

Advances in fasting aerobic exercise research

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Abstract: As of 2020, obesity has become a worldwide crisis and the rate of obesity in China has exceeded 50%, there's no doubt obesity has become a major problem that plagues the healthy development of China's economy and the well-being and health of national life. Not only exercise is a good doctor, but also to solve the problem of obesity efficient means. In order to reduce the obesity rate, we have taken many exercise methods, such as resistance exercise, aerobic exercise, special exercise, but most of them have the problems of inability to adhere to and inefficiency. At this time, fasting aerobic as a new method of weight loss came into the forefront, a large number of experimental studies have been conducted on fasting aerobic abroad, and thanks to the points that have been found, fasting aerobic has been used as an effective method to cope with cardiovascular diseases, metabolic diseases and obesity abroad. On the basis of a thorough reading of domestic and international literature, the authors summarize the existing studies on fasting aerobics, hoping to point out the direction for subsequent research, so that everyone can fully understand the benefits of fasting aerobics and actively promote it.

Keywords: fasting aerobic; glucose and lipid metabolism; insulin resistance

1. Backgrounds

Obesity has been confirmed to be closely related to a series of cardiovascular and cerebrovascular diseases, such as coronary heart disease, diabetes, stroke, etc., which has seriously endangered human health. With the economic development of human society, "obesity" has become a global problem (Wang Y, et al., 2017; Wang Y, et al., 2006), and the World Health Organization officially listed "obesity" as a disease in 2020. Our people are suffering from "obesity" for a long time (Wang Y, et al., 2007), besides, the obesity rate of our population has surpassed the United States and become the world's first obese country. Although the economic take-off in the past few decades has brought unprecedented material enrichment to Chinese people, the concept of health has not yet become popular, which leads to the rampage of hypertension, diabetes, stroke and other chronic diseases caused by obesity caused by unhealthy diet and lack of exercise in China (Estes C, et al., 2018). In 2019, the number of deaths caused by chronic diseases in China accounted for 88.5% of the total death population, and has now become a major burden on the medical system and the health of Chinese people in China. In addition, owing to the increasingly serious problem of adolescent "obesity" (Steinbeck KS, et al., 2018), many chronic diseases such as hypertension (Seeman T, et al., 2019), diabetes, and gout begin to show a visible tendency to adolescent group, which has become a tough problem afflicting the healthy development of Chinese society. How to carry out scientific exploration for the "obese" population and find a scientific and effective weight loss method is the starting point and desire of this review. At present, people have fully recognized the benefits of exercise for health and chronic diseases, and many exercise methods, such as aerobic exercise, resistance exercise (Piercy KL, et al., 2018), resistance plus aerobic combined exercise (Ho SS, et al., 2012), HIIT high-frequency intermittent exercise (Batacan RB, Jr., et al., 2017), and special exercise, have begun to be gradually accepted by the public, but there is a lack of an efficient and sustainable fat reduction exercise. Resistance exercise and dedicated exercise require professional venues and devices; although the combination of aerobic and resistance exercise can efficiently lose weight, it takes too much time; HIIT exercise is effective, but it requires a good training basis and cannot be introduced with a weak foundation; aerobic exercise was first proposed by Cooper and defined by the Oxford Dictionary in 1986 as — an exercise method that meets the increase and maintenance of moderate oxygen intake through exercise and is beneficial to the respiratory and circulatory systems (Fisher JP, et al., 2015; McKenzie DC, 2012). In decades of practical and scientific research exploration, it has been found that it can effectively improve body shape, fasting blood glucose, blood lipids and blood pressure and recognized as a safe and effective means of weight loss (Gollisch KS, et al., 2009). With the deepening

of research, Davis et al.(Davis JM, et al., 1989) proposed in 1989 that the thermogenic effect of premeal and post-prandial exercise were totally different, and once it was introduced, it set off a wave of research on the effect of post-fasting exercise on body composition. Since then, fasting aerobic has gradually entered the public career as an efficient and convenient way to reduce fat, and is widely used as a final "tool" to reduce stubborn fat among bodybuilders and enthusiasts (Robinson SL, et al., 2015; Hartgens F, et al., 2004). In addition, fasting aerobics has been a hot research topic in foreign sports circles and sports medicine in recent years (Hartgens, 2004).The research on its mechanism, molecules and phenotypes has become more and more in-depth and comprehensive. This review hopes to synthesize domestic and foreign research, summarize the current situation of fasting aerobic research, make a specific description of its mechanism, and provide a theoretical reference for future research.

2. Fasting aerobic mechanism and the current status of domestic and international research

2.1 Fasting aerobic mechanism

The fasting state refers to the physical state of fasting for more than 8 hours, while fasting aerobic refers to endurance exercise in fasting state(Meng H, et al., 2020). In fasting or hungry state, the body maintains a constant blood glucose level by isogenic glucose such as lysine and glycerol(Secor SM, et al., 2016). The process of conversion of non-sugar compounds, pyruvate, lactate, glycerol, amino acids, etc. into glucose is called gluconeogenesis. In a prolonged fasting state, the body with no exogenous energy intake and nearly complete glycogen depletion, will preferentially choose adipose tissue for catabolism to meet the needs of vital activities. A consensus at this time suggests that in the fasting state, the body's utilization of fat is excessive(Secor SM et al., 2016; Tinsley GM, et al., 2015), so the caloric deficit caused by fasting aerobic can cause body fat reduction in the short term and even regulate autophagy to delay aging(Blagosklonny MV, 2019; Kristensen CM, et al., 2018).Aerobic exercise alone inevitably loses more skeletal muscle during the long fat reduction process and even leads to the appearance of a fat reduction plateau (Maughan RJ, 2010), and Maughan argued that muscle augmentation is not suitable in the fasting state. Fasting aerobic exercise as a unique way to combine fasting and exercise, breaking the traditional concept of exercise after meals, and greatly improves the efficiency of exercise fat reduction(Li L, et al., 2013).

2.1.1 Status of foreign research

The hot wave of fasting aerobic research, in foreign countries, has continuous for decades, the research direction is all over the molecules, physiological mechanisms, appearance, etc., and it is precisely due to the benefits of fasting aerobic found in the past research that it has been very mature in foreign countries as a healthy and effective method for the prevention and treatment of hypertension, hyperlipidemia, coronary heart disease, diabetes and other chronic diseases.

In terms of the appearance of animal studies: Mc Sheer(Jospe MR, et al., 2020) and others used 12-month-old Wister rats for experiments and found that the weight loss effect of the experimental subjects in the fasting state was significantly greater than that of the control group; The study by Mark E Smyers et al. (Smyers ME, et al., 2021) specifically selected rats with low fat oxidation capacity and high fat oxidation capacity. The results showed that although the weight loss was not statistically significant, the "fat loss" of rats in the fasting aerobic exercise group was significantly greater than that in the feeding group, which was also confirmed by the study by Antonio Real-Hohn(Real-Hohn A, et al., 2018);In terms of human phenotypic and physiological mechanism research: Ferland (Ferland A, et al., 2007) convened 10 patients with stage II diabetes to conduct a randomized trial and found that fasting aerobic exercise had a wonderful effect on energy metabolism after the experiment; Milena Barbon (Carvalho MB, et al., 2020) discovered that it could significantly improve fat combustion efficiency compared with the placebo control group after ingesting 6 g taurine to 17 healthy men; SAMARMAR (Chacaroun S, et al., 2020) convened 23 healthy volunteers and conducted the experiment and found that the mixed exercise fasting aerobic group had a perfect weight reduction effect than the other single exercise groups, of which the fasting exercise group had a better fat loss effect than the mixed exercise group . Fereshteh et al. (Aliasghari F, et al., 2017) convened 83 patients with nonalcoholic fatty liver disease to perform fasting exercise intervention and found that it could effectively improve the condition ; Kristin K (Hoddy KK, et al., 2016) found that the satiety developed by fasting aerobic exercise facilitated long-term weight loss in 61 healthy volunteers after an eight-week exercise intervention, which is instructive for people's long-term weight loss; it's interesting that Victoria J(McIver VJ, et al., 2019) , after experiments with 12 people, found that gastrointestinal function, hunger and appetite regulating hormones were insensitive to low-intensity activities, which

suggested that people needed to perform a certain degree of high-intensity stimulation. Jenna B. Gillen performed thigh muscle biopsy after fasting aerobic exercise intervention experiments in 16 volunteers and found that fasting training-induced increased mitochondrial capacity and increased maximum activity of citrate lyase and β -hydroxycoenzyme A dehydrogenase (Gillen JB, et al., 2013); even in Alessio Nencioni (Nencioni A, et al., 2018) —on metabolic molecules and clinical applications of fasting and cancer —discovered fasting can alter cancer factors. Almost all of their studies found that fasting aerobic was effective in reducing blood glucose, blood pressure, blood lipids, and insulin resistance levels in "obese" people. In summary, fasting aerobic has enough advantages from the perspective of human physical status and physiological indicators to allow us to adhere to and use.

2.1.2 Domestic research status

Domestic research on fasting aerobics started late and is relatively small, but abundant results have still been achieved at the phenotypic, physiological and molecular levels. In terms of performance and physiological studies, researchers in China have conducted extensive studies on patients with metabolic syndrome, diabetes, and stroke, and have achieved good efficacy in terms of physiological parameters: body mass index (BMI), triacyl glycerides (TG), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (Fasting blood-glucose, FPG), 2-h plasma glucose (2-h protein-cholesterol), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C) and other parameters closely related to metabolic diseases of the body have achieved effective control and decrease; meanwhile, high-density lipoprotein-cholesterol (HDL-C) has increased. Recent studies have shown that the consumption of triglycerides in one hour has only 50% of the fat-burning effect in the fasting aerobic state, which can have higher levels of blood glycerol and fatty acid release, stimulate higher metabolic levels (Enevoldsen LH, et al., 2004), and have a positive feedback on the treatment of patients with nonalcoholic fatty liver disease and type 2 diabetes. In molecular research, fasting aerobic has not been done, but many aerobic levels have emerged that can provide guidance for fasting aerobic. Ji Lili found that vascular aortic molecules LOX-1, NF- κ Bp65 and caspase-3 protein expression increased; Wang Xiaoqiang, Li Xun and others found that exercise intervention miR-7/PDX-1/GLUT2-GCK with dietary plan can effectively improve islet function; Wang Tianyuan, Wang Xiaohui found the factors PPAR α , PPAR γ and PPARs after aerobic exercise intervention in diabetic rats for 4 weeks, 6 days a week, 60 min a day! / σ expression increased; Li Jun, Feng Lijie found that inflammatory factors decreased, Nrf2/ARE signaling was activated, and vascular oxidative stress was relieved after eight weeks of swimming exercise in diabetic rats; Zhang Qiang performed intervention experiments by dividing rats into ketogenic diet, ketogenic diet and aerobic exercise groups, ketogenic diet and high-frequency intermittent exercise groups and found that aerobic exercise may accelerate fat oxidation in liver tissue of diabetic mice by activating AMPK/ACC/CPT1A signaling pathway and slow down the process of fatty liver development, while high-intensity intermittent exercise did not rely on this regulatory pathway. Various domestic studies also lay a certain foundation for the future development of fasting aerobic. With the understanding of the public and researchers, fasting aerobic will certainly set off an upsurge in China in the future.

3. Benefits of fasting aerobic

3.1 Improving Insulin Sensitivity and Insulin Resistance

3.1.1 Insulin Sensitivity

In recent years, a large number of domestic and international studies have shown that fasting aerobic exercise can improve insulin sensitivity, but glucose and insulin metabolism under fasting exercise is a very complex and interesting thing. In the fasting state, the body's glycogen is consumed overnight and blood glucose is at a low level, when glucagon, which promotes catabolism, is high and insulin is low. It can promote glycogenolysis and gluconeogenesis, significantly increase blood glucose; in addition, it can also activate lipase, promote the notice of lipolysis to strengthen fatty acid oxidation, so that ketone bodies increase.

For example, the application of different relative exercise intensities significantly affected blood glucose and insulin concentrations. In trained cyclists, elevated blood glucose and insulin concentrations (above anaerobic threshold at 86% of VO₂ peak) were found during high-intensity exercise in the fasted state (as opposed to exercise in the fed state). In contrast, during moderate-intensity endurance exercise (below the anaerobic threshold at 79% of peak oxygen), fasting was comparable to fed state blood glucose and insulin concentrations. Thus, changes in blood glucose

levels during exercise depend, at least in part, on exercise intensity. It is well-known that high-intensity exercise is associated with greater epinephrine and growth hormone synthesis/release, which will stimulate hepatic glucose output. Blood glucose concentrations may increase during high-intensity exercise (above the anaerobic threshold) due to greater glucose production rather than glucose utilization (in skeletal muscle cells).

Lei Yu develops insulin resistance through an 8-week diet in rats. Aerobic exercise can inhibit or reduce the occurrence of insulin resistance in the body, acting through activation of IL-6 and AMPK, IL-6 may reduce blood glucose by activating GLUT4 mRNA; Guo Yin conducted a 4-week exercise intervention experiment in 126 obese adolescents at Shanghai Peak Training Camp and found that aerobic exercise can effectively improve the body morphology of obese children and adolescents, improve lipid metabolism disorders and insulin resistance, and prevent metabolic syndrome; Gui shukang performed an 8-week aerobic exercise intervention in mice with treadmill and found that aerobic exercise can reduce the concentration of insulin and IGF-1 in serum and significantly improve insulin sensitivity in insulin-resistant mice; Sun Min found that insulin resistance is related to extracellular matrix protein (EMC); Wang Zhengqing and others performed a 12-week aerobic exercise intervention in diabetic patients and found that 12-week aerobic exercise can effectively improve the metabolic abnormalities such as hyperglycemia, low insulin sensitivity, and insulin resistance in IGR population, regulate the secretory function of islet β cells, and reduce the risk factors of cardiovascular disease. It normalized blood glucose in 62.4% of patients with impaired glucose regulation (IGR).JA (Houmar JA, et al., 2004) conducted a study of 154 overweight subjects and found that 170 min of exercise per week better improved insulin sensitivity than 120 min of exercise, and there was a relationship between insulin sensitivity and sedentary.

3.1.2 Insulin Resistance

Insulin can promote the uptake and utilization of glucose by tissues and cells, accelerate the synthesis of glucose into glycogen, store in liver and muscle, inhibit gluconeogenesis, promote the conversion of glucose into fatty acids, store in adipose tissue, resulting in decreased blood glucose levels. In insulin deficiency, the blood glucose concentration increases, and once the renal glucose threshold is exceeded, sugar will appear in the urine, causing diabetes. Insulin resistance, on the other hand, refers to a decrease in the ability of insulin to maintain normoglycemia, which produces biological effects below normal levels, or a decrease in tissue responsiveness to insulin. It is mainly manifested in the reduced utilization of glucose uptake by peripheral tissues, especially adipose tissue and skeletal muscle, as well as the effect of reducing hepatic glucose output (Cheng S, et al., 2017). At present, obesity is considered to be the most important cause of insulin resistance, especially central obesity, which is mainly related to long-term insufficient exercise and excessive dietary energy intake. Patients with type 2 diabetes are diagnosed with obesity and insulin resistance is a more important risk factor leading to coronary heart disease or stroke. A large number of studies have shown that aerobic exercise can reduce insulin resistance in obese people and people with metabolic diseases, including college students, elderly patients with IGF, patients with IGF, obese patients, patients with early diabetes and elderly patients with diabetes, all of which have achieved good improvement results; Karen Van (Van Proeyen K, et al., 2010) found that systemic glucose tolerance and insulin sensitivity were significantly improved during fasting aerobic exercise intervention experiments on clerkships.

3.2 Improvement of diabetes and metabolic diseases

Type 2 diabetes is a chronic metabolic non-communicable disease characterized by chronic hyperglycemia and insulin resistance caused by various factors such as genes, environment and lifestyle (Yang SH, et al., 2010). Although insulin resistance and β -cell failure are considered to be the main causes of the development of type 2 diabetes, a large body of evidence suggests that diabetes is a systemic inflammatory metabolic disease. At present, diabetes is still incurable, so it is also known as chronic cancer.

Diabetes mellitus is currently the most serious chronic metabolic disease in China. It is reported that as of 2013, diabetic patients in China have accounted for 11.6% of the total population. Cardiovascular disease and insulin resistance caused by obesity caused by lack of exercise and unhealthy diet are the main causes of diabetes mellitus. Active and effective exercise therapy is currently being sought worldwide to improve diabetes and related metabolic diseases. Kristin I. Stanford (Stanford KI, et al., 2017) found that maternal exercise is especially important compared with the parental exercise after conducting an exercise intervention experiment in a diabetic rat model, and maternal exercise can significantly improve the ability of offspring to metabolically healthy, and the good glucose tolerance

produced by this exercise intervention can be transmitted from mother to offspring, thereby counteracting obesity and diabetes; Michael (Fedewa MV, et al., 2014) concluded that aerobic exercise can effectively improve diabetic conditions after META analysis of previous studies; AlissaA (Newman AA, et al., 2019) conducted a 12-week randomized aerobic experiment in thirty obese patients and found that fasting blood glucose increased after glucose sodium co-transporter 2 (SGLT2) inhibition and insulin sensitivity increased after (SGLT2) inhibition after endurance exercise training, suggesting that glucose sodium co-transporter 2 (SGLT2) induced an increase in insulin sensitivity.

3.3 Aerobic Capacity

Endurance exercise training in the fasted state significantly improves basal muscle fat transport and oxidative capacity, as evidenced by a significant increase in basal muscle fatty acid translocase CD36 (FAT/CD36) protein and fatty acid binding protein (FABP) content, which is superior to exercise training in the fed state in this regard ; Alexandra (Vieira AF, et al., 2016) conducted a META analysis of more than 10,400 participants and finally found that the fat oxidative capacity was enhanced in the fasting aerobic group; recent studies also showed that fasting aerobic can improve gastrointestinal sensitivity, obese people due to long-term massive excess diet lead to reduced gastrointestinal sensitivity to food, while small-intensity exercise does not ; high-intensity exercise can increase tissue oxygen supply, while leading to increased reactive oxygen species production (Wiecek M, et al., 2015).

3.4 Weight Loss

Obesity is one of the main culprits leading to cardiovascular disease. According to the 2020 Report on Nutrition and Chronic Diseases of Chinese Residents, overweight and obese people account for 50% in China. People have been making various attempts to reduce the obesity rate, and since people proposed that exercise is the slogan of good medicine, various exercise methods have emerged, but most of them have a threshold and cannot adhere to it for a long time, and since then fasting aerobic has come into front.

Past theories and practices have demonstrated that fasting aerobic brings greater benefits to weight loss than ordinary aerobic training. This is also the same as the results of the Michelle RJosep experiment, in which fasting aerobic decreased more significantly than fed aerobic weight through a 12-month participant self-supervision experiment, and because this experiment was performed by patient self-supervision it also reflected its sustainability from the side.

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The Su-JongKim-Dorner (Kim-Dorner SJ, et al., 2009) study found that optimistic psychological attitudes had a positive effect on insulin resistance through a study of 108 participants in the United States, and I suspect that mood pleasure may produce certain factors that activate insulin function, such as lowering cortisol; there is a very interesting study recently, through a group experiment of 873 students with obesity and health, and finally found that high levels of cardiopulmonary health function can counteract the harm caused by hyperlipidemia (Ruiz JR, et al., 2007), and if you really cannot reduce fat, it may be a good choice to improve cardiopulmonary capacity.

3.5 Autonomic Function

Heart rate variability (HRV), which reflects the function of cardiac autonomic nervous system, can reflect the control and regulation of heart by nervous system and reflect the degree of variation between successive sinus beats and cardiac cycle in obese people. This feature is the result of the common regulation of human neurohumoral and cardiovascular systems. Not only the odds of cardiovascular disease, hypertension, type II diabetes, in excessive weight predisposes obese individuals, will increase, but also will face a higher risk of death compare with normal. The disorders of autonomic nervous system in obese people have become the focus of attention in the health field, and recent studies have been found that obese people gain 10% of body weight and have reduced parasympathetic regulation; while obese or overweight people lose 10% of body weight and have increased parasympathetic nerves, and the increase in body weight leads to inhibition of parasympathetic nerves,

enhancement of sympathetic nerves, and disruption of the balance of cardiac rhythm, which is likely to be caused by disturbances in their own ANS (autonomic nervous system) function in obese people and is an important cause of cardiovascular disease. Guan Yuming et al. studied heart rate variability and vagus nerve in adolescent obese people, and the results showed that in people with reduced heart rate variability, the corresponding vagus nerve function was also reduced; Gao Arning observed the relationship between Body Mass Index (BMI) and heart rate variability in 70 obese children and found that BMI was positively correlated with triglyceride (TG) and high-density lipoprotein cholesterol (LDL-C) in obese children; BMI was negatively correlated with SDNN, SDANN, and RMSSD, and TG was negatively correlated with SDNN, SDANN, and RMSSD. The results showed that obese children may cause autonomic nerve damage due to high TG; Zhang Jingyang et al. found that the content of metabolic indicators in obese children was significantly correlated with heart rate variability indicators SDNN, SDANN, RMSSD, body cytokines, body adipocytokines and other indicators after observing 260 obese children. In summary, heart rate variability in obese children is closely related to the body's lipid metabolism, and excessive obesity can lead to abnormal cardiac function. Recent studies have shown that metabolism affects a variety of pathways in the human body, MarkP (Mattson MP, et al., 2018) proposed a hypothesis on the basis of previous experiments, that light fasting can improve nerve reactivity and brain health, improve brain resistance to injury and disease; simultaneously, he also proposed a conjecture which based on his long-term research on diet and brain nerves that excessive intake will damage some metabolism-related pathways which will affect people's cognitive and neurological function (Mattson MP, 2019).

Exercise is an auxiliary tool in the treatment of T2D, abundant time-tested evidence can prove aerobic exercise can have unique positive effects on autonomic function while improving glycemic control (Reddy R, et al., 2019; Yang Z, et al., 2014) and insulin resistance (Yang Z et al., 2014; Goulopoulou S, et al., 2010). Long-term moderate-intensity aerobic exercise can improve cardiac autonomic regulation and baroreflex function in T2D (Goit RK, et al., 2014; Goit RK, et al., 2018) is a consensus in the field of research on the effects of exercise on autonomic function in the fasting state of T2D. The effects of aerobic exercise and resistance training on autonomic function during fasting and glucose load in patients with type 2 diabetes were studied in China, and the results showed that aerobic capacity, muscle mass, glycosylated hemoglobin, fasting blood glucose, HOMA2-0, body weight, BMI, HDL-C, LDL-C and Framingham risk score and heart rate variability (HRV) were improved (Masroor S, et al., 2018; Kelley GA, et al., 2011; Ratajczak M, et al., 2020). In summary, exercise can improve cognition and autonomic function.

3.6 Other Benefits

Historic breakthrough has been discovered not long ago. Though we still can't figure out the mechanism, that can't obstruct the enthusiasm about the detection of the combination of rapamycin and fasting aerobic exercise have a magical effect in against anti-aging (Blagosklonny MV, 2019); Jenna B (Gillen JB et al., 2013) found by biopsy that fasting training-induced increased mitochondrial capacity and increased maximum activity of citrate lyase and b-hydroxycoenzyme a dehydrogenase.

4. Problems and Prospects

The current domestic research focuses on the aerobic exercise level and has not been advanced to the fasting aerobic stage. Fasting aerobic as a method for the treatment of cardiovascular diseases and obesity has been very popular abroad. There are many advantages of fasting aerobic itself, such as the previously mentioned increase of high density lipoprotein, insulin sensitivity, gastrointestinal sensitivity, insulin resistance, low-density lipoprotein, blood pressure, blood lipids, fasting blood glucose, body weight, body fat rate, waist circumference and so on. In addition to its many advantages of improving physical conditions, the cost performance of fasting aerobic is also very prominent. In terms of economy, compared with resistance and special sports requiring complete sites and professional devices, fasting aerobic requires only a simple treadmill or even a home bicycle to perform fasting aerobic; half an hour after the start of the morning will not occupy too much time.

There are few existing fasting aerobic studies in China, and its mechanistic concept is still vague and has great potential, and it is sincere to hope that domestic researchers can carry out more meaningful research in the future.

Tip: The fasting aerobic benefits addressed throughout this article are presented in Figure 1.

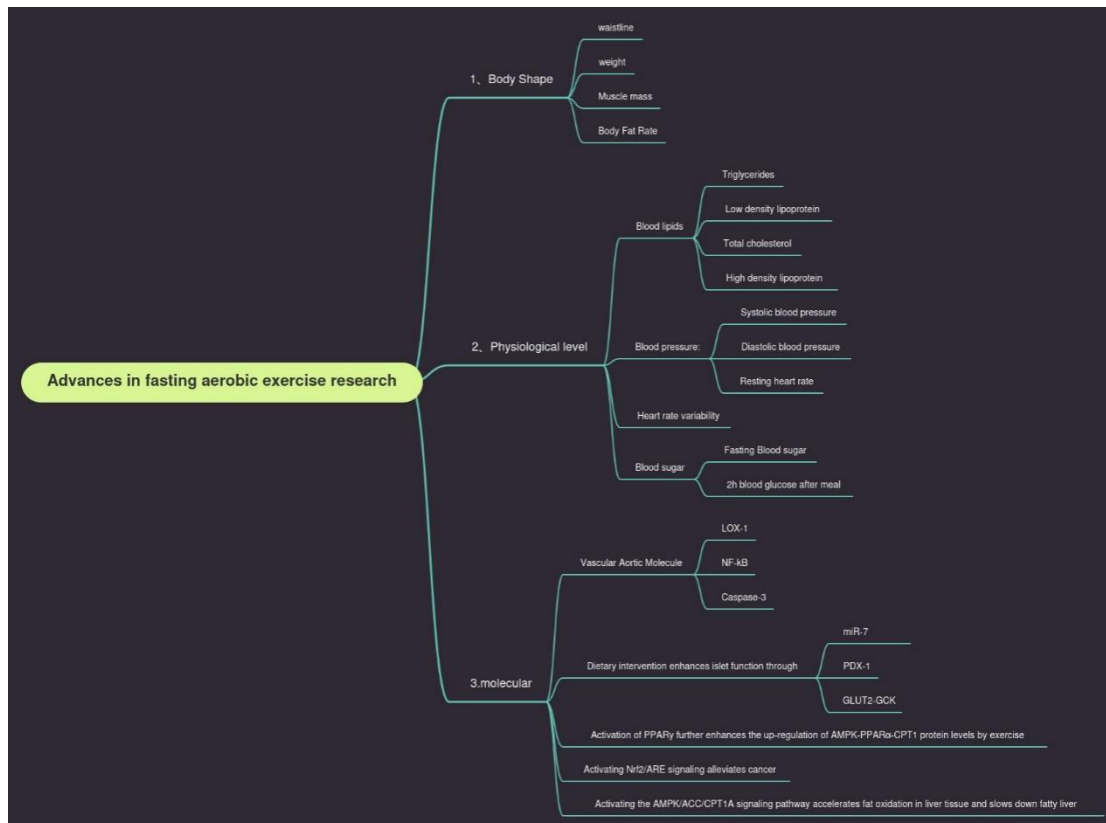


Figure 1: The fasting aerobic benefits

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