

Athletes Heart Sudden Death Hypertrophic Cardiomyopathy

Stanford University

June 26-27, 2009

Stanford University Presents – the world's foremost experts on athlete's heart, sudden death and Hypertrophic Cardiomyopathy.

Friday, June 26, 2009

7:00 – Registration and Breakfast

8:00 – Euan Ashley, Welcome & Introduction to Keynote Speaker

8:05 – Antonio Pelliccia, The athlete's heart: cardiac remodeling and the risk of sports

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Underlining the research from the past 20 years. Rowing and other type sports are changing wall thickness just in the sport. Relative impact of different sports on LV dimensions (Pelliccia A. Oxford Textbook of Sport Medicine table, 1998)

Upper limits of LV wall thickness in 738 male and 600 female athletes; differences in LV remodeling according to race, the upper limits for blacks can go as high as 1.6 as upper limits; LV remodeling for race and age.

LV cavity dimension in normal athletes and athletes with HCM: seems to be age levels

Quantitative analysis, global systolic function,

Left Ventricular Remodeling Index, showing the athletes among the varying people with HCM.

Distribution of LV cavity dimension in 1309 elite athletes, the left side shows large number of athletes with LV cavity above 6.0 and could be defined as diastolic dysfunction

LV cavity may be larger and the ejection fraction can be low, with values of 50 – 55; use the stress echo to show the true story with the heart

Distribution of left Atrial Dimensions in 1777 athletes, a small subset of athletes with a higher than normal capacity. 347 athletes with enlarged LA; 1430 athletes with normal LA. Study to determine the reason for the remodeling that occurred in the LA. Is the remodeling sufficient to cause Atrial Fibrillation?

Aortic Root Dimension in 1300 male athletes, 95% were 3.2 or lower, 44 mm should be viewed with caution. Long-term follow-up of athletes with enlarged Aorta, 41 mm or higher, 15 athletes with enlarged Aorta, 15 athletes followed for 8 year study.

What are the long-term consequence of these findings? 40 male elite athletes reevaluated 1 – 13 (mean 6) years after cessation. The heart reduced size, from 56 to 52 mm. LV cavity remodeling was evident after long-term detraining, with significant reduction in cavity size and wall thickness.

Questions – In the small group of athletes, was the athletic activity the cause of the enlargement? Should sports participation be allowed or not?

Answer – We don't have the data. These athletes were found from late follow-up, and should be considered to allow participation.

EXERCISE AND THE ATHLETE'S HEART – Moderator: Gordon Matheson

8:30 – Paul Thompson, Historical concepts of the athlete's heart

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Historical Concepts, two articles.

Pheidippides, 490 BC; story of his death was not actually true.

The historical concept has been writing about diet and exercise. Interest for sports for high class were not very exerting. The laboring class had more to provide.

Interest Increase in Competitive sports late 1800. The YMCA were founded and offered a godly effort for being fit.

In the 1800 the Mechanics Clause was inserted to exclude “professionals” from the Olympics. Concerns for lower classing exerting themselves was studying in published in 1867 for the over excursion.

Rower’s, bicyclist, and runners heart all have articles

Did “danger” add to the appeal? The public watched the Boston Marathon in hopes of watching someone die.

“Athlete’s heart” was coined by Swede, S. Henschen in 1899. The right and left side of the heart. Acute dilatation from cardiac fatigue.

Clarence De Mar – “Mr. Marathon” Ran the marathon 32 times, won 7 times. His concern and his fans for dangers to a person’s heart from running added to his own fear and retirement.

Before echocardiograms: Sinus Bradycardia, Cardiac enlargement, plumonic & aortic flow murupers, patholocial hearts

Paul Dudley White, MD the only cardiologist that had a stamp made in his image. De Mar was autopsied by Dr. White; heart was unusually large and the vessel sizes were large, too,

Studies in the past quantified the presence of Athlete’s Heart. Exercise does increase your risk of Sudden Cardiac Death.

Black’s Crack in the Placque

1984 – Davies studies about the placque as well

Most MI’s and their cause was due to the placque.

Sir Russel Brock 1957 – studied HCM; Donald Teare 1958 – described Asschemic disorders

RVC – Italy studies

Dr. Liaonel Opie

Peter Wood out of Stanford

Dr. Barry Maron, 1980 studies

Risks of exercise, throughout the years from various writers; Steve van Kamp for the high school athletes

Antonio Pelliccia – studies from Italy and written many papers

Personal connections with the past; his personal stories

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You who drink the water, do not forget the person who dug the well – Chinese Proverb

Questions: Coronary arteries large sized for animals that have been over exercised. How does that impact your work?

Answer: These seemed to be myths. There was no truth to the large size of the arteries, but it seems to have larger vascular capacity.

8:45 Mikael Mattsson – Physiological demands and cardiac fatigue during ultra-endurance exercise
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Background: Ultra endurance exercise: over 24 hours continuous exercise in various modes: extreme physiological strain: at the time of the event

Heart rate during competition – over 90 hours

Extreme competition, self chosen work rate, energy intake and time for rest
Average work rate 40 – 50% av VO₂ peaked (incl. rests and sleep)

Set up: 140 – 150 h adventure race

Circulatory measurements and blood samples for analysis of heart markers approx. every 24 hrs. during the study of the adventure race.

At the finish, the athletes were all healthy without any clinical signs of symptoms of heart failure.
Increased levels of Troponin T in 20% of the athletes. Increased levels of NP pro BNP in All athletes.

Decreased function aptitude tissue testing

Same as previous studies. Gained knowledge & remaining questions: Reversible even after 6 days of exercise; not a single athlete displayed a pathological heart. Some questions remain.

Differences between athletes are wide range. Pre-values as predictors as well.

Rating performances from within the athletes. Status – self and team reported

Novelty and conclusion

Reversed drive in HR after 6 h of exercise. High oxygen drift, despite relatively low work intensity;

9:00 Jonathan Myers – Placing the risks and benefit of exercise in perspective

The media gets a hold of a SCA incident and the public perspective that exercise is the cause of the death.

Exercise a transient increase in risk for sudden death

The overall risk of a cardiac event during exercise is extremely small

Those at higher risk are the people living a sedentary life style

The incidence of primary cardiac arrest during vigorous exercise:

Interviews with spouses of 133 men who had cardiac arrest, to determine the level of regular habitual activity levels. The inactive group has an 11 times more risk of having a SCA. 93% of the Cardiac events do not occur during exercise.

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Among men of low levels of activity – compared with that at other times was 56; risk during exercise was elevated only at a level of 5

Physical exertion as a trigger of acute myocardial infarction – German group: group that exercises less than 4 times a week is more at risk when they do exercise.

Strenuous physical activity is associated with temporary increase in the risk of MI; only 7.1% of MIs are associated with exercise.

People who are more physically active are less likely to have an MI during exercise. It doesn't mean that events don't occur during exercise, only that the probability is less likely.

Summary – exercise causes a transient increase in risk for a cardiac event/sudden death; highest risk are those of a sedentary life style; most cardiac events occur at rest, not during exertion.

Questions – What if you have an obese pt? How do you get them from the sedentary life style to more vigorous exercises?

Answers – Yes, start with a walking program and increase the exercise.

9:15 Gary Balady – Benefits and risks of exercise in cardiovascular disease: CHF and HCM

Exercise capacity during exercise testing and risk of mortality. Talk is leaning towards HF.

The situation is even worse around pts that have heart failure. Survival rate is only about 20% for people with CHF after 5 years.

Exercise intolerance can have contributing factors for other issues; muscle, lungs and health related issues that are associated with the sedentary life style.

Many studies were done but small in size. There was a large study done with 1100 group and found the improvements in peak $VO_2 = 5 - 41\%$

Exercise Training in Heart Failure: mechanisms that lead to improved functionality capacity; increased aerobic and muscular capacity; improved ejection fraction over time.

Balance of oxidative stress and NO in vasculature

Heart failure ACTION trail was recently published in JAMA. Multi center NIH funded study; purpose – to determine the efficacy to exercise a pt in heart failure; outcomes – the median change was a 5% improvement.

About 30% were doing what they were asked to do; 70% were doing less than asked.

After the adjustments, there was an increased value to benefits.

In terms of safety; there was a small group that had risk to the outcomes.

Exercise in HCM – no studies have been published for the pts that have exercise training. Only antidotal studies.

Much of the pts are low risk and only given exercise tests; arrhythmias occur, syncope, etc.

Questions – Did they do a sensitivity trial for the ACTION trial?

Answers – Have not seen that data, but it will be coming.

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Questions – Why they spent all that money, why didn't they keep the people exercising?

Answers – The medicare limits are 3 months for exercise training / rehab.

9:30 Rick Dewey – Does size matter? Scaling in sport.

Heart rate of a pigmy shrew – 1200 bpm; whale – 6 bpm

Why scale CV structure and function? Measurement accuracy is improving & advances in non-invasive imaging and invasive monitoring; proper consideration for pt size may resolve some of the issues around size matters.

A significant grey area exists between physiological responses to training and primary Cardiomyopathy; diagnosis means yearly clinical follow up; death of a young athlete is a tragic event and takes hold in the public.

Implementation of large screening programs have not been made available for our country.

Body size as a potential consideration with the average size of a man to the average size of an NBA player (athlete)

Scaling definitions – a calculation.

Current scaling practice.

Short comings of current methods; consider the LV mass index: LV mass should be proportional to BSA (body mass).

Dimensionally – consistent allometric scaling should be employed
Scaling

Evidence for allometric scaling resting stroke volume; over weight subjects are penalized for not considering the appropriate proportions.

Evidence of allometric scaling of cardiac output.

Dimensionally – lots of math studies to determine the appropriate measurement for the considerations of the size of pts.

Questions: Differences between men & women. Are there studies for the two sexes?

Answers: Yes, a great need for the differences in the populations.

Questions: Great to have these studies. But how do these scaling relationships translate to the risk of Sudden Death?

Answers: Height might be a very acceptable factor for that determination. More studies required.

9:45 Dan Garza – Joys and challenges of the team physician: SF 49ers

What we do at the NFL level? Academics to reality and professional sports.

Players are aware of concussions and the reality of sudden death.

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We are most concern was the death of Thomas Herron. He died from Coronary Artery disease, the autopsy was inconclusive.

Thomas's locker room remains in the training facilities today. The NFL is boys network and very difficult to navigate these issues.

The TV contracts are in the range of \$20 billion. It is hard to navigate the network.

Medical challenges: concussions; SCD; Morbidity of football after the game; MRSA.

How do we screen?

First at the Combine, for performance; now it is in Indianapolis in 1987; first one was in Tampa in 1982.

First for the modeling of a software package. Teams do share medical information. Multiple measurements of performance & physical examinations / imaging.

Players are coached by the physicians to be a not reveal everything with their team. Hence the relationship between the team doctor and the player begins.

The players are not the premedonas as perceived. The are great people, too.

The average lifespan in the NFL for a player is 3 ½ years.

These guys are a generous group of individuals that are willing to support the research and support of improvements with the game.

Questions: Barry Maron – concern about the thickness of the heart is classic. Why is the family have input in the diagnosis?

Answer: We are asked to respect the family and to not discuss the matters as a representative of the 49s.

Question: Lisa Salberg – she has spoken to the family and does have the permission of the family to share the autopsy report for the use of learning.

Question: Was this player we are talking about at a combine?

Answer: No.

BREAK

Met with Dr. Dan Garza, asked him to connect me to the SF 49ers for player involvement to community screening programs.

Met with Lisa Salberg & then Dr. Antonio Pelliccia for discussion of the above player, the history of athletes and the screening process in the professional sports.

HYPERTROPHIC CARDIOMYOPATHY – DIAGNOSIS AND ASSESSMENT – Moderator: Barry Maron

10:45 – Philip Yang, Nuances of imaging in HCM: echo and MRI

Echo is more cost effective and portable. MRI is becoming more available. Role of MRI is tissue characterization.

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Nuances – Echo Risk Stratification. Studies for the levels of risks to SCD with the size of septal wall, LV obstruction, etc.

Nuances – MRI Risk Stratification. Imaging is more intensified for the areas that echo are not able to reach (apex, etc).

Stanford study case of a 70 year old male with echo vs MRI. How do we put all these levels of information together? Allowing to take the information in real time tests to get to the prescription needed for the benefit of the pt.

Conclusion: Echo is still the gold standard in diagnosis of HCM. MIR add to the tissue characteristics to allow for the treatment.

Questions: Is this the stratification for the level of ICD needs?

Answer:

Questions: Do you perceive MRI will be the distinguishing factor from Athlete's Heart to a non-Athletic Heart?

Answer: I don't know. More studies required. Cardiac MRI will be able to assist in the revealing factors.

11:00 – Barry Maron, Differential diagnosis of HCM.

Massive Hypertrophy is the usual presentation of this disease. The magnitude of the wall thickness is equal to the risk factors of SD.

There are many genes (11 or more) with many mutations (over 500 and as many as 900).

Sarcomere

The heaviest heart ever recorded. 65 mm septal and 1416 g heart weight. This type of HCM would not be appropriate for an ICD as the heart would not respond to the therapy of an ICD shock.

The scarring is extensive throughout the heart which makes it unresponsive. This one heart had varying levels of sarcomere & other types of HCM.

Clinical implications of LAMP2 Cardiomyopathy

- Survival after age 25 years unlikely
- Requires molecular diagnosis
- Deserves consideration for heart transplantation

Carolyn Ho, continuation for this discussion – phono copies these types of HCM.

LAMP2 is LVH & EP & Systemic; abnormal lysosomes; severe arrhythmias are present.

Metabolic and storage cardiomyopathies; New paradym of inherited on the x Chromosome.

Multisystem Danon disease (neurologic, ophthalmologic, developmental delay, skeletal muscle)

Cardiac-isolated phenotypes

Cardiac Hypertrophy (autophagic vacuoles) and fibrosis

Phenotype of heterozygous females highly variable.

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Questions: At Stanford we have three families that have this. What is the prevalence?

Answer: Very rare and probably in the range of 1/50,000.

Questions: Is the requisition for families with HCM to have genetic testing?

Answer: Some of the testing could be related to the other conditions that are surrounding their condition. The ones with LAMP2 seem to have WPW. So considering the type of condition, there selection of pts with genetic testing will have to be considered based on Dr judgement.

Questions: will you also comment on the women that is displaying enlargement?

Answer: There is a small fraction of the estimated 600,000 with the HCM gene as identified. Many of them living the normal lifespan.

11:15 Sharlene Day, the role of stress testing in HCM.

Should stress testing be a routine component of evaluation of HCM pts? We have to know if this testing is safe & type of testing is the best process to determine the risk factors of normal life.

Type of stress: exercise; dobutamine; adenosine

Imaging modality: echo

Exercise testing in HCM pts is safe.

ACC/AHA guidelines 2002 – HCM a relative contraindication to exercise testing; can be superseded in benefits outweigh risks

Total of 516 HCM pts in 3 studies.

Total 465 HCM pts appeared to be safe for the process of testing.

Diagnosis: Latent obstruction, a Stanford pt.

Resting outflow 15 gradient; with exercise 89 gradient

40% of the HCM pts develop obstruction with exercise.

Implications for management of symptomatic pts.

- negative inotropes

Symptom reduction after septal reduction therapy

Exercise capacity

- quantifies degree of functional limitation
- guides medical therapy for diastolic dysfunction, heart failure, ischemia
- CP parameters correlate w/ invasive hemodynamics

Diagnosis of ischemic heart disease

Determines need for therapy

What exercise parameters are useful prognostically?

Abnormal blood pressure response w/upright exercise

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Is abnormal BP response to exercise a risk factor for sudden cardiac death?

Only found a risk factor for age < 40 y/o

A study later on with the BP factor found to be not conclusive.

If this is their sole risk factor that pt may not be a proponent for ICD implantation.

Are there other prognostic exercise parameters?

Exercise stress testing in HCM:

- majority of the opportunity is safe
- identifies provokable outflow obstructions
- provides prognostic information

Question: we do exercise testing and have a lot of protocol to handle emergencies.

Answer: Very good points: we do these tests in a well supervised location, we don't ask pts to NPO, ask them to be well hydrated, take BP frequently, rest for pts with expressed symptoms.

(Maron) discussion on drugs that are targets for the pts with provokable gradients.

Question: Standards to allow for limits to levels of heart exertion?

Answer: The tests levels have to be very individualized.

Question: question around the drugs

(Maron) not sure that there is specific data on the Diaperamide

11:30 Daniel Bernstein, Unique challenges in managing HCM in children.

Children are the future – but children with HCM are the future adults with HCM.

Children are not just small adults – their physiology, metabolism, expression of diseases are different to adults.

Diagnosed prevalence of children w/HCM is much lower than 1/500.

1.13/100,000 of incidence of HCM in children.

HCM in children: Concentric Hypertrophy, they seem to present with extreme concentric hypertrophy. Doesn't seem to have big amounts of capacity in their hearts.

HCM in Neonates: biventricular involvement. HCM in the fetus is possible as well.

Genes associated w/ sarcomeric proteins & myosin light chain is similar to the pattern in adults.

Modifier Genes influence HCM progression.

Genes associated with HCM Phenocopy – several listed issues outside of the typical adult HCM.

Look for other clinical signs to determine if there are other health issues that present within the children that have HCM.

Clinical evaluation

- symptom history
- detailed family history