Sedentary behavior, physical activity, epigenetics, and cardiovascular disease risk – A short review

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Abstract—Some adults who meet the minimal recommendations for physical activity time each week are still at an increased risk for developing cardiovascular disease (CVD) or coronary artery disease (CAD) because these physically active adults are spending most of their waking hours in sedentary behaviors. This underscores the importance of the amount of time spent per day in sedentary behavior during their waking hours. Most research studies exclude sleeping time as spending time in sedentary behavior, and use self-reported time spent sitting or time spent watching television or video monitor to assess sedentary behavior. The association between sedentary behavior and risk for CVD or CAD as well as developing risk factors for the disease is high. The health impacts of increasing physical activity and reducing sedentary time using various wearable technologies and recommended intervention strategies are a field that warrants further research. While genetic risk factors for CVD have been well-documented, emerging evidence has linked epigenetic mechanisms (heritable changes to gene expression that are not from differences in the genetic code) with many CVDs. Epigenetic mechanisms are regulated by many factors including diet and physical activity. Recent evidence provides support for the theory of epigenetic inheritance in which epigenetic alterations in gametes are transferable from parents to offspring. This new dimension of risk for CVD susceptibility and its interaction with other factors such as diet and physical activity underscore the complexity of CVD risk factors and their regulatory role in prevention, management, and possibly diagnosis of CVDs. This short review examines the interplaying role of sedentary behavior, physical activity, and epigenetics in CVD risk.

Keywords—Sedentary behaviour; physical activity; epigenetics; cardiovascular diseases; wearable technologies.

I. INTRODUCTION

What is sedentary behavior and do we have standardized and universal guidelines for describing sedentary behavior?

Sedentary behavior is defined as any behavioral task that induces less than 1.5 metabolic equivalent of task, simply metabolic equivalent, (MET) energy expenditure [1]. This amount of energy expenditure would include time spent in a seated position while performing desk work, driving a motor-driven vehicle, sitting in a bus, train or airplane, using a mobile phone or in a reclined position while watching television (TV). Thus, sedentary behavior does not mean complete rest; rather it includes tasks that are at the lower end of light-intensity activities range (1.1 MET to 2.9 MET), (as defined by the Physical Activity Guidelines for Americans 2008). Note that one MET represents the rate of energy expenditure while at rest or resting metabolic rate (RER). In terms of oxygen consumption, one MET requires 3.5 ml O₂/kg/min [2]. However, study has shown that using the 3.5 mlO₂/kg/min to represent baseline oxygen consumption tends to produce errors in estimating RER because this estimation of resting metabolic rate would exaggerate the cost of oxygen during activity [2]. Most research studies excluded sleeping time as spending time in sedentary behavior, and used self-reported time spent sitting, or time spent watching television or video monitor to assess sedentary behavior. The components of the twenty-four hours model of free living activities estimate 8 hours of sedentary behavior (less than 1.5 MET), 7.5 hours of sleep, 8 hours of light activities (1.5 to 3.0 MET), and 0.5 hour of exercise at moderate to vigorous activities (3 to greater than 6 MET) [21].

II. DESCRIPTION OF SEDENTARY BEHAVIOR

From the literature, we found two studies that describe sedentary behavior.

A. The first study by the Canadian Sedentary Behavior Guidelines recommended people avoid watching television screen time no more than 2 hours per day, or avoid motorized transport, extended sitting and time spent in doors throughout the day [3].

B. The second from the Australian Sedentary Behavior Guidelines recommended people avoid the amount of time spent in sitting, and take frequent breaks, as often as possible, from long periods of sitting [4].

III. DESCRIPTION OF PHYSICAL ACTIVITY

Physical activity is defined as any bodily movement that results in a substantial increase in energy expenditure over resting energy expenditure. For example, exercise or playing tennis is the example of physical activity. “Light” physical activity is defined as requiring < 3 METs of energy expenditure, “moderate” physical activity as between 3 and < 6 METs, and “vigorous” physical activity as equal to or greater than 6 METs [5]. Optimal or minimal physical activity level as recommended
by the American College of Sports Medicine (ACSM) and U.S. Centers for Disease Control and Prevention (CDC) is that all adults engage in regular physical activity of “moderate intensity” 30 minutes a day on 5 or more days a week (i.e., equal to or >150 minutes a week of moderate intensity, aerobic activity), preferably all days of the week [5]. This description highlights the importance of the amount and intensity of physical activity that is required for attaining health benefits and for lowering susceptibility to chronic disease and decreasing premature mortality. The recommendations also call for all adults engage in regular “vigorous intensity” physical activity, 20 minutes a day on 3 or more days a week (i.e., 75 minutes a week of vigorous intensity, aerobic activity) [5].

Research has shown that there is a dose-response relationship between physical activity and the risks of coronary artery disease (CAD) and cardiovascular disease (CVD) [6]. In addition, several large scale observational studies have clearly documented a dose-response relationship between physical activity and risk of cardiovascular disease and premature mortality in men and women [5]. With that the ACSM and CDC further recommended that additional health benefits can be obtained with 300 or more minutes per week of moderate aerobic activity [5].

Among those who meet the ACSM and CDC recommendations for physical activity time each week, some of these adults are still at an increased risk for developing cardiovascular disease. These physically active adults are spending most of their waking hours in sedentary behaviors. It should be noted that American adults spent 50% of his or her waking hours in sedentary behavior [7].

It has been reported that the prevalence of physical activity is lower among individuals with chronic disease. Among all adults engaging in sufficient volume of aerobic leisure-time physical activity the prevalence rate was 50.1% ± 0.5% (mean ± standard error) [8]. The prevalence of sufficient volume of aerobic leisure-time physical activity was lower for each chronic disease category (prevalence range = 26.1% to 48.6%) compared to apparently healthy adults (53.6% ± 0.7%) [8].

IV. SEDENTARY BEHAVIOR AND RISK OF CARDIOVASCULAR DISEASE

Evidence on sedentary behavior and risk of developing cardiovascular disease (CVD) is presented below. There are five major studies that reported the association between high sedentary behavior and cardiovascular disease incidence.

- From the Women’s Health Initiative Study, the authors followed participants free of CVD at baseline and found hazard ratio (HR) of 1.18 (95% confidence interval (CI) 1.09 – 1.29) in women spending more than 10 hours/day sitting, compared with those less than 5 hours/day sitting [9]. Chomistek’s et al. [9] analysis used multivariable models which include physical activity level, also found that women in the prolonged sitting group their risk of developing CVD were stronger in overweight persons, compared with those who were normal weight, and in women older than 70 years of age.

- From the NIH–AARP Diet and Health Study, Matthews et al. [10] examined the relationship between sedentary time and CVD mortality in adults. Participants with the most TV viewing time of > 7 hours/day compared with < 1 hour/day were at greater risk of CVD mortality (HR = 2.00, 95% CI = 1.33 – 3.00). The study population involved 240,819 adults free of CVD at baseline [10].

- The Scottish Health Survey from 2003 to 2007 reported 215 CVD events with a HR for CVD events of 2.30 (95% CI 1.33 – 3.96) for participants reporting more than 4 hours/day of TV screen time compared to those with less than 2 hours/day [11]. The HR was similar after the authors adjusted for the level of physical activity of these participants.

- The European Prospective Investigation into Cancer and Nutrition Study, observed a group of men and women who were free of known CVD at baseline for a total of 11 years [12]. For this group of men and women, the HR for CVD incidence based on sedentary time was 1.06 (95% CI of 1.03 – 1.09) [12].

- In a study conducted by Ford et al. [13] that 2 hours/day of sitting time and TV or computer screen time were associated with an increase of 5% and 17% in CVD events, respectively. The HR = 1.05 (with 95% CI = 1.01 – 1.09) and 1.17 (with 95% CI = 1.13 – 1.20), respectively [13].

V.GLOBAL EFFECT OF SEDENTARY BEHAVIOR ON CARDIOVASCULAR AND ASSOCIATED NON-COMMUNICABLE DISEASE

Analysis of disease burden and life expectancy revealed that sedentary behavior causes a worldwide average of 6% of the burden of disease from coronary heart disease with 3.9% in Africa, 7.1% in Latin America and Caribbean, 6.2% in North America, 7.8% in Eastern Mediterranean, 5.5% in Europe, 3.2% in Southeast Asia, and 7.2% in Western Pacific [14].

On the associated non-communicable diseases, sedentary behavior causes a worldwide average of 7% of type-2 diabetes, 10% of breast cancer, 10% of colon cancer, and 9% of premature mortality. It was estimated that if the worldwide prevalence of sedentary behavior is lowered by 25%, more than 1.3 million deaths per year would have been prevented [14].

VI. SEDENTARY BEHAVIOR AND CARDIOVASCULAR DISEASE RISK FACTOR

There are reports showing that there is high association between sedentary behavior and CVD risk factors which includes diabetes, dyslipidemia (such as high LDL cholesterol,
apolipoprotein B, total cholesterol, and triglycerides), insulin resistance, and development of the metabolic syndrome [15].

From the Brazilian Longitudinal Study of Adults Health (ELSA-Brasil) the authors reported that subjects with an ideal cardiovascular risk profile have lower coronary artery calcium when compared to subjects with fewer controlled cardiovascular risk factors [16].

Is there any beneficial effect of reallocating sedentary behavior time to replace physical activity time? Study has shown that replacing 2 hours/day sitting time with standing can improve biomarkers of glucose and lipid metabolism. However, greater significant improvement in body mass index (BMI) and waist circumference can be achieved with more active stepping time in place of standing time.

Which are the most sought intervention strategies recommended by the experts for reducing sedentary behavior? Researchers have proposed many strategies for adults to reduce sedentary behavior patterns. Reducing sedentary behavior can be accomplished by reducing sedentary time with physical activity time in commuting to work, at home, and in leisure activities [1].

Study also found that it is more convenient and easier to reduce sedentary time than to increase physical activity. For example, in a 2014 meta-analysis study by Martin et al. [17] who observed a 22 min/day reduction in sedentary time in the intervention group (95% CI = -36 to -9 min/day). When interventions that focus only on reducing sedentary time, sedentary behavior was lowered by 42 min/day (95% CI = -79 to -5) [17].

VII. SEDENTARY BEHAVIOR, PHYSICAL ACTIVITY AND MENTAL STRESS

From fifty-five prospective studies that examined the influence of stress on physical activity and observed psychological stress was associated with less physical activity (PA) or exercise or more sedentary behavior (76.4 %) [18]. Nearly all the 55 prospective studies investigating the effects of objective stress associated markers agreed that stress has a negative effect on PA. Approximately 18% of the prospective studies reported that PA was positively impacted by stress [18].

The reason for this is because some individuals use exercise to cope with stress or reduce stress. The study also reported that some physically active individuals exercise more when encountering stress, and those in beginning stages of encountering stress do less exercise [18]. In light of this, psychological or mental stress may have different impact on physical activity and exercise, suggesting that combining stress management programming with exercise interventions may improve stress-related increase in sedentary behavior or decrease PA. However, this hypothesis warrants further study.

VIII. MODERN TECHNOLOGY, WORKPLACE ENVIRONMENT AND SEDENTARY BEHAVIOR

Mobile health also known as eHealth is used to describe the use of mobile technology and the practice of medicine. Modern technology provides health care professionals with new and advanced miniaturized and wireless technologies that allowed for greater gains in Mobile health such as the use of smartphones, and wearable technology including pedometers, accelerometers, smartwatches, iPad, etc. [1]. These wearable devices can provide meaningful interactive feedbacks and thus promote motivation for the person wearing it.

The American College of Sports Medicine conducted a worldwide survey on most popular trend in fitness programs, and observed that one of the top 10 fitness trends for 2016 is wearable technologies such as accelerometers, motion sensor devices, iPod, iWatch and iPhone app, etc. [19]. These wearable devices can be used to track user’s sedentary behavior level.

Some mobile Samsung Galaxy S5 phone has a built in app called “S Health”, Apple iPhone6 built in app called “Health”, and there are other mobile phone apps called “Runkeeper” on Apple and Android as well as “FitBit”. These modern technologies can lower the error made in data collection based on “self-report” which is considered unreliable in research setting. In addition, individuals wearing wearable devices can be programmed to vibrate every 15 to 60 min if the individuals wearing i have been sitting or sedentary without bodily movement for too long [1]. Above all, these wearable technologies are convenient and easy to use by the participant as a motivational tool for monitoring his/her daily physical activity levels and reducing sedentary time.

In addition to the wearable technologies, another factor that can affect an individual’s sedentary behavior is one’s “built environment” which refers to all the physical surroundings in a person’s life. This includes urban planning for constructing pedestrian sidewalks for the roads and city streets, city park visitors’ walkways, and workplace environment [1]. The later includes activity-permissive workplaces build into the work environment, such as standing desk, treadmill desk, and giant medicine ball chair, etc. Study has shown that these activity-permissive workplaces can reduce office workers’ sedentary time by 77 min/8 hour workday (95% CI = -120 to -35 min), compared to the control group [20].

Undoubtedly, the health impacts of increasing physical activity and reducing sedentary time using various MODERN technologies and recommended intervention strategy are a field that warrants further research.

IX. EPIGENETICS AND CARDIOVASCULAR DISEASE

A. Epigenetic Mechanisms

In simple terms, the word epigenetic means “on top of or in addition to genetics” [22]. Unlike genetics which refers to the nucleotide triplet base sequence of the DNA code that translate genetic information into a particular peptide chain or protein, epigenetic are chemical tags that regulate the expression pattern of genes. Thus, epigenetic induces a change in phenotype without changes in genotype. The epigenome is capable of modifying the genome outcome through several processes that include DNA methylation, histone modification and non-coding RNA (ncRNA) mechanisms that have been correlated with various disorders and diseases including CVs [23]. DNA methylation involves the addition of a methyl group (CH3) to cytosine converting it into 5methyl-cytosine through the action
of DNA methyltransferase (DNMT). It occurs predominately (90%) at the CpG rich areas where cytosine is linked to guanine by phosphate [24]. CpG rich areas are generally found in promoter sites where transcription is initiated and methylation of cytosine inhibit transcription silencing gene expression [23].

Histone modifications are post-translational changes that could involve acetylation of lysines, methylation of lysine and arginines, and phosphorylation of serine and threonine [25]. Histone acetylation and deacetylation are epigenetic mechanisms that involve the addition or removal of an acetyl group (CH3CO) on lysines in the N-terminal tail through a group of Histone acetyltransferases (HAT) and Histone deacetylases (HDACs) enzymes. Acetylation results in euchromatin, where chromatin structure is relaxed keeping DNA accessible for transcription. Whereas, deacetylation condensing chromatin in heterochromatin preventing transcription due to inaccessibility of DNA [25].

Epigenetic related ncRNA such as micro RNAs (miRNA), small interfering RNAs (siRNA), and Pici-interacting RNA (piRNA) function to regulate gene expression at the transcriptional and post-transcriptional level. For example, miRNA can bind to complementary sequences in the 3’ untranslated region of specifically targeted mRNA resulting in their degradation and inhibition of protein expression [26].

B. Epigenetics Interplay in CVD and Physical Activity

Epigenetic studies in CVD have identified numerous epigenetic modifications that affect the development and progression of various CVDs including, arrhythmias [27, 28, 29], cardiac hypertrophy [30, 31], heart failure [32, 33], vascular diseases [34, 35].

Epigenetic mechanisms are affected by life style factors such as physical activity and diet [36]. Mononzygous twins are epigenetically indistinguishable during their early years of life however epigenetic differences across different tissue types arise in older mononzygous twins with different life style [37]. Acute physical exercise has been found to decrease global and gene-specific promoter methylation in human skeletal muscle following a dose-dependent response [38]. Six months of aerobic exercise in sedentary but healthy men resulted in decreased blood pressure, heart rate, waist circumference, and increased high-density lipoprotein (HDL), all of which are protective mechanisms of CVDs [39, 40]. DNA methylation where decreased in majority of skeletal muscle genes, while it was increased in adipose tissue [39, 40].

Recent evidence provides support for the theory of epigenetic inheritance in which epigenetic alterations in gametes are transferable from parents to offspring [41]. Researcher used in vitro fertilization (IVF) to produce various pairing of egg and sperm cells from parent mice that were fed high-fat, low-fat, or normal diet. Embryos were implanted into healthy surrogate females to eliminate parental influence beyond the contribution of gametes. Offspring were placed on high-fat diet for six weeks starting week 10 after birth. Offspring from two parents on high-fat diets were heavier than offspring with both parents on a normal diet [41].

X. CONCLUSION

In Summary, studies demonstrate that regular physical activity and, more recently, limited sedentary behavior are associated with reduced risk of CVD. While genetic risk factors for CVD have been well-documented, emerging evidence has linked epigenetic mechanisms with many CVDs. Epigenetic mechanisms are regulated by many factors including diet and physical activity. The new dimension of epigenetic inheritance risk factors for CVD susceptibility and its interaction with other factors such as diet and physical activity is still emerging and underscores the complexity of CVD risk factors and their regulatory role in prevention, management, and possibly diagnosis of CVDs.

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