Review Article

Physical Inactivity and Mortality Risk

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In recent years a plethora of epidemiologic evidence accumulated supports a strong, independent and inverse, association between physical activity and the fitness status of an individual and mortality in apparently healthy individuals and diseased populations. These health benefits are realized at relatively low fitness levels and increase with higher physical activity patterns or fitness status in a dose-response fashion. The risk reduction is at least in part attributed to the favorable effect of exercise or physical activity on the cardiovascular risk factors, namely, blood pressure, diabetes mellitus and obesity. In this review, we examine evidence from epidemiologic and interventional studies in support of the association between exercise and physical activity and health. In addition, we present the exercise effects on the aforementioned risk factors. Finally, we include select dietary approaches and their impact on risk factors and overall mortality risk.

1. Introduction

The conventional wisdom since antiquity has been that a healthy lifestyle leads to prolonged and healthy life. Although a precise definition of a healthy lifestyle is not established, data acquired from the Framingham Heart Study have helped identify several behaviors that predispose an individual to a higher risk for future cardiovascular events and early mortality. These behaviors, coined as risk factors, include age, gender, heredity (nonmodifiable) and diabetes mellitus, hypertension, dyslipidemia, smoking, physical inactivity, and obesity referred to as modifiable risk factors.

The modifiable risk factors are influenced by a number of variables including diet and exercise. In this review, we present a synopsis of some of the most influential studies examining the effects of physical activity and diet and the traditional CV risk factors and mortality. Finally, we consider the clinical applications of this evidence.

2. Physical Activity and Health

Interest in the relationship between physical activity, fitness, and health was generated by the landmark work by Morris

and coworkers who reported significantly lower mortality rates in civil servants with physically demanding occupations when compared to desk clerks [1]. The plethora of evidences accumulated since then from occupational, leisure time and fitness assessment studies support a strong, inverse, and independent association between physical activity, health, and cardiovascular (CV) and overall mortality in apparently healthy individuals [2–26] and in those with documented CV disease [23]. The association is as robust as that of established risk factors [2]. A detailed account of the most influential studies in each category follows.

3. Occupational and Leisure Time Studies

The findings of occupational studies on 6,351 longshoremen [3] and those of 16,963 Harvard alumni support an inverse association between physical work and cardiovascular mortality [6, 7]. The findings of these studies support a sharp reduction in fatal and nonfatal heart attack rates with increase in weekly energy expenditure of ≥ 2000 Kcal per week. Those who expended less than 2,000 Kcal per week had 64% higher risk for a heart attack. An important finding of this study was that reduction in risk was only

evident if physical activity was maintained throughout life. Those who played varsity sports, but did not maintain a physically active lifestyle had higher mortality rate compared to those who maintained a physically active lifestyle in adulthood. Moreover, those who avoided athletics in college but subsequently took up a more active lifestyle also had similarly low rates of mortality [6].

In the next two reports that followed on the same cohort, a consistent, inverse, and graded trend towards lower all-cause mortality rate was noted. As physical activity-related caloric expenditure increased from 500 Kcal to 2000 Kcal per week the mortality rate decreased. More specifically, the mortality risk for men whose weekly energy expenditure from leisure time activities total 2000 Kcal or more had about 25% to 33% lower mortality rate compared to those with caloric expenditure less than 2000 Kcal per week. An interesting observation of this study was that the mortality risk tended to increase slightly in those expending more than 3,500 Kcal per week suggesting that exercise beyond a certain level may be harmful to some [7]. This will be equivalent to about 30–35 miles of jogging per week.

In the more recent study, the relative risk of death based on different types of physical activity that included walking (miles/week), stair-climbing (floors), and sports playing in 10,269 Harvard alumni over a 9-year period was examined [8]. Particularly noteworthy in this study was the 30% to 40% reduction in mortality risk, evident in those individuals engaging in moderate to vigorous activity levels (≥ 4.5 METs) with only minimal additional benefits achieved by engaging in activities of greater intensity. The reduction was similar, when physical activity was expressed as kilocalories per week (the sum of walking, stair climbing, and sports participation) suggesting that a 40% reduction in mortality occurs by engaging in modest levels of activity (1,000 to 2,000 kcal/week, equivalent to three to five 1-hour sessions of activity).

Collectively, the findings of these studies [3, 6, 8] provided evidence in support of an exercise intensity threshold of about 5–6 METs and an exercise volume threshold somewhere between 1,000 to 2000 Kcal per week for significant reduction in mortality risk. Furthermore, the findings suggest that most of the benefits occur at moderate exercise volumes and moderate intensities.

Fatal and nonfatal coronary events were also assessed in 5,288 men and 5,229 women who lived in 58 settlements called kibbutzim [4]. A unique aspect of this study is that these settlements (kibbutzim) provided communal dining facilities and similar medical care for a relatively homogeneous group. Thus, many of the confounding factors present in epidemiologic studies were eliminated. In addition, risk factors were similar in between physically active and sedentary groups. The relative risk for coronary events of this 15-year followup study was 2.5-times higher in men in sedentary occupations compared to the men who performed more physically demanding jobs. For women, the risk was 3.1-times greater for the corresponding occupations [4].

Similar results have been reported from large studies that have followed cohorts for CHD morbidity and mortality in the range of 10 to 20 years among British civil servants,

U.S. railroad workers, San Francisco longshoremen, nurses, physicians, other health care workers, and other cohorts. The findings of these studies are summarized in two comprehensive reviews [9, 10].

The influence of genetic factors in the reduction of the mortality risk cannot be dismissed. A valid agreement can be made that it is not the physical activity that provides protection, but the genetic composition of these individuals. In this regard, the independent association of physical activity and mortality and the influence of genetic and other familial factors were assessed in a cohort of same-sex twins born in Finland before 1958 and with both alive in 1967 [12]. In 1975, healthy men ($n = 7,925$) and women ($n = 7,977$) responded to a questionnaire on physical activity, occupation, smoking habits, body weight, alcohol use, and physician-diagnosed diseases. Individuals who reported engaging in a brisk walk for a mean duration of 30 minutes, at least 6 times per month were classified as physically active. Those who reported no leisure time activity were classified as sedentary. The remaining individuals were classified as occasional exercisers. When compared to the sedentary twins, the adjusted risk of mortality was 33% lower among the twins who exercised occasionally and 44% lower among the physically active twins. These findings suggest that physical activity is associated with lower mortality independent of genetic and other confounding factors.

In contrast to these reports, a Finnish study found that the rate of coronary heart disease mortality was greater among lumberjacks compared to less active farmers of the same region [5]. However, these finding must be interpreted with caution for two reasons. Although farmers may have been less active than lumberjacks, they were not sedentary. Thus, the study compared highly active individuals (lumberjacks) to somewhat less active (farmers). This along with the higher fat consumption and smoking rates among lumberjacks is likely to have attenuated the positive effects of physical activity in the lumberjacks and showed more favorable outcomes for the farmers.

Clearly, the accumulated evidence from observational studies provided strong support for the existence of a strong inverse relationship between physical exercise and coronary heart disease risk. In a recent review that included 44 observational studies from 1966 to 2000, the findings are summarized as follows. First, there is strong evidence of an inverse linear dose-response relationship between volume of physical activity and all-cause mortality. Second, an exercise volume threshold can be defined beyond which a significant reduction in mortality risk occurs. Such threshold appears to be at caloric expenditure of approximately 1,000 Kcal per week was defined as the threshold for an average reduction of 20% to 30% in mortality risk. Further reductions in risk are observed with higher volumes of energy expenditure. The independent contribution of the exercise components of intensity, duration, and frequency to the reduction of mortality risk was not clear and the need for more research to better understand the contribution of each component is emphasized [11]. Efforts to define the intensity, duration, frequency, volume, and type of exercise necessary for cardiovascular health and longevity continue.

4. Physical Fitness Studies

A shift from assessing physical activity by questionnaires to a more objective assessment was provided by Blair and coinvestigators [13]. In study, 10,224 men and 3,120 women underwent a maximal exercise test exercise. They were then grouped into five fitness categories based on the MET level achieved. In a follow-up period of over 8 years, the adjusted relationship between exercise capacity, cardiovascular, and all-cause mortality inverse, and graded for both men and women. The major reduction in mortality risk occurred when moving from the least fit (<6 METs) to the next fit category of 7 METs, continued to decline with higher fitness levels and appears to plateau at approximately 9 to 10 METs for women and men, respectively. These findings suggest that health benefits are realized at relatively moderate fitness levels attainable by a brisk walk of 30 to 60 minutes each day. The investigators also reported similar findings in much larger cohort when the impact of fitness was assessed within groups who possess specific risk factors such as hypertension, diabetes, or smoking [14].

Although the physical activity-mortality relationship is well established by now, information on the intensity, duration, and type of physical activity is still speculative. An exercise intensity threshold of about 6 METs for a reduction in risk has been suggested by some [15]. Others have shown an independent effect of exercise type, intensity, and duration on the risk for coronary heart disease. It is noteworthy that this is the first study to provide evidence on the efficacy of weight training or resistance exercise on coronary heart disease risk reduction. The risk reduction was similar to that provided by a brisk walking 30 or more minutes [16].

Although exercise intensity, duration, and volume were inversely related to coronary heart disease, the much stronger association between intensity and risk suggests that walking intensity has a stronger effect on risk reduction than duration [16].

5. A Dose-Response Association

Recently, several studies have reported a more precise quantification of the dose (amount of exercise or degree of fitness) and response (mortality risk-reduction) relationship by expressing exercise capacity in the context of survival benefit per MET. These studies present the change in mortality risk for each 1-MET increases in exercise capacity assessed by a maximal exercise test. The reduction in mortality risk per 1-MET increase in exercise capacity ranges between 10% and 25% [17–27]. This is evident in both men and women. There is also evidence to suggest that the strength of exercise capacity in predicting risk of mortality may even be greater among women than men, reporting [19, 25].

It is well documented that the age-adjusted all-cause mortality rates in African-Americans are as much as 60% higher when compared to Caucasians. In a recent study we assessed the association between physical activity, exercise capacity, and mortality among 6,749 African-American and 8,911 Caucasian men [24]. We found exercise capacity to

be a more powerful predictor of risk for all-cause mortality than established risk factors (smoking, dyslipidemia, diabetes, and hypertension) among both African-Americans and Caucasians after adjusting for cardiac medications. The risk for mortality was 13% lower for every 1-MET increase in exercise capacity for the entire cohort with similar reductions observed for those with and without CVD. When fitness groups were considered, the relative risk for all-cause mortality was approximately 20% lower in those with an exercise capacity of 5–7 METs (Moderate-Fit category) when compared to those achieving <5 METs. The mortality risk was 50% lower for those with an exercise capacity 7.1 to 10 METs and 70% lower for those with an exercise capacity of more than 10 METs. This gradient for a reduction in mortality with increasing fitness was similar in African-Americans and Caucasians in the entire cohort and in individuals with and without CVD.

Similar findings were reported in men 65–92 years of age during a 20-year follow-up period. To account for the possibility that the higher mortality rates observed in the low-fit categories were the result of underlying diseases (such as cachexia), musculoskeletal, or peripheral vascular issues and not low fitness per se (reverse causality), the investigators undertook three approaches: (1) excluded those who died within the initial two years of followup, (2) excluded those who were not treated with beta-blockers but did not achieve at least 85% of their age-predicted maximal heart rate (to account for factors that may have impaired exercise performance), and (3) excluded those in the two lowest fit categories (≤ 5 METs) with BMI < 20; and finally excluded all those who met all three conditions. We then repeated the survival analyses separately (for each exclusion), as well as with all exclusions combined. In all four scenarios, the association between exercise capacity and mortality risk remained robust and the risk reduction did not deviate substantially from that observed in the entire cohort. The similarity in trends and magnitude of risk reduction observed between the findings of the entire cohort and these four separate analyses argues against the likelihood of reverse causality and supports the validity of fitness and mortality risk association. Another noteworthy finding in this study is that the mortality risk of individuals who were unfit during the initial evaluation but became fit during the followup was 35% when compared to those who remained unfit [26]. These findings are similar to those reported by Blair et al. [17].

These findings have significant public health implications. Mortality risk can be cut in half regardless of age or race by just engaging in brisk walk for 2–3 hours per week or 30 minutes per session 4–5 days per week. Collectively, the findings of the aforementioned studies support the concept that exercise capacity should be given as much attention by clinicians as other major risk factors.

6. Physical Activity, Risk Factors, and Mortality

As mentioned previously, the exercise-related health benefits are in part related to favorable modulations in CV risk factors that have been observed with increased physical activity

patterns or structured exercise programs [27]. In this regard, we present data to support the effects of physical activity or exercise capacity on select cardiac risk factors.

7. Hypertension and Physical Activity

Chronic hypertension is recognized as a major and the most common risk factor for developing cardiovascular disease [28–30]. This relationship is direct, strong, continuous, graded, consistent, predictive, and independent [31]. The mortality risk doubles for every 20 mm Hg increase systolic blood pressure above the threshold of 115 mm Hg and for every 10 mm Hg increase in diastolic blood pressure threshold of 75 mm Hg [32]. For an individual with normal blood pressure at the age of 55 years, the risk of developing hypertension during the remainder of his or her life is estimated to be 90% [33].

The potential of increased physical activity to lower elevated blood pressure or to prevent/attenuate the development of hypertension was suggested by several epidemiologic studies that used habitual physical activity as reported by the participants [34–36] or assessed more objectively by an exercise treadmill test [37]. The relative risk for developing hypertension in sedentary individuals with normal blood pressure at rest is approximately 35% to 70% higher when compared to their physically active peers [38–40].

8. Exercise Interventional Studies

The aforementioned epidemiologic evidence, an overwhelming number of well-controlled studies that followed have consistently shown that regularly performed aerobic exercise of mild to moderate intensity lowers blood pressure in patients with mild to moderate essential hypertension [41–43].

An overwhelming number of these studies reported that regularly performed aerobic exercise lowers blood pressure in patients with essential hypertension when compared to nonexercising controls. Although some variability exists among the several reviews and metaanalyses, the general conclusion is that aerobic exercise training is effective in lowering blood pressure in hypertensive individuals for all ages and both genders [41–44]. The average exercise-related blood pressure is about 7–10 mm Hg for systolic and 4–8 mm Hg for diastolic blood pressure [41, 42]. We also observed significantly lower blood pressure in individuals with Stage 2 hypertension after 16 weeks of exercise training. In addition, blood pressure in the exercise group was still significantly lower from baseline even after a 33% reduction in antihypertensive medication was achieved in those who exercised for an additional 16 weeks [45]. It is now well-recognized that a sedentary lifestyle increases the risk for hypertension whereas increased occupational or leisure time physical activity is associated with lower levels of blood pressure [31, 46]. Increased physical activity is now strongly recommended as part of the lifestyle modification along or as adjunct to pharmacologic therapy proposed by the Joint National Committee [29, 30].

9. Physical Activity and Mortality Risk in Hypertensive Individuals

We assessed the association between exercise capacity and mortality in 4,631 hypertensive men with and without additional cardiovascular risk factors. During a follow-up period of 7.7 ± 5.4 years (35,629 person-years), the adjusted mortality rate was 34% lower for the group next to the lowest fit individuals, and 59% and 71% for the next two highest fit categories, respectively. Exercise capacity was the strongest predictor of all-cause mortality. The adjusted mortality risk was 13% lower for every 1-MET increase in exercise capacity.

When additional risk factors were considered, the mortality risk was 47% higher for individuals within the lowest-fit category with additional risk factors, compared to individuals with no risk factors. This risk was eliminated for those in the next fitness category and was progressively reduced for the highest-fit categories regardless of the presence or absence of additional risk factors. These findings support that exercise capacity is a strong predictor of all-cause mortality in hypertensive males. The increased risk imposed by low fitness and additional cardiovascular risk factors is eliminated by relatively small increases in exercise capacity and declines progressively with higher exercise capacity [47]. Similar findings were observed in those with high to normal blood pressure [48] and in prehypertensive individuals [49].

10. PA and Mortality in Individuals with Type 2 Diabetes Mellitus

Findings from randomized, well-controlled exercise training studies supports that both aerobic and anaerobic (resistance training) exercises improve glucose uptake and insulin sensitivity after only a few weeks of training [50–53]. There is also evidence to suggest that resistance training may be more effective in lowering blood glucose levels [50–52].

11. Exercise and Diabetes Prevention

Strong evidence from large cohort studies also supports that exercise and physical activity in general, are highly effective in delaying or averting the development of diabetes. In addition, physical activity has been shown to reduce the risk of mortality in diabetics [54–57]. Support of the epidemiologic findings is provided by two interventional studies [58, 59]. In one study [58], overweight men ($n = 172$) and women ($n = 350$) with impaired glucose tolerance randomly assigned to either the intervention group or control group. The intervention group was instructed to follow a healthy diet, reduce weight, and increase physical activity. At the end of the follow-up period (3.2 years), the cumulative incidence of diabetes was 11% for the intervention group and 23% in the control group. The risk for diabetes was reduced by 58% in the intervention group. The investigators concluded that the observed changes in the incidence of diabetes were the direct result of the implemented lifestyle modifications.

In the Diabetes Prevention Program Research Group [59], 3,234 nondiabetic individuals with elevated fasting

blood glucose levels were randomly assigned to one of three groups: lifestyle-modification, metformin, and placebo. The lifestyle-modification group included weight reduction of at least 7% of initial body weight through a heart-healthy diet and engaging in moderate intensity physical activity (brisk walking) for at least 150 minutes per week. At the end of the follow-up period (2.8 years), both medication (metformin) and lifestyle interventions were equally effective in lowering blood glucose concentrations when compared to the placebo group. However, lifestyle intervention was significantly more effective in preventing the incidence of diabetes than metformin (58% versus 31% for lifestyle-modification and metformin groups, resp.). To prevent one case of diabetes, the investigators calculated that 6.9 persons have to participate in the lifestyle-modification group and 13.9 would have to receive metformin. Finally, lifestyle intervention resulted in more participants maintaining normal blood glucose values over a period of 4 years than the metformin or placebo groups.

12. Exercise Capacity and Mortality Risk

Poor exercise capacity is a well-established independent predictor of cardiovascular and overall mortality among healthy subjects, and patients with diabetes mellitus and/or cardiovascular disease (CVD) [23, 24, 60–65] whereas increased physical activity and higher cardiorespiratory fitness confer health benefits in proportion to the level of fitness [23, 24, 60–65], independent of body mass index (BMI) [60, 61, 64, 65]. Increases in physical activity patterns, have, thus, emerged as an integral part of the prevention and management of type 2 diabetes mellitus [60–65]. We assessed the association between exercise capacity and mortality risk in African-American ($n = 1,703$) and Caucasian ($n = 1,445$) diabetic men during a mean follow-up period of over 7 years. We noted a graded reduction in mortality risk with increased exercise capacity for both races. The association was stronger for Caucasians. Each 1-MET increase in exercise capacity yielded 19% lower risk for Caucasians and 14% for African-Americans. Similarly, the risk was 43% lower for moderate-fit and 67% for high-fit Caucasians. The comparable reductions in African-Americans were 34% and 46%, respectively. Our findings support that exercise capacity is a strong predictor of all-cause mortality in African-American and Caucasian men with type 2 diabetes. The exercise capacity-related reduction in mortality appears to be stronger and more graded for Caucasians than for African-Americans [65]. These findings support previous reports of an inverse relationship between aerobic fitness and total mortality in both healthy and diabetic populations [23, 24, 60–64]. They also confirm a previous report in predominantly male Caucasian diabetics that the largest proportional reduction in risk occurs between the least fit and the moderate fit categories [61].

13. Physical Activity and Obesity

Prior to 1998, obesity was not considered an independent risk factor for CHD. In June 1998, the AHA reclassified

overweight and obesity as a major, modifiable risk factor for CHD comparable in status to the other well-established CHD risk factors [66].

Obesity not only increases directly the CHD risk, but also amplifies it indirectly by the adverse effects of obesity on several established CHD risk factors. Evidence from multiple studies agreed that both $\text{BMI} \geq 27$ and the distribution of fat in the abdomen region as indicated by a waist to hip ratio > 0.85 in women and 0.98 in men or a waist circumference of ≥ 98 cm and ≥ 85 cm for men and women, respectively, are associated with hypertension, diabetes, abnormal lipids, and increased CHD mortality [67–72].

14. Physical Activity and Weight Loss

Weight reduction is principally determined and directly related to the net deficit in energy balance, either through a reduction in energy intake or an increase in energy expenditure regardless of the diet composition [73]. Both genetic factors and lifestyle are likely to contribute significantly to variability of body weight in humans [74]. A chronic energy imbalance that favors weight gain may be the outcome of a complex interaction between genetic and environmental factors [75, 76]. However it is virtually impossible to blame genes for the increase in obesity of epidemic proportion in the United States in the past 20 years, since the gene pool has not changed significantly [75]. It is more likely that the genetic makeup may not necessarily cause obesity, but in the presence of powerful environmental influences, the propensity for obesity is enhanced. The predominant environmental factors for obesity appear to be over-consumption of calories and reduction in physical activity. Of the two, physical inactivity appears to play the predominant role. According to the USA federal report on obesity, total caloric intake over the last two decades has not substantially increased while physical activity has decreased significantly [77].

The theoretical mechanism that chronic exercise promotes a reduction in body fat is by increasing total daily energy expenditure without a corresponding increase in energy intake [78]. Exercise alone results in favorable but modest reduction on body weight and body fat distribution [79]. This exercise-induced weight reduction is achieved by long-term aerobic exercises or physical activity of sufficient intensity, duration, and frequency. However, when the energy intake is held constant, exercise alone can achieve significant weight losses [78]. This was shown in at least one study where the investigators achieved 7.6 lbs of weight over a period of three months when an energy deficit of 700 Kcal per day was achieved by exercise only and energy intake was held constant to pre-exercise levels [80].

The effectiveness of exercise to induce weight loss is directly related to the total number of kcal expended [81]. In this regard, the duration of exercise becomes important. In a recent 18-month exercise study, overweight women exercising more than 200 minutes per week realized a significantly greater weight reduction (-13.1 kg) than those exercising 150 to 200 minutes/week (-8.5 kg) or less than 150 min/week (3.5 kg). This suggests a dose-response relationship between

amount of exercise and long-term weight loss and that a minimum of 150 minutes of exercise per week may be necessary for enhanced weight loss [82].

Although the exercise-induced losses in body weight may be viewed as relatively small and disappointing by some, it is worth pointing out that weight loss must be viewed as a long-term process. Excess weight accumulation did not occur over night and expectations that it will shed quickly are not realistic. In this regard, long-term exercise-induced weight loss is promising. In an 8-week-diet or diet-plus-exercise program consisting of 35–60 minutes of aerobic activity 3 days per week, weight losses were similar in both groups. However, those who did not exercise during the 18-month follow-up period gained about 60% of the weight back in 6 months and 92% of the weight back at 18 months. For those who continued to exercise during the 18-month follow-up period, body weight did not change significantly [83]. Finally, increased physical activity combined with a prudent diet and behavior modification is likely to be a more effective a way to maximize weight loss [84, 85]. Furthermore, the exercise program should focus on long duration and low intensity, tailored for expending calories rather than improving fitness [84].

Despite the small changes in weight reduction associated with physical activity, a number of studies provide convincing evidence that reduction in mortality risk is evident and inversely related to exercise capacity regardless of BMI levels [86–89]. Furthermore, in a number of these studies, fitness emerged as a more powerful predictor of mortality than BMI [86–88] independent of overall and abdominal obesity [87] and of comparable importance with that of diabetes mellitus and other cardiovascular risk factors [88].

15. Dietary Approaches to Lower Risk

Comprehensive dietary approaches favorably affect cardiometabolic risk factors, (diabetes, high blood pressure, obesity) and reduce CVD. They are now widely recommended and implemented in the prevention and treatment of cardiovascular disease [90, 91]. Decreased saturated fats and cholesterol and increased consumption of fruits, vegetables, and whole grain products are advocated in most dietary approaches. In this regard, data from the Lyon Diet Heart Study [92, 93] supports as much as 50% to 70% reduction in recurrent heart disease and all-cause mortality and suggests that a Mediterranean-style diet may be superior to the health benefits of step I diet advocated by the National Cholesterol Education Program committee (NCEP) [90]. Several studies now support health benefits associated with the Mediterranean or Mediterranean-type diet. Consequently, such dietary patterns are presented as an alternative to the less practical for most people, vegetarian diet [92–100]. The traditional Mediterranean diet is characterized by a high consumption of olive oil, legumes, cereals, fruits, vegetables, moderate to high consumption of fish, moderate consumption of wine, dairy products, mostly as cheese and yogurt, and low consumption of meat and meat products. This diet is low in saturated fat (less than about 9% of

energy), with total lipid intake ranging from less than 30% to more than 40% of energy from one area to another. Moreover, the ratio of monounsaturated to saturated fats is about two. The high content in the diet of vegetables, fresh fruits, and cereals, and the liberal use of olive oil guarantee an adequate intake of carotene, vitamin C, tocopherols, a linolenic acid, and various important minerals.

The unusually lower mortality rates reported by epidemiologic studies in Mediterranean populations are in support of suggestions [95] that such dietary pattern may be associated with lower risk of hypertension, coronary heart disease, and cancer. Recently, evidence from the CARDIO2000 study [97, 101] showed that the adoption of Mediterranean diet was related with an adjusted 7% to 10% reduction on the coronary risk in treated, untreated, or uncontrolled hypertensive subjects. In large prospective survey involving over 22,000 middle age and older Greeks, an inverse association was observed between death due to coronary heart disease and greater adherence to the Mediterranean diet regardless of sex, smoking status, level of education, body mass index, and level of physical activity [99].

Although the evidence strongly supports that Mediterranean dietary patterns lead to health benefits, some doubt that such dietary pattern is practical or can be adopted by other populations due to differences in cultural and environmental conditions [102]. Others, however, express optimism that the Mediterranean dietary pattern can easily be translated into other cultures, since it can utilize other food options to increase the intake of monounsaturated fats and consequently lead to similar effects in the health status [103]. Although this debate is likely to continue, current evidence strongly argues that the use of products that utilize olive oil instead of saturated fats should be encouraged in all cultures. In this regard, an ingenious and potentially promising approach to increase the consumption of olive oil has been introduced recently by at least one company. Saturated fats are removed from meat products (ham, cold cuts, etc.) and are substituted with olive oil. Similar findings have been reported by the Dietary Approaches to Stop Hypertension (DASH) clinical trial [94] that utilized very similar to the Mediterranean dietary pattern in hypertensive adults. The investigators reported that the diet, rich in fruits and vegetables, and contains reduced saturated and total fat, sodium held constant, was superior in reducing blood pressure [94] and lowering the risk of CHD and stroke among middle-aged women during 24 years of follow-up [104].

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