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Correlation between muscle tissue and type 2 diabetes

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Abstract

Diabetes is one of the most common diseases in the world. There are several types of it with different etiologies. The most common type of diabetes is type 2. Every year, DM2 contributes to the deaths of millions of people worldwide. Its complications pose a huge health as well as economic problem. Nowadays, pharmaceutical companies are outdoing themselves in synthesizing new drugs, using newer and newer mechanisms of action. This meets with the approval of patients – It is easier to take a pill instead of changing your lifestyle. However, it is worth considering and rethinking the pathophysiology of type 2 diabetes. How to effectively reduce the risk of pre-diabetes or developing DM2? In this research study, we will try to give an insight into how important our body's muscle tissue is in the context of diabetes and why it is important to take care of its proper amount and condition. It is hoped that paying attention to this aspect in relation to diabetes will allow for a less invasive and more effective treatment of carbohydrate disorders and contribute to benefiting from the other health effects of developing proper skeletal muscle tissue in the human body.

Introduction

Diabetes is one of the most prevalent diseases in the world, being also the most common metabolic disease worldwide [1]. Despite an increase in the variety and efficiency of diabetes therapies and the public's awareness of it, health care is struggling to cope with the growing number of people with carbohydrate disorders and is spending more and more on dealing with it. In recent years, a widespread trend towards being 'fit' has been noticed [2]. Social media is witnessing an increase in health-promoting content urging people to change their lifestyles for a healthier one. Can the popularisation of healthy lifestyles and body-strengthening exercises affect the health of the population? What is the relationship between the development of muscle mass and protection against the development of carbohydrate disorders, and the consequent reduction in quality of life and years in health? This paper will present the current scientific view on the relationship between skeletal muscle mass and risk of type 2 diabetes.

Epidemiology

Diabetes is a global health problem that is consistently increasing [3]. Some authors now describe DM2 as a pandemic disease. More than 90% of diabetes cases worldwide are type 2 diabetes [4][5]. Citing 2017 sources, approximately 462 million people had type 2 diabetes, equivalent to 6.28% of the global population (4.4% of 15-49 year olds, 15% of 50-69 year olds and 22% of 70+ year olds) and the prevalence rate was 6059 cases per 100,000. More than 1 million deaths per year can be attributed to diabetes alone, making it the ninth cause of human mortality worldwide [6]. Over the years, the number of hospitalised patients whose hospital stay is linked to diabetes is increasing. The rate is already as high as 27% of patients per year [7]. Healthcare expenditure on type 2 diabetes in 2017 globally amounted to USD 850 billion [8]. This is an amount equivalent to the GDP of Switzerland in 2023!

Pathophysiology

The pathophysiology of type 2 diabetes is characterised by 4 major metabolic abnormalities leading to its development: obesity, impaired insulin action, dysfunction of insulin secretion and increased endogenous glucose production (EGO) [9].

Considering muscle tissue, impaired insulin action on insulin receptors located in skeletal muscle, which is commonly referred to as tissue insulin resistance, is considered to be the factor most influential in the development of type 2 diabetes [10]. The mechanism for this disorder is based on abnormal signal transduction through insulin-binding INSR receptors located on the surface of cell membranes and trans-membrane transporters, mainly in the GLUT4 class [11]. INSR receptor dysfunction is the result of two components: a reduced number of INSR receptors (down regulation) on the cell surface and a reduced INSR kinase (IRK) response to receptor stimulation and, consequently, its down-regulation [12], [13], [14]. This results in a reduced capacity for the process of glycogen synthesis, which is the main target for glucose uptake by skeletal muscle cells from serum. It is the main safety guard of our body's carbohydrate balance. The effect of a disturbed glycogen balance is hyperglycaemia and, therefore, the development of type 2 diabetes.

Methodology

This article reviews the current knowledge on the effect of muscle mass on the prevention and incidence of type 2 diabetes. We selected articles with unrestricted access in several databases, mainly PubMed, Google Scholar and Web of Science. We only included in

the review articles written in English and with accessible full text. No restrictions were made due to article type.

Sport and metabolic processes in the muscle cell

According to a 2011 study, humans have an average of 500 grams of glycogen stored in skeletal muscle cells and 100 grams of glycogen distributed in liver cells [15]. Looking at the percentage of glycogen in its structure, the liver appears to be the more important glycogen storage organ in our body. However, considering the quantitative composition of glycogen in the organs, skeletal muscle is the main glycogen store in our body. The only effective way to utilise muscle glycogen stores is through exercise [15]. It has also been described in the literature that glycogen is a negative regulator of glycogen synthase [16]. Considering both pieces of information, it can be concluded that exercise is a key element in regulating the amount of glycogen in our bodies. During research into the physiology of human skeletal muscle cells, it has also been noted that skeletal muscle cells previously subjected to training are able to take up more glucose from plasma and thus accumulate more glycogen [17],[18]. Even a single bout of moderate-intensity exercise increases skeletal muscle glucose uptake by at least 40% [19]. Two enzymes, the previously presented glycogen synthase, hexokinase, and the glucose transporter GLUT4, are mainly responsible for this process [20]. One of the effects leading to increased plasma glucose uptake is the mechanism by which the amount of GLUT 4 transporters on the surface of skeletal muscle cells is induced by exercise [21],[22]. This allows more glucose to be taken up from the plasma, leading to more effective carbohydrate homeostasis of the body and providing a kind of protection against disruption of the body's carbohydrate metabolism. The effect of increased GLUT4 synthesis expressed by the amount of GLUT4 mRNA is elevated up to 24 h after cessation of exercise, but the induced amount of GLUT4 on the surface of muscle cells persists for up to 8 days [23]. However, as with glycogen synthase, excessive glycogen in muscle cells results in inhibition of GLUT4 receptor translocation to the surface of cell membranes [24],[25]. It was also discovered that the higher the concentration of glycogen in muscle cells, the slower glycogenolysis occurs which promotes fat metabolism [17] preventing excessive fat deposition, which is one of the factors in the development of type 2 diabetes. Another interesting observation is the phenomenon that occurs during human starvation. Namely, researchers have found that starvation does not reduce glycogen levels in human skeletal muscle [26]. The long-term state of storing a large amount of glycogen in

skeletal muscle through the above mechanisms can lead to a state of increased insulin resistance [15], which contributes to the development of type 2 diabetes.

Decline in muscle mass and chances of developing type 2 diabetes

Correlations between a decrease in muscle mass and an increased risk of developing type 2 diabetes have been reported in the literature. In the journal Nutrition & Diabetes, a correlation was described in which it was shown that the risk of diabetes was 1.31 times higher in men [OR 1.31 (1.18-1.45), p = 0.0001] and 1.24 times higher in women [OR 1.24 (1.05-1.46), p = 0.01] for each percentage point decrease in lean muscle mass/weight after accounting for age, race, height, smoking and education [27]. This effect is related to the fact that muscle tissue is the main store of glucose in the form of glycogen in the body. Muscle can account for up to 80% of plasma glucose uptake under hyperinsulinaemic conditions during the postprandial period [28],[29],[11]. It was also noted during studies on postprandial carbohydrate uptake that, in addition to a reduced rate of muscle glycogen synthesis, diabetic patients had a longer latency period before the onset of glycogen synthesis (35 ± 6 minutes) than healthy subjects (12 ± 5 minutes) [30].

Similar results were reported in a study published from the National Health and Nutrition Examination Survey in 2010. The HOMA IR index - representing the body's insulin resistance - was elevated in people struggling with little muscle tissue. Skeletal muscle atrophy was associated with insulin resistance in non-obese (HOMA IR index 1.39, 95% confidence interval (CI) 1.26 to 1.52) and obese (HOMA-IR index 1.16, 95% CI 1.12 to 1.18) individuals. Sarcopenia was associated with dysglycaemia in obese subjects (HbA1C ratio 1.021, 95% CI 1.011 to 1.043), but not in normal-weight subjects. Associations were stronger in people under 60 years of age. Those over 60 years of age showed increased levels of insulin resistance, but this did not translate into an increased risk of dysglycaemia [31].

A study of nearly 1,500 Japanese aged between 18 and 85 years showed that those with muscle mass less than 1 degree of deviation for their age had significantly elevated HbA1C levels than peers with normal skeletal muscle mass [32].

A trap that confuses even the most experienced physicians is sarcopenia coexisting with obesity. Excess body weight suggests that muscle tissue mass is also elevated. Unfortunately, the two coefficients are not correlated. Contrary to popular opinion, the phenomenon of sarcopenia in obesity may affect up to 34.8 per cent of obese men and 50.1 per cent of obese women [33]. The effect resulting from low muscle mass compounded by

chronic inflammation or increased tissue resistance to insulin resulting from obesity contributes to carbohydrate disorders overlooking the obvious impact of excessive body weight and abnormal lifestyle [34]. It is also an interesting observation that while low muscle mass has an impact on the development of type 2 diabetes, the way in which adipose tissue is distributed (android, gynoid) does not in itself affect the chances of developing carbohydrate disorders [27]. Thus, physical exercise aimed at increasing muscle tissue as well as muscle quality can greatly contribute to reducing the risk of DM2 despite obesity.

Increased muscle mass versus reduced chance of dysglycaemia and DM2.

There are also studies in the literature showing a directly proportional effect between increased muscle mass and a reduction in insulin resistance and the chances of developing type 2 diabetes [35]. In the study in question, the study group was divided into groups based on total skeletal muscle mass. A correlation was observed that as total skeletal muscle mass increased, insulin resistance decreased and the risk of developing DM2 decreased. Of the factors examined - HOMA IR, HbA1C, pre-diabetes status and diabetes - an increase in skeletal muscle mass had the greatest effect on reducing the risk of diabetes - by 63%. The smallest effect was observed with respect to HbA1C concentration - 5.8%. Similar results were obtained by researchers in Korea [36]. The study groups were divided by MMI - muscle mass index corrected for body weight. It was noted that people in the group with the smallest MMI used in this study were more than 2.3 times more likely to develop type 2 diabetes than those in the group with the largest MMI. Moreover, even obese people who had a higher MMI than those with the corresponding BMI but less muscle mass had a lower risk of developing diabetes. The difference in risk for the group with the smallest MMI and the risk for the group with the largest MMI was 1.42 [95% CI 1.03, 1.95]) [36].

It is also worth noting that the effect of skeletal muscle mass on glycaemic reduction is significantly greater in people who have not developed diabetes [37]. Individuals with type 2 diabetes respond less with a reduction in glycaemia with an increase in muscle mass. This is due, among other things, to the generalised inflammation that accompanies obesity, which is often co-present with DM2 [38]. Through localised inflammation in skeletal muscle, cell metabolism is targeted to produce pro-inflammatory factors [39],[40], resulting in dysregulation of metabolic processes including glycogen synthesis, resulting in increased insulin resistance in the body, as well as promotion of catabolic transformation of muscle cells, resulting in decreased muscle strength and increased risk of disability [41].

Discussion

It is unequivocal that muscle tissue affects the carbohydrate metabolism of the human body. This effect is often overlooked in discussions about type 2 diabetes. It is worth encouraging patients to exercise as it shows pleiotropic effects. Regular participation in amateur sport improves mood and mental health [37]. Physical activity is also known to increase the quantity as well as the quality of muscle mass [42] - we use this against the development of diabetes by improving metabolic pathways, in particular synthesising muscle glycogen. It is an effective way to prevent the development of overweight and obesity [43] - which in effect reduces generalised inflammation and insulin resistance in tissues. It increases quality of life for people with disabilities (HRQoL) [44]. A large positive impact can also be noted on the cardiovascular system, whose diseases are one of the most common causes of health loss worldwide [45]. According to the WHO, sufficient physical exercise to maintain health and reduce the chances of developing metabolic diseases including type 2 diabetes is 150min of moderate exercise per week or 75min of vigorous exercise and exercise that strengthens the major muscle groups 2 or more times per week. [46]. Doctors, particularly GPs, should educate patients about the impact of regular exercise and its effects on health. This is an effective approach. It has been shown that people with a higher level of education have more muscle tissue as well as greater muscle strength than less educated people [47]. This phenomenon should encourage physicians to devote more of their patients' time to health education. Particularly when data show that the majority of those with type 2 diabetes do not meet weekly physical activity targets [48].

Conclusions

The amount of muscle tissue correlates with the chance of developing type 2 diabetes. The more muscle tissue, the lower the chance of developing type 2 diabetes or pre-diabetic conditions [35]. This effect is present even with unfavourable conditions such as obesity. Regular physical activity that develops muscle tissue is an effective method of reducing the risk of pre-diabetic conditions and the incidence of type 2 diabetes. It is worth starting to develop an optimal exercise protocol to take advantage of the phenomena described in the current study, resulting in improved therapy against carbohydrate disorders.

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