarcomere, the basic contractile apparatus of the heart. However, because we are defining this condition simply by an increased wall thickness, we now recognize that there are many other genetic, and indeed some acquired diseases that cause this phenotype of hypertrophic cardiomyopathy.

On this slide, you see causes that are age-related. Some more prevalent in the young, some more prevalent in older individuals. If we focus on the clinical presentation, many patients present with symptoms. Here you see in this advice from the patient charity Cardiomyopathy UK, patients may complain of peripheral edema, chest pain, dizziness, breathlessness, often of fatigue and

palpitations.

Interestingly, when you ask patients what their priorities are in terms of symptoms, they will also say in addition to these physical symptoms, there is a significant emotional and psychological burden of living with this disease, one which we need to pay increasing attention to. For clinicians, the diagnosis may be first suspected from an electrocardiogram in someone with symptoms or performed incidentally. We can see a range of abnormalities on the ECG reflecting different patterns of hypertrophy. But the electrocardiogram also provides us with additional information. So if we move beyond the, if you like, the standard way of reading an ECG, we can, in the case of hypertrophic cardiomyopathy, also infer the severity and distribution of hypertrophy, the presence of fibrosis, and in some cases, the electrocardiogram may be diagnostic.

So here you see an individual with apical hypertrophic cardiomyopathy who has 2:1 AV block and on the conducted beats, pre-excitation. And this is highly suggestive of one of the rarer genetic subtypes caused by variants in PRKAG2.

Clinical examination of hypertrophic cardiomyopathy may reveal the signs that you see and indeed hear on this slide. And these classical signs and symptoms reflect the phenomenon of left ventricular outflow tract obstruction. Here you see in this end-hole catheter pressure reading from the left ventricle being withdrawn into the outflow tract into the aorta, this pressure gradient between the body of the left ventricle and the outflow tract.

And this is caused by this phenomenon that you see on this slide, which is systolic anterior motion of the mitral valve, such that the mitral valve makes contact with the septum during systole. This phenomenon is dynamic, and it is affected by loading conditions. Here you see the classic Brockenbrough phenomenon where you see a post ectopic accentuation of the outflow tract gradient.

Here you see the same, this time during a Valsalva maneuver. The importance of this is that probably as many patients with symptoms will only have obstruction with provocation. So if one should perform bedside maneuvers such as the Valsalva maneuver, and if they are negative, you should then consider exercise provocation.

Finally, with regard to obstruction, the mitral valve is the critical component of outflow tract obstruction. The mitral valve itself may be abnormal with the elongation of the leaflets and accessory connections, and in some cases, anomalous insertions of the papillary muscle into the mitral valve leaflet. We may also see obstruction at different levels in the ventricle, in the mid cavity as shown on this slide, or indeed, down at the apex of the left ventricle, sometimes associated with the formation of a left ventricular apical aneurysm.

So hopefully you can see that the phenotype of hypertrophic cardiomyopathy is very variable with hypertrophy of different patterns of different severities. We may also see, as the disease progresses, end-stage dilatation, and in some individuals, there may be restrictive physiology.

In some cases, when we look at a phenotype, we may also see clues to the underlying diagnosis. So in this older male patient, he has concentric hypertrophy with impaired systolic function, which is an important red flag for cardiac amyloidosis. And this approach of using diagnostic red flags is reinforced by multimodality imaging and, in particular, using cardiac MRI to characterize the left ventricular substrate and detect signals which may be indicative of one of the less common mimics of hypertrophic cardiomyopathy.

Finally, hypertrophic cardiomyopathy is associated with a number of complications, sudden cardiac death, heart failure, atrial fibrillation, and stroke. While sudden cardiac death is the complication that probably patients and cardiologists fear the most, actually, over a lifetime, the major complications are those of atrial fibrillation and heart failure. With respect to atrial fibrillation, there are a number of predisposing factors, including age, symptoms, but the most important is left atrial size. And as you can see in this relationship between the left atrial size and the risk of AF, we can superimpose upon that the risk of stroke because stroke in hypertrophic cardiomyopathy is nearly always related to the occurrence of atrial fibrillation. And then finally, the progression to heart failure. Some patients will have long periods of clinical stability, but a proportion, maybe 10% to 15%, will develop left ventricular thinning and impairment of systolic and diastolic function.

So I hope you've seen that hypertrophic cardiomyopathy is a highly variable phenotype which can present with severe cardiac symptoms and is associated with significant cardiac complications. In the other presentations in this series, you're going to see the beginning of a new and exciting era of new drugs and approaches to treatment that may allow us to modify the severity and the progression of this important clinical disease.