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EXCESSIVE EXERCISE

CAN YOU REALLY DO TOO MUCH?

BY DR PAUL BATMAN

PREAMBLE

Since the 1950s it has been extensively reported that regular physical activity, strength and increased cardiorespiratory levels all contribute to improvements in general health and longevity.

The current physical activity guidelines were revised in 2020 to increase the amount of physical activity required for these benefits to 150-300 minutes (600-1,200 MET Minutes) of moderate intensity or 75-150 minutes (or 525-1,050 MET Minutes) of vigorous intensity, almost a doubling from previous recommendations.

In addition to these new ranges, it is also recommended to break up prolonged sitting and reduce the duration of any activity from a previous bout of 10 minutes to any time span, even 60 seconds, and that some physical activity is better than none.

In the past decade there has been some suggestion that there could be upper limit of exercise where the health benefits are reduced or even attenuated.

Dr Ralph Paffenbarger in his famous longitudinal Harvard Alumni studies started in the 1960s, found there was a decline in the death rates for those who expended <500, while for those who exceed 3,500kcals per week death rates increased. This was one of the first epidemiological studies that questioned the potential upper threshold for the benefits of exercise.

Recently, an increased number of authors and studies reported the possibility of a U-shaped or reverse J-shaped curve to explain this upper limit. It is at this level where the benefits of the activity are attenuated or even possibly lost, with the focus largely on subjects who participated in long-term vigorous to highly vigorous exercise (>9 METs).

Overuse conditions such as atrial fibrillation, severe bradycardia, coronary atherosclerosis ventricular hypertrophy, atrial and myocardial fibrosis have been reported due to excessive exercise. For example, vigorous exercise >3,000 MET Minutes per week has been reported to increase the risk of atrial fibrillation, coronary atherosclerosis and myocardial fibrosis.
The dose response curve for vigorous-intensity health improvements appears to plateau off at 660 MET Minutes, indicating that larger volumes up to 3,000 MET Minutes is unnecessary.

One risk factor that has been studied closely over the past decade has been the causal role that excessive exercise plays in accelerating atherosclerosis as measured by an increase in coronary artery calcium scores (CAC). It has been reported that prolonged high heart rates, blood pressure, atrial and ventricular pressures create turbulent arterial blood flow producing large quantities of free radicals that deplete the buffering system of antioxidants after 50-60 minutes of continuous intense exercise. The prolonged effect of this response can lead to atherogenic modifications of cholesterol, increased oxidative stress, reduced nitric oxide release and, ultimately, endothelial dysfunction.

While many of these conditions have been noted in older athletes who train intensely, they still live on average three to six years longer when compared to control older non-athletes.

It is important to note that the intensity and duration of training for improved performance is very different to training for improved health. The largest risk reduction in mortality and greatest health improvements occur in individuals who progress from the most inactive, least active and very sedentary groups to moderately active. It only takes an improvement of 1 MET in VO2max to reduce all-cause mortality by 15%.

Individuals with low physical activity levels and cardiorespiratory fitness are two to three times more likely to die prematurely than their physically active and fitter equals, when matched for age, gender and coronary risk profiles.

It seems that no amount of moderate-intensity physical activity (3-6 METs) can cause adverse health effects and so should form a significant part of any exercise-related prescription model across the lifespan. Vigorous exercise (6-9 METs) is an important component of any exercise programme and should be used in combination with adequate recovery techniques.

Most would still agree that the benefits of exercise at any intensity for any duration still far outweigh the potential increased risks. While it is important to acknowledge the risks at the upper limit of exercise, how to motivate and encourage more people to reduce sedentary time and be more physically active every day should take greater precedence.

This paper reviews a sample of studies that examine the effects of prolonged intense exercise on cardiovascular functioning and recommendations to be employed to avoid any possible detrimental side effects.

RESEARCH REVIEW1

Title: *Exercise volume versus intensity and the progression of coronary atherosclerosis in middle aged and older adults: findings from the MARC 2 study*

Authors: V L Aengevaeren et al (2023)

Source: Circulation, 147. DOI: 10.1161

Introduction

While there is overwhelming evidence that exercise significantly reduces the risk of cardiovascular disease between 30-40% in active individuals, there is also emerging evidence that amateur athletes have a higher risk of coronary atherosclerosis when compared to their less-active counterparts.

Coronary artery calcification as measured by computed topography imaging is now being used to identify coronary atherosclerotic risks. It allows a more detailed picture of the extent and concentration of the plaques present and the prediction of future coronary events.

The purpose of this study was to investigate the association between exercise volume and intensity in the progression of coronary atherosclerosis in middle aged and older male athletes.

Method

Middle aged and older males who participated in the first Measuring Athletes Risk of Cardiovascular Events (MARC 1) were invited to participate in the MARC 2 follow-up. The purpose of the first study was to investigate the presence of subclinical coronary atherosclerosis in healthy middle aged and older athletes.

Participants reported the type of sport, the duration for each sport, the frequency and duration of each sport and the level of performance. METs were assigned from the Compendium of Physical Activities for all sports. Volume of exercise was calculated by the MET score multiplied by the frequency of participation per month per by year. Exercise was classified as light with MET scores <3 Mets, moderate at 3-6 METs and vigorous at >9 METs.

Results

A total of 291 males aged between 50 and 60 years at the MARC 1 and between 56 and 66 years at the MARC 2 follow-up study made up the sample size. Participants exercised for 41 MET hours per week or 2,460 MET Minutes at moderate intensity (0%) and vigorous intensity (44%) and very vigorous intensity (34%). The prevalence of coronary artery calcification (CAC) per 10% increases was associated with higher CAC scores. Very vigorous exercise produced the highest CAC scores per 10% increases.

Discussion

The results of this study suggest that exercise intensity was associated with greater increases in coronary calcium scores than exercise volume. Vigorous exercise at 6-9 METS was associated with less CAC progression, while very vigorous exercise >9 METs was responsible for increases in the progression of calcified coronary plaques.

The MARC 1 study, which continued for 36 years, reported a positive relationship between volume and prevalence of coronary atherosclerosis, indicating that the most active athletes did present with higher coronary calcium scores.

In the follow-up MARC 2 study six years later, exercise intensity increased the risk of higher coronary calcium scores. The very vigorous exercise intensity at 9 METs produced the highest coronary calcium scores. This could be due to the higher catecholamine levels produced. At moderate to vigorous levels of intensity catecholamine levels are reasonably stable and low. The increased levels cause increases in heart rate and blood pressure increasing coronary artery mechanical stress, turbulent blood flow and inflammation potentially accelerating atherosclerosis.

In a Korean study of >25,000 young males it was reported that seven days of vigorous activity >3,000 MET Minutes increased the risk of higher coronary calcium scores after five years.

It is possible that the initial increase in coronary calcium scores could be caused by the volume of vigorous intensity exercise (6-9 METs) with further increases caused by very vigorous intensity exercise (>9 METs).

Even though CAC and atherosclerosis plaques are strongly associated with heart disease and life-long athletes demonstrate a propensity for increased levels, on average they still have a longer life expectancy than the general population with the same condition.

In the short term, exercise intensity >9 METs appears to be the main precursor for the development of coronary artery calcification.

RESEARCH REVIEW2

Title: *Association of all-cause and cardiovascular mortality with high levels of physical activity and concurrent coronary artery calcification*

Authors: L F Defina et al (2019)

Source: JAMA Cardiol., 4(2): 174-181

Introduction

Recent publications have focused on the adverse effects that high levels of endurance exercise have on the progression of coronary artery atherosclerosis. Varying degrees of coronary calcification have been reported in studies, with some reporting low risks while others report more significant plaque formation in the more active groups.

One study examined 284 active males who trained >2,000 MET Minutes per week and had a high prevalence of CAC with calcified plaques suggesting they were more stable and less prone to rupture.

Questions are being raised of the potential increase in calcified plaques and its effect on mortality outcomes. Given the stability of the plaques, active males with increased CAC levels reportedly live longer lives than their sedentary and less active counterparts.

The purpose of this study was to examine the effect of high levels of physical activity on CAC levels and to evaluate if these high levels were associated with increased mortality rates.

Method

Subjects from the Cooper Centre Longitudinal Study who had a history of moderate to vigorous exercise and had CAC scanning seen from 1998 to 2014 were analysed in this study. A total of 21,758 males with an average age of 51 years and who also had undergone CAC scans formed the study sample.

Subjects were asked to fill out a self-reported questionnaire that tallied their exercise sessions per week against frequency and duration in walking, jogging, running, treadmill, bicycling, stationary cycling, swimming, aerobic dance and vigorous activity. MET values were assigned to physical activities and multiplied by duration in minutes to give workloads of MET Minutes per week.

Physical activity levels were grouped into three sections: <1,500 MET Minutes, 1,500-2,999 MET Minutes and >3,000 MET Minutes.

Results

The mean volume of the most active group was 4,600 MET Minutes per week, which equates to running 10km per day at 6-7 minutes per kilometre – a pace typical of masters athletes' training programmes. The subjects in this group tended to be older and have lower BMI, triglycerides and blood glucose levels.

Males training at least 3,000 Met Minutes per week at moderate to vigorous intensity were likely to have higher CAC scores compared to the other two groups. These males did not present with increased levels of all-cause or cardiovascular mortality compared to the other two groups.

Discussion

Male subjects who trained in >3,000 Met Minutes per day after 10 years of training had an adjusted risk of CAC 11% greater than those with low levels. This suggests that high-volume endurance training of more than 60 minutes per day did not increase the risk of all-cause or cardiovascular mortality regardless of CAC scores.

Even though overall mortality risks were not significant, the highly active males with high CAC scores still had a greater risk of cardiovascular disease and atherosclerosis compared to those who had low CAC scores.

While the mortality risks were reportedly lower than sedentary people, the question is whether these atherosclerotic changes continue to progress and become worse when the physical activity levels are reduced or stopped. It seems that continual physical activity at a certain level of physical activity might be a prerequisite in maintaining plaque stability and reducing risk factors.

RESEARCH REVIEW 3

Title: *The physical activity paradox in cardiovascular disease and all-cause mortality: the contemporary Copenhagen General Population Study with 104,046 adults*

Authors: A Holtermann, P Schnohr, B G Nordestgaard, JR Marott (2021)

Source: European Heart Journal, 42: 1,499-1,511

Introduction

While the health benefits of leisure time physical activity have been widely reported, similar activity performed in an occupational setting has been met with mixed reviews. Some researchers have reported that males in high volume occupational activities have an increased risk of cardiovascular events, osteoarthritis, poor sleep quality and all-cause mortality.

The contrasting health effects between leisure time and occupational physical activity have been termed the physical activity paradox. A likely reason given for some of the observable differences is the different environment that each is performed in.

Leisure physical activity is usually performed in blocks with ample time for recovery, while occupational physical activity often requires unusual postures and is performed for many hours without adequate recovery.

The purpose of this study was to investigate the risk of adverse major cardiovascular events and deaths from all causes against occupational physical activity and leisure time physical activity in a large sample size measured between 2003-2014.

Method

Males and females between 20 and 100 years from the Copenhagen area were randomly invited to participate in this study. Data was taken from the Copenhagen General Populations Study from 2003-2014. From 256,761 potential subjects invited to participate, 43% responded with a final sample size of 104,046.

Subjects completed a questionnaire on leisure time physical activity, occupational physical activity, educational background, living conditions and socio-economic status, income, employment, smoking and alcohol consumption. They also undertook a physical health examination including height, weight, resting blood pressure and heart rate.

Results

During the 10-year follow-up period of the study, 7.6% of the subjects suffered a major adverse cardiovascular event and 9.5% died from all causes.

The lower leisure time group reported with higher fatigue scores, resting heart rates, LDL cholesterol and triglycerides than the very high leisure time activity group.

Males and females both reported moderate to high levels of occupational physical activity, with more males reporting very high occupational activities. Those in the very high occupational group also presented with poorer lifestyle factors including increased smoking, low education, low adherence to dietary guidelines and high alcohol consumption.

The risk of major adverse cardiovascular events was higher in the high occupational groups compared to all other groups. In the high levels of leisure time activity groups there was a lower risk of major adverse cardiovascular events and all-cause mortality.

Discussion

The overall result indicated that higher leisure time physical activity was associated with a lower risk of major adverse cardiovascular events and all-cause mortality, while higher levels of occupational physical activity increased the risk. While this was evident in this study, other research has suggested that moderate to vigorous occupational physical activity can contribute to longevity in males.

The main reasons given for the difference between leisure time and occupational physical activity was the high levels of fatigue, insufficient recovery, elevated 24-hour blood pressure, and heart rate, without an improvement in cardiorespiratory fitness. The higher mortality rates and increased risk of cardiovascular events could have been amplified by the poor lifestyle habits and living conditions also reported. For an occupational physical activity to be regarded as vigorous/high, it must exceed 6 METs.

Another variable to occupational physical activity is an environment that creates little or no movement or prolonged sitting such as office and management jobs. With the intensity at base levels and the long periods in the one position, numerous adverse health outcomes have been reported.

The physical activity paradox is explained by the different characteristics of physical activity performed in a work environment compared to leisure time physical activity. Leisure time physical activity encourages more dynamic muscle contractions over a shorter time, higher intensity with adequate recovery time while occupational physical activity encourages static and constrained activities for long durations and lower intensities.

The group that showed the lowest risk for MACE and mortality was the high leisure time and low occupational group, while those who had high levels of occupational physical activity and high levels of leisure time physical activity reduced their risk factors. It appears that to reduce the side effects of excessive occupational, it is necessary to have higher levels of fitness and leisure time physical activity.

Another possible explanation for the possible physical activity paradox is the potential global reduction in maximum aerobic fitness (VO2max) across many populations. As the demand for some occupational tasks remains the same, those participating workers present with reduced aerobic fitness levels making them unable to meet the demands of the job.

Lower aerobic fitness levels translates into higher heart rate, higher blood pressure responses, and higher inflammation while on the job. A Swedish study of over 350,000 male and female workers reported declining cardiovascular fitness over the past 20 + years. This is particularly concerning for older workers in demanding occupations as they typically present with lower cardiorespiratory fitness levels.

Data extracted from health profile assessments reveal that the average occupational workload should not exceed 30% of a worker's VO2max to maintain these workloads without adverse health effects.

The same principle could be followed by leisure physical activity, as high intensities and workload demands are prescribed before they can meet the requirements. In all physical activity environments there should be a progressive improvement in VO2max to a specific level before performing high-intensity activities.

RESEARCH REVIEW 4

Title: *25 years Physical Activity Trajectories and development of subclinical coronary artery disease as measured by Coronary Artery Calcium: the coronary risk development in young athletes*

Authors: D Laddu et al (2017)

Source: Mayo Clinic Proc., 92(11): 1,660-70

Introduction

Coronary artery calcification has been reported as a strong predictor of atherosclerosis.

It has been reported extensively that moderate to vigorous exercise provides significant health-related benefits, reducing the risk of cardiovascular disease and all-cause mortality. However, there has been some debate as to the optimal dose of exercise required to achieve these benefits.

Some recent epidemiological studies suggest that exercise beyond the recommended physical activity levels could potentially cause a U-shaped response where health benefits might be adversely affected.

In the Coronary Risk Development in Young Adults study population, increased physical activity levels and high levels of cardiorespiratory fitness were associated with lower CAC or no detectable CAC scores some 15 years later.

As physical activity levels vary significantly over the life course, longitudinal studies need to be conducted to analyse the effects of long-term participation in physical activity.

The purpose of this study examined the effects of long-term physical activity participation on CAC scores during a 25-year transition from young adulthood to middle age (CARDIA study).

Method

Subjects in this study included 3,175 participants (56.6% were females) in the CARDIA study. Subjects reported their physical activity participation in recreational activities, exercise, home maintenance and occupational activities during the previous 12 months by completing a questionnaire at eight examinations over 25 years (1986-2011).

Coronary artery calcium (CAC) scores were also measured at year 25 and a group-based trajectory model was used to identify physical activity trajectories with increasing age.

Intensity for activities was expressed in METs, with vigorous activities >6 METs and moderate activities at 3-5 METs.

Results

Three trajectory pathways were identified: 1) PA below recommended guidelines (<600 MET Minutes); 2) PA at recommended guidelines (600-1200 MET Minutes); 3) PA three times recommended guidelines (1,800-3,600 MET Minutes).

Physical activity levels decreased with advancing age in those who exercised at three times the recommended guidelines, while participants below and at recommended guidelines plateaued with advancing age. Participants in three times recommended guidelines were predominantly males, while those in less than recommended guidelines were primarily females.

Hypertension and type 2 diabetes were highest in the below recommended guidelines group.

At year 25, those engaged in three times the recommended guidelines presented with the highest coronary calcium scores, with white males scoring the highest.

Discussion

Those subjects who exercised three times above the recommended PA guidelines had 27% higher odds of a higher CAC score compared to the other below the guideline groups, with white males at the greatest risk, suggesting a U-shaped or reverse J-shaped relationship between high doses of PA and CV and all-cause mortality.

White males generally reported with lower levels of HDL-C levels across all groups. High HDL-C levels often provide a protective role in cardiovascular disease. In this study, the low HDL-C levels demonstrated might not have provided enough protection against the development of CAC and atherosclerosis.

Other studies have reported potentially adverse cardiovascular effects such as elevated cardiac troponin levels and increased incidence of atrial fibrillation, both of which are predictors of subclinical myocardial damage as a result of long-term vigorous extreme exercise.

Marathon runners have been reported with higher CAC scores mainly due to the sheer stress of higher heart rates and systolic blood pressure during training. This is contrary to some other studies that challenge the extreme exercise hypothesis by reporting that these athletes have increased diameter and dilation of coronary arteries that might mitigate any potential adverse effects caused by atherosclerosis.

Even though higher CAC scores have been reported, it has also been suggested that physical activity has a possible atherosclerotic benefit by promoting plaque stabilisation and preventing its rupture and thrombosis.

RESEARCH REVIEW 5

Title: *Excessive exercise training causes mitochondrial functional impairment and decreases glucose intolerance in healthy volunteers*

Authors: M Flockhart et al (2021)

Source: Cell Metabolism, 33: 957-70

Introduction

Mitochondria is the powerhouse of the cell and is the site for energy metabolism. It houses the Krebs cycle and is responsible for the production of ATP. It is a critical cell organelle in maintaining metabolic health. If the mitochondria are dysfunctional, whole-body functions will be affected, including blood glucose control and insulin sensitivity.

It is also highly trainable and responds very well to physical activity at any intensity and has a strong relationship with maximal oxygen consumption. While high to extreme amounts of exercise have been reported to contribute to increased coronary calcification, no clear threshold has been reported for disturbances in mitochondrial function.

In competitive sport it is well established that, without adequate recovery and planning, too much training can lead to an initial state of overreaching, which could lead to overtraining. A study of 12 subjects trained in sprint interval training demonstrated significant decreases in mitochondrial functioning due to changes in oxidative stress. Mitochondrial health is linked to metabolic health and adverse changes could cause negative metabolic outcomes.

The purpose of this study was to examine the effects of high-intensity interval training on mitochondrial function.

Method

Six female and five male healthy subjects were recruited for the study. They were trained using a four-week HIIT protocol. During the first three weeks, the workload progressively increased from baseline to light and moderate to excessive intensity, followed by a recovery fourth week.

Muscle biopsies and glucose tolerance tests were administered at different times in the four-week study.

Results

Power output improved throughout the first two weeks and then stagnated during the excessive exercise phase, possibly due to the accumulation of fatigue from the previous phases without adequate recovery. Maximal heart rate was also suppressed after the excessive training phase.

Intrinsic mitochondrial function, which represents the respiratory capacity of the muscle increased during the base, light and moderate phase, was reduced by 40% during the excessive phase. This also translated into a reduction in glucose control.

Discussion

In this study there is an upper limit of exercise where metabolic homeostasis is disrupted due to mitochondrial partial shutdown of the hydrogen peroxide by 50% (a key reactive oxygen species or free radical necessary for muscle contractions). This reduced the production of free radicals or ROS, disrupting the balance between free radicals and the antioxidant defence system and increasing oxidative stress.

The mitochondrial dysfunction also caused disturbances in glucose tolerance and a decreased capacity to oxidise lipid-based molecules, leading to insulin resistance.

The training stimulus responsible for the mitochondrial dysfunction consisted of daily intervals of all-out efforts that only the fit and very motivated individuals could maintain on a daily basis. This supports the importance of progressive overload and adequate recovery time between intervals and between sessions.

In this group, 90 minutes of HIIT per week could be tolerated, while the tipping point for mitochondrial dysfunction occurred at 152 minutes per week.

RESEARCH REVIEW 6

Title: *Risk of atrial fibrillation in athletes: a systemic review and meta-analysis*

Authors: W Newman et al (2021)

Source: Br J Sports Med., 55: 1,233-38

Introduction

While physical activity and exercise training improve both mental and physical health and is associated with healthy ageing, it has also been reported that high volumes of high-intensity exercise can impair many of these positive benefits. The prevalence of atrial fibrillation in the general population can be as high as 3.3%, with exercise reportedly reducing its burden.

Atrial fibrillation is a cardiac arrhythmia that has been cited as a potential side effect of excessive exercise. The mechanisms responsible for this condition include chronic inflammation, adrenal activation, atrial dilation, interstitial fibrosis and vagal tone. It is the most common of the arrythmias and can increase the risk of stroke, heart failure and dementia.

The purpose of this study was to calculate the risk of athletes suffering from atrial fibrillation and to investigate the role of different sports in its development.

Method

A meta-analysis was performed on 13 research articles with a sample size of 70,478 subjects on atrial fibrillation in athletes written between 1990 and 2020 and sourced from PubMed, MEDLINE, Science Direct, Sports Discus and the Cochrane Library.

Results

In athletes and non-athletes with no CV risk factors, athletes had the greatest risk of atrial fibrillation. Younger athletes <55 years were at the greatest risk of developing atrial fibrillation.

Mixed sports conferred the highest risk of developing atrial fibrillation compared to endurance sports, while cycling produced the highest risk in endurance sports.

Discussion

This study reported that athletes were at greater risk of atrial fibrillation, particularly those <55 years, compared to non-athletes.

Studies have reported that non-athletes participating in physical activity between 500 and 1,000 MET Minutes per week showed the largest benefit in reducing the risk of atrial fibrillation by 12%, while <500 MET Minutes and >1,000 MET Minutes increased the risk of atrial fibrillation in this population.

Moderate intensity reportedly produces lower atrial fibrillation risks than high-intensity exercise that is responsible for increased oxidative stress, accompanying inflammation, atrial dilation and fibrosis. Those exercising at high intensity >1,000 MET Minutes per week appear to be at the greatest risk of developing atrial fibrillation.

Males tended to be more sensitive to changes in atrial fibrillation compared to females.

RESEARCH REVIEW 7

Title: *Frequent physical activity may not reduce vascular disease risk as much as moderate activity*

Authors: E G Armstrong et al (2015)

Source: Circulation, 131: 721-729

Introduction

While it has been reported extensively that physical activity can reduce the risk of coronary heart disease (CHD) in general, there is little information on the specific effects of particular types of vascular disease, including stroke and venous thromboembolism.

Venous thromboembolism is a condition where blood clots form in the vein and includes deep vein thrombosis and pulmonary embolism due to blood clots forming in the legs, thigh and pelvis.

The purpose of this study was to study the effects of frequency, duration and type of physical activity on the incident of CHD, cerebrovascular disease and venous thromboembolism.

Method

Subjects were recruited from the National Breast Cancer clinics into the Million Women Study. A final total of 1.1 million women aged between 50 and 64 years consented to be part of the study.

Three years after an initial assessment that included a questionnaire on physical activity, anthropometry, lifestyle, health and socioeconomic factors, the subjects were tested and questioned again.

Measurements of physical activity were taken from questions about physical activity patterns and estimated MET hours for each activity.

Analyses were done for intracerebral haemorrhage, cerebral infarction, pulmonary embolism and deep vein thrombosis.

Results

During the initial three-year follow-up there was a progressive increase in hypertension, weight, mean BMI and an increase in MET hours per week in physical activity levels. Those subjects who reported gardening and walking as their main physical activity modes had lower mean BMI and weight.

In nine years after the initial testing, 49,113 women had a first coronary heart disease event, 17,822 had a first cerebrovascular event and 14,550 had a first thromboembolic event.

When compared to inactive women, those who reported moderate physical activity had a significantly lower risk of coronary heart disease, cerebrovascular disease and thromboembolic disease, while those who reported daily strenuous physical activity had a higher risk of coronary heart disease, compared to those who reported two to three times per week.

Discussion

From a sample size of 1.1 million women, those who engaged in moderate amounts of physical activity reduced their risk of coronary heart disease, cerebrovascular disease and thromboembolic disease compared to inactive people.

Positive changes that have a favourable effect on reducing coronary heart disease include increases in HDL cholesterol, improvements in endothelial function, decrease in chronic inflammation, reduction in fibrinogen and a decrease in plasma viscosity.

Women who participated in daily strenuous physical activity had a better vascular profile and a reduced risk than inactive women. However, there was little improvement in the risk reduction of heart disease when strenuous physical activity was performed every day compared to moderate amounts of physical activity performed two to three times per week. This result has been supported in a study of men and women runners, where the lowest risk cardiovascular mortality was found in those running three times per week compared to more than four times per week.

This study suggests that, to maximise the coronary benefits of strenuous daily physical activity, adequate recovery within sessions and between sessions with easier days or rest days might be necessary.

Encouraging inactive middle-aged women to engage in moderate forms of any physical activity that can be maintained could benefit their vascular health profile, rather than prescribing more strenuous alternatives.

RESEARCH REVIEW 8

Title: *Dose of jogging and long-term mortality: the Copenhagen City Heart Study*

Authors: P Schnohr et al (2015)

Source: Journal of American College of Cardiology, 65(5)

Introduction

Over the decades, exercise and physical activity have been recommended to combat many chronic diseases associated with inactivity. More recently, the general recommendation has centred around 150 to 300 minutes of moderate-intensity exercise (3-6 METs) or 75-150 minutes of vigorous exercise (6-9 METs) per week. It has been reported that physically active people have at least a 30% lower risk of death compared to inactive groups.

Very rarely has an upper threshold been identified where exercise could create a U-shaped curve, causing adverse health conditions.

One mode of exercise now receiving attention is running or jogging and its effect on longevity. One study from the Copenhagen Heart Study reported that the relative intensity of walking and cycling and not the duration was critical to increasing longevity and reducing mortality. Male and female joggers lived on average 6.3 years longer than non-joggers, with 2.5 hours per week at a slow or average pace for three times per week producing the best results. It was reported that those who jogged more than four times per week at a fast pace appeared to attenuate many of the positive benefits.

The purpose of this study was to assess the likelihood of a U-shaped curve between mortality and the dose of jogging or running.

Methods

Data collected from the Copenhagen City Heart Study was used in this study. From a sample size of 19,329 subjects of between 20 and 93 years, 1,098 healthy joggers and 3,950 healthy non-joggers were selected for this study. Those with coronary heart disease, cancer and stroke were eliminated from the sample.

Subjects were asked to complete a physical activity and leisure time questionnaire detailing their intensity, frequency and duration of activities, all of which were graded 1-4. Group 1 was mainly the sedentary group interspersed with light walking or biking for more than two hours per week. Group 2 was light activity for two to four hours per week. Group 3 was light activity for more than four hours per week or more vigorous activity for two to four hours per week. Group 4 was high vigorous activity for more than four hours per week.

Joggers were grouped into three sections: light joggers had a slow or average pace of 8kmph (6 METs) at 2.5 hours per week, three times per week. Moderate joggers jogged at the same pace but for >2.5 hours per week more than three times per week. Strenuous joggers ran at 11.5kmph (12 METs) for more than four hours three times per week.

Results

The results of this study indicated that the lowest mortality rates were found at a duration of 1-2.5 hours per week, at a frequency of two to three times per week at a slow to average pace. The lowest heart rate for mortality was found in the light joggers, followed by the moderate joggers and then the strenuous joggers and inactive people.

Discussion

This study reported a U-shaped curve between jogging doses and mortality rates in 1,098 healthy joggers aged between 20 and 86 years over a 12-year period, suggesting an upper limit of exercise that is conducive to improvements in health.

The lowest mortality rates were found in light joggers who ran at a slow to average pace at 6 METs (kmph) between 1-2.5 hours per week at three times per week.

The highest mortality rates were found in strenuous joggers who ran at 12 METs (11.5kmph) for more than four hours per week at three times per week.

It should be noted that exercising at 6 METs is at the highest level of moderate intensity bordering on vigorous, while 12 METS is regarded beyond vigorous to highly vigorous to high intensity. Given that the VO2max of older subjects would have been lower than their younger counterparts due to normal ageing, the intensity of 6 METs could be regarded as very vigorous.

Other studies have reported decreases of 30% in all-cause mortality rates and a 45% decrease in cardiovascular disease mortality rates in runners compared to non-runners. The most effective dose for reducing risk factors was noted at a dose of 10-20km per week, durations of 50-120 minutes per week, at a frequency of three times per week at a maximum pace of 10-12km per hour.

Even the wonderful longitudinal studies by Dr Paffenbarger reported increased mortality rates in physical activity levels beyond an energy expenditure of 3,500kcals per week, which is equivalent to running 60km per week.

Extensive epidemiological studies suggest that the upper limit of health benefits from jogging occurs at 60km of running and 75km of walking.

Long-term strenuous exercise can reportedly cause remodelling of the heart and large arteries by transient high loads in the atria and ventricles, causing reductions in right ventricular ejection fraction and increase in cardiac biomarker levels, resulting in myocardial fibrosis and atrial and ventricular arrhythmias. Also reported are increases in coronary calcium levels, diastolic dysfunction and artery wall stiffening.

Those subjects running at the strenuous intensity (12 METs) were obviously running for more than general fitness and improved health outcomes. Higher doses of running at high-intensity levels can create positive health benefits but not without an increased potential risk of adverse cardiac events.

The dose required for running for health can be achieved by largely concentrating on low to moderate levels of intensity with forays into more intense workouts with adequate recovery periods.

RESEARCH REVIEW 9

Title: *Influence of half marathon race on aortic stiffness in amateur runners*

Authors: M Standiszewska, A Puto, A Pawlik (2017)

Source: Arch Med Sci., 4

Introduction

Low levels of physical activity and small improvements in fitness can promote improvement in health and longevity without any potential adverse side effects. Improvements as low as 1 MET can reduce mortality rates by 15%.

Alternatively, high-intensity long-term exercise can be challenging to the cardiovascular system, contributing to vascular remodelling and increasing the risk of coronary atherosclerosis.

The purpose of this study was to investigate the hemodynamic response of the cardiovascular system in a half marathon in amateur runners by estimating cardiovascular risk factors including arterial stiffness. A new method for determining cardiovascular risk factors is the oscillometric method that measures pulse waves and central aortic pressure.

Method

Eight healthy amateur male runners were randomly selected through medical screening for this study. All subjects completed the full half marathon course. Blood pressure and pulse waveform were evaluated in a supine position after 15 minutes of rest using the oscillometric method.

Results

No significant difference in peripheral or central blood pressure was noted between pre- and post-half marathon.

At the conclusion of the race a significant decrease in aortic pulse pressure was noted. Heart rate and ejection duration was decreased while heart rate was increased.

Discussion

This study reported that running a half marathon was accompanied by a significant increase in aortic stiffness, increase in blood flow to the heart and heart rate, while blood pressure remained unchanged.

The increased arterial wall stiffness also contributed to a decrease in stroke volume, which is a critical contributor to cardiac output necessary for an improved oxygen delivery to the exercising muscle. When stroke volume is reduced the heart rate must increase to maintain the required cardiac output, putting more strain on the heart.

The temporary response of large artery stiffness from very high endurance demands in amateur runners can contribute long term to coronary artery calcification and potentially myocardial fibrosis.

RESEARCH REVIEW 10

Title: *Prevalence of sub clinical coronary artery disease in Master endurance athletes with low atherosclerotic risk profile*

Authors: A Merghani et al (2017)

Source: Circulation, 136: 127-136

Introduction

While national physical activity guidelines of 150 minutes of moderate-intensity exercise have been prescribed to reduce coronary artery disease, some masters athletes engage in several hours of intense exercise per day, many times the daily recommendations.

Recent studies have reported an increased risk of coronary artery disease in older masters athletes, through high coronary artery scores compared to sedentary groups. Many of these studies have included small sample sizes, males only and athletes with known risk factors.

However, few studies have assessed the prevalence of coronary artery disease in masters athletes without an atherosclerotic risk profile.

The purpose of this study was to investigate the coronary arteries of a large cohort of masters athletes, both males and females, without established risk factors for coronary artery disease.

Method

152 masters athletes were assessed with an average age of 54 years with low Framingham 10-year coronary disease risk scores from echocardiogram, stress test, coronary angiogram, MRI imaging and a 24 hours BP Holter. Athletes had a training age 31+-12.6 years with 70% males.

Results

Most athletes (60%) investigated and 63% of control had a normal CAC score. Male athletes had a higher prevalence of atherosclerotic plaques of any luminal irregularity compared to sedentary males and only male athletes presented with high CAC values >300 Agaston units and luminal stenosis.

Male athletes had calcified plaques compared to sedentary males who had mixed morphology plaques. Male athletes also had multiple plaques compared to sedentary males.

Coronary plaques were evident in main left coronary arteries in both athletes and the sedentary group, while athletes showed a greater distribution of irregularities throughout the coronary tree that were more common in the right coronary artery.

Both male and female athletes demonstrated an increase in the thickness of the wall of the left ventricle compared to sedentary group.

The only variable associated with an increased risk was the number of years of training.

Discussion

Although 60% of middle-aged athletes with a low atherosclerotic risk profile had no CAC, there was a proportion without pre-existing risk factors that had higher CAC scores compared to healthy sedentary males' (>300 Agatston units) CAC scores and a greater number of atherosclerotic plaques including multivessel locations and an increased luminal narrowing. In this study, the majority of subjects with a low risk for coronary artery disease showed no evidence of CAD as a result of years of training.

In earlier studies that reported an increased risk of coronary artery calcium scores due to excessive exercise, some subjects who already had a degree of atherosclerosis might have skewed the results towards high CAC scores. It might suggest that athletes with a high risk for coronary artery disease could be at further risk by long-term excessive exercise.

Those low-risk subjects that did present with an increased CAC score had more stable calcified plaques, potentially promoting a lower risk of plaques disruption. It has been reported that subjects with subclinical CAD (CAC score >100 Agaston units) who had a high degree of fitness reduced their risk of an adverse cardiac event by 75% possibly by more stable plaques.

The mechanism for the increased plaque formation could be due to hyperdynamic of coronary blood flow creating an increase in sheer forces against the endothelium of the artery, the increased force caused by the bending of the artery, the exercise-induced spasm of the coronary arteries, exercise-induced hypertension and the increased oxidative stress. An increased concentration of parathyroid hormones from repeated intense exercise bouts could accelerate coronary calcification.

THE BOTTOM LINE

1 In the follow-up MARC 2 study six years later, exercise intensity increased the risk of higher coronary calcium scores. The very vigorous exercise intensity at 9 METs produced the highest coronary calcium scores. This could be due to the higher catecholamine levels produced. At moderate to vigorous levels of intensity, catecholamine levels are reasonably stable and low. The increased levels cause increases in heart rate and blood pressure, increasing coronary artery mechanical stress, turbulent blood flow and inflammation, potentially accelerating atherosclerosis.

2 Male subjects who trained in >3,000 Met Minutes per day after 10 years of training had an adjusted risk of CAC 11% greater than those with low levels. This suggests that high-volume endurance training of more than 60 minutes per day did not increase the risk of all-cause or cardiovascular mortality regardless of CAC scores.
Even though overall mortality risks were not significant, the highly active males with high CAC scores still had a greater risk of cardiovascular disease and atherosclerosis compared to those who had low CAC scores.

3 Higher leisure time physical activity was associated with a lower risk of major adverse cardiovascular events and all-cause mortality while higher levels of occupational physical activity increased the risk. While this was evident in this study, other research has suggested that moderate to vigorous occupational physical activity can contribute to longevity in males. The main reasons for the difference between leisure time and occupational physical activity was the high levels of fatigue, insufficient recovery, elevated 24-hour blood pressure and heart rate, without an improvement in cardiorespiratory fitness. The higher mortality rates and increased risk of cardiovascular events could have been amplified by the poor lifestyle habits and living conditions also reported. For an occupational physical activity to be regarded as vigorous/high it must exceed 6 METs.

4 Subjects who exercised three times above the recommended PA guidelines had 27% higher odds of a higher CAC score compared to the other below the guideline groups, with white males at the greatest risk suggesting a U-shaped or reverse J-shaped relationship between high doses of PA and CV and all-cause mortality. Marathon runners have been reported with higher CAC scores mainly due to the sheer stress of higher heart rates and systolic blood pressure during training. This is contrary to some other studies that challenge the extreme exercise hypothesis by reporting that these athletes have increased diameter and dilation of coronary arteries that might mitigate any potential adverse effects caused by atherosclerosis.

5 There is an upper limit of exercise where metabolic homeostasis is disrupted due to mitochondrial partial shutdown of the hydrogen peroxide by 50% (a key reactive oxygen species or free radical necessary for muscle contractions) to reduce the production of free radicals or ROS to maintain a balance between free radicals and the antioxidant defence system and reduce oxidative stress. The mitochondrial dysfunction also caused disturbances in glucose tolerance and a decreased capacity to oxidise lipid-based molecules leading to insulin resistance.

6 Athletes were at greater risk of atrial fibrillation, particularly those <55 years compared to non-athletes. Studies have reported that non-athletes participating in physical activity between 500-1,000 MET Minutes per week showed the largest benefit in reducing the risk of atrial fibrillation by 12%, while <500 MET Minutes and >1,000 MET Minutes increased the risk of atrial fibrillation in this population.

7 From a sample size of 1.1 million women, those who engaged in moderate amounts of physical activity reduced their risk of coronary heart disease, cerebrovascular disease and thromboembolic disease compared to inactive people. Women who participated in daily strenuous physical activity had a better vascular profile and a reduced risk than inactive women. However, there was little improvement in the risk reduction of heart disease when strenuous physical activity was performed every day compared to moderate amounts of physical activity performed two to three times per week. This result has been supported in a study of men and women runners, where the lowest risk cardiovascular mortality was found in those running three times per week compared to more than four times per week.

8 A U-shaped curve existed between jogging doses and mortality rates in 1,098 healthy joggers aged between 20 and 86 years over a 12-year period, suggesting an upper limit of exercise that is conducive to improvements in health. The lowest mortality rates were found in light joggers who ran at a slow to average pace at 6 METs (kmph) between 1-2.5 hours per week at three times per week. The highest mortality rates were found in strenuous joggers who ran at 12 METs (11.5kmph) for more than four hours per week at three times per week. Other studies have reported decreases of 30% in all-cause mortality rates and a 45% decrease in cardiovascular disease mortality rates in runners compared to non-runners. The most effective dose for reducing risk factors was noted at a dose of 10-20km per week, durations of 50-120 minutes per week, at a frequency of three times per week at a maximum pace of 10-12km per hour.

9 Running a half marathon was accompanied by a significant increase in aortic stiffness, increase in blood flow to the heart and heart rate, while blood pressure remained unchanged. The increased arterial wall stiffness also contributed to a decrease in stroke volume, which is a critical contributor to cardiac output necessary for an improved oxygen delivery to the exercising muscle. When stroke volume is reduced, the heart rate must increase to maintain the required cardiac output, putting more strain on the heart.

10 Although 60% of middle-aged athletes with a low atherosclerotic risk profile had no CAC, there was a proportion without pre-existing risk factors that had higher CAC scores compared to healthy sedentary males' (>300 Agatston units) CAC scores and a greater number of atherosclerotic plaques including multivessel locations and an increased luminal narrowing. Most of the subjects with a low risk for coronary artery disease showed no evidence of CAD with years of training. The mechanism for the increased plaque formation could be due to hyperdynamic of coronary blood flow creating an increase in sheer forces against the endothelium of the artery, the increased force caused by the bending of the artery, the exercise-induced spasm of the coronary arteries, exercise-induced hypertension and the increased oxidative stress. An increased concentration of parathyroid hormones from repeated intense exercise bouts could accelerate coronary calcification.