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THE EFFECT OF OBESITY ON THE CARDIOVASCULAR AND ENDOTHELIAL SYSTEMS

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Resume: Obesity is one of the most common chronic diseases in the world. To date, many epidemiological studies have been conducted to determine the relationship between an increase in the prevalence of obesity and an increase in the number of other diseases. It has been proven that the development of obesity contributes to the occurrence of many cardiovascular diseases, type 2 diabetes mellitus, cholelithiasis, oncological diseases, diseases of the musculoskeletal system. Many scientific studies have also noted that this disease causes inflammatory processes in the vascular endothelium and contributes to the development of atherosclerotic cardiovascular diseases.

Keywords: obesity, cardiovascular diseases, endothelial dysfunction, NLRP-3, sVCAM-1

Relevance

Obesity is a complex, multifactorial disease characterized by excessive accumulation of adipose tissue in the body, leading to the development of serious health problems such as type 2 diabetes mellitus, cardiovascular diseases, hypertension, and dyslipidemia. Over the past 50 years, obesity has gradually evolved into a global epidemic. After smoking, obesity is the second leading preventable cause of death worldwide [31].

This disease is characterized by an imbalance between white and brown adipose tissue and leads to alterations in glycolysis, gluconeogenesis, and lipid metabolism. The increasing prevalence of obesity is more commonly observed among urban populations and is a consequence of an imbalance between energy intake and expenditure. Currently, approximately one third of the world's population—around 2.2 billion people—are overweight, and nearly 712 million people (about 10%) suffer from obesity [16].

The prevalence of obesity is 11% among men and 15% among women. By 2030, it is projected that 60% of the global population—approximately 3.3 billion people—will be overweight, and 1.1 billion will have obesity [39].

As of 2019, Uzbekistan ranked 123rd globally in terms of obesity prevalence. Among adults aged 18 years and older, obesity prevalence was 16.6%, while 48.2% were overweight [23]. In Uzbekistan, cardiovascular diseases—particularly arterial hypertension—rank first among causes of mortality, followed by hyperglycemia, obesity, and hypercholesterolemia. Notably, in 2019, obesity-related deaths accounted for 16.7% of total mortality [23].

Obesity is considered a major risk factor for the development of several severe diseases, including cardiovascular, metabolic, and oncological conditions [20]. An increase in obesity

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prevalence inevitably leads to an increase in obesity-associated diseases. For example, due to the rising incidence of type 2 diabetes mellitus, the American Diabetes Association (ADA) lowered the recommended age for screening for carbohydrate metabolism disorders from 45 to 35 years in 2021 [28].

Several malignancies are associated with high body mass index (BMI): 11% of colorectal cancer cases, 9% of postmenopausal breast cancer, 39% of endometrial cancer, 25% of kidney cancer, and 37% of esophageal cancer are linked to obesity. Moreover, more than 65% of all obesity-related cancers are endometrial, postmenopausal breast, and colorectal cancers [30].

In addition, obesity causes excessive mechanical load on joints, leading to impaired function and mobility, disrupts pulmonary function, and contributes to the development of obstructive sleep apnea [27].

Obesity in Asian Populations

In recent years, due to nutritional imbalance and low physical activity, a rising trend in obesity prevalence has been observed in Asian countries. Asian populations have specific characteristics of obesity: despite having similar or even lower BMI values, individuals of Asian descent tend to have a higher percentage of body fat and lower skeletal muscle mass compared to Caucasian populations. At the same time, excessive fat accumulation in the abdominal organs and liver (non-alcoholic fatty liver disease) is observed, which worsens cardiometabolic risk, morbidity, and mortality prognosis [21].

These factors necessitated changes in diagnostic criteria for overweight and obesity in Asian populations compared to non-Asian populations [21]. It is well known that waist circumference has higher prognostic value than BMI in identifying metabolic syndrome. However, waist circumference does not account for height, which may limit cardiovascular risk prediction in very tall or very short individuals. Despite this, BMI has important advantages: it is easy to measure and convenient for rapid and early identification of obesity in primary healthcare settings.

Even at the same BMI, the percentage of body fat may differ among various Asian ethnic groups. Overall, Asians have a higher cardiometabolic risk at lower BMI values compared to non-Asian populations. Therefore, BMI remains a key anthropometric indicator for diagnosing overweight and obesity in Asian populations [29]. Lower BMI cut-off points are generally recommended, although these criteria are still under discussion and may vary across Asian countries depending on ethnic characteristics. In 2019, the ADA outlined BMI thresholds for Asian Americans in the “Obesity Management” section of the Standards of Medical Care in Diabetes [10].

Obesity and Cardiovascular Diseases

Cardiovascular diseases are among the leading causes of death worldwide, accounting for approximately 31% of all deaths, or about 18 million deaths annually [26]. Regardless of its severity, abdominal obesity plays a central role in the development of cardiovascular risk [2].

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If not corrected in a timely manner, abdominal obesity leads to metabolic syndrome, characterized by visceral obesity, elevated blood pressure, hypercholesterolemia, hypertriglyceridemia, and fasting hyperglycemia [3].

According to the INTERSALT study, each 4.5 kg increase in body weight is associated with a 4.5 mmHg increase in systolic blood pressure [19]. Hypertension remains one of the leading causes of death from cardiovascular diseases worldwide, resulting in approximately 182 million deaths and 10.4 million cases of disability annually [23].

Obesity is linked to arterial hypertension through multiple mechanisms. Excess body weight leads to adipose tissue dysfunction, activation of the renin–angiotensin–aldosterone system, systemic inflammation, and oxidative stress. As a result, endothelial dysfunction develops, peripheral vascular resistance increases, vasoconstriction occurs, and vascular wall hypertrophy progresses [18].

Recent studies suggest that leptin may also contribute to obesity-related hypertension. Leptin produced by adipocytes can activate the sympathetic nervous system via the melanocortin pathway, leading to increased blood pressure [37].

Another major cardiovascular risk factor associated with obesity is decreased insulin sensitivity and hyperglycemia, which are predictors of type 2 diabetes mellitus [36]. Ectopic fat accumulation and excess metabolites disrupt insulin signaling, autophagy, and the gut–brain axis, ultimately leading to β-cell dysfunction and progressive hyperglycemia [35].

Obesity and Endothelial Dysfunction

There is no doubt that obesity leads to endothelial dysfunction [4]. As body weight increases, visceral fat accumulation contributes to multiple cardiovascular risk factors, including dyslipidemia, insulin resistance, hyperinsulinemia, impaired fibrinolysis, and endothelial dysfunction. Even in individuals with normal BMI, excess visceral fat may lead to ectopic fat deposition in the heart, liver, and skeletal muscles, increasing cardiovascular risk [17].

Central fat distribution promotes the production of inflammatory cytokines such as TNF-α and IL-6, which contribute to muscle mass loss and sarcopenia [14]. Increased oxidative stress markers, including F2α-prostaglandins, have also been detected in plasma and urine [33].

Visceral adiposity induces hypoxia in the endoplasmic reticulum, stimulating inflammatory gene expression. Elevated leptin levels and reduced adiponectin levels further activate immune cells [12].

Numerous studies demonstrate that metabolic (bariatric) surgery reduces visceral fat, leading to improvements in leukocytosis, systemic inflammation, and endothelial dysfunction. Significant reductions in C-reactive protein, interleukin-6, and tumor necrosis factor-α have been reported after bariatric surgery [12]. Improvements in endothelial dysfunction markers such as sVCAM-1 persist for up to 24 months postoperatively [38].

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Obesity also triggers the expression of sVCAM-1, an endothelial dysfunction marker that facilitates adhesion and migration of circulating monocytes and lymphocytes into the endothelium, playing a key role in chronic inflammation and atherogenesis [1,7].

Conclusion

In conclusion, obesity has a detrimental effect on the cardiovascular and endothelial systems and contributes to the development of life-threatening diseases. Despite extensive research aimed at understanding and preventing obesity, it remains a highly relevant global health problem. Therefore, further research in this area is of critical importance.

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