Substantial evidence suggests that regular physical activity and/or higher cardiorespiratory fitness delay the development of atherosclerotic CVD and reduce risk of CHD.

Biomarker

“a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions”

What are cardiac biomarkers?

- Released in blood when heart is damaged or stressed
- Measurement aids in diagnosis & management of cardiovascular disease
  - Determines risk of having these conditions
  - Monitor patients with these conditions

Cardiac biomarkers

- Heart attack? Angina? Heart failure? Other heart condition?
  - Important to distinguish
  - May have similar signs and symptoms
  - Treatment and monitoring requirements are different
- Diagnosis in “golden period” is vital
Timeline for cardiac biomarkers

Classification of cardiac biomarkers

Creatinine kinase (CK)
- CK-MB specific to heart
- CK-MB rise of 5% that of total CK indicates myocardial damage
- Appears 4-6 hours after onset of chest pain
- Peaks at 10-12 hours
- Multiple measurements provides best information

Myoglobin
- Heme protein in muscle
- Sensitive early indicator of cardiac damage
  - Released within 1 hour of chest pain
  - Peaks in 8-10 hours
  - Returns to normal within 24 hours

Discovery of troponin
- Discovered in 1965
- Late 1990s radioimmunoassay developed
  - Appear 4-10 hours after onset of AMI
  - Peak at 12-48 hours
  - Remain elevated for 4-10 days
- Sensitivity for TnI and TnT approached 100% when sampled 6-12 hours after onset of chest pain

What is troponin?
- Component of contractile apparatus within skeletal and cardiac myocytes
  - Regulate & facilitate interaction between actin and myosin filaments
    - Part of mechanism of muscle contraction
Cardiac troponin (cTn)

- Three subunits:
  1. Tn-T attaches troponin complex to actin filament
  2. Tn-C acts as calcium binding site
  3. Tn-I inhibits interaction with myosin heads in absence of sufficient calcium

- Tn-C → skeletal & cardiac muscle
- Tn-I & TnT → highly specific and sensitive to cardiac myocytes → cardiac troponins

High-sensitivity cardiac troponin

- Most hospitals replaced cTn with hs-cTnT or I
- Higher sensitivity & precision at earlier point of time
- Now, role of cTn expands beyond acute cardiac care
  - Risk stratification & prognostic medicine

Detection range for cTn assays

Causes of elevated hs-cTn

- Variety of mechanisms may explain ↑ cTn
  - Normal cell turnover
  - Myocyte necrosis
  - Apoptosis
  - Proteolytic fragmentation
  - Membranous blebs
  - Detectable/elevated levels dependent on interdependent factors

Natriuretic peptides

- Involved in sodium and water excretion → affects BP
- Increase blood flow into heart causes ventricular wall to stretch
- Induces transcription of NP
- proBNP cleaved into BNP (active) and NT-proBNP (inactive)
- Significant rise in BNP in HF

PHYSICAL ACTIVITY
Regular exercise promotes optimal health
- 30 min moderate exercise, 5 days/week

Physical exercise possesses similar traits of a pharmacological agent

Highly effective for prevention & treatment of: CHD, hypertension, heart failure, depression, diabetes

Benefits of exercise
- Meta-analysis of ~88,000 participants
  - 30-50% risk reduction in cardiovascular mortality
  - 20-50% risk reduction in all-cause mortality
- Nurses Health Study (~79,000) and Health Professionals Follow-up Study (~44,000)
  - Increase of 7-8 years life expectancy in men and women

If a moderate amount of exercise is good, then more MUST be better!

A bit of history...
- 490 BC during the Greco-Persian War
- 40-yr old Greek herald ran almost 150 miles over two day span delivering military messages
- Day 3, he ran 26 miles, announced “Victory is ours!”, collapsed and died
• Born to Run, by Christopher McDougall
  • Writes about a long distance runner, ran up to 100 miles on some days
  • Went on short, 12-mile run and suddenly died

Excessive endurance exercise

• Prolonged exercise training >60-90 min/session
• Evidence that high levels of excessive endurance exercise may be associated with cardiotoxicity
  • Increased risk of atrial fibrillation, CAD, & malignant ventricular arrhythmias

Endurance athletes >35 yr old
• Increased myocardial late gadolinium enhancement
  • Suggestive of fibrosis and elevated CAC scores
• Acute bouts of this high-level exercise may lead to cardiac dilation and dysfunction
  • Results in increased BNP and cTn

The athlete's heart

• Chronic training (especially cardiac work) forces increased hemodynamic demands
  • Alters loading conditions of the heart
• Develop cardiac adaptations:
  • Enlarged LV & RV volumes
  • Increased LV wall thickness and cardiac mass
  • Increased left atrial side

SCD in these instances is RARE! Benefits of moderate exercise far outweighs the potential risks.

• SCD in marathons: 1 in 100,000 participants
  • 50% of SCDs occur in final mile
• Fatality rate for triathlons almost double that of marathons
  • Increased CV events and drownings
• SCD in collegiate athletes: 1 in 40,000

SCD in these instances is RARE! Benefits of moderate exercise far outweighs the potential risks.

• Long-term training and competing in extreme endurance events may predispose to CV issues not observed in moderate forms of exercise
• Young athletes (under 30) often had genetic predisposition for SCD
• Athletes over 30 often suffered from CHD, AMI, or ischemia, causing exercise-related SCD
Sudden cardiac death (SCD)

- Risk of SCD and MI is increased during and shortly after bouts of vigorous exercise
- 61-80% of SCDs in athletes occur during or just after physical exertion
- SCD following acute exertion
  - Incidence is higher in competitive athletes
  - Absolute numbers is greater in recreational sports (usually >35 yr old)

High catecholamines during excessive endurance exercise
+ Pre-existing exercise-induced structural heart abnormality
= Most logical explanation for SCD

Exercise-related SCD in young

- Previous AHA statement: congenital cardiovascular abnormalities most common cause of PA-related SCD in people under age 30
- Most common cause in US – hypertrophic cardiomyopathy
- Recent studies contradict this report
- High school/college athletes with exercise-related SCD – most likely due to sudden arrhythmic death or SCD with structurally normal heart

Study Population | Estimated Annual Incidence Rates of Exertion-Related SCD* |
---|---|---|
Overall | 0.3-2.1 | |
Age | | |
<35 yr | 0.3 | |
>35 yr | 3.0 | |
Sex | | |
Female | 0.04-0.3 | |
Male | 0.5-3.5 | |
Athletics | | |
Competitive | 0.4-0.9 | |
Non-competitive | 0.2 | |
*Rates reported per 100,000 individuals. For comparison, annual incidence of SCD not related to exertion are estimated to be 0.5-3.5 per 100,000.

Exercise-related SCD in young

- Meta-analysis of SCD in individuals <35 yr
  - 10.3% HCM
  - 26.7% structurally normal heart
  - 608 athletes
    - 13.6% HCM
    - 18.1% structurally normal heart
- Overall, prevalence of any causative condition for SCD is variable

Biomarkers after exercise training

- Uninterrupted, long distance running → adverse CV effects in some people
  - Increase cTn, CK-MB, BNP in 50% of marathon participants
  - May reflect myocardial damage
  - Significance of elevation is uncertain
Hs-cTnT in marathon participants

Proposed pathogenesis of cardiomyopathy in endurance athletes

Impact of endurance exercise on CAD

Copenhagen City Heart Study

Aerobic Center Longitudinal Study

Hs-cTn & exercise

- Elevated baseline hs-cTn associated with increased risk of adverse cardiac events
- Suggested exercise-induced cTn elevation related to cardiomyocyte injury or subclinical myocardial ischemia during exercise

- Male marathon runners had increased coronary artery calcification
- Men that complete one marathon each year for 25 years (compared with sedentary controls) demonstrated higher plaque volume

- Followed 1878 runners and 10,158 non-runners over 35-year span
- Runners had 44% lower mortality
- J-shaped curve for mortality with respect to running dose
  - Peak benefit → slow/moderate running speed 3x/week
  - Lower survival → very high doses of running

- 13,000 runners and 42,000 non-runners followed for 15 years
- Runners had 30-45% reduction in mortality
  - Persistent runners had greatest reduction
- Lower dose of running demonstrated maximal protection against CV mortality
Short-term relative risk

• Several studies estimated relative risk (RR) of SCD and MI during and 1 hour after exercise

• Consistent findings:
  • RR of SCD or MI is transiently elevated during and immediately after exertion

Cardiorespiratory fitness (CRF)

• Cardiovascular stress of vigorous exertion determined by person’s CRF
  • Identical physical tasks evoke lower cardiac demands on person that is fit
  
  • Those that exercise vigorously on a frequent basis, have lower RR for each exercise bout

US Physician’s Health Study

• Risk of SCD in men transiently elevated ~17 fold during and up to 30 minutes after vigorous exertion
  • Most active people, that regular participated in vigorous exercise had decreased magnitude of the increased SCD risk
  • Highest risk were the least active individuals

Higher risk

• Strenuous physical activity, especially when sudden and/or unaccustomed, increases risk for SCD and MI
  
  • Extreme exercise → at risk for further deterioration of cardiac function, acute cardiac events, or SCDs
Higher risk

• People with a "susceptible" heart are more likely NOT to benefit from extreme levels of exercise
• Heart failure or prior MI with left ventricular dysfunction
• Age (over 35 yr. old)

Other cardiovascular risks of exercise

• AMI occurs during or soon after physical exercise
• Often associated with underlying CHD or acute plaque rupture
• Triggers acute type A aortic dissection
• Reported in alpine skiers and weight lifters
• Only 2-3% athletes have sudden death caused by aortic dissection or rupture of aortic aneurysm

Despite the high profile of sports-related SCD, majority of exercise-related SCD occur during recreational exercise

Activities associated with acute cardiac events

What can we learn from the research?

Regular physical activity & level of CRF are inversely related to risk of cardiovascular morbidity and mortality

What can we learn from the research?

• Exercise may acutely, yet transiently, increase relative risk for SCD and MI
• Risk is highest in those unaccustomed to exercise
• Most common cause of exercise-related SCD in adults over 35 is atherosclerotic CAD
• Most common cause in younger individuals is controversial
What can we learn from the research?

• Recognize the J-shaped association between physical activity and risk for AF
  • Possible long-term training induces cardiac remodeling

Conclusion

• Lack of physical activity is more prevalent than excessive exercise
  • Very few people actually meet the minimal recommendations
  • Benefits of long-term exercise training outweighs the risks for most of the population

Conclusion

• Moderate intensity physical activity - 30 min for 5 days/week
  • Vigorous activity – 20 min for 3 days/week
  • Are you inactive? Just start out slowly, then increase intensity and duration

“If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health.”

- Hippocrates

References