**Title: ACC 23: LIVE HCM: Lifestyle and Excercise in Patients with Hypertrophic Cardiomyopathy and Long-QT Syndrome**

**Participants: Dr Rachel Lampert, Dr Sharlene Day and Dr Michael Ackerman**

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"- Hi, I am Dr. Rachel Lampert from Yale School of Medicine.

- Hi, I'm Dr. Sharlene Day. I'm from the University of Pennsylvania.

- And hello, I'm Mike Ackerman, a genetic cardiologist at the Mayo Clinic in Rochester, Minnesota.

What is the importance of the LIVE HCM trial?

Dr Ackerman:

Well, we're really excited about presenting LIVE-HCM here at ACC 2023. And it actually it takes us back a decade ago, when the three of us were all shared decision-making minded physicians and we've been letting our patients young and old be very active. And we said, why don't we look at this? We know that there are patients with HCM out there, some who are very active in terms of exercise, some, because of recommendations of their cardiologists, are very sedentary. And so we really sought out to test the hypothesis that those people with HCM who exercise the most, will they have any different degree of HCM triggered events compared to those patients with HCM who exercised the least? And here it is.

Can you tell us about the study design and methods?

Dr Lampert:

- The study design was a prospective observational study. We identified individuals from age eight to age 60 who had either hypertrophic cardiomyopathy or a genetic variant for HCM. And we enrolled them in a prospective study to follow them over three years. Every six months, they received an online survey asking whether they had had any of our outcome events, which included a resuscitated cardiac arrest, a shock from their ICD, which we later adjudicated to confirm it was appropriate for ventricular arrhythmias. That, of course, was for individuals who did have an ICD, as well as syncope which was felt to be arrhythmic by our events committee. And we also quantified all cause mortality. We analysed the data both primarily for non-inferiority, hypothesising that those who exercised vigorously would not have a higher risk of our composite endpoint, as well as looking for superiority on either side. Individuals were enrolled across the whole spectrum of exercise, from those exercising vigorously and even competitively to those who were just doing moderate exercise to those who had less active lifestyles. So our patients were enrolled through 42 centres worldwide. We had sites in not only the United States, but then a number of sites in the United Kingdom as well as Canada Australia and New Zealand.

Can you please summarise the baseline characteristics of the patients?

Dr Lampert:

So we enrolled 1,660 individuals, of whom 92% had overt hypertrophic cardiomyopathy, that is, they had left ventricular hypertrophy, and 8% carried the genetic variant along without LVH. Six hundred and sixty-one of them were the vigorous exercisers. And the remainder we combined into the moderate and sedentary group. It was about a quarter paediatric less than 18, another quarter between 18 and 25, and then the rest were adults from age 26 to 60.

What data did you present at ACC?

Dr Lampert:

So, we are very pleased to present data describing that first of all the overall event rate was low, less than 5% across the three years, which calculated out to a rate per thousand person years, of 15.3 for the the less vigorous compared to 15.9 for the vigorous per a thousand patient years. So this gave us a hazard ratio of 1.01, pretty close to unity, comparing the vigorous exercisers with those who are less active. This hazard ratio did not, the confidence intervals for the hazard ratio did not cross our pre-specified boundary for non-inferiority of 1.5. We also looked at a variety of subgroups, including those who, including only those who had overt hypertrophy, as well as some other subgroups, and we found hazard ratios which were very similar. Although in these smaller groups of course, the confidence intervals were wider.

How should this data impact patient care and guidelines?

Dr Day:

- Well, we find these data very reassuring in that the absolute risk of arrhythmic events in these patients was very low, and that the relative risk in those exercising vigorously, or even competitively, was not higher than those who are less active. So we think that these data challenge a widely held belief that patients with HCM who engage its vigorous activity or organised competitive sports are at heightened risk of arrhythmic events. This has been held for over four decades. And so we are excited that these data can now inform discussions around individualised shared decision-making for patients with their providers, and their family and their athletic teams.

What are the next steps?

Dr Lampert:

- So, we're looking to take even more deeper dives into this data, looking at some subgroups, for example, those who have defibrillators, looking at some other questions in this group itself. We also have, at the same time we initiated the LIVE-HCM study, we also initiated another study that was parallel called Livelong QT, asking the same questions about a different population, the individuals with the channelopathy or electrical disease of Long QT syndrome, but for whom similar questions existed. As far as next steps, so that studies in a phase where we should be analysing that fairly soon, and we're looking to present that data within the year. Next steps, I think we'll be wanting to look at some wider populations as well. There are many other channelopathies, many other cardiomyopathies, for whom these same questions exist.

Dr Ackerman:

- I think in terms of next steps, is getting out the message of of good news. This is really good news for our patients with hypertrophic cardiomyopathy. For far too long, I think the guidelines probably have inadvertently resulted in a sedentary lifestyle for our patients with HCM, and we have essentially deprived them of what we all know, that exercise is good medicine, and is probably the best pill that we have for all patients with all heart diseases. And now even patients with HCM, we can tell them with a very rigorous study, that there's no signal of heightened risk among those who exercise the most compared to those who are the most sedentary. So I think people, not only patients, families, but also the cardiology community, ought to be able to take this as really good news.