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The Cardiometabolic Burden of Sedentarism and Its Implications on Health

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Abstract: Sedentary behavior is spreading in society, a phenomenon especially aggravated by the rise of modern technology. Sedentary lifestyle habits are being adopted by young people, who increase the time they spend in stationary activities like video games, TV and, most recently handheld digital devices like smartphones and tablets. Today many daily activities can be carried out without greater muscular activity, transforming an active and dynamic being into a sedentary one, with less energy expenditure. It has been demonstrated that both sedentary behavior and physical inactivity impact negatively on cardiometabolic well-being, and they become a serious problem for public health, as it has been claimed in several studies and by scientific statements. People need to reduce the amount of time they waste being sedentary, especially during infancy and youthhood to avoid the increase in cardiometabolic risk during adulthood and reach the advanced age with a better functional capacity and more active. Further observational and experimental studies are needed to define relationships between total sedentary time and patterns of sedentary time with biomarkers of cardiometabolic risk and its impact on health outcomes. This review intends to outline the facts of sedentarism as a cardiometabolic risk factor specially in youngest people and claim for more attention by medical care to this problem.

Keywords: Sedentariness, Physical Inactivity, Cardiometabolic Risk, Atherosclerotic Cardiovascular Disease, Type 2 Diabetes

1. Introduction

The link between exercise and health with a dose/response style relationship is well known: more physical activity equals better general health; furthermore, it has also been proven that those people committed to regular physical activity, in general, also partake in a heart-healthy diet and other habits that promote better general health. Sedentary lifestyle and physical inactivity, however, have received very little publicity in past decades, although their negative impact on well-being, in general, and on cardiometabolic health, in particular, has been recognized recently due to a higher mortality and incidence of chronic non-communicable diseases. Thanks to the numerous distractions provided by modern electronic devices in general, there is an increasing and alarming trend for sedentarism within the child and youth population [1, 2].

It is well known that the human being is the result of several million years of biological transformation, so nearly its genome was shaped during pre-agricultural evolution and allowed it to adapt to the challenges that our ancestors faced during the evolution until the recent past [3]. Wandering from place to place and looking to get food significate a high expenditure of energy so the human being from the first days was very active. The metabolic ability to adapt to cyclical periods of food abundance and scarcity made a vast difference in the primitive homo [4]. When food was plentiful, the sparing metabolic processes were set in motion, and energy was built up as fatty storage and muscle glycogen. When famine occurred, they used the energy accumulated in their reserves more efficiently with the conservation of their muscular mass which allowed them to be more likely to find food, overcome the crisis and survive [4]. Additionally, physical activity strengthened both muscle cells and the central nervous system as it is the organ that controls body movements in all-time variables supporting the evolutionary growth of certain areas of the cerebral cortex and putting apart from all other hominids.

The spreading of the human being allowed them to develop a transcendental cognitive revolution, redefining the ways they were interacting with the environment and enhancing the maturation of prodigious abilities, come to know, understand, and develop complex phenomena such as fire or painting, predict the changes of seasons, and set up contacts with their neighborhoods, especially in socializing with other ancestors of the same specie [5].

For many thousands of years, primitive humans were moving from one place to another until they discovered how to grow and crop certain grains, so they were forced to settle in fixed places, abandon nomadic life and begin the complex task of agriculture with its sowing and harvest seasons and knowing the opportune time for grazing [5]. In short, the human being is active by nature and has been wandering for much of its evolutionary history; paradoxically, while Humanity´s transformation to sedentarism occurred just 10,000 years ago when they became farmers, it has hardly taken them less than a century to adopt an inactive lifestyle, thanks to the pervasiveness of current technology, with so little physical activity that large reserves of energy are accumulated in the organism, giving rise to a series of cardiometabolic alterations, such as overweight / obesity with a significant impact on their health from an early age.

This review aims to highlight the dangers of a sedentary lifestyle in public health in general for two main reasons; the first one lies in the little to no physical activity carried out by children and adolescents, in conjunction with the explosive increase in overweight and obesity in these groups; the second reason is that most of these cases are attended and treated by non-specialist doctors in the cardiometabolic area, who do not pay attention to biochemical alterations due to several reasons i.e., alterations found are marginal or they consider that weight gain is an attribute of development or that they can be treated later. In this sense, the main protagonist is time, a factor that must not be underestimated; the golden rule is that the earlier any metabolic alteration is controlled or eradicated in a young person, the better.

2. Sedentarism: Its Evolution as a Problem

Like many other fields of medicine and other sciences, the first known observations about the harm of physical inactivity come from the flourishing Greek culture. One of the fathers of philosophy, Plato, founder of the Academy (Athens, ca. 427-347 BC) and an athlete rewarded with several Olympic awards, wisely warned about the need for scrupulous physical education from childhood and for continued exercise throughout life, starting almost from the womb itself, so that pregnant women regularly perform the appropriate physical exercises to give birth to healthy and strong children [6], anticipating by many centuries what we know today as the prenatal care and fetal programming.

His contemporary Hippocrates (377 BC), considered the father of Medicine, also established the benefits of physical activity and glimpsed the potential risks of a sedentary lifestyle [7], quoting "All parts of the body which have a function if used in moderation and exercised in labors in which each is accustomed, become thereby healthy, well developed and age more slowly; but if unused and left idle they become liable to disease, defective in growth and age quickly."

However, it would take several centuries to better understand the potential risks of a sedentary lifestyle. It is not until the middle of the 1950s that the close relationship between physical inactivity and risk of chronic disease is known with scientific rigor [8]; in consequence, the interest and research on sedentarism has increased due to of the pathophysiological evidence of specific adverse effects that occur with the appearance of cardiometabolic conditions such as obesity, type 2 diabetes mellitus (T2DM), high blood pressure (HBP), atherosclerosis and atherosclerotic cardiovascular disease (ACVD) [1, 2, 9, 10] with its two major clinical expressions: coronary artery disease (CAD) and cerebral vascular disease. Furthermore, today we know that just like physical activity, sedentary behavior also shows a dose/response relationship, but in the opposite direction; more sedentary time translates into a higher risk of mortality and / or adverse outcomes, especially cardiometabolic ones; indeed, the longer the sedentary behavior, the greater aggregation and burden of cardiometabolic risk factors will be [1, 2, 9-11].

Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents while in a sitting, reclining, or lying posture [12] and includes smartphone / tablet use, TV viewing, video game playing, computer use, driving or riding in a car, and reading / studying while sitting. Although sedentary behavior is not simply less physical activity, but also includes a set of individual unhealthy habits such as a rise in caloric intake, smoking or alcohol consumption.

Nearly two decades ago, a sedentary lifestyle has turn into severe trouble that has grown by leaps and bounds with the arrival of new technological inventions aimed at facilitating daily activities, without realizing that humanity is becoming increasingly immobile in comparison to half a century ago [11]. Today many daily activities can be carried out without greater muscular activity, transforming an active and dynamic being into a sedentary one, with less energy expenditure. Of course, such behaviors have been exacerbated by the confinement resulting from the COVID-19 pandemic that we have been experiencing during the last two years, with no end in sight for the immediate future.

More recently, the World Health Organization (WHO) updated the 2010 Global Recommendations on Physical Activity for Health which, for the first time, provided population-based guidelines on sedentary behavior [12, 13]. To summarize, there is evidence of moderate certainty that a higher time of sedentarism is associated with an increased risk of mortality from cardiovascular disease, cancer, and all-cause, as well as an elevated risk of atherosclerotic

cardiovascular disease (ACVD) and type 2 diabetes mellitus (T2DM). Nevertheless, no recommendation for a quantified (time-based) limit for sedentary periods was provided in these guidelines, due to current insufficient evidence. Moderate certainty of the evidence also suggests that the association between sedentary behavior and mortality due to all-cause, ACVD, and cancer varies according to the level of moderate-to-vigorous physical activity (MVPA). On the other side, the evidence is insufficient or low-certainty degree on the type or domain of sedentary habit, or the frequency and/or duration of bouts or breaks linked to the health outcomes mentioned.

3. The Burden of Sedentary Behavior

Sedentary lifestyle has become a serious public health problem in recent times, especially in schoolchildren and adolescents, which has been gradually increasing in importance with the arrival of new technological inventions, aimed at facilitating everyday life or providing means for distraction, without realizing the consequences on cardiometabolic health. Given the dimension of the problem, the WHO identifies sedentary lifestyle as a fourth risk factor in terms of global mortality, with 6% of deaths recorded worldwide, amounting to 3.2 million people [14], which means one death every 10 seconds; and responsible also for 6% of cases of CAD, 7% of T2DM, 10% of breast cancer and 10% of colon cancer, 9% of premature mortality, adding up to more than 5.3 million deaths caused in 2008. The risk of death from any cause is higher in adults whose physical activity is insufficient compared to those who practice at least 150 minutes of exercise per week or its equivalent.

The magnitude of the problem of physical inactivity around the globe was highlighted in the study by Guthold et al [15], where they analyzed data in 168 countries from 358 population surveys between 2001 and 2016 that included almost two million participants. Briefly, the results showed that [15]:

1) 27.5% of adults aged 18 and over are not active enough.
2) Women are less active than men (31.7% vs. 23.4%, respectively) and older people less so than young people.
3) The highest percentages occurred among women from Latin America and the Caribbean (43.7%), Southeast Asia (43.0%) and high-income Western countries (42.3%); while the lowest values corresponded to men from Oceania (12.3%), East and Southeast Asia (17.6%), and sub-Saharan Africa (17.9%).

The figure for the prevalence of insufficient physical inactivity remained the same, with very little variation between 2001 and 2016.

4. Impact of a Sedentary Lifestyle on Children and Adolescents

Promoting healthy practices from childhood is essential to incorporate them as life habits and help prevent or reduce the risk of suffering from certain diseases as adults. The point is that early childhood, during which there is rapid growth and cognitive development, is the period when children's habits are formed, family routines are more open to change and more adaptable. On the other hand, a sedentary lifestyle in childhood means a high predisposition to obesity and, therefore, to T2DM in adulthood; and in this process, the time in front of a screen (call it a computer, television, console, etc.) play a causal role of the first magnitude. Data from various biomedical publications warn about the high proportions of insufficient physical activity in this age group [11, 16, 17]. Worldwide, 1 in 4 adults, and 3 in 4 adolescents (aged 11–17 years), do not currently meet the global recommendations for physical activity set by WHO [11], and over 80% of school-aged adolescents worldwide (85% of girls and 78% of boys) do not meet the minimum one hour of daily physical activity level recommended [11].

In another publication by Guthold et al. [17], they give a more up-to-date perspective of the situation regarding adolescents: the prevalence of insufficient physical activity was significantly reduced between 2001 and 2016 for males (from 80.1% to 77.6 %), while for females there were no changes (85.1% to 84.7%), without distinctions regarding the economic position of the countries. The region with the highest prevalence of insufficient physical activity in 2016 was the high-income Asia-Pacific region for both males (89.0%) and females (95.6%); while the region with the lowest prevalence corresponded to the Western countries with the highest income for males (72.1%) and Southeast Asia for females (77.5%) [17]. For Latin America, there was no favorable change in global prevalence (2001 versus 2016: 84.8% versus 84.3%), with a slight reduction among men (81.1% versus 79.9%), but not in females (88.6% versus 88.9%) [17].

Regarding the impact on health, research on children between 5 and 17 years of age with sedentary habits, compared to those who are less sedentary, have shown [2, 18-20]:

1) More frequency of overweight/obesity.
2) Less muscle development and tone with reduced tolerance to exertion.
3) Slightly elevated systolic and diastolic blood pressure.
4) Greater frequency of insulin resistance, favorable for the appearance of T2DM.
5) Lower concentrations of high-density lipoprotein cholesterol (HDL-C) and higher concentrations of low-density lipoprotein cholesterol (LDL-C) and triglycerides.
6) Greater tendency to depression in youth, emotional and/or behavioral disorders.
7) Tendency to remain isolated with little social participation.

In summary, those persons in charge for the family group are responsible for motivating and helping children to be more active and reduce or leave aside activities that promote a sedentary lifestyle, reducing screen time, since a more

energetic childhood will be more beneficial for cardiometabolic and mental health in adulthood [21].

5. The Cardiometabolic Burden of Sedentary Lifestyle

The central pathophysiological alteration lies in insulin resistance, and from there a series of negative modifications are generated in the different systems of the organism, which are responsible for the metabolic balance of carbohydrates and lipids [22]. But, in addition, this resistance to insulin, which is greater the longer the time spent in a sedentary attitude, also determines other changes that are closely related to the cardiovascular system, such as favoring sympathetic tone (vasoconstriction, increased in heart rate), promotion of an inflammatory and oxidative environment, thereby accelerating the progression of arterial damage and atherosclerosis or favorable conditioning for the appearance of cancer and even cognitive deterioration (Figure 1).

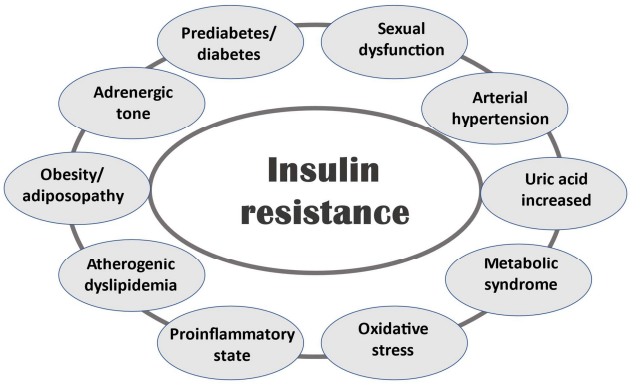

Figure 1. *Target area and consequences of insulin resistance.*

The clinical consequences of a sedentary lifestyle on the various systems of the body are extensive and interconnected, summarized below [1, 9, 10, 14, 22-30]:

1) Metabolic: Obesity, decreased sensitivity to insulin, T2DM, dyslipidemia, metabolic syndrome, hyperuricemia.
2) Cardiovascular: Atherosclerosis, coronary heart disease, unstable angina, myocardial infarction, heart failure, stroke, intermittent claudication, thrombosis, and arterial hypertension.
3) Deterioration of vascular function: Increased vascular tone due to sympathetic hyperactivity, endothelial dysfunction, and arterial stiffness.
4) Pulmonary: Asthma, chronic obstructive pulmonary disease (COPD), reduced ventilatory capacity.
5) Neurobiological aspects: Cognitive decline, depressive disorders, mood, and anxiety alterations, and increased risk for Alzheimer's disease, particularly in the elderly.
6) Muscle disorders. If the stimulus of exercise does not exist, the muscle fiber is lost with which there is a decrease in muscle strength, resistance to fatigue, loss of balance, and increased risks of fallings with the consequent fracture. Considering current knowledge, muscle mass is a large endocrine organ that produces a series of hormones, plays fundamental roles in glucose and lipid metabolism, and supports the immune system. Sarcopenia will be developed with its characteristic reduction in muscle mass and fiber cross-sectional area, infiltration of the muscle by fat and connective tissue, decreased size and number of type 1 and 2 muscle fibers, mitochondrial dysfunction, proliferation of the sarcoplasmic reticulum and dysfunction of the progenitor cells.
7) Greater physical frailty, especially in the elderly.
8) Quality of life: Decline sense of well-being, psychological frailty, difficulties to carry out routine activities and social interactions, functional restriction, and sleep alterations.
9) Constipation, sedentary microbiota network less efficient.
10) Increased risk of cancer and cancer mortality due to a diversity of mechanisms including an effect on endogenous sex steroids and metabolic hormones, insulin sensitivity, chronic inflammation, oxidative stress, DNA methylation, telomere length, immune function, and gut microbiome are under investigation.
11) Shorter life expectancy with risk of premature death.

6. The "Chair Effect" and Its Repercussions on Health

This term was recently coined to define the time we spend sitting during the day and/or night, whether at work, housework, social gatherings, etc.

As mentioned at the beginning, the current lifestyle flows with a greater time without physical activity, which increases the risk of cardiometabolic conditions due to the constellation of functional abnormalities that occur. Zhao et al. [1] showed in a review of 24 clinical studies that there is a dose-response relationship between sitting time and its association with cardiovascular disease (CVD), cancer, and total mortality, this relationship being closer to time spent watching television. Previously, Bailey et al. [31] in their meta-analysis of nine studies had revealed that the longer the sitting time, the greater the risk of CVD and T2DM, independent of physical activity.

Rezende et al. [32] showed that more than 60% of people spend more than three hours a day sitting (the average in adults is 4.7 hours/day) and this time is responsible for 3.8% of mortality (approximately 433,000 deaths/year). Ekelund et al [33] in their systematic review and meta-analysis asked the question of how much physical activity was necessary to counteract long periods of sitting and the risk of premature mortality. They included 16 prospective studies that included 1,005,791 participants with follow-up between 2 and 18.1 years, during this period 84,609 (8.4%) died. The results suggested the existence of a curvilinear relationship between the least amount of physical activity with the longest sitting

time and increased mortality, this relationship being more evident if physical activity was below 35.5 MET/hour/week.

Consequently, according to these findings, although long periods of sitting cannot be avoided, the negative effect on health associated with sedentary time can be counteracted by physical activity of sufficient intensity during any time of the day or by breaks for physical activity for 10 minutes every hour. However, Stamatakis et al. [34] in their study aimed at analyzing the joint association of sitting time and physical activity with all-cause and cardiovascular mortality in a large sample of middle-aged Australian adults, conclude that the most effective option is a combination of increased time spent on physical activation with shorter sitting time.

7. Discussion

Unless there is an eradication or drastic reduction in sedentary habits with increased physical activity and better nutrition, next generations can expect high cardiometabolic risk for ACVD in their future. Young people must be aware that it is essential to routinely practice some demanding physical activity from early age, adapted to the possibilities of each person, regardless of sex, in order to enjoy a good general state of health in old age. Of course, this practice will also have immediate effects on good health in general and to the extent that it lasts over time, the benefit will be greater, in a dose-response style: the more health care, the better functional capacity in the last decades of the golden years.

It is important to assimilate the fact that sedentary lifestyle is a behavior that is also deleterious for health in the elderly, as much or more impactful than in children and young people, since in those years there is already a marked decrease in functional capacity with a decrease in body mass, muscle deterioration and restricted joint movement, which favors the adoption of comfortable postures with as little physical activity as possible. Such attitudes in old age are prominent contributors to restricted socialization, impaired manual or gait skills, loss of cognitive ability, and the onset or progression of dementia. For these reasons, regular and vigorous physical activity should be mandatory for the elderly and its numerous benefits for physical and mental health have been scientifically proven, although they occur to a lesser extent and intensity compared to those obtained in the young adult. It is well known that older people are the most sedentary and less physically active age group, most of their time is spent on leisure pursuits at home, and often in social isolation [35]. Of course, greater levels of sedentary behavior negatively impact overall active aging, including physical (e.g. functional impairment), psychological (e.g. cognitive function, depression) and social (e.g. sense of belonging, loneliness) components of aging [36]. The matter is not just how long we live, but how long we remain healthy and independent.

In adolescents, being physically active is the most significant and protective strategy to reduce cardiometabolic risk.

Based on the available evidence, sitting time should be considered in people who are not physically active or do not meet the recommended level of physical activity, because the longer the sitting time, more risk of developing a cardiometabolic condition. This is particularly relevant in young subjects with low physical activity, where sedentary behavior should ideally be eliminated or reduced as a potentially effective approach in improving cardiometabolic health, replacing one hour of sitting time with the same lapse in moderate to vigorous physical activity can reduce overall cardiovascular risk by up to 20% [33, 34].

Nonetheless, the evidence is not fully sufficient to describe the dose-response curve between MVPA and inactivity, and if this association changes by category or class of exercise, or duration of sedentary behavior.

Finally, it is important to pay more attention to sedentarism due to the huge number of people affected or living with this unnoticed risk factor for cardiometabolic disease.

8. Conclusions

Sedentarism has increased dramatically over the last 2 decades, particularly in developed countries, although more recently in developing countries as well, and become a heavy problem for public health due to the negative consequences on cardiometabolic risk since the first years of life and linked to a range of chronic health conditions like cardiovascular disease, high blood pressure, T2DM, and obesity and can also increase the risk of dying, either from heart disease or other medical problems. In fact, sedentarism has been identified as the fourth leading risk factor for death worldwide (6% of global deaths) [14].

People need to reduce the amount of time they waste being sedentary, especially during infancy and youthhood to avoid the increase in cardiometabolic risk during adulthood and reach the advanced age with a better functional capacity and more active.

Further observational and experimental studies are needed to define relationships between total sedentary time and patterns of sedentary time with biomarkers of cardiometabolic risk and its impact on health outcomes.

Conflict of Interest

The author declares no competing interests.

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