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Review

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Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR (Part II)

L Vanhees[1], N Geladas[2], D Hansen[3], E Kouidi[4], J Niebauer[5], Ž Reiner[6], V Cornelissen[1], S Adamopoulos[7], E Prescott[8] and M Börjesson[9] (on behalf of the writing group)

Abstract

In a previous paper, as the first of a series of three on the importance of characteristics and modalities of physical activity (PA) and exercise in the management of cardiovascular health within the general population, we concluded that, in the population at large, PA and aerobic exercise capacity clearly are inversely associated with increased cardiovascular disease risk and all-cause and cardiovascular mortality and that a dose–response curve on cardiovascular outcome has been demonstrated in most studies. More and more evidence is accumulated that engaging in regular PA and exercise interventions are essential components for reducing the severity of cardiovascular risk factors, such as obesity and abdominal fat, high BP, metabolic risk factors, and systemic inflammation. However, it is less clear whether and which type of PA and exercise intervention (aerobic exercise, dynamic resistive exercise, or both) or characteristic of exercise (frequency, intensity, time or duration, and volume) would yield more benefit for each separate risk factor. The present paper, therefore, will review and make recommendations for PA and exercise training in the management of cardiovascular health in individuals with cardiovascular risk factors. The guidance offered in this series of papers is aimed at medical doctors, health practitioners, kinesiologists, physiotherapists and exercise physiologists, politicians, public health policy makers, and individual members of the public. Based on previous and the current literature overviews, recommendations from the European Association on Cardiovascular Prevention and Rehabilitation are formulated regarding type, volume, and intensity of PA and regarding appropriate risk evaluation during exercise in individuals with cardiovascular risk factors.

Keywords

Physical activity, exercise, prevention, cardiovascular, risk factors, physical training

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Introduction

Over the last decades, researchers have given increased attention to the effects of physical activity (PA) on health and disease, morbidity and mortality. Numerous epidemiological studies have provided strong evidence that there are inverse associations between PA and the risk for cardiovascular mortality

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and morbidity. We have reviewed these studies in a previous paper on the importance of characteristics and modalities of PA and exercise in the management of cardiovascular health within the general population in part I.[1] We concluded that in the population at large PA and aerobic exercise capacity clearly are inversely associated with increased cardiovascular disease risk and all-cause and cardiovascular mortality and that a dose–response curve on cardiovascular outcome has been demonstrated in most studies.[1]

Several studies have also shown the importance of engaging in regular PA for reducing the severity of cardiovascular risk factors, such as obesity and abdominal fat, high blood pressure (BP), metabolic risk factors, and systemic inflammation.[2–7] However, at present it is not clear if the type of PA or exercise intervention (endurance exercise, dynamic resistive exercise, or both) or characteristic of exercise (frequency, intensity, time, volume, and duration) would yield more benefit for each separate risk factor.

The present paper, therefore, will review and make recommendations for PA and exercise training in the management of cardiovascular health in individuals with cardiovascular risk factors (part II). After some exercise physiological definitions and background, this paper will focus on the current literature regarding the influence of type and characteristics of exercise on the various cardiovascular risk factors. Part III will then deal with the importance of exercise characteristics in the management of individuals with cardiovascular disease. The guidance offered in this series of papers is aimed at medical doctors, health practitioners, kinesiologists, physiotherapists and exercise physiologists, but also politicians, public health policy makers, and individual members of the public.

Definition and characteristics of exercise interventions

This section briefly covers the various types and characteristics of exercise training interventions. For a more complete definition of PA and physical fitness, we refer the reader to part I of this series of papers.

Aerobic exercise training

The most common modes of exercise are walking, jogging, cycling, and swimming, which, when carried out at moderate intensity, represent good examples of aerobic activity. To achieve a safe exercise training effect, the appropriate intensity, duration, and frequency of exercise should be chosen.

Exercise intensity. Submaximal prolonged walking, jogging, cycling, and swimming are representative types of exercise, usually called aerobic or endurance. Of all the basic elements of exercise prescription, exercise intensity is recently claimed to be an important factor in the development of aerobic fitness and reversion of risk factors.[8,9] Absolute intensity refers to the rate of energy expenditure during exercise and is usually expressed in kcal/min or metabolic equivalent tasks (METs).[1,10] Relative exercise intensity refers to a portion of maximal power (load) that is maintained during exercise and is usually prescribed as a percentage of maximal aerobic capacity (VO_{2max}) on the basis of a cardiopulmonary stress test.[10] Training intensity can also be expressed as a percentage of maximal heart rate (HR_{max}) recorded in a stress test[11] or predicted on the basis of an equation stating that HR_{max} equals 220 minus age.[12,13] We do not recommend the use of prediction equations of HR_{max} for individuals, because of the large standard deviation.[14] Alternatively, exercise intensity can be expressed relative to a percentage of a person's HR reserve (HRR) which uses a percentage of the difference between HR_{max} and resting HR and adds it to the resting HR (Karvonen's formula).[15] There are caveats and cautions to the use of HR for prescribing and evaluating exercise intensity in persons under β-blocker medication.[16] Ideally, the HR derived for training should only be used if the functional capacity (or stress test) was performed under actual medication. Intensity could also be easily monitored using the rate of perceived exertion scale or the breathing rule – 'to be able to talk while exercising'[14] – or arterialized blood lactate concentration[1,17–19] (Table 1).

Exercise training zones. According to Galen (180 AD), not all movement constitutes exercise but only vigorous movement, which is indicated by remarkable alteration in respiration.[20] Nowadays it is accepted that, to enhance cardiorespiratory fitness, exercise should be sufficiently intense to overload the aerobic system. Aerobic fitness is improved when exercise intensity is above the aerobic threshold[21] and within the aerobic training zone, the boundaries of which are indicated in Table 1. The first aerobic threshold, measured by gas exchange or by lactate levels, is indicative of everyday activities and presumably corresponds to 2 mmol/l lactate, while the second anaerobic threshold emerges from more intense aerobic activities which usually lead to a blood lactate accumulation of 4 mmol/l.[21,22] For both primary and secondary cardiovascular disease prevention, the target intensity is usually recommended to be close to the second anaerobic threshold.[11,23] Subsequent to the aerobic threshold is the anaerobic training

Table 1. Relationship among indices of exercise intensity and training zones

Intensity	Lactate (mmol/l)	METs	VO_{2max} (%)	HRR (%)	HR_{max} (%)	RPE scale	Training zone
Low intensity, light effort	2–3	2–4	28–39	30–39	45–54	10–11	Aerobic
Moderate intensity, moderate effort	4–5	4–6	40–59	40–59	55–69	12–13	Aerobic
High intensity, vigorous effort	6–8	6–8	60–79	60–84	70–89	14–16	Lactate, aerobic, anaerobic
Very hard effort	8–10	8–10	>80	>84	>89	17–19	Lactate, aerobic, anaerobic

HR_{max}, maximum heart rate; HRR, heart rate reserve; METs, metabolic equivalents, 1 MET = individual metabolic resting demand, when sitting quiet, about 3.5 ml oxygen/kg/min or 1 kcal (4.2 kJ/kg/h in the general population; RPE, Borg rating of perceived exertion (6–20 scale).

zone (Table 1).[19,21,22] Cardiorespiratory endurance is also effectively improved as far as training stimulus is applied within this zone (6–10 mmol/l lactate and 14–20 rate of perceived exertion scale), but indicated more for athletic purposes.[21,22]

Training volume. Exercise intensity is inversely related to exercise time. Their product (in kcal or kJ) defines the volume of each training unit which in turn multiplied by frequency of occurrence results into the energy expenditure of the training bout or session. The rate of applying training sessions and the duration of training period provide total energy expenditure of a training programme. Training volume should increase every week either by 2.5% in intensity[7] or by 2 min in duration[24] although progressiveness of exercise dose is prudent to be tailored according to the biological adaptation of the individual. Training adaptation is also influenced by genetic potential[25] and environmental factors, such as dehydration, heat, cold, and high-altitude hypoxia.[26–28]

Mode of training. Aerobic exercise training can either be continuous or interval. There is a huge amount of evidence and guidance on continuous aerobic exercise which this paper will distil in the following sections. There is also strong evidence emerging for the benefits of interval-type training. The interval design enables the individuals to complete short work periods at high intensities, which are assumed to challenge the pumping ability of the heart.[29,30] Since intermittent training exposes subjects to near maximal capacity, long-enough rest intervals, preferably active ones, are recommended.[31] The exercise to rest ratio would ideally be one to one.[32] Moreover, interval training is reported to be motivating, since there is a varied procedure during each training session instead of a continuous boring exercise mode and mimics everyday activities.[29,30] Interval training does not appear to be less safe than continuous training since the higher power output and blood lactate levels in the former type of exercise are accompanied by lower cardiac stress (rate-pressure product), rate of perceived exertion, and plasma catecholamines.[33,34]

Resistance training

Exercise intensity. The intensity of resistance exercise is prescribed relatively to 1 repetition performed at maximum weight (1RM). Even though, the performance of 1RM appears to be a safe approach for evaluating strength stimulus[35,36] and no significant cardiovascular events were reported during it,[37] for convenience and compliance reasons the prediction of 1RM from multiple (usually 5) repetition testing (5RM) is suggested.[37] It is found that 5RM data produced the greatest prediction accuracy and that 1RM can be accurately estimated from multiple repetition testing.[38]

Exercise training zones. Training with less than 20% 1RM is considered aerobic endurance training. With more than 20% 1RM, the muscular capillaries start to become compressed during muscle contraction resulting in a cyanotic stimulus responsible for training effects. The number of repetitions should be inverse to the training intensity. A moderate training intensity of 30–50% 1RM with 15–30 repetitions is considered muscular endurance training. Higher training intensities of 50–70% 1RM with 8–15 repetitions are optimal for strength gain.

Training volume. Exercise resistance design could follow a station or a circuit approach. In the former approach, individuals have to finish all the sets for a given exercise per muscle group first and then to move on to another exercise and muscle group. In the second approach, individuals have to perform 1 set of exercise per muscle group and then move on to another exercise and muscle group until completing 1 set. Afterwards, the circuit is followed again until trainees have completed the prescribed sets of each exercise. One to three sets of 8–15 repetitions should be performed for the flexion and extension of each muscle group. Multiple sets are superior to a single set.[39,40] A variety to 8–10 resistance exercises should be prescribed to cover most of the muscular groups.[10] Muscular power is best maintained when prescribing 3–5 min rest intervals instead of short rest intervals (<1 min).[41]

Mode of training. Resistance training can either be isometric (i.e. unchanged muscle length without joint movement) or dynamic. Isometric (static) muscle actions may, at moderate to high loads, induce Valsalva manoeuvre, if not intentionally avoided by regular breathing, and may lead to an unnecessary fluctuation of BP. Contraction with shortening of the muscle and movement of the joint throughout a range of motion is referred to as dynamic. Dynamic training may include constant or variable resistance through the range of motion using either free weights or weight machines. In both these modes, the type of contraction and the velocity of movement vary throughout the range of motion. This type of muscle activity mirrors muscle loading faced in daily activity. There is one other mode of resistance training and muscle assessment, called isokinetic exercise, where the angular velocity remains constant. Isokinetic muscle action does not exist in daily life but the modality remains popular as a means of assessing muscle strength. Muscles can contract concentrically, when during the movement shortening is exhibited or eccentrically when a lengthening of the muscle occurs. Plyometric resistance training is an advanced application of resistance training where participants carry out a series of rapid concentric and eccentric muscle actions often at a relatively high load. Plyometric training is often used to improve sports-related performance and is beyond the scope of this paper.

It is well known that resistance exercise can result in an extreme increase in BP, but it is also recognized that this does not necessarily have to be the case if an appropriate training volume (weight, number of repetitions, sets) is chosen. The actual BP response to resistance exercise is dependent on the amount of static (isometric) muscle contraction, the actual load (% of individual's 1RM) and the amount of muscle mass involved, the number of repetitions, and total duration of muscular contraction. The highest BP response is reached when multiple repetitions are performed at 70–95% of 1RM to exhaustion.[38] Dynamic resistance training with low-to-moderate intensity allows a high number of repetitions (muscular endurance training (15–30 reps); moderate hypertrophy training (10–15 reps) without evoking any major rise in BP. The BP response during this type of training is lower compared to the increase in BP seen during moderate endurance training. If the Valsalva manoeuvre is carried out during resistance exercise the rise in BP is more pronounced.

Effective exercise training for bodyweight control

Effects of exercise intervention on bodyweight loss in overweight/obesity

In obese individuals, fat mass loss can be achieved with endurance training.[42–46] As a result of 16 weeks of endurance training without diet, an average weight loss of ~3 kg can be achieved.[42] A decline of approximately 5–10% of initial bodyweight is associated with significant health benefits, such as a decreased risk for insulin resistance, type 2 diabetes mellitus (T2DM), cardiovascular disease, an improvement in lipid profile, bone metabolism, and BP.[43–46] However, a different selection of training modalities might be instrumental to further optimize exercise intervention effectiveness. In overweight/obese patients, it is important to reduce fat mass as effectively as possible. The effect of different training modalities during exercise interventions on changes in fat mass in overweight/obese patients, as well as the maintenance of bodyweight loss will be examined and recommendations made in the following section.

Weight loss and characteristics of aerobic exercise training. The impact of training frequency on fat mass loss during endurance exercise intervention in obese patients was assessed in one study with 23 females: a greater exercise frequency (5 vs. 3 days/week) had the desired effect with a greater fat mass loss (16 ± 4 vs. 13 ± 4 kg, respectively) when following a 12-week exercise intervention.[47] When comparing low- vs. high-intensity continuous exercise training programmes (with matched energy expenditure between trials), three studies unequivocally report no difference in fat mass loss in obese subjects.[48–50] In a study comparing the effects of a 12-week high-intensity interval vs. a moderate-intensity continuous exercise regimen (matched for energy expenditure) in obese adults,[8] it was demonstrated that fat mass declined to a similar extent (by 2.2 vs. 2.5%, respectively). A large number of studies indicate that prolonged exercise intervention results in a significantly greater reduction in fat mass in obese patients, as opposed to short exercise intervention.[51] Studies targeting <150 min/week of PA do not yield a significant change in bodyweight in obese subjects,[52] >150 min/week of PA reveal modest bodyweight loss of approximately 2–3 kg, whereas PA between 224 and 420 min/week induce a bodyweight loss of approximately 5–7.5 kg. Extreme amounts of PA result in substantial greater weight loss.[53,54]

Weight loss and characteristics of resistance training. Resistance training is reported to be medically safe in people with obesity[52,55,56] and may affect positively cardiovascular disease risk factors,[57–59] fat-free mass, muscle function, and resting energy expenditure,[57,59–64] especially when diet is implemented.[64–66] However, some studies have reported reductions in fat mass after resistance training,[57,63,67–74] while others failed to reproduce such finding.[8,52,55,64,75–81] It seems that resistance training in obese people primarily improves body composition by increasing fat-free mass.[51] The contradiction in the literature regarding the impact of resistance training on fat mass in the overweight/obese might, at least in part, be related to the selection of training modalities.

No study has examined the effects of different resistance training frequencies (days/week) during exercise intervention on fat mass in obese subjects.[8,67,68,80,82] Regarding intensity of resistance training used in the literature, they vary from 50% 1RM[68] up to 90% 1RM.[8] In older men, neither moderate- nor low-intensity resistance training, added to endurance training, for 20 weeks affected body composition.[83] As to whether isometric, concentric, or eccentric resistance training exercises should be applied to reduce fat mass in the obese remains to be studied. Short-term resistance training (6–8 weeks) significantly improves body composition in overweight or obese subjects.[73,74,84] Prolonged resistance training intervention results in greater muscle hypertrophy in obese people.[66,85–87] There seems to be a dose–response relationship between resistance training intensity and biochemical and functional adaptation.[80,87,88] Multiple resistance training sets were found to be associated with significantly greater strength gains than a single set per exercise during a resistance exercise programme. However, no further benefits for volumes greater than 3 sets were observed.[89,90]

Combination of types of exercise training and/or diet. The addition of endurance training on top of diet increases bodyweight loss in the long term,[42] as well as improves cardiovascular disease risk factors and insulin sensitivity.[91] It has been suggested that the combination of resistance training and diet is needed to reduce fat mass in obese subjects.[84,92,93] In combined interventions even low-volume high-intensity resistance training protocols are found to cause reductions in total and regional fat mass.[69,94] The effect of implementation of resistance training within an endurance exercise training programme generally does not induce greater fat mass loss in obese patients.[51]

Prevention of bodyweight gain after weight loss as result of exercise intervention

It is reported that individuals who engage in greater amounts of PA after bodyweight loss experience less bodyweight regain than individuals with low-to-moderate PA volumes.[52,95,96] For general health and disease prevention[82] or prevention of overweight,[97] 30 min of accumulated moderate-intensity activity on most, preferably all days of the week is recommended. However, in previously obese subjects, greater exercise volumes might be required to effectively prevent weight regain. Further studies on the impact of exercise modalities to prevent weight regain in the obese are required.[98]

Mini summary

In general, exercise training has positive effects on bodyweight in the overweight/obese. However, it is still debated which PA is most effective e.g. mode, duration or intensity, for reducing fat mass in obesity. Endurance exercise intensity, and addition of resistance training to endurance training intervention, seems not to modulate fat mass loss, while an increase in exercise volume and programme prolongation are effective strategies to augment fat mass loss. The impact of resistance training modalities on fat mass in the obese remains obscure. Further investigation for the prevention of weight and fat mass regain after exercise intervention in the obese seems warranted.

Effective physical activity and exercise training for control of insulin/glucose dynamics

Several studies have clearly shown that regular PA and exercise training is associated with improved insulin sensitivity and a reduced incidence of T2DM.[99–102] Very few studies compared the different modalities of exercise training on insulin/glucose dynamics.[103]

Control of insulin/glucose dynamics and aerobic exercise training

Sixt et al.[104] assessed the effects of intensive endurance training (4 weeks of 6×15 min/day of cycle ergometry followed by 5 months of daily 30-min cycle ergometry at 70% of the maximum HR in addition to supervised group exercise sessions for 1 hour twice a week) as compared to an antidiabetic, insulin sensitizer drug (rosiglitazone) or usual care on glucose metabolism and endothelial function in patients with established coronary artery disease and impaired glucose tolerance. Four weeks of exercise training, but not rosiglitazone or usual care, improved endothelium-dependent flow-mediated vasodilation. After 6 months of follow up, similar effects were observed.[105] There was a significant improvement in fasting glucose but not in HbA_{1c} both in the exercise as well as the rosiglitazone group, suggesting an independent effect of exercise training on the vessel wall.[106] In a further study, Sixt et al.[107] applied the same protocol as previous outlined and demonstrated, in patients with T2DM, that 6 months of multifactorial intervention led to a significant improvement in coronary endothelial function. There was no correlation between improved markers of acute or chronic hyperglycaemia and improved coronary endothelial dysfunction, suggesting that chronic hyperglycaemia is not the primary factor linking T2DM to endothelial dysfunction. Fasting insulin plasma concentrations and values of the Homeostatic Model Assessment (HOMA) for insulin resistance (IR) and beta-cell function (HOMA-IR) correlated with attenuated coronary vasoconstriction in response to acetylcholine. This suggests that beneficial effects may be primarily mediated by improved insulin sensitivity. In accordance with these findings, there was a continuous increase in the expression of glucose transporters in skeletal muscle (GLUT-4 mRNA) in response to training.

The STENO-2 study called for light-to-moderate exercise of at least 30 min from 3–5 times/week. After an average study period of 7.8 years of intensified therapy, fasting glucose levels as well as glycated haemoglobin (HbA_{1c}) were significantly better in the intervention group than in the control group. Most importantly, a reduction of cardiovascular and microvascular events by 50% was observed.[108,109]

Control of insulin/glucose dynamics and resistance training

Several study protocols assessed resistance training of all major muscle groups at an intensity of 70–80% 1RM for 2–4 sets per muscle group performed 2–3 times/week.[110,111] Castaneda et al.[110] performed progressive resistance training 3 times/week for 16 weeks in addition to usual care in T2DM. They observed improvements in glycaemic control (HbA_{1c}, muscle glycogen storage), lean body mass, abdominal fat mass, and systolic BP. Fasting plasma glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels did not significantly change between groups. Furthermore, progressive resistance training coincided with a reduction in the dosage of antiglycaemic medication as compared with the control group.

Dunstan et al.[112] reported that HbA_{1c} decreased significantly during 6 months of supervised resistance training, but this effect was not maintained after 6 months of home-based training. Increases in upper and lower body muscle bulk were maintained over 12 months. There were no between-group differences for changes in bodyweight, fat mass, fasting glucose, or insulin at 6 or 12 months.

Ishii et al.[113] examined the effect of resistance training on insulin sensitivity in non-obese, T2DM patients. The training programme consisted of nine exercises, 5 times/week (2 sets, 10–20 repetitions) for 4–6 weeks. After training intervention, glucose disposal rate during the hyperinsulinemiceuglycaemic clamp increased in the training group but remained unchanged in the control group. No significant change in body composition was observed, whereas quadriceps strength increased as anticipated in the intervention group. Similarly, a 20-week resistance training that induced an overall improvement in glucose tolerance did not lower fasting glucose.[114]

Contrary to the above studies, Dela and Kjaer[115] reported improved insulin-stimulated glucose uptake and improved muscle strength induced by resistance training in both elderly healthy individuals and elderly individuals with chronic diseases like T2DM. Recent data from Sato et al.[116] have suggested that the improved effectiveness of insulin on skeletal muscle tissue following resistance training is attributable, at least in part, to increases in local expression of GLUT-4, IRS-1, and PI3 kinase.

Control of insulin/glucose dynamics and the combination of dynamic and resistance exercise training

Praet et al.[117] used a combined training protocol of progressive resistance and interval exercise training and reported an increase in muscle strength and exercise performance whereas mean arterial BP, fasting plasma glucose, and non-esterified fatty acids decreased significantly. No significant changes were observed in VO_{2peak}, muscle oxidative capacity, intramyocellular lipid or glycogen storage, and blood glycosylated haemoglobin, adiponectin, tumour necrosis factor α and/or cholesterol concentrations.

Baldi and Snowling[118] reported that 10 weeks of resistance training leads to improved glycaemic control, fastening glucose, HbA_{1c}, insulin, fat free mass, muscle strength, and endurance.

Cuff et al.[119] compared combined aerobic and resistance training with aerobic training alone and found no differences in HbA_{1c} levels between groups. The Diabetes Aerobic and Resistance Exercise Study[120] randomized 251 T2DM patients into one of four groups: aerobic training, resistance training, combined exercise training, and a sedentary control group. Patients in the training groups trained 3 times/week for 22 weeks. The absolute change in HbA_{1c} in the combined exercise training group was superior to changes documented in the control, aerobic, or resistance training groups. Both aerobic or resistance training alone improved glycaemic control, but improvements were greatest with combined aerobic and resistance training.

Marcus et al.[121] compared a 16-week intervention of combined aerobic and high-force eccentric resistance exercise with aerobic exercise only and reported similar improvements in HbA_{1c}, glycaemic control, thigh composition, and physical performance in both training modalities, whereas changes in thigh lean tissue and body mass index were more pronounced in the combined training protocol.

Cauza et al.[122] reported that resistance training was superior to endurance training with regard to improved HbA_{1c}, blood glucose, and insulin resistance.

Egger et al.[123] compared the effects of endurance training combined with either hypertrophy strength training (70–80% of 1RM; 2 sets of 10–12 repetitions) or endurance strength training (40–50% of 1RM; 2 sets of 20–30 repetitions). Hypertrophy strength training led to a significant reduction in fasting glucose levels and fructosamine, whereas no significant differences were detected in the endurance strength training group. A recent review summarized the current evidence about the effects of resistance training on glycaemic control[124] (Table 2).

Mini summary

Aerobic and resistance exercise alone have beneficial effects on glycaemic control, while a combination of both appears to be superior. If current guidelines on exercise prescription are being followed (Table 3),[125–128] beneficial effects on glycaemic control seems to be guarenteed.

Effective physical activity and exercise training for control of blood lipids

Physical activity and exercise in normolipidaemic subjects

It has been demonstrated that increase in PA and exercise training can improve lipid profile, primarily by increasing HDL-C and decreasing triglycerides (TG).[129–134]

Short-term effects. A single session of exercise in sedentary individuals does not have any effects on lipids. By contrast, athletes display a reduction in plasma TG and an increase in HDL-C following prolonged a single intensive competition, such as marathon running or Nordic skiing. However, these effects last only a few days.[135,136] It seems that more short-term exercise periods on the same day have a modestly greater effect for achieving transient increases in the HDL-C compared to a continuous similar duration of exercise.[137,138] Both intermittent and continuous exercise in sedentary subjects decrease TC and LDL-C and increase HDL_2-C as well as the LDL particle size, which are all favourable.[139]

Long-term effects of aerobic activity. Studies on athletes involved in aerobic or endurance activities, such as marathon running, Nordic skiing, and cycling, showed slightly lower levels of TC and LDL-C, markedly lower TG, and significantly higher HDL-C due to a selective increase in the HDL_2-C.[136,140–142] With regard to plasma apolipoproteins, athletes display higher levels of apoA-I and slightly lower levels of apoB, resulting in a higher apoA-I/apoB ratio while no difference in apoA-II, apoC-II, apoC-III, and

Table 2. Effects of resistance training on glycaemic control – review of the current literature

	Studies	Pre training	Post training	∆Pre/Post
HbA_{1c} (%)	27	8.2 ± 0.8	7.1 ± 0. 6	−1.1
Glucose (mg/dl)	17	158.8 ± 23. 8	138. 6 ± 28.3	−20.3
Insulin sensitivity (clamp) (mg/kg LBM min)	1	6.9 ± 2.8	10.1 ± 3.2	+3.3
Muscle glycogen storage (mmol glucose/kg muscle)	1	60.3 ± 0.0	79.1 ± 5.0	+18.8
Insulin resistance (HOMA)	6	8.1 ± 1.4	4.7 ± 2.2	−3.4
Insulin (pmol/l)	9	131.6 ± 30.8	103.7 ± 15.1	−27.9

Values are mean ± SD; HOMA, Homeostatic Model Assessment; LBM, lean body mass.

Table 3. Exercise prescription in the prevention and management of diabetes: recommendations of selected international associations

	Training mode	Intensity range	Exact intensity	Duration/sets/repetitions
ACSM (2000)	Endurance training	Low – moderate	40–60% VO_{2max}, RPE 11–13	40–60 min, 3–5 days/week
	Strength training			
	Circuit training	Low–moderate		8–10 repetitions (up to 20), 1–3 sets, 2–3 days/week
	Interval training			
	Free weights			
	Stretching	Moderate		10–30 s/exercise, 2–3 days/week
ADA (2009)	Endurance training	Moderate–high	40–60% VO_{2max}, 50–70% HR_{max}	150 min/week, 3 days/week
			$>$60% VO_{2max}, $>$70% HR_{max}	90 min/week, 3 days/week
	Strength training	Moderate		8–10 repetitions, 1–3 sets, 3 days/week
AHA (2009)	Endurance training	Moderate–high	$<$70% VO_{2max}	150 min/week
			$>$70% VO_{2max}	90 min/week
	Strength training	Moderate		8–10 repetitions, 3 sets, 3 days/week
ESC (2010)	Endurance training	Moderate		30 min, 5 days/week

ACSM, American College of Sports Medicine;[127] ESC, European Society of Cardiology;[128] ADA, American Diabetes Association;[125] AHA, American Heart Association.[126]; HR_{max}, maximal heart rate; RPE, Borg rating of perceived exertion (6–20 scale); VO_{2max}, maximal oxygen uptake.

apoE has been reported.[139] Prospective controlled studies on sedentary subjects have also documented variable, slight reductions in LDL-C, significant reductions in TG, and increases in HDL-C induced by aerobic training.[136–142] A threshold value of about 1000 kcal has been identified, which is the equivalent of running about 12 km/week, as the energy expenditure required in order to achieve a significant increase in HDL-C.[143]

It can be concluded that aerobic activity in general has favourable effects on plasma lipoprotein profile.

Long-term effects of anaerobic activity. Data are conflicting. While some authors claim that the lipid profile of athletes engaging in anaerobic activities is similar to that seen in those who perform aerobic activities, others have reported no change or even a worsening profile.[144–146]

It can be concluded that at the moment there are not enough data to claim that anaerobic activity exerts any favourable effects on the lipoprotein pattern.

Long-term effects of resistance training and combined aerobic and resistance training. A recent meta-analysis of the impact of progressive resistance training on lipids indicated that caution may be warranted.[147] Others suggest that combining aerobic and resistance-type exercise may confer better effect on lowering TG and LDL-C, improving LDL particle size and increasing HDL-C in healthy subjects than aerobic exercise alone.[148–151]

Physical activity and exercise in hyperlipidaemic patients

Hypertriglyceridaemia. Studies on the effects of exercise in subjects with mildly to moderately elevated TG showed a more marked and longer-lasting reduction of TG in the subjects on diet plus exercise.[152] However, in patients with hypertriglyceridaemia who underwent training, a significant reduction in TG was shown in spite of the fact that the subjects' dietary intake of calories increased.[153] In moderately hypertriglyceridaemic patients, exercise reduces TG, VLDL, and TC/HDL-C ratio.[154] The degree of TG reduction seems to be independent of the weight loss that accompanied the training and is proportional to the TG level.[155,156] By contrast, in patients with severe hypertriglyceridaemia, the effects of training are modest and variable.[157]

It can be concluded that in moderate hypertriglyceridaemia aerobic physical exercise seems to reduce TG by about 30–40% and to increase HDL-C by about 20%, while only slightly modifying total and LDL-C.[158,159] There is not enough data to make clear recommendations about the effects of any type or form of exercise in patients with severe hypertriglyceridaemia.

Hypercholesterolaemia. In patients with moderate hypercholesterolaemia, exercise seems to increase HDL-C and decrease TG, while TC and LDL-C do not correlate with the amount of exercise.[160–163] In patients with mild hypercholesterolaemia and ischaemic heart disease, exercise training within the framework of a programme of cardiovascular rehabilitation, in addition to exerting positive haemodynamic effects and improving physical performance also increases HDL-C[164,165] but induces only a slight reduction in TG.[166] It seems that, in high-risk subjects, exercise induces a decrease in apoB and an increase in LDL-C/apoB ratio thus suggesting favourable changes in the size of LDL particles, i.e. less small dense LDL particles which are more atherogenic.[167]

There are only a few studies on patients with severe hypercholesterolaemia and combined dyslipidaemia, i.e. with elevated cholesterol and TG.[168,169] Such studies have often been non-controlled and have yielded somewhat conflicting results. Studies on familial hypercholesterolaemia and on combined familial dyslipidaemia are totally lacking.

In conclusion, exercise does not seem to substantially modify TC or LDL-C in hypercholesterolaemic patients. It does appear, however, to reduce TG by 6–18% and to increase HDL-C by 7–16% in patients with increased both TC and TG, i.e. in combined hyperlipidaemia. [158,159]

Mini summary

It has not yet been established how much exercise is required in order to improve the lipid pattern and, more generally, to reduce cardiovascular risk. The data currently available seem to indicate that a moderately intense aerobic exercise programme is sufficient to improve TG and HDL-C, while a more demanding regimen does not offer further significant advantages. It seems that the amount of exercise, in terms of overall energy expenditure, is of greater importance than the intensity of training. A threshold value of about 1000 kcal/week has been identified as the energy expenditure required in order to achieve a significant increase in HDL-C. Moderate PA involving energy expenditure greater than 1000 kcal/week, and carried out at intensity equal to 75–85% of the HR_{max} would therefore prove efficacious, safe, and easily practicable for the majority of individuals. Recent data, however, seem to suggest that high-intensity aerobic interval training could increase HDL-C more than moderate-intensity continuous training in patients with metabolic syndrome. Exercise training should be scheduled in 3–4 sessions/week of at least 20 min each and should involve aerobic activity, such as brisk walking, jogging, or cycling. Moderate-intensity resistance exercise can efficaciously be combined with this in order to improve musculoskeletal efficiency and to increase lean body mass.

Effective physical activity and exercise training for control of blood pressure and arterial compliance

Hypertension is defined as a systolic BP $\geq$140 mmHg or diastolic BP $\geq$90 mmHg or being on antihypertensive treatment. BP in excess of 140/90 mmHg is further categorized in terms of severity, defined as stage 1–3.[170,171] Although BP <140/90 mmHg was once considered normal, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High BP now includes the category of prehypertension, defined as the pressure range between 120/80–139/89 mmHg.[170] Only pressures below 120/80 mmHg are considered optimal[171] or normal.[170] Further, a decrease in arterial compliance has been recognized as an important independent cardiovascular risk factor and has been implicated in the development and progression of hypertension.[172] Lifestyle changes, including an increase in PA, are recommended in the prevention, treatment, and control of BP.

Endurance exercise training, blood pressure and arterial compliance

A number of meta-analyses investigating the effect of endurance training on BP have been performed.[173–177] The most recent meta-analysis, including 72 randomized controlled trials, 105 exercise training groups, and 3936 participants, showed that the average net change of systolic BP/diastolic BP was −3.0 (−4.0 to −2.0)/−2.4 (−3.1 to −1.7) mmHg ($p < 0.001$). Further, net BP changes were greatest in the hypertensives compared to the normotensives. These results were obtained with training programmes that involved endurance exercises for an average of 40 min/session, 3 times/week, at an intensity of 65% of HRR.[177] The effect of endurance training on arterial compliance showed significant, clinically meaningful, positive effects in healthy individuals[178,179] dominantly on central arterial compliance, but no impact on arterial compliance in hypertensive subjects.[180,181]

Investigating the role of different exercise characteristics, it was shown that training frequencies of 3–7 times/week lowered BP to a similar extent.[177] However, Tully et al.[182] observed a slightly larger, although not significant, BP reduction in participants randomized to the 5-day walking group compared to those randomized to the 3-day walking group. Similarly, Jennings et al.[183] in normotensives and Nelson et al.[184] in hypertensives found that the fall in BP was significantly greater on a 7 times/week schedule than when the participants exercised 3 times/week. Importantly, during the last two decades, several investigators have shown that a single bout of exercise may result in immediate BP reductions that persist for a major portion of the day.[185]

Current guidelines recommend endurance training at 'moderate intensity'.[82,170,171,186] However, meta-regression analysis could not demonstrate a significant relation between changes in BP and training intensity.[173,177] In addition it has recently been shown that exercise at lower intensity (30% of HRR) was as effective for reducing resting SBP (SBP during submaximal exercise and recovery from exercise) as an identical exercise training programme at higher intensity (66% of HRR), and this was in older sedentary subjects.[187]

Given that a lack of time is a frequently cited barrier to PA a recommendation that allows individuals to perform short bouts of activity throughout the day rather than having to put aside a continuous time slot of 30–40 min seems attractive. Chronic intervention studies comparing continuous (e.g. 40 min) vs. intermittent exercise (e.g. 4×10 min) found similar decreases in BP, with no differences between the two patterns of exercise.[188] Furthermore, roughly similar BP reductions were observed following an acute session of 10, 15, 30, and 45 min of aerobic exercise at 70% of VO_{2peak}.[189]

Finally, no difference in BP reduction has been observed between these different types of endurance training, like walking, jogging, cycling, or a combination of these.[177]

Resistance training, blood pressure, and arterial compliance

Contrary to the large amount of evidence on the benefits of endurance training on BP, research on the effect of resistance training is less compelling. According to two different meta-analyses[190,191] a distinction should be made with regard to type of resistance training, i.e. dynamic resistance training vs. isometric/static resistance training.

In a meta-analysis[190] involving mainly supervised progressive dynamic resistance training programmes which were performed on average 3 times/week at a mean intensity of 76% of 1RM and incorporated approximately eight exercises/session for arms, legs, and trunks and 3 sets/exercise, an overall weighted net change in resting systolic BP of −2.7 (−4.6 to −0.78) mmHg and in diastolic BP of – 2.9 (−4.1 to −1.7) mmHg was found. Though, contrary to dynamic endurance training, reductions in BP were smaller and not significant in the 101 hypertensive individuals.[190] Training intensity was not a significant determinant of the observed BP reductions after dynamic resistance training.[190] Similarly no significant difference could be observed after static or isometric leg exercise, 3 times/week for 8 weeks at low (10% of 1RM) or high intensity (20% of 1RM).[192]

Results on the effect of dynamic resistance training on arterial compliance are heterogeneous. A 4-month dynamic resistance training programme (80% of 1RM) in 28 healthy men caused a significant decrease in carotid arterial compliance of 19% and an increase in stiffness index of 21% returning baseline levels during a 4-month detraining period.[193] By contrast, others could not demonstrate a significant change in arterial compliance after 3 months of concentric exercise of big muscle groups at 70% of 1RM[194] or 80% of 1RM[195] in healthy men and/or women, respectively.

No more than three randomized controlled trials, involving 81 men and women, could be included in the most recent meta-analysis on the effect of isometric resistance training on BP.[191] The observed reduction in BP (−13.5 (−16.5 to −10.5)/−6.1(−8.3 to −3.9) mmHg) suggests that isometric handgrip exercise may be efficacious for reducing resting SBP and DBP; however, the generalization of these findings is limited given the small number of studies included. No data are available with regard to the effect of isometric resistance training on arterial compliance. High-intensity isometric exercise such as heavy weightlifting should be avoided.[171,186]

With regard to the mode of dynamic resistance training, all dynamic resistance exercises involve movements of the arms, legs, and/or trunk, which is likely to introduce an aerobic component to the work out as suggested by the significant increase in VO_{2max}.[190] Furthermore, there were no differences in the BP reduction between conventional resistance training programmes or circuit protocols.[190]

Mini summary

The recommendations in Table 4 are expected to result in a control and/or lowering of BP. Ideally, exercise prescription aimed at prevention or management of hypertension requires endurance exercise, supplemented by resistance exercise on most, preferably all days of the week. Exercise should be performed at moderate intensity for a minimum of 30 min of continuous or accumulated PA day. Given that a single bout of low-intensity exercise can cause acute reductions in BP that lasts several hours, augmenting or contributing

Table 4. Minimum exercise prescription recommendations in the prevention and management of hypertension

Mode	Intensity	Duration	Frequency
Aerobic (endurance) (walking, cycling, jogging, running)	Moderate: 40–60% of HRR or 12–13 RPE	30 min	5 days/week
	OR		
	Vigorous: 60–84% of HRR or 14–16 RPE	20 min	3 days/week
	AND		
Resistance (strength) (progressive weight training using major muscles, bodyweight exercise, theraband exercise)	8–12 repetitions resulting in substantial fatigue	One set of 8–10 exercises (multiple sets if time allows)	2 or more non-consecutive days/week

HRR, heart rate reserve derived from individual maximal exercise testing; RPE, Borg rating of perceived exertion (6–20 scale). Combinations of moderate- and vigorous-intensity aerobic activity can be performed to meet the weekly recommendations (e.g. 2×30 min moderate sessions and 2×20 min vigorous sessions). Adapted from Sharman & Stowasser.[196]

to the reductions in BP resulting from chronic exercise, daily exercise should be emphasized in the hypertensive patient. Furthermore, just as one BP drug and one dose are not suitable for all patients, one exercise prescription is unlikely to fit all individuals but requires individualization. With regard to arterial compliance, endurance training dominantly improves arterial stiffness while resistance exercise may have either a positive or a negative effect dependent on the intensity of exercise. However, clearly more research is needed before firm recommendation can be made on exercise and arterial compliance.

Effective physical activity and exercise training for control of new emerging cardiovascular risk factors (haemostasis, inflammation)

Inflammatory responses after acute and chronic endurance exercise are well documented[197,198] while the evidence regarding the post-exercise haemostatic state is limited. Large variability in exercise protocols, training, and health status of studied populations and analytic methods may influence the expression of the circulating markers of inflammation and haemostasis and interfere with the objective interpretation of study results.[199] Interleukin-6 (IL-6) is the earliest and most marked cytokine response after strenuous exercise, which also triggers the hepatic C-reactive protein (CRP) synthesis exponentially.[198,200–202] The increases in IL-6 with resistance training seem to be of a lesser magnitude than those seen in endurance exercise.[203] A single bout of high-intensity exercise is also accompanied by a protective up-regulation of the anti-inflammatory cytokines including the IL-1 receptor antagonist, tumour necrosis factor (TNF) receptors, IL-10, IL-8.[198] Similarly, bouts of resistance training produce an increase in IL-10[204–205] but there were no changes in levels of TNF-α and IL-1 β.[203] Studies comparing different levels of exercise intensities indicate that significant activity of factor VIII (FVIII) with concomitant variations of the von Willebrand Factor is observed only at the highest work intensities.[206,207] Dynamic exercise is associated with shorter activated partial thromboplastin time whereas alterations of prothrombin time and plasma fibrinogen remain equivocal.[208,209] A global increase in fibrinolytic activity has also been reported after acute exercise.[210]

Accumulating data from cross-sectional studies point consistently to an inverse association between inflammatory markers and long-term PA.[197,211–215] Individuals with high physical fitness level have CRP levels 25–40% lower than those of the least fit or least active individuals. The type of exercise (greater in swimmers than in rowers, in joggers than in cyclists) influences the effects of exercise training on CRP even after adjusting for confounding factors.[197,212,216] Only few studies failed to confirm this inverse relationship, most likely because of the high proportion of sedentary subjects recruited.[216,217] Physical activity decreases resting levels of IL-6 and TNF-α and, ultimately, CRP production, by reducing obesity and leptin, by increasing adiponectin and insulin sensitivity, and possibly by its antioxidative effects.[198,202] The exercise-related anti-inflammatory effect is characterized by the modification of cytokine production from other sites besides adipose tissue, such as skeletal muscles and mononuclear cells, and by stimulating the production of atheroprotective mediators such as IL-10, IL-1 receptor antagonist, and TNF receptors.[197]

The overall effect of long-term resistance training appears to attenuate inflammation but with unclear effects on specific markers. Several studies demonstrated significant increases in anti- and in pro-inflammatory cytokines after resistance training, but the magnitude of the pro- to anti-inflammatory ratio is not yet well defined.[218] High-intensity work load appears to elicit a more favourable response of cytokine release whereas adaptations to training may be responsible for blunted cytokine responses.[203,219] Limited research has examined the effects of different exercise training modalities or characteristics on inflammatory system in controls. One study assigned 87 older adults to cardiovascular, flexibility, and resistance exercises and showed reduced serum levels of IL-6, IL-8, and CRP post intervention in the cardiovascular exercise group but there were no differences in the flexibility and resistance exercise groups.[214]

Regular PA is associated with lower levels of fibrinogen, von Willebrand Factor, coagulation FVIII and FIX, and D-dimer.[216,220] Studies have shown that long-term exercise stimulates endogenous fibrinolysis, as expressed by dose-dependent reduced plasma tissue plasminogen activator antigen levels.[216,220] Contradictory results on post-exercise coagulant and fibrinolytic responses may reflect differing adaptations with ageing and endothelial responses to exercise protocols.[209]

Consideration of age and sex

Exercise training is associated with reduced systemic inflammation also in the elderly but because of their physical or cognitive limitations the appropriate intensity is difficult to be determined.[216] Resistance training programmes may assist in improving age-related loss of muscle mass and muscle strength and reducing low-grade inflammation.[221] Advanced age appears also to influence the behaviour of many haemostatic parameters, by age-dependent endothelial dysfunction.[207,209]

Gender-related differences in baseline inflammatory status are largely attributable to body fat. Some studies reporting on sex differences with respect to inflammation have shown an inverse association between PA level and CRP in men but not in women even after adjusting for menopausal status and hormone therapy use.[222,223] The lack of association between CRP and PA in women may be due to the greater tendency of women vs. men to be inactive during leisure time or to the adaptation of different types of PA.[224]

Mini summary

Regular PA improves inflammatory profile and exerts antithrombotic effects, thereby contributing to the cardioprotective impact of exercise. Further research is required to identify the pathophysiological links between inflammatory pathways and cardiorespiratory fitness along with the underlying genetic regulatory elements. Randomized controlled trials are warranted to investigate the type, dose, and intensity of PA needed to achieve beneficial effects.

Effective physical activity and exercise training for control of anxiety and depression

Anxiety

A level of anxiety exists in the general population and is particularly common in people with heart conditions, with prevalence up to 70% in patients who have experienced an acute cardiac event and long-term prevalence in up to 25% of patients with cardiovascular disease.[225,226] Whether anxiety increases risk of coronary heart disease or leads to a poorer prognosis is still uncertain.[225,227–231] Early meta-analyses have reported on the effect of exercise on anxiety symptoms in primarily healthy adults and in coronary patients.[232,233] A recent systematic review and meta-analysis of exercise training of anxiety in patients with a chronic illness included 40 randomized controlled trials published between 1995 and 2007 with a total of 2914 patients (mean age 50 years, 59% women). The review compared exercise training with no treatment or as an addition to standard care and concluded that 3 or more weeks of exercise training resulted in significantly reduced anxiety symptoms.[234] The overall mean effect was 0.29 SD (95% CI 0.23–0.36), i.e. a moderate effect. Effect did not differ with age, gender, or type of chronic disease, which were mainly cardiovascular disease, musculoskeletal disorders, cancer, chronic obstructive pulmonary disease, and psychological disorders. Also acute bouts of exercise have been demonstrated to result in a reduction in anxiety and panic symptoms, including in experimental settings.[232,235–239]

Type and dosage of exercise. The intensity of exercise necessary to produce an anxiolytic effect is unclear. One study comparing six sessions of exercise at low-intensity (walking) with high-intensity (60–90% HR_{max}) exercise in 54 patients found that, whereas both reduced anxiety sensitivity, high intensity was more efficient.[240] In contrast, a study of 80 healthy elderly patients found that light exercise improved anxiety scores but higher intensity did not have additional beneficial effect.[241] In the meta-analysis described above, effect did not differ with exercise intensity or whether intervention resulted in increased levels of fitness. There was, however, a significantly greater effect of exercise sessions that exceeded 30 min compared with shorter or unspecified durations and, surprisingly, also greater effect of programmes running over 3–12 weeks than of longer duration. No difference with type of exercise (aerobic, resistance, or combined) could be found.[234] However, few studies focused on exercise modality and further research is needed to clarify the dose–response relationship between exercise training and alleviation of anxiety.

Depression

Depression is a common condition affecting one in five over a lifetime. Major depression affects 15–20% of myocardial infarction patients[242] and is associated with poorer prognosis[227,243–245], although whether the association is directly causal or mediated/confounded by behavioural risk factors remains unclear.[245] There is no clear evidence that pharmacological treatment of depression alters prognosis in coronary heart disease.[246,247]

Exercise and depression have a bidirectional relationship: physically active persons are less likely to develop depression[248] and, conversely, depression is a significant risk factor for development of a sedentary lifestyle.[249] Regardless of causality, exercise may alleviate symptoms of depression and is part of established treatment of depression.[250]

A Cochrane systematic review and meta-analysis including 23 randomized controlled trials comparing exercise with no treatment or a control intervention comprising 907 patients found that exercise improved depression by SD −0.82 (95% CI –1.12 to −0.51), i.e. a large clinical effect.[251] There were more women than men in the studies and a wide range in mean ages (22–87.5 years). When including only the three highest quality studies comprising 216 patients, effect size was reduced to –0.42 SMD (95% CI −0.88 to –0.03), i.e. a moderate improvement of borderline significance. Other recent reviews have reached similar conclusions.[237,252–256] Exercise training also appears to be a viable treatment option for elderly patients[254,255] and medically ill patients with co morbid depression: exercise has been shown to reduce depressive symptoms in patients with coronary heart disease[257–259] and pulmonary disease[260] and may improve cognitive function in the elderly and patients with signs of dementia.[261,262]

Type and dosage of exercise. Most studies showing effect of exercise have employed aerobic exercise (endurance training). In the systematic review, the SD for aerobic exercise indicated a moderate clinical effect (SD −0.63, 95% CI −0.95 to −0.30), whilst the SDs for both mixed exercise (SD −1.47, 95% CI −2.56 to −0.37) and resistance exercise (SD −1.34, 95% CI −2.07 to −0.61) indicated large effect sizes, but confidence intervals were wide.[251] Studies directly comparing endurance training with resistance training in patients with depression are lacking. Results, however, suggest that resistance training and mixed exercise may be substituted for aerobic training according to patient preference.

The Cochrane review could not determine the role of different intensity, duration, and frequency of exercise delivery.[251] Role of intensity of exercise was included in two studies. In one study, high- and low-energy exercise 3 or 5 times/week over a 12-week period were compared ($n = 80$). The study showed superior effect of high-energy exercise on depressive symptoms whereas frequency (3 vs. 5 times/week) was not of importance. In another study of elderly depressed persons ($n = 60$), high-intensity resistance training 3 days/week for 8 weeks was superior to low-intensity training.[263] Higher-intensity exercise will lead to higher level of fitness. However, improved cardiovascular fitness may not be necessary to improve symptoms and correlations between level of fitness and effect on mood have not been consistent.[251] The meta-analysis has shown no clear relationship between duration of intervention and effect and no effect of whether exercise was supervised or not or whether it was performed indoor or outdoor.[251] These findings suggest that it is the effect of exercise itself, which is of benefit, rather than potential side-effects such as social support. However, concerns about methodological quality of trials leading to possible overestimation of treatment effects should be considered.[251,255] Future research should also focus on defining the optimal dose of exercise training to achieve a favourable effect, as well as differences in effectiveness between aerobic exercise and other forms of training, such as resistance training, in individuals with depressive disorders.

Mini summary

Anxiety and depression have been linked to development of ischaemic heart disease and both are common in patients who have established heart disease. Based on randomized controlled trials, exercise training has been shown to alleviate both anxiety and depression. Most studies have used moderate-intensity aerobic exercise. At present there is insufficient data to give more specific recommendations on type, dosage, and intensity of exercise.

Lifestyle approaches to increase physical activity and exercise in persons with increased cardiovascular risk

Individuals with increased cardiovascular risk factors are targeted with lifestyle approaches to increase PA, as they constitute a high-risk group for future cardiovascular events.[264] Different intervention methods are needed, with the ultimate goal of all these lifestyle approaches is the increase in PA and the continued adherence to a higher level of activity.

In the promotion of PA in individuals with increased cardiovascular risk factors, the healthcare sector has a unique role. It reaches a large part of the population, and can offer individual expertise advice. About 65–70% of the population will meet a doctor at least once during a year,[265] providing opportunities for lifestyle information. US figures are even higher.[266] Healthcare professionals are considered as the most credible and respected source of health-related information[267] and are recommended to routinely inform and council the patient on how to be regularly physically active,[268–272] i.e. to 'act in the best interest of the patient' and ideally to involve activity counselling.[273]

Patients with increased risk of cardiovascular disease may be identified as part of a population screening strategy,[272] applying risk score stratification, or as opportunistic screening in a general practitioner setting.[264] Patients with first degree relatives with early onset cardiovascular disease, patients with T2DM, hypertension, hypercholesterolaemia, and obesity, for example, should be targeted for intervention following existing guidelines,[264] which include increased PA.

The evaluation of various approaches to increase PA in patients is difficult, because of the vast difference in the methods used, the type of activity prescribed, and the evaluation method chosen. Importantly, there is a gap between research in controlled conditions and the real life situation in everyday practice. Thus, the translation of health promotion research to practice remains a challenge.[274,275] Furthermore, many of the suggested approaches to increase PA have been studied in the normal population, and not specifically in patients with increased risk.

General advice

The most common and the least complex approach to increase PA is general advice. Many physicians in primary care believe this is important, but advice is still underutilized,[274,276–278] as only about 50% of them counsel sedentary patients on PA.[277,279] In US studies, only 20% of consultations resulted in advice on increasing PA[280] and only one-third of adults report exercise counselling at their last medical visit.[281]

Most earlier reviews had shown a moderate increase in PA level in the short term (up to 8 weeks) by advice, but no significant long-term effects.[282–284] The Swedish Council on Technology Assessment systematic review found that PA could be increased by 12–50% in 6 months by advice and counselling on PA only,[271] but the recent systematic review from the Swedish National Board of Health and Welfare found low efficacy of this method for increasing PA in patients with cardiovascular risk factors.[285]

Advice on PA with additional support

In addition to oral advice on increasing PA, the physician may offer adjuvant therapy such as written advice, step counters, and follow ups. In a US study, only 40% of the individuals receiving oral advice, also received support in the form of a plan for PA or a follow-up visit.[276] Counselling of PA supplemented by written prescription, diaries, pedometers, and information brochures may increase PA by another 15–50% in 6 months.[271] A Cochrane review[286] found that advice on PA and continued support could increase PA in adults. A review of four systematic reviews found that brief advice from the general practitioner, supported by written materials, has a modest short-term effect on PA lasting 6–12 months.[287] Importantly, the Swedish 2010 systematic review concluded that advice on PA with additional support (step counters, prescriptions, and follow up) had good efficacy for increasing the PA level in individuals with increased cardiovascular risk factors, giving this method a high priority within health care.[285]

Advice on PA using theoretical behavioural techniques

Additional support by cognitive and behavioural strategies in promoting PA have been tried.[288,289] Most studies are based on the transtheoretical model or on similar models, with some positive effects.[271,290] However, the US Preventive Services Task Force study concluded that there was insufficient evidence for the efficacy of behavioural counselling in the primary care setting,[291] as did the recent Swedish review of 'methods to change lifestyle behaviour'.[285]

Exercise prescription and exercise referral

More complex methods or approaches for promotion of PA have also been tried. The most common methods are the 'PA on prescription' and the closely related method of 'exercise referral schemes'.[292–295]

Exercise referral scheme.

The exercise referral scheme includes, by definition, referral of the individual by an appropriate professional to a service with a formalized process of assessment of the status and need of the patient, development of a individualized PA programme, and monitoring of the individual and follow up.[296] This model is currently used in the UK and Denmark and often includes a referral to a 2–3-month exercise programme run by the local exercise facilities.[293,297,298] Exercise referral schemes have been evaluated in several (systematic) reviews[293,297–300] showing an effect on the level of PA after 12 months[299] and a small effect on the level of PA in sedentary people.[300] Morgan[293] found that exercise-related schemes may increase PA in slightly active individuals, older adults, and patients who are overweight. Sorensen et al.[294] found a positive effect of PA counselling in six out of 12 studies. Exercise referral schemes in England and Wales resulted in a statistically significant increase in the proportion of sedentary people becoming moderately active.[287]

Physical activity on prescription

PA on prescription (PAP) involves counselling by the healthcare professional, resulting in a written prescription. However, the actual extent of the intervention may vary greatly in different countries and in different healthcare settings. PAP is used in Sweden,[295,301,302] Australia, New Zealand, and Finland with variations on who gives the advice on PA, the use of written prescriptions or not, the actual PA prescribed, and the extent of additional support (pedometers, motivational support, and follow up), used.

A recent randomized controlled study in Spain[303] showed a small, but significant increase in PA in physically inactive patients receiving information on PA and an exercise prescription, without other support. A more extensive approach of PAP has been evaluated in Sweden by several studies in the last years. Kallings et al.[295] showed the efficacy of PAP in the setting of general practice, increasing the PA level after 6 months. In a randomized controlled setting, PAP was shown to increase the level of PA in overweight individuals and to reduce cardiovascular risk factors.[304] Furthermore, the self-reported adherence to the PA prescribed was 65% at 6 months,[301] which is in line with earlier reports on adherence to medications (World Health Organization). Leijon et al.[302] subsequently showed that the efficacy of PAP to increase PA was extended to at least 12 months. Further studies are needed to explore the long-term effects of PAP over 24 months or longer.

Barriers to increased PA

Studies have shown that healthcare professionals think that the main obstacles to exercise advice is the low motivation of the patient,[305,306] the lack of time, and support from the healthcare system (by reimbursements for example)[307,308] as well as lack of knowledge and education on benefits of PA.[308,309] Interestingly, the PA level of the healthcare professional themselves influence their counselling habits,[310] as recently reviewed by Lobelo et al.,[267] indicating the importance of the physicians own level of motivation. Unfortunately, the proportion of medical students perceiving PA counselling as highly relevant decreased significantly from the first year to the fourth year of medical school.[311]

Mini summary

Different lifestyle approaches to increase PA and exercise in persons with cardiovascular risk factors are needed in the healthcare system. The traditionally most common method, general advice without additional support, seems to have a low efficacy for increasing the PA level in persons with increased cardiovascular risk.

Systematic lifestyle approaches in health care, such as exercise referral schemes and exercise on prescription, have shown promising results in improving the level of PA and also on the reduction of cardiovascular risk factors. These approaches need further evaluation regarding long-term effects and cost–benefit aspects, as well as for external validity in routine clinical care in different countries and healthcare systems.

Precautions and safety for at risk individuals participating in PA and exercise

For the benefits of PA to be realized, the safe participation in exercise has to be ensured. In this perspective, requisite safety measures in the healthcare setting and at sports and exercise facilities are also part of the overall preventive strategy as recommended by the European Association for Cardiovascular Prevention and Rehabilitation (EACPR).

There is evidence that increasing PA is associated with a beneficial effect on the general health[264] but also that vigorous physical exertion in risk individuals is associated with an increased risk for sudden cardiac death (SCD).[312,313] In middle-aged male athletes, the incidence of SCD is around 6/100,000.[314] The appropriate precautions and safety measures will vary according to the individual (age, risk factors) as well as the setting (elite sports, exercise programme, type of activity).[315]

Advice for safe exercise and sports participation in the young and apparently healthy individual

A higher rate of SCD has been reported (2.1 cases/100,000 athletes/year),[316] in young (<35 years) competitive athletes compared to non-athletes. The most common cause of death in younger athletes is inherited and/or unknown cardiac abnormalities,[317] the most common being hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, congenital coronary artery anomalies,[316,318] and to a lesser extent ion channelopathies (long QT-syndrome or Brugada syndrome).[316,319,320]

Cardiovascular screening of athletes recommended by the European Society of Cardiology (ESC) to decrease SCD during sports consists of personal history (family history and alarming symptoms), physical examination, and resting electrocardiogram[321] and has shown promising results on mortality.[322] Cardiac screening programmes are now widely implemented by the sporting organizations.[323]

Advice for safe exercise and sports participation in adult/senior individuals

In untrained individuals that are subjected to high-intensity exercise, the acute physical stress is linked to an elevated risk for sudden cardiac arrest,[312,313,324,325] with sedentary individuals with underlying coronary artery disease having the highest risk.[312,326] Habitual exercise training may diminish the risk of acute myocardial infarction and SCD in patients with coronary artery disease.[327]

In adult and senior individuals (>35 years), silent or symptomatic coronary artery disease is by far the most common underlying cause of SCD. Advice for safe exercise participation must deal primarily with identification of individuals at increased risk of coronary-induced events, by means of systematic risk stratification before starting a training programme/leisure-time exercise.[315] The risk stratification includes:

1. Self assessment of risk and habitual exercise: the first step in the risk stratification may be self-assessment, using standardized protocols for example PAR-Q.[315] In case of a positive self-assessment, further evaluation by a physician should take place.
2. Medical history and physical examination: specific attention should be given to current discomforts (in particular if these are induced by exercise), pre-existing cardiovascular illness, risk factors, family history, and medication use.[328] The individual risk profile could thus be estimated from:
   The burden of known classical risk factors, age, sex, smoking, BP, and total cholesterol level together with diabetes, according to SCORE.[264]
   The current level of habitual PA, undertaken by the individual as a marker of the cardio respiratory fitness.[329]
3. Exercise test: if risk stratification according to I-II identifies patients with increased risk, the next step is to rule out or confirm the presence of coronary artery disease.[315,330] Based on the individual risk profile and the type/intensity of intended PA, different levels of cardiovascular evaluation are recommended as appropriate for sedentary senior individuals and regularly active senior individuals, as outlined by the EACPR in 2010.[315]

Safety at exercise facilities

The 'chain of survival', including early cardiopulmonary resuscitation, early defibrillation, and early advanced cardiac life support when needed, may increase the survival of out-of hospital sudden cardiac accidents from 2–5% to >50%.[331] The major determinant of survival is the time to defibrillation, the critical time being within 3–5 min.[332] Public access defibrillation using automated external defibrillator programmes may increase the number of patients receiving bystander cardiopulmonary resuscitation and early defibrillation,[333] especially in locations where witnessed cardiac arrest is likely to occur[334] at least once in every 2 years (e.g. sports arenas and exercise facilities).[333] Automated external defibrillators are therefore recommended when normal access to defibrillation exceeds 5 min.[335] European recommendations on cardiovascular preparedness at sports arenas were published in 2011.[336]

Mini summary

While PA is associated with a beneficial effect on the general health, vigorous physical exertion is associated with an increased risk for cardiac events, especially in risk individuals. Recently, practical and pragmatic algorithms for the cardiovascular evaluation of individuals (≥35 years) prior to engaging in regular PA and sports has been proposed, where appropriate precautions and safety measures will vary according to the individual's characteristics (age, risk factors, habitual exercise) as well as the setting of PA (elite sports, exercise programme, type and intensity of activity).

General conclusion

In general, there is strong evidence that a sufficient level of PA and exercise can have beneficial effects on various cardiovascular risk factors. For reducing fat mass in obesity, an increase in exercise volume and programme prolongation are effective strategies to augment fat mass loss but it is still debated which PA is most effective e.g. mode, duration, or intensity. Increasing endurance exercise intensity and addition of resistance training to endurance training intervention seem not to modulate fat mass loss. The impact of resistance training modalities on fat mass in the obese remains obscure. For glycaemic control, both aerobic and resistance exercise have beneficial effects while a combination of both appears superior. In order to improve the lipid profile, the data currently available seem to indicate that a moderately intense aerobic exercise programme is sufficient to improve TG and HDL-C, while a more demanding regimen does not offer further significant advantages. It seems that the amount of exercise, in terms of overall energy expenditure, is of greater importance than the intensity of training. Exercise prescription aimed at prevention or management of hypertension requires endurance exercise, supplemented by resistance exercise on most, preferably all, days of the week. Exercise should be performed at moderate intensity for a minimum of 30 min of continuous or accumulated PA day. With regard to arterial compliance, endurance training dominantly improves arterial stiffness while resistance exercise may have either a positive or a negative effect dependent on the intensity of exercise. Regular PA improves the anti-inflammatory response and exerts antithrombotic effects. Moderate intense aerobic exercise has been shown to alleviate both anxiety and depression. At present there is insufficient data to give more specific recommendations on type, dosage, and intensity of exercise for prevention or treatment regarding new emerging risk factors or anxiety and depression.

Various lifestyle approaches to increase PA and exercise in persons with cardiovascular risk factors are needed in the healthcare system. General advice without additional support, the traditionally most common method, seems to have a low efficacy for increasing the PA level in persons with increased cardiovascular risk. Systematic lifestyle approaches in health care, such as exercise referral schemes and exercise on prescription, have shown promising results in improving the level of PA and also on the reduction of cardiovascular risk factors. With regard to safety, also appropriate individual exercise prescription, preferentially based on exercise testing, in patients with an increased risk profile and the presence of other safety measures, such as the availability of automated external defibrillators in fitness facilities, is mandatory.

It is clear that PA and exercise make a significant contribution to health and that the characteristics and mode of PA and exercise can be highly influential in defining the type and extent of impact in a range of cardiovascular disease risk factors.

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