

## The Good, the Bad, and the Ugly about VO<sub>2</sub> Max as a Biomarker of Healthy Aging and Life Expectancy

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### ABSTRACT

The VO<sub>2</sub> max is generally considered as the ultimate value for characterizing the maximal capacity at a given point in time of the cardiovascular, respiratory, and muscular systems to use oxygen as main source of energy for aerobic performances. It is therefore often measured to assess quantitatively the efficacy of an aerobic training program on corresponding physiological functions as well as to make prediction about the quality of life and life expectancy of individuals performing endurance training on a regular basis. Paradoxically, however, VO<sub>2</sub> max gains may also be associated with the development of chronic pathological conditions depending on the type of training approach used. Increasing evidence suggests indeed that intensive training and repeated exhausting performances such those performed by marathon and triathlon athletes can increase the incidence of sudden cardiac death, atherosclerosis, coronary artery calcification, thrombophilia, impaired ventricular size, ventricular arrhythmias, myocardial fibrosis, and late gadolinium enhancement. This short article summarizes recent findings on pathological conditions and life-threatening consequences associated with VO<sub>2</sub> max increase induced by extreme endurance training.

### **KEYWORDS**

Marathon; Running; Cardiac arrest; Calcium plaque; Atherosclerosis; Inflammation; Cardiovascular capacity; Aerobic; Aging; Overtraining

### LETTER TO EDITOR

The VO<sub>2</sub> max is a quantitative value measured to assess the maximum amount of oxygen an individual can absorb, carry, and consume (by skeletal muscles) to perform a motor performance at a given moment in time. As such, it is generally used as an indicator or a biomarker of cardiorespiratory fitness (CRF). VO<sub>2</sub> max values are thus expressed as an absolute rate in liters of oxygen per

minute (L/min) or as a relative rate in milliliters of oxygen per kilogram of body mass per minute (mL/kg/min). In sedentary adults, average VO<sub>2</sub> max values normally range between 47.4 ml/kg/min (men) and 35.6 ml/kg/min (women) whereas, in active people, normal values range instead between 50.6 ml/kg/min and 38.9 ml/kg/min (men and women, respectively) [1]. Among high-performance athletes, Bjørn Daehlie, an Olympic cross-country skier, holds the highest score ever

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recorded officially - 96 ml/kg/ml [2] although Oskar Svendsen, a Swedish cyclist, reported to have reached unofficially 97.5 ml/kg/ml. In patients with a cardiac rehabilitation exercise program or in athletes who train for high performances and competitive races,  $VO_2$  max is generally used as a measure of progress [3]; (University of California School of Medicine, health.ucdavis.edu).

### **THE GOOD**

It is well-known that a sedentary lifestyle and physical inactivity may increase the incidence of metabolic disorders and obesity (CDC data - [www.cdc.gov/physicalactivity/basics/adults/index.htm](http://www.cdc.gov/physicalactivity/basics/adults/index.htm)).

Aging, also a factor increasing the incidence of those health problems, is associated with  $VO_2$  max values that generally decline by about 2% per year after 30-years old (health.ucdavis.edu). Yet, active walking at least 30 minutes per day, 5-days a week has clearly been shown to prevent or reverse metabolic disorders and other cardiovascular problem. Since  $VO_2$  max values typically increase with levels of aerobic training and active walking, swimming, biking or running, they are considered as the best marker of cardiorespiratory fitness. Its increase in percentage induced by training, although dependent on many variables, can normally be increased by 5% - 30% with greatest effects in those who are the least fit (health.ucdavis.edu). The  $VO_2$  max is therefore also considered by generalists and cardiologists as one of the best predictors or biomarkers of longevity - a  $VO_2$  max increase of 1 mg/kg/min is associated on average with an estimated 45-days increase in life expectancy [4]. Others have determined that an increase of 1 metabolic equivalent or MET can be associated with an increase of survival of 12% [5]. Higher METs,  $VO_2$  max values and CRF levels are also associated with numerous health benefits including better quality of life, improved mood and self-esteem, and improved sleep patterns (health.ucdavis.edu). More specifically, they are generally believed to prevent the development or the incidence of

dyslipidemia, osteoporosis, breast cancer, cognitive dysfunction, colon cancer, constipation, deep vein thrombosis, depression and anxiety, hypertension, immune problems, metabolic syndrome, and obesity, to name a few.

### **THE BAD**

However, long-term or excessive endurance exercise has also been shown recently to impair (e.g., scars, plaques, deformation) and stress (e.g., inflammation) the cardiovascular systems. Del Coso, et al. [6] reported that biomarkers of cardiovascular stress such as myoglobin concentration and electrolyte imbalances increase significantly in full marathon runners compared with athletes running shorter distances such as half-marathons. Less than 24 hours after a marathon, high levels of inflammatory and clotting factors such as creatine kinase - MB are found [7] - Biomarkers of inflammation such as c-reactive protein (CRP) and calcium plaque build-up increase significantly (American College of Cardiology July 28, 2017). According to experts from the Baylor Heart and Vascular Institute, running more than three hours induces a pathophysiological augmentation of right atrium and right ventricle volume (size) associated with an increase of heart injury biomarkers.

### **THE UGLY**

The study of Clausen and colleagues also revealed paradoxically that higher levels of  $VO_2$  max and cardiorespiratory fitness (CRF) are associated with an increased incidence of cardiovascular mortality [4]. This may be explained by the type of training programs used to increase  $VO_2$  max and CRF values. During many years, it was believed that long-distance were not at risks for cardiovascular problems [8]. However, sudden cardiac deaths (SCD) and other life-threatening complications have increasingly been found in recent years. SCD has been found to affect 135 people among 9 million endurance athletes since the 1990s. In general, data from

the literature indicate that about one of every 100,000 marathon runners experience SCD but a near two-fold increase (one of every 57,000 participants) occur during a long-distance race (e.g., 42 kilometers) [9]. Unheralded ventricular arrhythmias, myocardial fibrosis, and late gadolinium enhancement have been reported in experienced endurance athletes who also express a 5-fold increase in the prevalence of atrial fibrillation [10,11]. In fact, myocardial fibrosis (patchy interstitial or dense scars) found in long-distance runners and other elite athletes was shown recently to underlie the expression of arrhythmias [12]. High incidence of coronary artery calcification, atherosclerosis, and damaged myocardial cells in long-term marathon, ultramarathon, and extreme runners (much less in submarathon runners) have also been found [13-15].

### **TAKE-HOME MESSAGE**

All in all, the cardiovascular and respiratory benefits of endurance exercise training are well accepted but the tipping point where the physiologic remodeling of the cardiovascular and respiratory systems becomes pathologic is yet somewhat unclear. This said, a large study revealed that health benefits generally increase in a dose-dependent fashion with exercising up to about an hour per day, beyond which more aerobic training does not yield more benefits [10] which may suggest that shorter distances (e.g., 10 Ks or less) should be performed by athletes rather than marathons, triathlons, ultra-

marathons, ultra-triathlons or corresponding extreme training programs associated with them. In fact, high-intensity interval training or HIIT - i.e., short bursts of intense exercise alternated with low-intensity recovery periods - are increasingly being proposed by medical doctors, cardiologists, and physiotherapists for patients who have had cardiac problems [16,17].

### **6. CONCLUSION**

Exercising 15 minutes (e.g., high-intensity) or 30 minutes (e.g., moderate intensity) per day, 5 days a week is generally recognized as the threshold level for cardiovascular, respiratory, metabolic and immune benefits. On the other hand, long-distance runners are generally at the risk of developing life-threatening acute or chronic cardiovascular problems including SCD and adverse structural remodeling of the heart and large arteries. A safer limit probably exists, beyond which adverse effects on health out-weight the cardiovascular benefits of regular aerobic exercise training. HIIT 75 minutes per week (e.g., 15 minutes per training session) or moderate-intensity training 150 minutes per week (e.g., active walking or mild jogging) may be considered as a reasonable option for better and faster results on VO<sub>2</sub> max/CRF increase, long-lasting physiological benefits, and longevity without the deleterious and life-threatening acute and chronic consequences of excessive endurance training, marathons, and triathlons [18,19].

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