Cardiorespiratory Fitness as Vital Sign for Assessing Mortality Risk, Cardiovascular Risk and Cancer Risk Factors

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For many decades, it has been reported that an improvement in cardiorespiratory fitness translates into a decrease in mortality rates, cardiovascular disease and many other non-communicable diseases.

Seminal studies from the 1950s and 1960s by Dr Jeremy Morris and Dr Ralph Paffenbarger produced high-quality epidemiological evidence that supports higher levels of cardiorespiratory fitness with decreased mortality rates.

The importance of being aerobically fit has been known for many years, yet physical activity has reportedly decreased by 33% and sedentary lifestyle has increased by 28% and so it remains a global concern.

Exercise professionals typically promote the positives of exercise as a means of motivating people to maintain a programme long term. The reality is that attrition rates are still historically high and retention rates low, culminating in many clients starting an exercise programme and dropping out within a few months.

To gain the benefit of physical activity, clients need to be motivated to maintain the activity programme for the long term. Many of the goals that are set appear to be well beyond the ability of the client, with excessive intensity or volume often prescribed to receive the health benefits they seek. Sometimes meeting the national exercise guidelines is well beyond the capabilities and skillset of most inactive sedentary people, so they may not be motivated to even start an exercise programme.

One current theme from epidemiological studies is the association between the level of fitness at all levels and adverse health outcomes, with low-fit subjects especially susceptible not only to higher mortality rates but to higher rates of cardiovascular disease, cancer, Type 2 diabetes, stroke, hypertension and other diseases.

It is also reported that levels of cardiovascular fitness could be a stronger predictor of mortality and cardiovascular events than the traditional risk factors used by medical and allied health professionals, leading to some governing authorities recommending physical activity as an intervention to improve population health and to also reduce the national healthcare budget.

Improvements in cardiorespiratory fitness (CRF) are reliant on the integration of all body systems and seen as a direct reflection of total health. It reflects the body's ability to transport oxygen to the mitochondria of all tissues and organs to burn energy for the resynthesis of adenosine triphosphate (ATP).

The minimum amount of oxygen required to fuel all tissues in the body is equated to 1 Metabolic Equivalent (MET), which is the required oxygen consumption at rest, equivalent to 3.5ml/kg/min-1. The increased oxygen cost of physical activities can be expressed as multiplies of 1 MET (e.g., running on a treadmill at 7kph can be expressed as 6 METs, which is six times' resting oxygen consumption at rest).
To gauge the impact of CRF on health, studies express CRF as a survival benefit per MET. They further report from meta-analysis that a 1 MET improvement in CRF can result in a 10%-20% improvement in survival or decrease in mortality risk factors.

To give a comparison to how much of an improvement is required to gain a significant 10-20% decrease in mortality risk factors gained from an improvement of 1 MET in CRF; if a client was walking at 2.5mph or 4kph, they would be moving at 3 METs. If that client improved their CRF by 1 MET to 4 METs, they would be able to walk at 3.5mph or 5.8kph.

By participating in a low- to moderate-intensity exercise programme, a client would be able to improve their CRF by 1 MET with much less effort required than the current national exercise guidelines. Perhaps, initially, clients should be prescribed realistic achievable programmes to reach smaller goals before they are expected to commit to a currently prescribed medical exercise programme.

While it is desirable to have a higher CRF, it is important to understand that the greatest gains in health and mortality rates occur from moving from the least-fit group to the next least-fit group. More than 50% of the reduction in mortality rates occurs from a CRF of <5 METs (least fit) to 5-7 METs, which is the next least-fit category. This supports the fact that initially modest improvements in CRF can have a dramatic impact on a client's health status.

As the client moves up to the higher fitness groups, health improvements occur at lower rates but require more effort.

To make an impact on healthcare costs and reduce physical inactivity, interventions should focus on the least fit groups and set realistic improvement in CRF of at least 1 MET to show significant improvements in health to eventually reach CRF levels of 5-7 METs.

The purpose of this review is to report on the emerging importance of cardiorespiratory fitness and its effect on all aspects of health and to increase the awareness of using CRF as a clinical vital sign in association with other risk factors to improve risk prediction.

RESEARCH REVIEW 1

Title: *Cardiorespiratory fitness and mortality risk across the spectra of age, race and sex*

Authors: Peter Kokkinos et al (2022)

Source: Journal of the American College of Cardiology, 8(6)

Introduction

In recent times, epidemiological research has strongly supported an inverse and independent relationship between cardiorespiratory fitness and mortality. Data has been analysed from objectively measured VO2max using a treadmill testing protocol. The available research suggests that subjects in the lowest CRF groups of VO2max <5 METs have the greatest risk for cardiovascular disease and mortality when compared to those in the moderately fit group with a VO2max of between 5-7 METs or 17.5ml/kg/min-1 – 24.5ml/kg/min-1. More moderate declines in risk occur up to 10 METs or 35.5ml/kg/min-1 indicating that significant health benefits could be obtained by just moving from a very low fitness level to a moderate fitness level.

The purpose of this study was to analyse the results from a very large sample size of >750,000 subjects to determine and more accurately assess the association between cardiorespiratory fitness and all-cause mortality.

Methods

The authors identified 822,995 US veterans who were part of the Exercise Testing and Health Outcome Study between 1999-2020. After exclusions, the remaining sample consisted of 750,302 subjects. Detailed information was gathered including demographic, clinical, medications, risk factors and comorbidities. The authors randomly selected 3,000 samples of physician clinical notes and identified workload data as expressed as METs. From this data, peak MET levels were calculated by treadmill speeds and gradients.

Age-specific CRF categories were then established for five age groups: 30-49, 50-59, 60-69, 70-79 and 80-95 years. Hazard models were then developed, comparing hazard ratios with exercise capacity and mortality rates across all age categories.

Results

The results showed a significant difference between all six cardiorespiratory categories, with bodyweight, BMI and cardiovascular risk factors higher in lower fitness categories. Over 7,803,861 person years over 10 years were reviewed.

The most significant predictors of all-cause mortality included age, BMI, chronic kidney disease, smoking, atrial fibrillation, cardiovascular disease, all cancers and hypertension.

There was a positive relationship between higher levels of cardiorespiratory fitness with every 1 MET improvement in VO2max resulting in a significant lower mortality rate.

For every 1 MET improvement in CRF, the mortality risk was on average 12% lower for all ages. Mortality risks decreased by 15% for <60 years of age and 11% for >60 years.

Approximately 80% of men and 95% of women in the highest cardiorespiratory categories lived an average of 20 years longer compared to 40% of men and 75% of women in the lowest CRF categories.

Discussion

The literature suggests that the mortality risks increase at a CRF threshold of between 5-6 METs and can be used as a reference point to predict mortality risk.

According to age categories and CRF, a 50% reduction in mortality risk at the peak MET level was reached at 11 METs for 30-49 years, 10 METs for 50-59 years, 8 METs for 60-79 years and 7 METs for >80 years. The lowest mortality risk was observed at a maximum of 14 METs.

Males with a maximum CRF of 10-12 METs (fit and highly fit) lived 4.5 years longer than males in the lowest CRF group (77.7 years compared to 73.2 years). Those subjects in the extremely fit group >98th percentile or >14 METs lived six years longer than the lowest CRF group.

Women in the highest CRF group at 10-11.5 METs (fit and highly fit) lived 2.5 years longer than those in the lowest CRF group (71.5 years compared to 69 years) while those in the extremely fit group lived 6.7 years longer.

In the older age group >70 years those with a CRF of >7 METs lived 2.7 years longer than those with a CRF of 4.7 METs.

The mortality risk for the least fit group of males (4.7 METs) was >4 times higher compared to the extremely fit group.

The overall result of this study suggests that CRF is a strong predictor of mortality across all ages and sexes with a 50% reduction in risk factors with moderate levels of cardiorespiratory fitness.

The greatest reduction in risk factors occurs from being unfit to moderately fit, which indicates that even with a minimum commitment to fitness, important improvements in health can be made.

RESEARCH REVIEW 2

Title: *Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women*

Authors: Satoru Kodama et al (2009)

Source: JAMA, May (301)19

Introduction

It is becoming increasingly apparent that there is a strong relationship between cardiorespiratory fitness (CRF) and all-cause mortality. It is now regarded as a major cause of death and disability. Yet, it is rare for clinicians to consider CRF as a risk factor for cardiovascular events.

The purpose of this study was to undertake a meta-analysis to determine the relationship between CRF and all-cause mortality, and coronary heart disease and cardiovascular disease in healthy individuals.

Methods

A systematic literature review was conducted of MEDLINE from 1980-2008. Research papers included: CRF assessed by an exercise stress test and/or a maximum aerobic test (VO2max), association between CRF and all-cause mortality, expressed in METs, and identified other risk factors. A meta-analysis was performed on 33 selected studies and 102,980 subjects and 6,910 cases.

All considered data was converted to MET values and sex.

Dose response analysis was performed and three CRF ranges were identified. Low fitness was 7.9 METs, intermediate fitness was 7.9-10.9 METs and high was >10.9 METs.

Results

Data analysis indicated a strong association between a high CRF and reduced all-cause mortality across the three fitness categories in both healthy men and women. Results between the two variables was stronger in studies that used an ergometer for assessing CRF or conducted using maximal aerobic testing procedures.

Individuals with a low CRF <7.9 METs had a high risk of all-cause mortality and CHD/CVD than those in the immediate (7.9-10.8 METs) and high CRF groups (>10.8 METs).

Discussion

According to this study, a 1 MET improvement in CRF reduced the risk of all-cause mortality by 13% and CHD/CVD by 15%. This indicates that even a small improvement in maximal aerobic fitness can significantly reduce risk factors.

Based on risk estimates from the National Cholesterol Council, a 1 MET improvement in CRF is comparable to a 7cm decrement in waist circumference, 5-mmHg decrement in systolic blood pressure, 1-mmol/L decrease in triglyceride levels and a 1 mmol/L decrease in fasting blood glucose and an increase of 0.2 mmol/L high-density lipoproteins (HDL good cholesterol).

The analysis also suggests that a minimal CRF of 7.9 METs could be used clinically as a strong indicator of all-cause mortality and CVD/CHD for all groups.

Reduced mortality rates could be age specific with different levels of CRF required. The minimal level for men and women at 40 years is a CRF between 7-9 METs; at 50 years it is a CRF between 6-8 METs; and >60 years CRF of 5-7 METs.

To put these levels into perspective and to reduce all-cause mortality, risk individuals <60 years should be able to complete stage 1 of the standard Bruce protocol of walking on a treadmill at 3kph (1.7mph) at 0 degrees' gradient and stage 2 walking at 4kph (2.5mph) at 12 degrees' gradient.

If CRF requirements to reduce risk factors were expressed as simply a walking speed, a 50-year-old male would be required to walk at 6.5kph or 4mph, while females would be required to walk at 5kph or 3mph.

Higher levels of CRF can reduce all-cause mortality rates and CVD/CHD rates significantly with improvements in CRF as low as 1 MET making significant changes.

RESEARCH REVIEW 3

Title: *Age specific exercise capacity threshold for mortality risk assessment in male veterans*

Authors: Peter Kokkinos et al (2014)

Source: Circulation, 130: 653-658

Introduction

Current epidemiological studies report a robust association between higher CRF levels and lower all-cause mortality rates. More recently, the focus has been on identifying the threshold where these health benefits occur with respect to age, race, gender or comorbidities.

Studies have reported that a threshold of approximately 5-6 METs is where mortality rates begin to decrease. While this is a general recommendation, different age groups will respond differently to different thresholds and, as such, peak exercise capacity thresholds need to be developed to assess mortality rates across all age groups. As cardiorespiratory fitness declines with age, absolute single threshold across all age groups skews the mortality risk.

Methods

Subjects in this study consisted of 18,102 male veterans who completed an exercise test between 1986 and 2011. The follow-up test averaged 10 years, with data collected on 208,108 person years. The sample group was divided up into age categories such as <50 years, 50-59 years, 60-69 years and >70 years.

Groups were further divided up into fitness categories of least fit, low fit, moderate fit and high fit.

Results

Higher CRF levels were inversely related to mortality rates for all subjects, irrespective of age group. Those subjects in the higher CRF categories reported a lower risk for all additional predictors of CVD, smoking, diabetes and hypertension.

For every 1 MET increase in CRF, there was a 12% lower risk in all-cause mortality for the entire sample size. Each specific age group reported a different risk reduction rate. For example, those subjects <60 years had a 15% reduction, while those >60 years had an 11% reduction in mortality rates.

There were significant differences observed between all four fitness categories. The biggest differences were between the least fit and high fit groups. Subjects in the lowest fit group were older than those in the high fit group. They were also heavier and with higher BMI, higher blood pressure, poor lipid profiles, greater alcohol and drug abuse and used more medications.
The thresholds for improvement in mortality rates for the four age groups were 8-9 METs for <50 years, 7-8 METs for the 50-59 years, 6-7 METs for 60-69 years and 5-6 METs for the >70 years.

One notable trend was that the 5-10 years' mortality risks for subjects in the lower fitness categories were three times higher than those in the higher fitness groups.

The study reported that approximately 32% of deaths in this population group were attributed to lower fitness levels that could possibly have been avoided with a modest improvement in their CRF.

Discussion

This study suggests there are age-specific CRF thresholds where mortality rates are altered in a graded fashion, ranging from 30-80% across the age categories.

Higher mortality rates were observed in subjects in the least fit categories. The five years' mortality rates for subjects >60 years with a CRF of 4 METs above their age group threshold (10-11 METs) were similar to those subjects <50 years with a CRF 2 Mets above their age group threshold (10-11 METs).

This study collected data across a broad range of ages from 25-92 years. It revealed that low fitness may be more detrimental in subjects <60 years than in those >60 years.

The mortality risk was 40% to 82% higher for subjects <50 years in the two lowest fitness categories compared to 41% to 79% higher for those 50-59 years.

For subjects in the 60-69 years' group, the mortality risk ranged from 30-48%, while the >70 years' age group mortality risk ranged from 2-30%. This could be attributed to the increased number of other comorbidities contributing to the health reported for the older subjects.

The results of this study indicate that significant improvements can be made in reducing mortality risk, with modest CRF gains for middle-aged or older adults achieved by moderate levels of physical activity. For example, a brisk walk for >60 years to a slow jog for the <50 years – no need for higher intensity activity.

RESEARCH REVIEW 4

Title: *Association between cardiorespiratory fitness and cancer incidence and cancer-specific mortality of colon, lung and prostate cancer among Swedish men*

Authors: Elin Ekblom-Bak et al (2023)

Source: JAMA Network Open, 6(6): e2321102

Introduction

Even with medical advances and improved screening and the need for lifestyle changes, cancer is still increasing at an alarming rate. By 2030 it has been estimated there will be an increase and reach of 21.4 million cases. This is partly due to the increasing ageing population, as well as a greater number of cases that can now be detected.

Physical activity is now regarded as a modifiable risk factor for many cancers. As the risk of cancer generally increases with age and CRF deceases with age, the relationship between both might depend at what age CRF is assessed.

The purpose of this study was to examine the interactive role of CRF and colon cancer, prostate cancer, lung cancer and mortality in men.

Methods

Data was collected on a cohort of men who completed an occupational health profile assessment between 1982-2019 and had a maximum oxygen consumption assessment completed on a cycle ergometer.

Data was obtained from national registers on prostate cancer, lung cancer, colon cancer and mortality rates.

The sample size consisted of 177,709 subjects ranging from 18-75 years.

Maximum oxygen consumption values were used to categorise the cohort into fitness levels. Low fitness = <7 METs, moderate = 10-13 METs and high = >13 METs

Results

The study revealed those with cancer had a lower mean CRF (VO2max) than those without cancer, while subjects who died during the interim period also had lower CRF.

Higher CRF was associated with a significantly lower risk of colon cancer and lung cancer but with a higher risk of prostate cancer.

Higher CRF was associated with lower risk of death for both prostate cancer, lung cancer and colon cancer.
More specifically, low, moderate and higher CRF levels were associated with lower risk of death due to prostate cancer. Higher CRF levels were associated with lower risk of death from lung cancer. Moderate and high CRF levels were associated with a lower risk of colon cancer.

Discussion

The main findings were that higher CRF was associated with lower risk of colon cancer incidence, lung cancer incidence and death and prostate cancer death. An explanation given for the poor relationship between CRF and prostate cancer incidence is the higher screening rates in those with higher CRF levels.

A study reported that males with a higher CRF had a 28% higher risk of completing the prostate screening compared to those with low CRF. Also, prostate cancer is the most inheritable cancer in men, with a reported 58% variability due to inherited risk factors.

It was noted that avoiding very low levels of CRF could have prevented 4-8% of colon cancer deaths, 4% of lung cancer deaths and 4-19% of prostate cancer deaths. One interesting finding was that higher CRF levels reduced the risk of death in lung cancer only in those >60 years.

A possible reason why high CRF levels can affect all cancers is due to its action on systemic inflammation levels, abdominal obesity, insulin sensitivity and dyslipidaemia.

The clinical implication of this study emphasises the importance of CRF in potentially reducing the incidence of cancer and improving mortality rates in the main cancers affecting men.

Different levels of intensity would be required to specifically reduce these cancers, as they all require a different exercise dose.

RESEARCH REVIEW 5

Title: *Exercise capacity and mortality in older men: A 20 years follow up study*

Authors: Peter Kokkinos et al (2010)

Source: Circulation, 122: 790-797

Introduction

While it is reported extensively that low CRF levels are a risk factor for higher mortality rates and chronic diseases and cancers, most of the studies have been conducted on middle-aged individuals, with very few examining the relationship in older adults.

By 2030 it is estimated that the population over 65 years will double in the USA. This will also bring with it higher rates of poor physical and mental health and an increase in the overall public healthcare budget.

To combat some of these additional health problems, governments should be looking towards interventions such as physical activity to prevent or control these conditions by improving the quality and length of life for older adults.

Methods

The association between exercise capacity and all-cause mortality rates was assessed between 1986 and 2008 on 5,314 males aged between 65-92 years who completed an exercise test to measure their CRF. Fitness categories were established based on METs achieved. Hazard ratios for exercise capacity for the entire cohort for each category were calculated. Relative mortality rates were also calculated across all categories. Age-specific hazard ratios were also calculated across all fitness categories. All assessments were followed up after an eight-year period.

Results

During the interim period between tests, 2,137 subjects died. The CRF among survivors was 6.3 + or - 2.4 METs compared to 5.3 + - 2 METs in those that had died.

For every 1 MET improvement in CRF, the adjusted hazard for death was 12% lower.

When compared to the least-fit subjects (<4 METs) the mortality rates were 38% lower for those who had a CRF of 5.1-6 METs and further declined to 61% when CRF reached 9 METs regardless of age.

Discussion

Overall, for every 1 MET, increase in CRF mortality rates decreased by 12% across the age categories. In studies conducted at the Mayo Clinic, greater decreases of 18% have been reported.

It is apparent from these results that a CRF of >5 METs (17.5ml/kg/min-1) is necessary to obtain significant health benefits in those >65 years.

Those subjects that went from unfit in the first test to fit in the second test reduced their mortality rates by 38%. Those that were fit in the first test and remained fit for the second test had a 61% lower mortality risk than those who were unfit in test one and remained unfit in test two.

This finding suggests that important and significant health benefits can be gained for older men just from improving from low-fit to fit status. Interestingly, those who were fit in the first test but became unfit for the second test still presented with a 41% lower mortality risk profile than those who were unfit and stayed unfit. Apparently, some of the health benefits from being initially fit were maintained, even though they had lost much of their fitness by the second test, indicating some type of carryover effect that could last indefinitely.

This study suggests that age has little bearing on improving health through increasing CRF. The 5 MET threshold is readily attainable in this older age group with moderate levels of physical activity across all activity modes and should be the basis for public health recommendations.

RESEARCH REVIEW 6

Title: *Cardiorespiratory fitness in middle age and healthcare costs in later life*

Authors: Justin Bachmann et al (2015)

Source: Journal of American College of Cardiology, 66(17)

Introduction

More than 30% of the population does not participate in enough daily physical activity to make any significant difference to their general health.

Globally, physical inactivity accounts for 6-10% of deaths from non-communicable diseases such as coronary heart disease and Type 2 diabetes.

It is projected that by 2035 the US Medicare costs will grow from 3.7% of the GDP to 5.7%.

It is widely reported that cardiovascular risk factors and increases in BMI are associated with increased healthcare costs.

To reduce this financial burden, an improvement in cardiorespiratory fitness in midlife could be associated with lower healthcare costs in old age.

Methods

This study comprised 19,571 subjects who had undertaken a cardiorespiratory assessment at the Cooper Longitudinal Centre between 1999-2009 and who had also received Medicare coverage for an average of 6.5 years before they turned 65 years over the same period, totalling 126,388 person years of follow-up. Mortality data was obtained from the death indicator from the Medicare data.

Results

Subjects presented with a low level of CRF at the beginning of the study, with women having lower average METs than men. Younger subjects made up a significant cohort of the low fitness group.

All-cause mortality rates were greater in the low CRF group. Subjects who increased their CRF in midlife demonstrated lower average annual healthcare costs during the Medicare coverage.

Subjects in the lowest CRF group had the highest annual healthcare costs, more physician visits, greater hospital rates and longer inpatient lengths of stay.

Healthcare costs were significantly lower in men than women who had high levels of CRF at midlife.

Discussion

Higher levels of CRF were associated with lower total healthcare and CVD-related healthcare costs from midlife to end of life.

Every 1 MET increase in CRF in midlife resulted in a decrease in healthcare costs in later life.

The average annual healthcare cost for low CRF in men was $12,811 and $7,569 for men in the high CRF group, a difference of $5,242. A difference of $1,875 was also noted between low CRF and high CRF male groups for cardiovascular-related healthcare costs.

Healthcare costs in later life decreased incrementally with every 1 MET improvement in CRF in midlife. A 6.5% decrease in annual healthcare costs for men and a 6.7% decrease in healthcare costs for women were reported with every 1 MET improvement in CRF.

The World Health Organization (WHO) estimated that 499.2 million new cases of non- communicable diseases and mental health conditions would occur globally between 2020-2030.

Those conditions that contribute the most to a country's healthcare budget are hypertension, depression and anxiety. The global costs of all preventable non-communicable diseases and mental health conditions are expected to reach $USD $27.4 billion.

The healthcare costs invariably increased differentially according to the NCD and mental health condition. Although dementia only accounts for 3% of NCD, it accounts for 22% of the total direct healthcare costs. Type 2 diabetes accounts for 2% of preventable cases but incurs 9% of total healthcare costs and cancer, which accounts for 1% of all cases, incurs 15% of the total healthcare costs.

In those individuals suffering from diabetes, for every 1 MET improvement in CRF, the annual cost saving per person was $5,193, which was an 11.5% decrease in total costs and, for a non-diabetic, the cost saving was $3,603 per person, a 9.7% decrease in total costs.

RESEARCH REVIEW 7

Title: *Importance of assessing cardiorespiratory fitness in clinical practice: A case for fitness as a clinical vital sign*

Authors: Robert Ross et al (2016)

Source: Circulation, 134: e653-e699

A scientific statement from the American Heart Association

Summary of main points

The purpose of this paper was to provide evidence to support CRF as a legitimate risk factor as a vital sign to be assessed in the clinic, as well as to improve patient management.

It has been extensively reported that higher levels of cardiorespiratory fitness (CRF) are associated with a reduced mortality rate. However, it is the only major risk factor that is not routinely assessed in clinical practice.

Many studies support CRF as a potentially stronger predictor of mortality than smoking, hypertension, high cholesterol and type 2 diabetes.

Cardiorespiratory fitness (CRF) recruits all the systems of the body to supply increased amounts of oxygen to all tissues and systems of the body. Approximately 45-50% of improvements in CRF are due to inherited factors, while the remaining are due to lifestyle factors.

Recent studies have expressed CRF as a survival benefit per metabolic equivalent or METs. One MET is equivalent to the body consuming 3.5ml/kg/min-1 with each improvement of 1 MET in CRF equivalent to a 10-15% improvement in survival.

In a study completed by Blair et al (1989), and after testing >13,000 asymptomatic clients and following up eight years later for all-cause mortality, reported rates were lower in the most fit group and highest in the least fit group.

The Lipid Research Group reported that a decrease in CRF by 2 METs resulted in a 2-5-times' increase in cardiovascular disease and all-cause mortality. Conversely, in the fitter groups, a 20% lower survival rate was noted for every 1 MET improvement in CRF.

Studies reviewed reported that the greatest improvement in mortality (up to 50%) was noted when moving from the lowest CRF group (<5 METs) to the next lowest CRF group (5-7 METs). It demonstrates that the greatest health gains from an improved CRF occur at the lower end of the CRF continuum.

Clients who have a CRF >13 METs are exercising more for a performance improvement than a health gain. There is little additional health benefit above these levels due to the significant workload and effort required to reach these levels.

Those in the lowest CRF group with <5 METs with CVD and 6 Mets without CVD were at a >4 times' increased risk of all-cause mortality when compared to the highest CRF, demonstrating that CRF level was a stronger predictor of all-cause mortality than smoking, hypertension, high cholesterol and type 2 diabetes.

Across all studies reported, a 13-15% reduction in all-cause mortality and cardiovascular disease was observed for every 1 MET improvement in CRF. It is reported that every 6% increase in CRF over three months was associated with a 4% lowered risk of cardiovascular mortality.

The explanation for the inverse relationship between CRF and mortality rates is still open to discussion. Reasons given include lower risk of thrombotic effects, lower visceral adiposity, improved insulin sensitivity, lower levels of inflammation, better lipid profiles and lower blood pressure and improved endothelial function.

Observation suggests that individuals with CRF <5 METs are at greater risk of all-cause mortality and CVD, while those >8 METs to 10 METs tend to have the greatest protection.

This indicates that very high CRF levels are not a requirement, as relatively less is gained by the extra work required to reach the highest CRF levels. This could be a strong motivator for those who struggle to start or sustain a long-term exercise programme, as sedentary groups find it almost impossible to maintain the current WHO exercise guidelines.

Improvements in CRF could be very helpful for patients undergoing surgical procedures. Assessing CRF could be a vital indication of the success of the surgery post operatively. ➤

A report indicated that for every one-minute decrease in exercise test duration, there was a 7% increased risk of death. An improvement of 1 MET in CRF in midlife could result in a 17% lower risk for hospitalisation. Patients who improve their CRF before surgery present with a lower risk of adverse health and clinical outcomes than those whose CRF decreases.

In a 10 years' study, males in a high CRF group (>13.4 METs) had a 68% lower risk of stroke death than the lowest CRF group (>8.5 METs).

When CRF is added to the traditional risk model of age, BMI, systolic blood pressure, type 2 diabetes, high levels of cholesterol and smoking, a lower level of CRF fitness (<8 METs) for men and (<6 METs) for females was associated with a greater 30-years' risk of dying of CVD and all risk factors, further improving risk prediction.

Several studies report a 36% reduced risk of dementia and Alzheimer's disease in the highest CRF groups, compared to the lowest CRF groups.

In type 2 diabetes, there is only a small difference in mortality rates between those in the highly fit and moderately fit groups, while the largest improvements occurred with small improvements in CRF in the least fit groups. Perhaps initial interventions should focus on targeting the least fit, as these are likely to experience the greatest changes.

Overall, the consensus is that moderate levels of physical activity can improve CRF to moderate levels from unfit to moderately fit to receive a significant reduction in all-cause mortality rate and cardiovascular disease rates. This is particularly relevant for sedentary populations, older adults and dropouts from traditional exercise programmes.

RESEARCH REVIEW 8

Title: *Cardiorespiratory fitness and mortality from all causes, cardiovascular disease and cancer: Dose response meta-analysis of cohort studies*

Authors: Minghui Han et al (2022)

Source: British Journal of Sports Medicine, 56: 733-739

Introduction

The two most common causes of death are cardiovascular disease and cancer, accounting for 48.9% of deaths globally.

Cardiorespiratory fitness is a measure of the body's ability to utilise oxygen and supply energy to tissues, organs and systems and, from numerous studies, is an integral measure of CVD mortality.

Of particular interest is how much of the risk reduction in cancer could be attributed to incremental increases in CRF.

The purpose of this study was to assess the qualitive and quantitative associations between CRF and all-cause mortality and cancer in a healthy population.

Methods

Researchers analysed data from 34 studies from PubMed, EMBASE and Web of Science 2019 on risk estimates for all-cause mortality, CVD and cancer mortality by level of CRF. Studies were limited to those whose subjects were assessed by exercise stress test.

Results

For every 1 MET increase in CRF there was a significant reduction in CVD and cancer risk factors, with the higher fitness groups producing the most significant changes. The lower fitness groups presented with a higher risk for CVD and cancer.

Discussion

The does response interaction between mortality rates and CRF showed that a 1 MET increase in CRF was associated with a 12% reduced risk in all-cause mortality, 13% reduction in CVD and 7% reduction in cancer mortality.

Comparing the intermediate to the lowest CRF groups, there was a 33% reduction in risk factors for all-cause mortality, 40% reduction for CVD and 24% reduction in cancer, all favouring the intermediate fitness group.

Comparing the highest CRF to the lowest CRF, there was a 53% reduction in risk factors for all-cause mortality, 51% for CVD and 43% for cancer, all favouring the highest CRF group.

Given the large number of epidemiological studies reporting an inverse relationship between CRF and all-cause mortality, the public health message should be reframed that small increases in CRF can lead to significant improvement in long-term health.

This further supports the emerging hypothesis that physical activity can be potentially a powerful mediator for improving immunity during the ageing process and offsetting immunosenescence. Regardless of physical activity levels, both groups experienced an increase in T cell mobilisation immediately during and after the exercise bout. The results tended to be higher in the physically active group, indicating the gains are much greater with ongoing participation in all movement experiences.

T cell mobilisation was reported to be higher at rest in the inactive group, suggesting a heightened immune response leading to long-term chronic inflammation.

The mobilisation of T cells during exercise and then a return back to normal levels as observed in the physically active group is the most favourable profile for improved immunity against infection of bacterial invasion.

Both cardiorespiratory training and resistance training can be prescribed to increase the mobilisation of the adaptive immune system through the increased mobilisation of T cells and their subpopulations.

It could be possible that multiple bouts of physical activity throughout the day could produce repeated bouts of heightened immunity to fight infection and delay the onset of immunosenescence given that, after the exercise bout and during recovery, T cell mobilisation reverts back to its normal pre-workout levels.

RESEARCH REVIEW 9

Title: *Relationship to exercise capacity to incident heart failure among men and women with coronary heart disease (from the Henry Ford Exercise Testing Project)*

Authors: Sarah Giogis et al (2022)

Source: Am J Cardiol., 181: 66-70

Introduction

It has long been recognised that cardiorespiratory fitness is inversely related to the risk of cardiovascular disease and heart failure, yet conversely heart failure continues to increase with an estimated eight million Americans suffering from the disease at a cost of >USD $70 million by 2030.

It would seem an obvious choice to develop physical activity interventions that would appeal to this group and be sustained in the long term.

The purpose of this study was to compare exercise capacity (CRF) and the risk of heart failure in patients with known coronary heart disease.

Methods

A cohort of 8,387 subjects with a history of myocardial infarction or coronary revascularisation and no history of heart failure completed an exercise stress test between 1991-2009. This cohort came from the much larger Ford Exercise Testing Project that tested >69,000 subjects. CRF was estimated in METs from the results of the exercise testing procedure and incidents of heart failure were identified up to June 2010 from administrative databases. Data from a post-test was collected 8.2 years later.

Results

Following 8.2 years, a post test was conducted with 22.5% of subjects reporting an incidence of heart failure. The mean age of subjects was 61 years + - 12 years.

The most common cardiovascular co-morbidity was hypertension with 87.9%, MI with 78.3%, prior revascularisation with 57.7%, smoking with 44.1% and diabetes with 26.8%.

The typical profile of someone who reported an incidence of heart failure was hypertension, diabetes, atrial fibrillation and prior MI, while those who did not have an incident of heart failure had hyperlipidaemia, were on statins and had a prior MI.

Subjects with a CRF <6 METs had a 3.8 times' more likely risk for incident heart failure compared to subjects who had a CRF of >12 METs.

Subjects with a CRF of <6 METs had a 43% higher risk of heart failure, between 6-10 METs had a 25% increased risk, 10-12 METs had a 15% increased risk, while >12 METs had a 7% greater risk.

Discussion

In a cohort of subjects who had known cardiovascular disease and no history of heart failure, CRF was inversely related to a risk of future heart failure. For every 1 MET improvement in CRF in this CVD group there was a 12% lower adjusted risk for future incident heart failure. This improvement is similar to other studies that have reported on healthy subjects.

Great results have been obtained by formal cardiac rehabilitation programmes but, historically, only 20-30% of eligible patients participate in these programmes. It would seem obvious that physical interventions focusing on any modality that can improve CRF and can be maintained into the future should be considered a viable option.

The lower risk of incident heart failure with improved CRF was not affected by gender, race, age or comorbidities, indicating that the CRF benefits transcend other variables.

Interesting to note is that the risk per 1 MET was higher in those subjects that had not undergone coronary revascularisation or bypass at 14%, compared to those who had a bypass at 4%.

This study supports the long-term benefit of higher CRF levels in those with CVD, with the rate of incidence of heart failure six times higher at a CRF <6 METs compared to higher CRF at 12 METs.

In another study by Myers et al (2017), a modest level of CRF at 6 METs was associated with lower risk for heart failure compared to a least fit CRF. Subjects with a CRF >12 METS had a 76% lower risk for heart failure compared to the least fit CRF group.

Every 1 MET improvement in CRF was associated with a 20% lower risk for heart failure hospitalisation after the age of 65 years in both males and females.

RESEARCH REVIEW 10

Title: *Cardiorespiratory fitness and adiposity as mortality predictors in older adults*

Authors: Xuemei Sui et al (2007)

Source: JAMA, 298(21)

Introduction

Over the past 20 years, there has been an increase in obesity levels and a decrease in physical activity participation resulting in high mortality rates and a low level of functioning.

With an increase in age comes a marked decrease in physical activity and an increase in obesity levels. By 2030 22% of the US population will be over the age of 65 years, totalling some 70 million people, creating a dramatic increase in the healthcare costs.

The purpose of this study was to examine the joint and independent associations among fitness, adiposity and mortality among older males and females.

Methods

A cohort of 2,603 subjects aged 60 years or older enrolled at the Cooper Clinic for the Aerobic Longitudinal Study and those who had completed an exercise test and examination between 1974-2001 were eligible for this study. Other measures taken include BMI, waist circumference and % body fat.

Results

The average age of subjects was 64.4 years, of which 20% were females. There were 450 deaths in the 12 years of the follow-up with most being older, with lower fitness levels and with more cardiovascular risks than those that survived.

Subjects in the higher CRF groups were less likely to have risk factors for hypertension, diabetes and high cholesterol levels.

Subjects with higher abdominal obesity had higher mortality rates compared to lower abdominal obesity levels.

Subjects in the high CRF groups had lower death rates even with high levels of adiposity.

Discussion

Interestingly, BMI and waist circumference were associated with higher mortality risk, while % body fat and fat free mass were not related to mortality. It appears that abdominal obesity in older groups as measured by waist circumference is a better mortality predictor than BMI.

Higher levels of CRF were linked inversely to all-cause mortality in normal weight, overweight by BMI, normal waist circumference, those with abdominal obesity and those with excessive body fat.

Obese subjects defined as having a BMI >30 and unfit were at a higher risk for mortality than fit obese subjects. This supports the notion that moderate and high CRF levels favourably influence mortality risks across all levels of body composition, with normal weight subjects only reducing risk factors if they were physical fit.

In subjects >60 years, improved CRF reduces mortality risk factors significantly when compared to unfit groups. It is almost apparent that mortality risk factors can be reduced in obese populations by improving CRF levels.

Obese groups should be encouraged to participate in any/all regular physical activities of their choice at whatever intensity to improve their CRF to moderate levels, reducing their mortality risk factors. Initially, it is possible to improve health by increasing CRF without significant weight loss.

In a recent study by Adriano et al (2023) it was reported that physical activity for 30-35 minutes per week of vigorous intensity can offset the association of Grade 1 abdominal obesity (30-35kg/m2) and cardiovascular disease.

Alternatively, physical activity at moderate intensity for 500 minutes per week can also offset the association between Grade 1 abdominal obesity and cardiovascular disease. Subjects with a BMI >35kg/m2 may not receive the same decrease in cardiovascular disease at any intensity of physical activity.

THE BOTTOM LINE

1 Generally, mortality risk increases at a CRF threshold of between 5-6 METs and is used as a reference point to predict mortality risk. According to age categories and CRF, a 50% reduction in mortality risk at the peak MET level was 11 METs for 30-49 years, 10 METs for 50-59 years, 8 METs for 60-79 years and 7 Mets for >80 years. The lowest mortality risk was observed at a maximum of 14 METs. Males with a maximum CRF of 10-12 METs (fit and highly fit) lived 4.5 years longer than males in the lowest CRF group (77.7 years, compared to 73.2 years). Those subjects in the extremely fit group >98th percentile or >14 METs lived six years longer than the lowest CRF group.

2 Based on risk estimates from the National Cholesterol Council, a 1 MET improvement in CRF is comparable to a 7cm decrement in waist circumference, 5-mmHg decrement in systolic blood pressure, 1-mmol/L decrease in triglyceride levels and a 1mmol/L decrease in fasting blood glucose and an increase of 0.2mmol/L high-density lipoproteins (HDL good cholesterol).

3 Collecting data across a broad range of ages 25-92 years it is reported that low fitness may be more detrimental in those <60 years compared to >60 years. The mortality risk was 40% to 82% higher for subjects <50 years in the two lowest fitness categories compared to 41% to 79% higher for those aged 50-59 years. For subjects in the 60-69 years group, the mortality risk ranged from 30-48%, while the >70 years age group mortality risk ranged from 2-30%. This could be attributed to the increased number of other comorbidities contributing to the health reported for the older subjects.

4 Higher CRF was associated with lower risk of colon cancer incidence, lung cancer incidence and death and prostate cancer death. An explanation given for the poor relationship between CRF and prostate cancer incidence is the higher screening rates in those with higher CRF levels. It was noted that avoiding very low levels of CRF could have prevented 4-8% of colon cancer deaths, 4% of lung cancer deaths and 4-19% of prostate cancer deaths. One interesting finding was that higher CRF levels reduced the risk of death in lung cancer only in those >60 years.

5 Overall, for every 1 MET increase in CRF, mortality rates decreased by 12% across the age categories. In studies conducted at the Mayo Clinic, greater decreases of 18% have been noted. It is apparent from these results that a CRF of >5 METs (17.5ml/kg/min-1) is necessary to obtain significant health benefits in those >65 years.

6 Higher levels of CRF were associated with lower total healthcare and CVD-related healthcare costs from midlife to end of life. For every 1 MET increase in CRF in midlife there is a decrease in healthcare costs in later life. The average annual healthcare cost for low CRF in men was $12,811 and $7,569 for men in the high CRF group, a difference of $5,242. A difference of $1,875 was also noted between low CRF and high CRF male groups for cardiovascular-related healthcare costs. A 6.5% decrease in annual healthcare costs for men and a 6.7% decrease in healthcare costs for women were reported with every 1 MET improvement in CRF.

7 The greatest improvements in mortality (up to 50%) were noted when moving from the lowest CRF group (<5 METs) to the next lowest CRF group (5-7 METs). It demonstrates that the greatest health gains from an improved CRF occur at the lower end of the CRF continuum. Clients who have a CRF >13 METs are exercising more for a performance improvement than a health gain. There is little additional health benefit above these levels due to the significant workload and effort required to reach these levels. Those in the lowest CRF group with <5 METs with CVD and 6 METs without CVD had a >4 times' increased risk of all-cause mortality when compared to the highest CRF, demonstrating that CRF level was a stronger predictor of all-cause mortality than smoking, hypertension, high cholesterol and type 2 diabetes.

8 The dose response interaction between mortality rates and CRF showed that a 1 MET increase in CRF was associated with a 12% reduced risk in all-cause mortality, 13% reduction in CVD and 7% reduction in cancer mortality. Comparing the intermediate to the lowest CRF groups, there was a 33% reduction in risk factors for all-cause mortality, 40% reduction for CVD and 24% reduction in cancer, all favouring the intermediate fitness group.

9 In a cohort who had known cardiovascular disease and no history of heart failure, CRF was inversely related to risk of future heart failure. For every 1 MET improvement in CRF in this CVD group, there was a 12% lower adjusted risk for future incident heart failure. This improvement is similar to other studies that have reported on healthy subjects. Great results have been obtained by formal cardiac rehabilitation programmes but historically only 20-30% of eligible patients participate in these programmes. It would seem obvious that physical interventions focusing on any modality that can improve CRF and can be maintained into the future should be considered a viable option.

10 Higher levels of CRF were linked inversely to all-cause mortality in normal weight, overweight by BMI, in normal waist circumference, those with abdominal obesity and those with excessive body fat. Obese subjects defined as having a BMI >30 and unfit were at a higher risk for mortality than fit obese subjects. This supports the notion that moderate and high CRF levels favourably influence mortality risks across all levels of body composition, with normal weight subjects only reducing risk factors if they were physical fit.