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Survival of the fittest: VO_2max, a key predictor of longevity?

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1. ABSTRACT

Cardiorespiratory fitness, as measured by maximal oxygen uptake (VO_2max), is related to functional capacity and human performance and has been shown to be a strong and independent predictor of all-cause and disease-specific mortality. The purpose of this review is to emphasize age-related physiological adaptations occurring with regular exercise training, with specific reference to the main organs (lung, heart, skeletal muscles) involved in oxygen delivery and utilization as well as the importance of exercise training for promoting life expectancy in clinically referred populations. As yet, it is not possible to extend the genetically fixed lifespan with regular exercise training, but to give the years more life. This is where physical fitness plays an important role.

2. INTRODUCTION

There is little doubt that an active lifestyle has positive influences on the human organism but that physical inactivity may be seen as pathology. Regular exercise training increases a variety of physiological parameters, and all of them may contribute to the training-induced increase in maximal oxygen uptake (VO_2max), which is an indicator of the system's ability to deliver oxygen to active muscle as well as a biomarker of health. These include an elevated cardiac output, augmented blood volume, skeletal muscle angiogenesis, increased skeletal muscle mitochondrial volume density as well as function, and a shift in skeletal muscle fiber distribution toward more oxidative fibers (1). Cardiorespiratory fitness (CRF), as measured by VO_2max, is related to functional capacity and human performance and has been shown to be a strong and independent predictor of all-cause and disease-specific mortality regardless of sex and race (2). Recent advances underscore the importance of lifelong structured exercise to enhance or maintain CRF but particularly in early adulthood, as a higher CRF at younger ages confers the greatest survival benefit (3, 4). Moreover, there is a large body of epidemiological and clinical evidence

demonstrating that the addition of CRF to traditional risks factors significantly enhances risk prediction so that the American Heart Association recently strongly recommended the assessment of CRF during routine clinical visits to improve patient health care (5). To understand how exercise may facilitate overall health and may further extend life expectancy, this review briefly highlights age-related physiological adaptations occurring with regular exercise training, with specific reference to VO_2max as a biomarker of health and long-term survival. Furthermore, muscular strength is a crucial component of physical fitness with an independent role in the prevention of illness and disability, and becomes vital at older ages.

3. VO_2MAX AND OXYGEN DELIVERY TO WORKING MUSCLES

VO_2max is defined as the oxygen uptake when activating large skeletal muscle groups at maximal intensity, e.g., during running or cycling. According to Hill and Lupton (1923), this upper limit value of oxygen uptake cannot be increased further despite continued increment in exercise workload, and may therefore primarily be limited by the maximal oxygen delivery (6).

Skeletal muscles rely on an adequate oxygen supply (aerobic energy supply), which is accurately adjusted to metabolic requirements. When these requirements cannot be met aerobically, anaerobic energy supply will transiently compensate for the lack of oxygen accompanied by lactate production, resulting in lactic acidosis. There is a series of steps transporting the oxygen from the environment to the mitochondria of the working skeletal muscles (7). First, the respiratory system insures the delivery of oxygen from the environment into the alveoli and the bloodstream and the elimination of carbon dioxide from the blood into the alveoli and the environment (gas exchange). Second, the oxygenated arterial blood is pumped by the heart to the mitochondria of the skeletal muscles. Gas exchange between the alveoli in the lung and the pulmonary capillary blood and the capillary blood and the mitochondria of the skeletal muscles is driven by gas (oxygen and carbon dioxide) pressure differences (diffusion). As oxygen is primarily carried by hemoglobin, the hemoglobin concentration (Hb) constitutes, besides the cardiac output (Q), another important factor for oxygen delivery (DO_2). DO_2 is determined by Q, Hb, and the amount of its saturation with oxygen (SaO_2). $DO_2 = Q \times Hb \times SaO_2 \times K$ (coefficient for the hemoglobin-oxygen binding capacity, which is 1.3.3 ml/g). According to the Fick principle, VO_2max equals Qmax times arterio-venous oxygen difference, representing the oxygen extraction by the mitochondria of the contracting muscle cells. Consequently, VO_2max depends on the integrated functioning of the lung, the heart, and the skeletal muscles exercising at maximal intensity, and may range from more than 90 ml/kg/min in elite endurance athletes to values below 20 ml/kg/min in elderly individuals (7). Aging may progressively affect the functioning of all organs involved in the delivery and use of oxygen.

4. PHYSIOLOGICAL EFFECTS OF AGING

4.1. The aging respiratory system

Structural and functional changes in the respiratory system with age, e.g., loss of elastic recoil, increasing rigidity of the chest wall, and decreasing respiratory muscle strength, declining alveolar surface area and capillaries perfusing the lung might all affect sufficient ventilation and pulmonary gas exchange, resulting in VO_2max limitation. However, the existing literature does not generally support this view because the exercise-related maximal metabolic demands in healthy elderly people occur at a rate equal to or greater than the structural and functional changes in the respiratory system with aging (8). Whereas VO_2max decreases at a rate of about 10% per decade, the maximal voluntary ventilation only decreases at a rate of about 6%, and the diffusion capacity of the lung by about 5% per decade (7, 8). Nevertheless, exercise-induced arterial hypoxemia may occur in some circumstances, being more prevalent in well-trained older individuals, similar to known values for young athletes (9). Moreover, older fit subjects will more likely experience expiratory flow limitation compared with less fit elderly subjects or their younger counterparts (8, 10). Taken together, the aging respiratory system will not essentially limit VO_2max in the healthy elderly but might sometimes affect particularly fit older individuals and of course those suffering from lung diseases.

4.2. The aging cardiovascular system

Nowadays, it is widely accepted that Qmax represents the predominant factor limiting VO_2max in healthy individuals, accounting for about 80% of VO_2max limitation (11, 12). After 30 years of age, VO_2max progressively decreases with age at a rate of about 10% per decade (13). Whereas age-related structural and functional changes in the heart may affect maximal stroke volume, the decline in maximal heart rate (HRmax) has been suggested to largely explain the decrease in Qmax and related VO_2max (14). An important role for the changing intrinsic heart rate primarily accounting for the decline in HRmax with aging has been demonstrated, but decreasing chronotropic responsiveness to β-adrenergic stimulation might add to this decline (15). Besides lowering of HRmax, β-adrenoceptor desensitization may also cause decreasing inotropic properties of the heart, which may significantly contribute to the impairment in Qmax and VO_2max with age (16).

Furthermore, macrovascular and microvascular dysfunction associated with stiffening of central elastic arteries and peripheral endothelial dysfunction are typical consequences of aging negatively affecting blood flow and oxygen delivery to the working skeletal muscles. Nitric oxide bioavailability is diminished with advanced age, thereby contributing to the endothelial dysfunction (7, 17). Finally, the blood oxygen-carrying capacity, which is generally lower in females than in males, declines slightly with age (about 10% from 30 to 80 years) and may also contribute to the VO_2max decrease with age (18).

4.3. The aging skeletal muscle

Skeletal muscles account for approximately 40% of total body mass in humans and decrease by 3–10% per decade starting at the age of about 25 years (19). Thus, the decreasing muscle mass and strength (sarcopenia) represents a hallmark of the aging process in humans. Common structural and functional changes in skeletal muscle are likely related to muscle mitochondrial dysfunction (19). The extent of these changes profoundly depends on lifestyle aspects such as regular physical activity and nutrition. It has been shown that mitochondrial respiratory capacity and mitochondrial dynamics (fusion and fission) are negatively associated with body mass index and positively associated with CRF, but not with the chronological age *per se* (20). In general, the angiogenic adaptability and the aerobic capacity of mitochondria in human skeletal muscle are well maintained in older individuals (21, 22). It has also been demonstrated that the oxidative capacity of small muscle groups is at least twice as high as that used during whole body exercise (22). The arterio-venous oxygen difference, as a marker for the muscles' ability to use oxygen, is only slightly reduced in older individuals, but again somewhat more pronounced in the trained compared with the untrained (12). Taken together, although skeletal muscle is considerably affected by aging, its limiting effect on VO_2max is rather minor.

5. THE EFFECT OF TRAINING

5.1. Training and VO_2max

Although the VO_2max has a significant genetic component and is affected by the aging process, it can improve significantly at any age with regular endurance training by approximately 15–20% or 0.5.l/min, depending on exercise intensity, in healthy sedentary/recreationally active humans (23). Accordingly, it is possible that a trained 70-year-old can exhibit the biological age of an untrained 50-year-old based on the VO_2max, which declines at about 7% (women) to 10% (men) per decade from the age of around 25 years, but in an endurance-trained person starting from a higher level (24, 25) (Figure 1). Healthy untrained men at the age of 25 years exhibit a relative VO_2max of ≈42 ml/kg/min, corresponding to 12 metabolic equivalents (METs). The respective values are 20% less in healthy untrained women, hence ≈36 ml/kg/min and 10.5. METs. After five decades, at the age of 75 years, the VO_2max is about 21 ml/kg/min (6 METs), with no significant sex differences. Thus, men demonstrate a greater absolute decline in VO_2max with age compared with women. Similarly, endurance-trained adults reveal greater absolute (ml/kg/min/year) rates of decline in VO_2max with advancing age compared with healthy sedentary adults, with no differences in the relative (%) rate of decline (24). However, despite the subsequent decrease, endurance performance remains about 3.5.-fold higher in lifelong endurance athletes up to 70+ years compared with their untrained peers (26). This is of great importance as the superior aerobic capacity of the trained adults provides a large functional reserve above the aerobic frailty threshold and is associated with lower risk of disability and mortality (7). Recently, a population-based follow-up study of 579 middle-aged men suggested that a 1 ml/kg/min higher VO_2max at reexamination at 11 years was associated with a 9% relative risk reduction in all-cause mortality, emphasizing the importance of maintaining good CRF over the decades (27). As described by Myers *et al.* (28), a VO_2max of 17.5. ml/kg/min (5 METs) is necessary for an independent lifestyle and a higher survival rate. If the VO_2max decreases below 3 METs, the basal metabolism requires more than 30% of VO_2max. This situation very soon leads to exhaustion and decompensation of the circulatory and respiratory system, and thus to natural death. Aging plus physical inactivity initiates a circulus vitiosus dramatically affecting the oxygen delivery and utilization systems, and thus VO_2max (7). Whereas in the healthy elderly, this circulus vitiosus is starting from inactive locomotor muscles, the heart and/or the lung constitute the origin in patients who suffer from cardiorespiratory diseases. Appropriate exercise training programs undoubtedly represent the most important and effective intervention to prevent or break this circulus vitiosus.

5.2. Training and skeletal muscle

Both endurance and resistance training programs elicit rapid (within weeks) and pronounced effects on strength and muscle mass, aerobic and anaerobic capacity, and the related beneficial implications on the cardiovascular and respiratory systems of healthy adults. Even a 6-week resistance training program (2–3 sessions per week) may result in a 50% strength gain in sedentary healthy elderly individuals (29). Resistance training activates satellite cells, myogenic progenitor cells that are responsible for renewal and repair of myofibers (30). In addition,

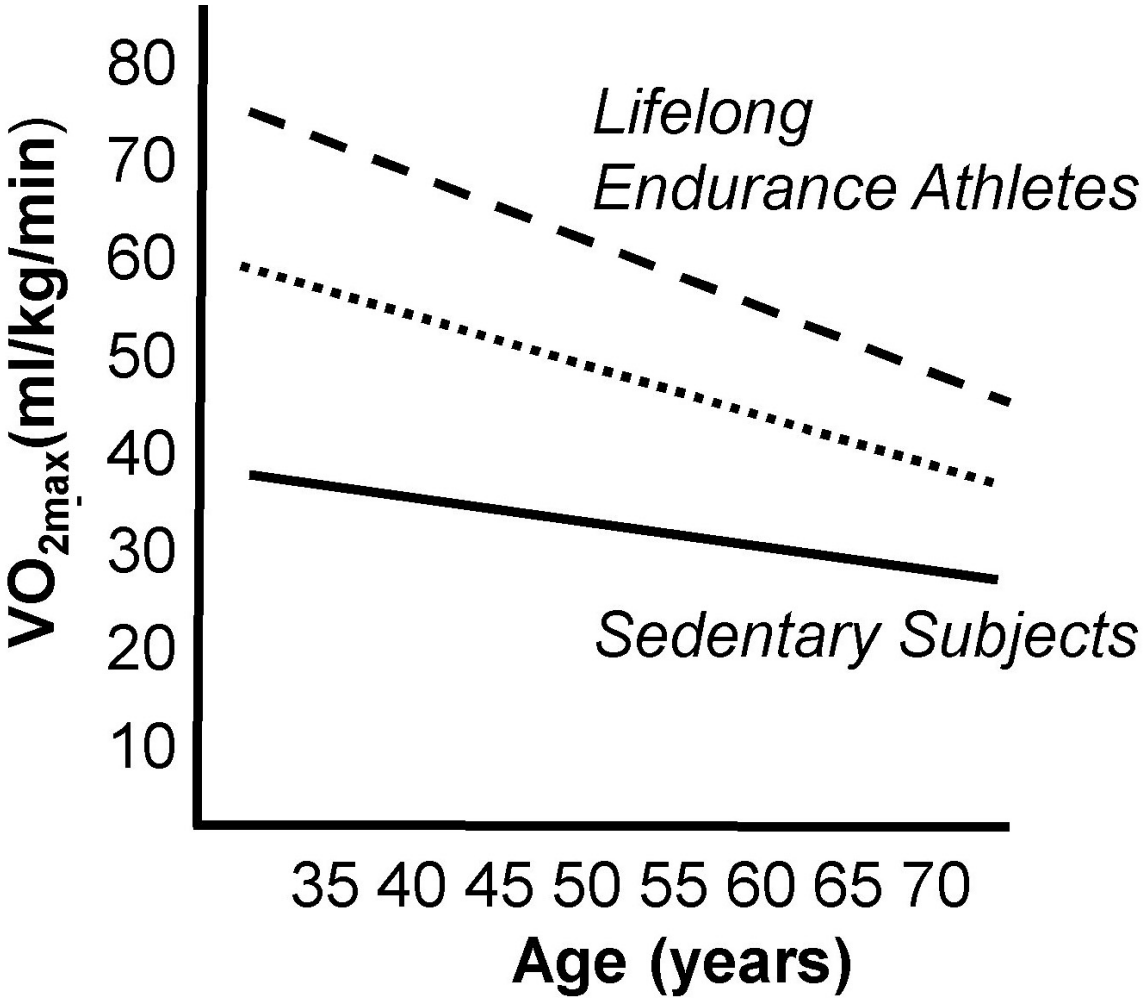

Figure 1. Age-related decline of maximal oxygen uptake (VO_2max) in endurance trained male (- - -) and female (···) athletes versus sedentary control subjects (—); (as described by ref. 24, 25).

resistance training is also capable of promoting mitochondrial biogenesis, thereby improving oxygen extraction within the working muscle, and finally VO_2max (31, 32). Whereas resistance training is the method of choice to maintain or improve skeletal muscle mass and strength, endurance training represents the preferred intervention to improve CRF. A considerable increase in VO_2max has also been demonstrated in young and elderly subjects in response to a 12-week endurance training period (33). The 30% VO_2max improvement in the elderly was achieved by both an increase in cardiac output (70%) and an increment in oxygen extraction (30%) in working muscles. Adaptations resulting from endurance training at the level of the locomotor muscles include improved capillary supply and increases in mitochondrial key enzyme activities (7). Consequently, the trained muscles work at a higher rate of fat oxidation at the same exercise intensity, spare muscle glycogen with less lactate accumulation, finally resulting in improved exercise tolerance. High exercise tolerance is an important prerequisite to perform prolonged exercise during daily physical activities, leisure time activities, or exercise training. VO_2max can only be maintained for a few minutes, but such prolonged exercises are typically performed for a longer duration (up to hours). Obviously, the individual VO_2max value does not determine the ability to perform sustained exercise, but represents an upper limit. The capability of using a high percentage of VO_2max is a typical consequence of adaptations in skeletal muscle due to chronic exercise training (34).

5.3. Training and the cardiorespiratory system

Whereas training adaptations in skeletal muscles are especially important to perform sustained exercise, the cardiovascular system represents the primary limitation of VO_2max in the young and the elderly as well. VO_2max is negatively affected by aging, but training can dramatically improve VO_2max

values in sedentary elderly people (33). Whereas HRmax inevitably declines with age and will not change markedly with training, the increase in stroke volume represents the main adaptation to endurance training responsible for the increment in Qmax and related VO_2max. Even after short-term (6 days) endurance training, improved left ventricular function, Qmax, and VO_2max have been demonstrated (35). These short-term effects have been attributed to the exercise-induced rapid expansion of plasma volume associated with improved ventricular filling and increased stroke volume secondary to a Frank–Starling effect. During subsequent continuation of the training stimulus, these short-term effects might cause the well-known structural adaptations of the heart. Besides, endurance training can increase nitric oxide bioavailability, which has been suggested to represent the most important modulatory factor in vascular aging (17). As is true for other skeletal muscles, respiratory muscle strength and endurance are also negatively affected by advancing age (36). Usual endurance exercise training, especially when combined with specific training of the respiratory muscles, has been shown to prevent or improve respiratory muscle dysfunction, thereby supporting the preservation or improvement of exercise tolerance, and finally VO_2max (37).

5.4. How much exercise is needed?

Considering the benefits of physical exercise in improving functional capacity, an important question is: how much physical activity is needed to confer such benefits? Implicit within current guidelines for physical activity and health is the observation that 75 minutes of weekly higher intensity exercise is equivalent to 150 minutes of moderate-intensity exercise to achieve a total energy expenditure of ≥500–1000 METs/min/week (38). However, even less than the currently recommended amount of time seems to be effective. A study by Wen *et al.* (39) found that a 5-min run generates the same benefits as a 15-min walk, and a 25-min run is equivalent to a 105-min walk in terms of mortality reduction. Likewise, the study by Lee *et al.* (40) showed reduced mortality from all-cause (30%) and cardiovascular disease (45%) from 5- to 10-min runs per day. Accordingly, in contrast to traditional high-volume endurance training (at 3–6 METs), higher intensity exercise (at ≥6 METs) can be a time-efficient strategy to improve health and increase life expectancy.

A growing body of evidence also suggests that muscular strength is inversely and independently associated with all-cause and cardiovascular mortality even after adjusting for CRF and other cofactors such as age, body fat, smoking, and hypertension (41). Especially in the oldest old population, poor handgrip strength has been linked to premature mortality, and this association tended to be stronger in women (42). Regular resistance training not only increases muscular strength and functional mobility, but also has the potential to increase the intrinsic function of mitochondria in skeletal muscles and may offer an alternative approach to improve mitochondrial oxidative capacity (43), which is particularly important for older adults and patients with chronic conditions resulting from sarcopenia and muscle weakness (44). A resistance training program should be performed on a minimum of two, non-consecutive days per week (38). The loading intensity to promote hypertrophy should approach 60–80% of one repetition maximum with an exercise volume ranging from three to six sets per muscle group per week of 10–15 repetitions per exercise (45).

6. CRF IN THE CLINICAL SETTING

6.1. Measurement of CRF

CRF can be measured directly, expressed as VO_2max, ideally via a cardiopulmonary exercise test (CPX) to exhaustion. The subject cycles on an ergometer, while his/her oxygen consumption (VO_2) and carbon dioxide production (VCO_2) is measured by indirect calorimetry. During the test, expired air is collected by a facemask to analyze ventilation (V_E) and gas fractions breath-by-breath at each power level and before completion of the test. VO_2max is generally reached if the following criteria are met: a respiratory exchange ratio (RER = VCO_2/VO_2) greater than 1.1.0 and a respiratory equivalent for O_2 (V_E/VO_2) to 35 or more. Conversely, the respiratory equivalent for CO_2 (V_E/VCO_2) has high clinical utility as it is abnormally elevated (≥45) in patients with cardiovascular or pulmonary disease (46). But because it is easier to obtain, CRF can also be estimated from the maximal work rate, expressed as watts, achieved on a cycle ergometer according to the formula proposed by Wasserman *et al.* (47): VO_2 (ml) = body mass (kg) × 6.3. + 10.2. × maximal power (W). The protocol usually consists of a 5-min warm-up period, after which the workload is set at 50 W and is increased by 25 W every 2 min until exhaustion.

Numerous studies have reported that CRF has a significant influence on survival rate in patients suffering from lung and/or cardiovascular diseases and cancer. Moreover, CRF is a strong predictor of postoperative complications in patients undergoing cardiovascular and noncardiovascular surgery (5). The next sections provide the reader with a view of clinically relevant studies, with specific reference to the main organs (lung, heart, skeletal muscles) involved in oxygen delivery and utilization as well as the importance of exercise training for promoting life expectancy in clinically referred populations.

6.2. Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a progressive disorder characterized by progressive airflow limitation that leads to substantial morbidity and mortality. Muscle wasting and dysfunction is common and associated with limitation of exercise capacity and poor disease prognosis (48). Although the diseased respiratory system represents the origin in patients suffering from COPD, rapid deadaptation of skeletal muscles and cardiovascular function further contribute to exercise intolerance promoting physical inactivity, thereby negatively affecting cardiorespiratory health (7). Physical training is considered as the cornerstone of pulmonary rehabilitation to improve exercise tolerance and muscle function (49). However, exercise outcomes after pulmonary rehabilitation depend on the contribution of limiting factors of the main organs involved in oxygen delivery and utilization. For example, only small training adaptations occurred with regard to VO_2max in patients who were primarily ventilatory limited, whereas the improvements were three times higher in patients who were solely cardiovascular limited (5)). The prevention and treatment of muscle weakness and dysfunction is of most importance in COPD patients as enhancements in lower limb muscle strength enable higher training intensities and thus cardiovascular adaptations, resulting in more pronounced increases in VO_2max. Based on our own results, progressive resistance training increased not only muscle strength and quality of life, but also exercise capacity in patients with COPD (51). Furthermore, a key finding of a meta-analysis of randomized clinical trials was that resistance training may indeed improve respiratory function in patients with COPD due to a fall in ventilatory demand during exercise and improved ventilatory capacity by increases in maximum minute ventilation (52). The objective of the NUTRAIN trial was to study whether nutritional supplementation targeting muscle derangements enhances the outcome of exercise training in COPD patients with low muscle mass (53). Interestingly, no additional effect of nutritional intervention was shown on lower limb muscle strength as a primary outcome measure, supporting the notion that the training component *per se* is of primary importance when it comes to improving muscle strength and exercise performance in COPD patients with moderate airflow obstruction. Importantly in this context, a recent study using 2003–2006 NHANES data found that participation in muscle-strengthening activities is independently associated with reduced all-cause mortality in COPD (54). Specific exercise training programs, such as training of the small muscle groups of the lower limbs (e.g., one-leg knee extensions) as well as one-leg high-intensity interval cycling are effective interventions to improve exercise tolerance and VO_2max and to break the circulus vitiosus, thereby promoting life expectancy in aging COPD patients (7).

6.3. Heart failure

Chronic heart failure (HF) increases with age and is associated with a high mortality rate and poor quality of life due to low exercise tolerance and shortness of breath. While low CRF and obesity are risk factors for HF in general (55), myocardial infarction is the leading cause of the development of HF characterized by a dilated and poorly functioning ventricle. During exercise, HF patients exhibit diminished cardiac output and a reduction in muscle blood flow, which subsequently lead to deadaptation of skeletal muscles (7). On the other hand, current evidence provides promising results from exercise training in patients suffering from HF (56), with significantly greater VO_2max improvements in older adults with preserved ejection fraction compared with individuals with reduced ejection fraction (57). In particular, local skeletal muscle training (e.g., isolated quadriceps training) is a powerful approach to combat exercise intolerance in HF. Small muscle mass training stimulates intramuscular adaptations contributing to O_2 transport and oxidative metabolism (e.g., increased capillarity and mitochondrial density) and significantly enhances skeletal muscle O_2 delivery and diffusive conductance, yielding a significant increase in VO_2max, without a change in cardiac output (58). The physiologic adaptations attributed to muscle training may allow trained older adults with HF to better tolerate submaximal workloads such as those encountered during day-to-day functional activities. For example, a typical older HF patient with a VO_2max of 15 ml/kg/min may have difficulty walking faster than 3 km/h for a sustained period of time and usually cannot climb more than 10 steps/min, as these tasks represent an increasing percentage of the individual's maximum aerobic power. Above all, however, high-intensity training (e.g., 4-min intervals at 85–95% of maximum heart rates, separated by 3-min active pauses, performed on 3 days per week) seems to provoke both systemic and skeletal muscle adaptations (59). Indeed, the findings of a recent meta-analysis indicate that the magnitude of gain in CRF is greater with increasing exercise intensity, accompanied by lower study withdrawal and hospitalization in exercising patients (60). Thus, the intensity of exercise may be an important factor in reversing left ventricular remodeling, improving aerobic capacity, and quality of life in patients with HF.

6.4. Cancer

Epidemiologic studies have reported that higher levels of CRF are associated with a lower risk of developing certain cancers, including breast and lung cancer (61, 62). Based on a recent meta-analysis, increased CRF represents a strong predictor of decreased total cancer mortality risk, independent of adiposity (63). Furthermore, randomized controlled

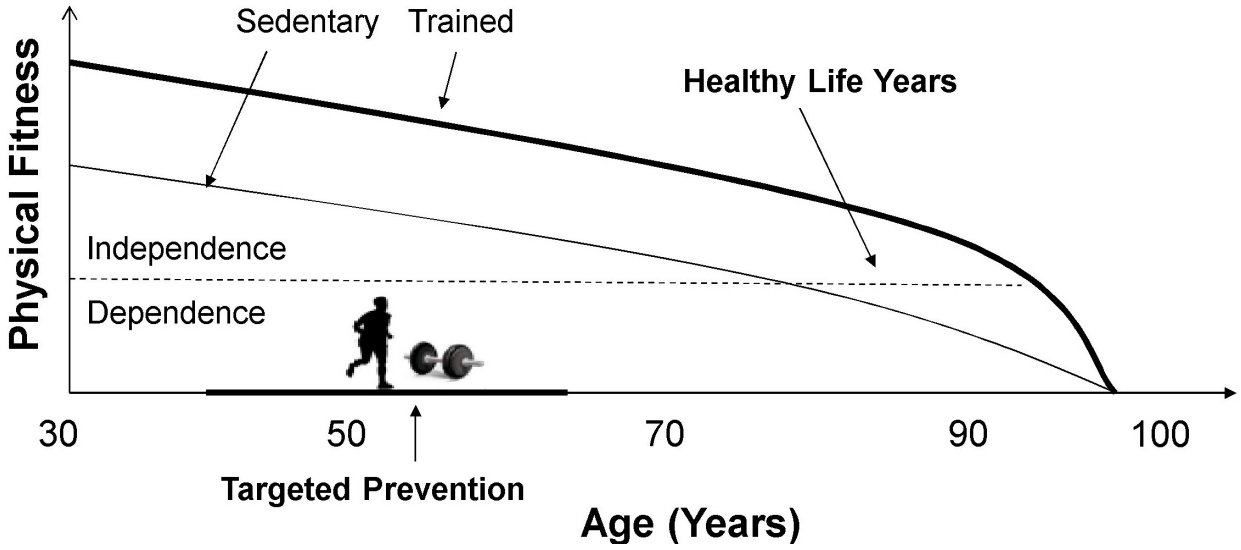

Figure 2. Hypothesis of physical fitness (cardiorespiratory fitness and muscle strength) on Healthy Life Years (disability-free life expectancy) in trained versus sedentary subjects. The dotted line represents the prognostic exercise capacity generally necessary for an independent lifestyle and associated with an increased risk for mortality. The cut-off values are: 17.5. ml/kg/min (5 METs) for aerobic capacity (28); 30 kg and 18 kg for grip strength in men and women aged over 65 years, respectively (42).

trials show a beneficial effect of physical activity on CRF, body composition, and quality of life in cancer survivors (64). In general, cancer patients exhibit marked and significantly impaired cardiopulmonary function during and after chemotherapy (65). Hereby, chemotherapy appears to impair CRF by influencing the oxygen delivery system. Moreover, muscle atrophy is an unfortunate effect of many wasting diseases and can compromise physical function and impair vital metabolic processes (66). The consequences of muscle wasting are serious, leading to weakness, disability, impaired quality of life, increased hospitalization, morbidity, and mortality (44). Thus, early interventions to enhance aerobic and muscular fitness in cancer patients are of vital importance. The Physical Exercise During Adjuvant Chemotherapy Effectiveness Study (PACES) suggests that a supervised, moderate- to high-intensity, combined resistance and aerobic exercise program is most effective for patients with breast cancer undergoing adjuvant chemotherapy in minimizing decline in CRF and muscle strength, limiting fatigue and symptom burden, and facilitating return to work (67). Results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study found that both a high-intensity and a low- to moderate-intensity resistance and endurance exercise program over 12 weeks are effective in reducing general and physical fatigue, but favoring high-intensity training when it comes to improving VO_2max (mean VO_2max improvements of 4.4. ml/kg/min after high-intensity versus 3.3. ml/kg/min after low- to moderate-intensity training) (68). Even shorter term high-intensity endurance training over 4 weeks appears to offer superior and clinically meaningful improvements in VO_2max (+ 3.5. ml/kg/min) in comparison to current physical activity guidelines for colorectal cancer survivors following treatment (69). There arises the question whether short-term preoperative exercise training enhances CRF before cancer surgery and thus reduces the risk of postoperative complications?

The preoperative period may provide an opportunity to increase the physiologic reserve (functional capacity) before surgery with the intention of improving outcomes and accelerating recovery (70). Recently, preoperative high-intensity interval training (median 25 days) resulted in significant improvements in VO_2max (median +15%), whereas aerobic capacity declined in the usual care group (median –8%) (71). Furthermore, the incidence of pulmonary complications was significantly lower in the training compared with the usual care group (23% versus 44%). Although preoperative exercise therapy may have beneficial effects on various physical fitness variables and postoperative complications in cancer patients scheduled for surgery, future research has to focus on developing patient-tailored exercise programs based on objective assessments of CRF and muscle function and investigating the influence of co-existing comorbidities (e.g., protein-energy malnutrition) on the outcome measures.

7. CONCLUSION

As yet, it is not possible to extend the genetically fixed lifespan with regular exercise training, but the chance to reach the later end of natural lifespan increases with higher physical fitness in midlife, where targeted preventative efforts may be launched. CRF (VO_2max) is the strongest

independent predictor of future life expectancy in both healthy and cardiorespiratory-diseased individuals. In addition, muscle stimulation is essential in order to prevent muscle wasting, disability, and increased hospitalization in old age, all crucial ways to avoid long-term care, thereby promoting quality of life in aging humans (Figure 2). Thus, extending life is not as important as giving those years more life. This is where physical fitness plays an important role.

8. ACKNOWLEGEMENT

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