Is obesity a real cardiovascular risk factor?

Je obezita skutočným kardiovaskulárnym rizikovým faktorom?

Tamás Forster

2nd Department of Medicine and Cardiology Center Albert Szent-Györgyi Medical Center, University of Szeged, Hungary

✉ **prof. Dr. Tamás Forster, MD, PhD, FESC, FACC, FAHA** | forster.tamas@med.u-szeged.hu | www.med.u-szeged.hu

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Abstract
Obesity has strong relationship to cardiovascular diseases. Cardiovascular morbidity and mortality increased in overweight and obese individuals. Abdominal (visceral) obesity is a part of metabolic syndrome which is also responsible for increased cardiovascular risk. However, according to certain observations, a subgroup of obese patients presented decreased cardiovascular mortality which is called obesity paradox. Similar term is healthy obesity although cardiovascular events become more frequent in overweight or obese patients during long-term follow-up. Summarizing all pathophysiological data, it can be stated that obesity substantially increases cardiovascular risk and significantly contributes to morbidity and mortality.

Abstrakt
Obezita má silný vzťah ku kardiovaskulárnym ochoreniam. Kardiovaskulárna morbidita a mortalita narastá u pacientov s nadváhou a obezitou. Abdominálna (viscerálna) obezita je súčasťou metabolického syndrómu, ktorý je tiež zodpovedný za zvýšenie kardiovaskulárneho rizika. Podľa niektorých pozorovaní bol v podskupine obéznych pacientov nižší výskyt kardiovaskulárnej mortality, tento stav bol nazvaný ako paradox obezity. V literatúre sa môžeme stretnúť s často diskutovaným termínom zdravá obezita, hoci vieme, že kardiovaskulárne príhody sa počas dlhodobého sledovania častejšie vyskytujú u pacientov s nadváhou alebo obezitou. Po sumarizácii všetkých patofyziologických údajov môžeme skonštatovať, že obezita podstatným spôsobom zvyšuje kardiovaskulárne riziko a významne prispieva k morbidite a mortalite.

Introduction

Cardiovascular diseases are still the leading cause of morbidity and mortality, especially in the developed countries. The prevalence of weight excess is increasing worldwide and pose serious burden to healthcare systems. According to recent data, overweight and obesity affect more than half of the population worldwide. It seems to be that obesity is the epidemic of the 21st century. Obesity has strong relationship to hypertension, diabetes, hyperlipidemia, atrial fibrillation, heart failure and OSA (obstructive sleep apnoea). Thus, obesity is a negative determinant for longevity.

Obesity as a risk factor

The basis of cardiovascular diseases is multifactorial. Risk factors can be categorized as non-modifiable, modifiable and novel ones. Age, gender and genetic disposition are non-modifiable, other risk factors such as hypertension, diabetes, hyperlipidemia, sedentary life style and stressful environment are modifiable. Novel risk factors comprise lipoprotein(a), homocystein, hyperuricemia and some others. Risk factors may affect endothelial function and the atherosclerotic process initiated and "cardiovascular continuum" will start [1].

In a small, north-american city a project was introduced following all inhabitants (approximately 6000 people) continuously for years. This was the Framingham Heart Study collecting epidemiological information about health status. They proved strong relationship between modifiable risk factors and cardiovascular morbidity and mortality. Relationship between body weight and incidence of cardiovascular events was separately analyzed [2]. With increasing body weight the number of cardiovascular complications become greater both in men and women which was more pronounced at older ages. Every 1 kg/m^2 increase in body mass index (BMI) increased the risk of heart failure by 5 % in men and 7 % in women during 14-year observation period

[3]. They observed that with increasing weight the cumulative incidence of heart failure linearly rising or even after 15 years endurance the frequency became exponential. Later, numerous publications confirmed this observation.

Further studies drew the attention to body fat distribution, i.e. not all types of obesity are dangerous for health. Abdominal obesity – visceral adipose tissue appeared to be responsible for cardiovascular problems. The most frequently used BMI is the less accurate method to assess body fat distribution. Therefore other methods are advised like waist circumference, waist-to-hip ratio or waist-to-height ratio. New imaging techniques (dual energy X-ray absorptiometry – DEXA, MDCT or MRI) can quantitatively measure body fat allocation. In a study, the increasing amount of visceral adipose tissue positively correlated with cardiovascular events, whilst the amount of lower body fat showed negative association with cardiovascular problems [4].

Some data suggest that body weight and fat distribution are related to arterial stiffness and early vascular changes. In our earlier observation, an increased arterial stiffness was demonstrated by echocardiography among patients with obesity even in young adults [5]. Increased arterial stiffness is an important risk factor and predictor of cardiovascular mortality. Fortunately, physical training-induced weight reduction is associated with improved aortic distensibility [6].

These data positively supported the maleficent effect of obesity on cardiovascular health.

Metabolic syndrome

Reaven introduced the term of metabolic X-syndrome in 1988 [7]. Originally, parts of the syndrome were abdominal (visceral) obesity, insulin resistance, hypertension and dyslipidemia. These are called the "deadly quartet". Later, other components are associated with this syndrome but the original four elements pose the majority of cardiovascular risk. In a Finnish study (Kuopio Ischemic Heart Disease Risk Factor Study), cardiovascular events were evaluated in men with vs. without metabolic syndrome [8]. In this study, men with metabolic syndrome had the chance to die more than 3 times more frequently as compared to men with normal metabolic state. Even death of any cause was more than 2 times likely. It is frequently debated whether the origin of metabolic syndrome is abdominal obesity or insulin resistance. Adipose tissue is not only a fat storage site but it is also an endocrine organ. Adipose tissue produces more than 50 metabolically active substances called adipokines (leptin, adiponectin, resistin, visfatin, omentin and others). Adipose tissue produces leptin which regulates appetite and energy balance. Leptin resistance is predominantly the cause of obesity. Elevated leptin level leads to sympathetic overactivity (tachycardia, hypertension) which reduces insulin sensitivity. It seems to explain that abdominal fat might play a dominant role in metabolic syndrome.

Obesity paradox

Surprisingly, numerous publications reported better survival among obese patients suffering from hypertension, ischemic heart disease, heart failure or atrial fibrillation as compared to their normal weight counterparts. This phenomenon is called "obesity paradox" which questioned all previous observations. Lavie et al. [9] investigated the 3-year survival of patients with stable coronary heart disease. They payed more attention to body composition than to the standard BMI. Body fat (BF) was measured as a sum of skin-fold method and Lean Mass Index (LMI) was calculated using the equation of (1-BF) x BMI. Patients falling in the category of High BF/High LMI had better survival as compared to Low BF/Low LMI category. This observation draw the attention to awareness of body fat composition. In a short communication Neeland I. J. et al. clearly demonstrated that high amount of visceral adipose tissue positively correlated with the incidence of cardiovascular diseases [4]. On the contrary, lower body subcutaneous adipose tissue inversely related to the risk of cardiovascular events. Visceral adipose tissue seems to have causative effect in cardiovascular risk. Advanced imaging tools (DEXA, MRI) may provide more accurate characterization of obesity than BMI, allowing better refinement of cardiovascular risk.

A direct relationship can be deducted from pathophysiologic considerations between excessive adipose accumulation and heart failure occurrence. In a large meta-analysis comprising 9 observational studies almost 30.000 patients were followed up for 2.7 years. It is demonstrated that overweight and obese patients with heart failure had reductions in both cardiovascular and all-cause mortality [10]. Other studies also confirmed this statement. There are speculations explaining this observation. Concerning that heart failure is a catabolic state, obese patients may have more metabolic reserve. Adipose tissue produces cytokines which may be protective in obese patients. RAAS activity may be attenuated which also may explain better prognosis [11]. Other confounding factors including hypertension, ischemic heart disease, atrial fibrillation, diabetes etc. might have impacted prognosis.

"Healthy obesity"

Furthermore, it still exists the term of "healthy obesity" which covers obese patients without risk factors and cardiovascular diseases. A subgroup approximately 10–30 % of obese patients has no metabolic risk factor in spite of extreme accumulation of body fat. Metabolically healthy obesity is more frequent among women. With increasing age, the percentage of metabolically healthy obesity decreasing. Metabolically healthy patients have no higher risk for cardiovascular diseases and mortality as compared to healthy non-obese individuals [12]. During long-term observation, it is confirmed that metabolically healthy obese patients have four times higher risk to develop type 2 diabetes as compared to metabolically healthy normal weight subjects in the future [13]. This observation

suggests that metabolically healthy obesity is not absolutely harmless alteration.

Conclusion

Obesity clearly alters cardiovascular structure and function leading to systolic and, especially, diastolic dysfunction. In general population, cardiovascular morbidity and mortality increased. Nevertheless, many studies described "obesity paradox" phenomenon – a more favorable outcome among overweight and obese patients. Until now, there is no exact explanation for this observation although speculations are given.

Summarizing all pathophysiologic and epidemiological data, obesity has to be considered as a real cardiovascular risk factor.

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