

**EFFECTS OF WHEY PROTEIN ASSOCIATED WITH RESISTANCE TRAINING:
EVIDENCE IN ANIMAL AND HUMAN MODELS**

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ABSTRACT

Objective: This abstract aims to synthesize the literature on the effects of resistance training combined with whey protein supplementation, highlighting evidence from both animal and human models, as well as benefits, potential risks, and knowledge gaps. **Materials and Methods:** This study is an literature review, which consists of constructing an analysis of the results and methods applied and reflections on future studies, obtaining, throughout the research, an understanding of the phenomenon, used based on previous studies. **Results:** Evidence shows that whey protein, due to its high biological value and rapid digestibility, enhances the responses to resistance exercise. Studies report significant increases in muscle mass, improved post-exercise recovery, and greater cardiac contractile capacity. In addition, reductions in fat mass and improvements in metabolic profile, including glycemia and insulin sensitivity, have been observed. Leucine, an amino acid abundant in whey protein, plays a central role by directly stimulating protein synthesis. Although high protein intake still raises concerns about potential renal or hepatic risks, investigations indicate that supplementation at recommended doses is safe in healthy individuals. **Conclusion:** The combination of resistance training and whey protein supplementation is an effective strategy to improve body composition, physical performance, and metabolic parameters, in addition to promoting beneficial cardiac adaptations. Despite the promising results, further studies are needed to elucidate the underlying mechanisms, assess long-term effects, and establish optimal supplementation protocols.

Key words: Whey protein. Resistance training. Cardiac hypertrophy. Wistar rats. Protein supplementation.

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RESUMO

Efeitos do whey protein associado ao treinamento resistido: evidências em modelos animais e humanos

Objetivo sintetizar a literatura sobre os efeitos do treinamento resistido associado à suplementação com whey protein, destacando evidências em modelos animais e humanos, bem como benefícios, potenciais riscos e lacunas do conhecimento. Este estudo, trata-se de uma revisão integrativa da literatura, que consiste na construção de uma análise sobre os resultados e métodos aplicados e reflexões sobre estudos futuros, obtendo ao decorrer da pesquisa um entendimento do fenômeno, usado com base estudos anteriores. Evidências demonstram que o whey protein, devido ao seu elevado valor biológico e rápida digestibilidade, potencializa as respostas ao exercício resistido. Estudos apontam aumento significativo de massa muscular, melhora na recuperação pós-exercício e maior capacidade contrátil cardíaca. Além disso, verificou-se redução da massa gorda e melhora do perfil metabólico, incluindo glicemia e sensibilidade à insulina. A leucina, aminoácido abundante no whey protein, exerce papel central ao estimular diretamente a síntese proteica. Embora o consumo elevado de proteínas ainda gere preocupações sobre possíveis riscos renais ou hepáticos, investigações apontam que a suplementação em doses recomendadas é segura em indivíduos saudáveis. A associação entre treinamento resistido e suplementação com whey protein constitui estratégia eficaz para a melhora da composição corporal, desempenho físico e parâmetros metabólicos, além de favorecer adaptações cardíacas benéficas. Apesar dos resultados promissores, são necessários estudos adicionais para elucidar os mecanismos envolvidos, avaliar efeitos a longo prazo e estabelecer protocolos de suplementação ideais.

Palavras-chave: Whey protein. Treinamento resistido. Hipertrofia cardíaca. Ratos Wistar. Suplementação proteica.

INTRODUCTION

The cardiovascular system is fundamental to maintaining life, as it ensures the transport of oxygen, nutrients, hormones, and metabolites through an integrated network of blood and lymphatic vessels, with the heart as the regulatory center of this entire process.

From the early stages of development, this system guarantees the necessary conditions for growth and cell differentiation, remaining essential to the organism's balance at all stages of life. Circulation, organized into pulmonary and systemic circuits, allows both the oxygenation of tissues and the removal of metabolic waste products, ensuring homeostasis.

The heart, mainly composed of muscle tissue, has four chambers that regulate the unidirectional flow of oxygenated and deoxygenated blood. Cardiac myocytes, specialized cells that make up the myocardium, have a high capacity for structural and functional adaptation, a characteristic that allows the organ to respond to both physiological stimuli and pathological conditions. Among the factors that modulate these responses are aging, physical inactivity, and, conversely, regular exercise.

Physical exercise, especially resistance training, is considered a stimulus with a great impact on the cardiovascular system. It promotes a series of biochemical, electrical, morphological, and functional adaptations that increase the efficiency of the heart and favor metabolic health.

Cardiac hypertrophy is an example of an adaptive response that can manifest physiologically, when it occurs as a consequence of exercise, or pathologically, when it results from diseases such as hypertension or obesity. In the first case, an increase in the size of myocytes is observed, accompanied by a proportional expansion of the capillary network, without impairing cardiac performance.

Another factor that plays a determining role in this process is nutrition. The intake of high-quality proteins is essential for maintaining lean mass, protein synthesis, and tissue repair.

In this context, whey protein stands out as a widely used supplement due to its rapid absorption and high content of essential amino acids, especially leucine, capable of directly stimulating protein synthesis. When associated with resistance training, the supplement

enhances muscle mass gains, promotes recovery after exercise, improves metabolic parameters, and can contribute to positive cardiovascular adaptations.

Thus, the combination of resistance training and whey protein supplementation represents a promising strategy for both promoting health and optimizing physical performance.

However, there is still a need to deepen the knowledge about the appropriate dosage, the long-term effects, and the molecular mechanisms that support these adaptations, which makes the topic relevant for future scientific investigations.

The increasing prevalence of chronic diseases associated with sedentary lifestyles and inadequate eating habits highlights the need for effective strategies to promote health.

Resistance training is recognized as an intervention capable of improving body composition, increasing muscle strength, and inducing beneficial cardiac adaptations, distinguishing itself from the changes observed in pathological conditions.

Nutrition, in turn, plays an essential role in enhancing the effects of exercise. Among the resources available, whey protein stands out for its high nutritional quality, rapid digestibility, and high concentration of essential amino acids, particularly leucine, which is fundamental for activating muscle protein synthesis.

When combined with resistance training, this supplement contributes to lean mass gain, improved recovery, and optimization of energy metabolism, including parameters such as blood glucose and insulin sensitivity.

Despite the promising results, important gaps remain regarding the mechanisms involved in cardiac remodeling and the effects in different contexts and populations. Issues related to prolonged consumption and the safety of protein supplementation still generate debate, especially regarding the most appropriate doses to maximize benefits and avoid potential risks.

Therefore, investigating the association between resistance training and whey protein supplementation is justified by the possibility of expanding knowledge about muscle and cardiac adaptations, as well as supporting safe and effective intervention strategies to improve metabolic health, prevent disease, and optimize physical performance.

This study aims to synthesize the literature on the effects of resistance training

combined with whey protein supplementation, highlighting evidence from animal and human models, as well as benefits, potential risks, and knowledge gaps.

MATERIALS AND METHODS

This study is characterized as literature review, whose purpose is to gather, analyze, and synthesize results from previously published research, allowing for a broad understanding of the investigated phenomenon. This method enables the construction of a critical view of the findings, as well as reflections on the methodologies used and perspectives for future studies.

The diversity of samples and the multiplicity of objectives contemplated by the integrative review favor the elaboration of a consistent overview of concepts, theories, and problems related to the topic.

For the study, scientific journals indexed in databases were consulted using previously defined descriptors. Inclusion criteria were: original articles from primary studies, published in English or Portuguese. Studies published more than ten years ago were

excluded, as well as those that did not meet the established search criteria.

After applying the criteria, five articles were selected and subjected to a detailed analysis. The data obtained were organized, evaluated, and interpreted in accordance with the objectives of this study, serving as a reference for discussion and for defining directions in future investigations.

RESULTS

Cardiovascular System

In vertebrates, the circulatory system is basically a set of connected tubes responsible for transporting fluids. This system includes the vascular systems of blood and lymph (Carniatto et al., 2019).

The cardiovascular system is a direct connection between a pump, a circuit that generates high pressure, with channels for nutrient exchange and a collection and return system that exerts low pressure on the organism (McArdle, Katch and Katch, 2003). It consists of blood, vessels, and the heart (Bergwerff et al., 1999; Monahan-Earley; Dvorak; Aird, 2013).

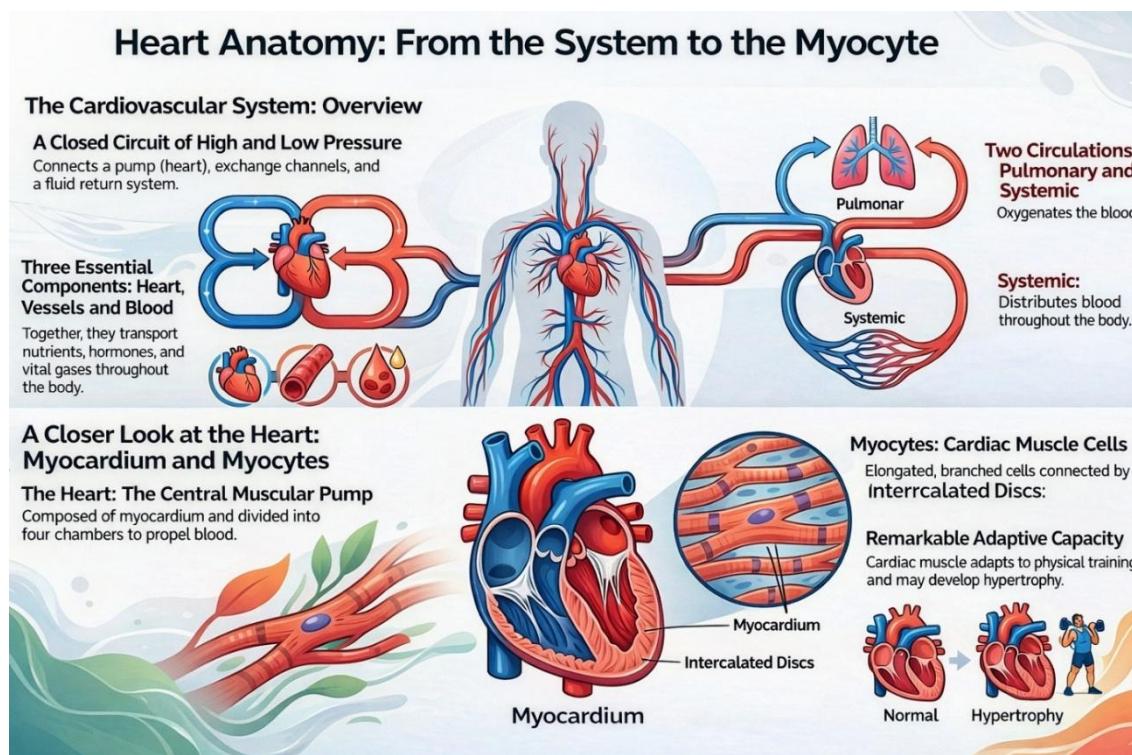


Figure 1 - Heart anatomy : From the system to the myocyte.

The cardiovascular system is the first system to become functional in embryonic development, as the differentiation and growth of the embryo depend on internal transport (Pelster, Bemis, 1991; Kardong, 2016).

According to Robergs and Roberts (2002), blood is pumped throughout the body in a closed circuit. This blood circulation is divided into pulmonary and systemic circulation, the latter being responsible for the rest of the body.

Myocardium and Myocytes

The heart is the central organ of the cardiovascular system, composed essentially of cardiac muscle, the myocardium, which forms a sac divided into four chambers: right atrium, left atrium, right ventricle, and left ventricle. Together with the blood vessels, the heart chambers form a single cavity in which blood circulates continuously (Silverthorn, 2017).

The heart is the pump responsible for moving blood through the cardiovascular system. It also functions to transport deoxygenated and oxygenated blood to their appropriate parts, thus preventing the mixing of blood. Another function is to transport hormones from their place of origin to the target tissues (Kardong, 2016).

According to Bishopric (2005), in vertebrates the myocardium is located ventrally. Since this group presents several anatomical adaptations, in species that have adopted the bipedal position, the heart is located in the anterior region of the body (Hickman et al., 2016).

The myocardium of mammals is composed of cardiac muscle fibers, blood vessels, and connective tissue. In the normal heart, this connective stroma is distributed, forming the epimysium, which surrounds all the cardiac musculature (subepicardial connective tissue); the perimysium, which separates bundles of fibrocellular tissue; and the endomysium, which is arranged around each myocyte. This connective tissue plays an important role in maintaining the functional integrity of the myocardium (Burlew and Weber, 2000).

Histologically, the heart is composed of cardiac muscle, restricted to this organ. This muscle is formed by cardiac cells called cardiac myocytes.

Cardiac myocytes are elongated and branched cells that are joined together by means of intercalated discs. These cells exhibit

transverse striations and have one or, at most, two centrally located nuclei (Junqueira and Carneiro, 2000).

For Anversa et al., (1994), the structural modifications that occur in the myocardium depend on a normal developmental process, as well as the functional demands required by the organ. Therefore, aging processes and physical inactivity can promote significant changes in the organ, affecting not only its cells, but also the blood conduction system (terminal vascular bed) in the myocardium.

The cardiac muscle is composed of tissue that exhibits significant adaptation to physical training, making it capable of supporting changes in its biochemical, functional, and morphological properties, and among the cardiac adaptations we have cardiac hypertrophy (Droge, 2007).

Physical exercise and cardiovascular adaptations

The practice of physical exercise promotes adjustments to the myocardium resulting from the required increases in metabolic and mechanical activities. This causes various biochemical, electrical, morphological, and mechanical adaptations in the heart muscle, resulting in improved cardiac function. These adaptations basically occur to reduce stress on the ventricular walls and, at the same time, meet the increased demand for blood supply to the exercising muscles (Kemi et al., 2007).

Physical exercise generates physiological stress in the body by considerably increasing energy demands compared to rest. In addition, it causes morphological and functional changes in practitioners that enable them to respond to the stress caused by the physical activities they perform.

The changes caused by physical training are widely studied and complex because they involve an interaction between several systems of the body, such as the musculoskeletal, cardiovascular, respiratory, metabolic, and autonomic nervous systems (Carniatto et al., 2019).

In this sense, physical activities can cause, for example, specific adaptations in skeletal muscle, such as an increase in muscle mass; Morphological cardiovascular adaptations, such as cardiac hypertrophy, and functional adaptations, such as bradycardia and respiratory changes, for example, increased

oxygen consumption (VO_2 max), which can be caused by an increase in the practitioner's metabolic rate (Pinho, et al., 2010).

The practice of physical exercise acts on the mechanism of prevention and promotion of health, and can slow down the physiological changes of aging and chronic-degenerative diseases, providing positive morphological and functional adaptations in the cardiac muscle (Gonçalves and Alchiere, 2010).

As a result, studies involving physical training (PT) have been developed, with the aim of verifying the morphological adaptations of the myocyte and myocardium. In which many studies with animal models have been carried out with varying protocols and intensities (Kemi et al., 2004; Kemi et al., 2005).

Among the exercises that promote adaptations in the cardiovascular system are resistance exercises.

Physical Exercise and the Heart: Strengthening Adaptations

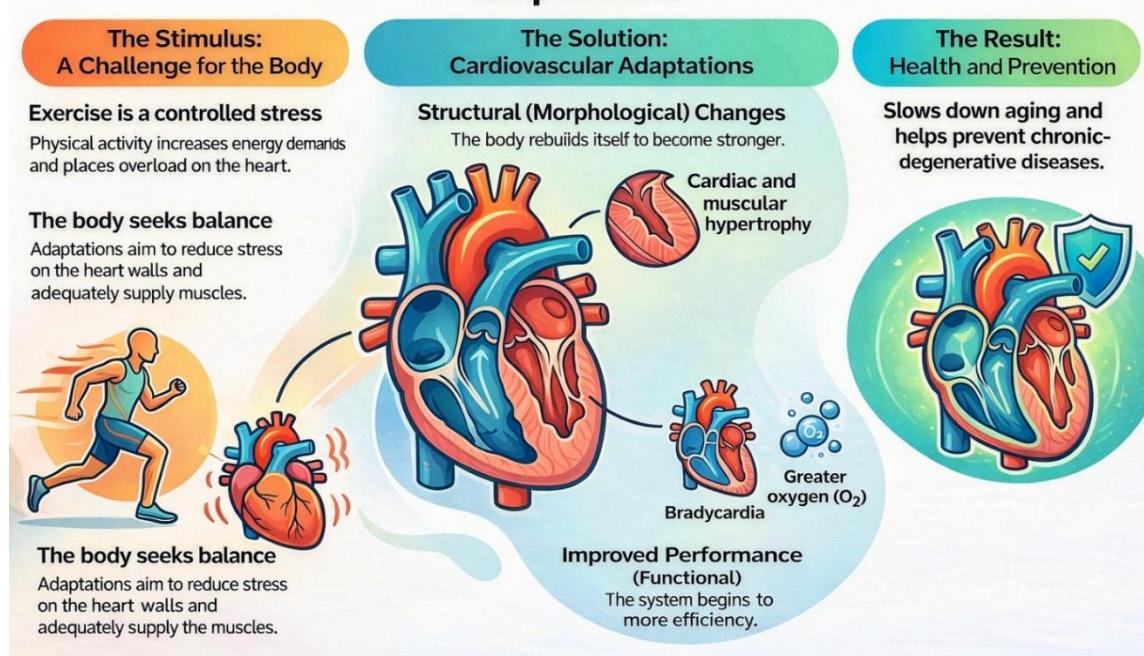


Figure 2 - Physical exercise and the heart : strengthening adaptations.

Resistance Training

Resistance training, also known as weight training or strength training, when applied correctly, can promote significant changes in body composition and health in clinical groups (adolescents, pregnant women, the elderly, hypertensive individuals, diabetics, among others).

Resistance training is a specialized conditioning procedure that involves the progressive use of a range of resistive loads and a variety of training modalities (NSCA, 2009).

Resistance training is characterized by repeated series of contractions against resistance, resulting in the rapid recruitment of

type 2 muscle fibers, and is also a potent stimulus for skeletal muscle protein synthesis (Phillips, 2009).

Endurance exercises are those that require the athlete to maintain a certain effort for as long as possible, involving significant muscle masses and the entire cardiovascular and respiratory system (Fernandes, et al., 2015).

According to resistance exercises can be applied with free weights, with body weight, in weight training machines or other equipment, being performed in most cases, in uninterrupted sequences of repetitions with varying intervals between sets.

According to Gianolla (2003), this type of training has been gaining popularity among

diverse audiences and consequently an increase in the number of followers.

Resistance training offers notable benefits in various areas, such as the development of important physical capacities like strength, power, muscular endurance, and flexibility (Gianolla, 2003), treatment for the low rate of sports injuries (Rios, 2017), treatment against heart disease (Lima, 2016; Jaenisch and Faralozzo, 2017) and obesity (ACSM,

2001), in addition to important systemic regulations, including the development and/or maintenance of muscle mass (Marques, 2016), as well as functional capacity for the elderly (Câmara, Bastos and Volpe, 2012).

Chronic resistance training promotes adaptations in the cardiovascular system, including cardiac hypertrophy in the myocardium.

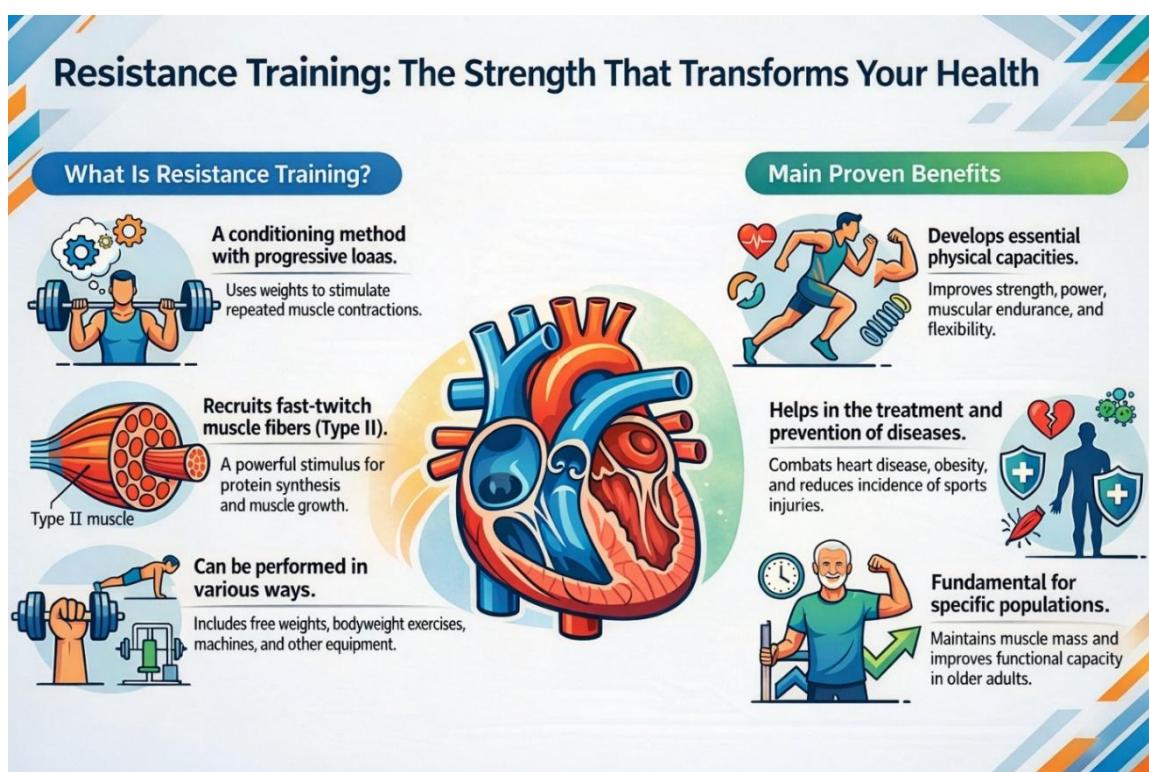


Figure 3 - Resistance training : the strength transforms your health.

Cardiac Hypertrophy (CH)

Cardiac hypertrophy (CH) is characterized by an increase in heart mass, due to an increase in protein synthesis and consequently in the dimensions of cardiomyocytes.

This process causes an increase in oxygen and nutrient consumption in cardiomyocytes and, as a consequence, promotes functional and biochemical changes in the cells (Maron and Pelliccia, 2006; Gupta, 2007).

The heart muscle adapts to hemodynamic overloads, causing changes in the structure of the myocardium in two ways: eccentric hypertrophy, caused by volume

overload, training, such as aerobic physical training (running, swimming, among others). The other form is concentric hypertrophy, caused by overload of blood pressure, observed with resistance/isometric training such as weightlifting (LPO).

Cardiac hypertrophy, in response to physical exercise, which corresponds to physiological hypertrophy, includes morphological and functional changes.

This type of hypertrophy occurs in both ventricles, but to a greater degree in the left ventricle. The main adaptations to physical training with regard to heart morphology are changes in muscle size and volume of the cardiac chambers (Wang et al., 2008).

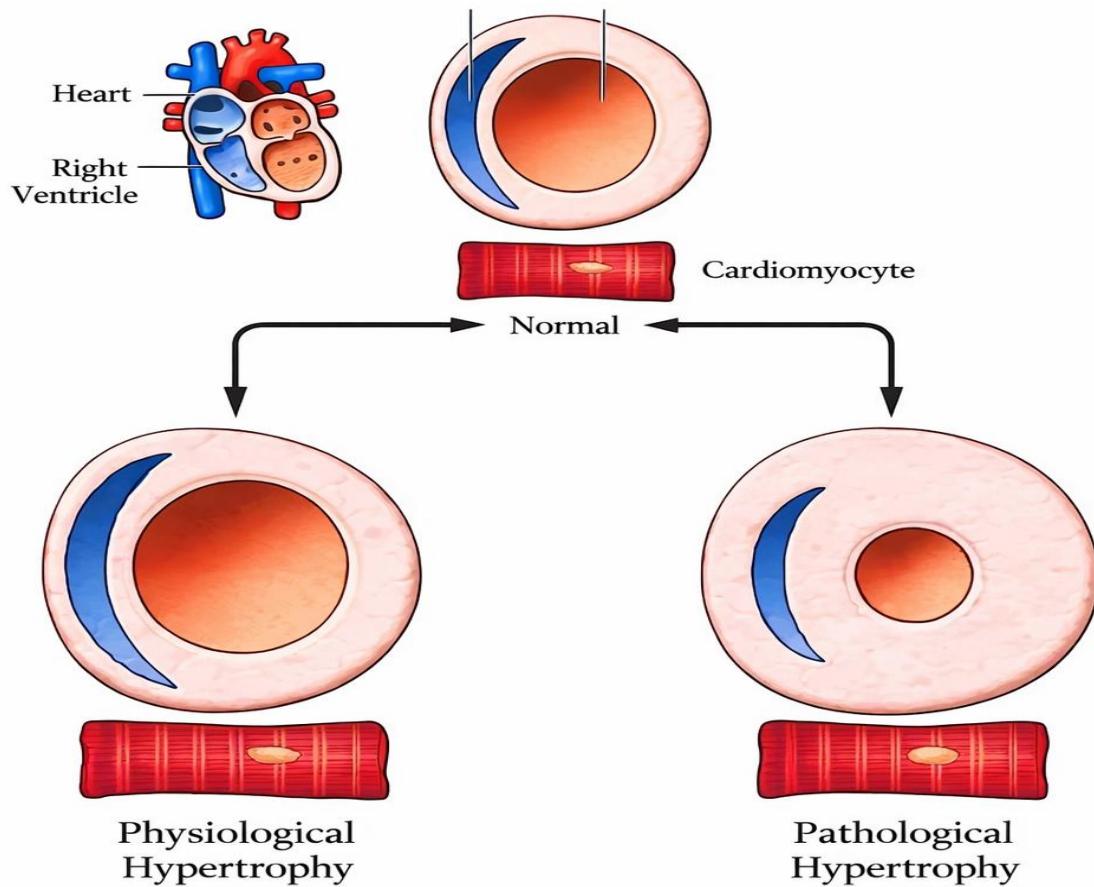


Figure 4 - Comparison of Eccentric (Physiological) versus Concentric (Pathological) Hypertrophy and its Implications in Ventricular Geometry. (Source: Van Berlo et al., 2013).

According to the type of stimulus received by the cardiac tissue, the structural and biochemical changes in cardiomyocytes can determine whether the hypertrophy present in the tissue is physiological or pathological in nature (Braunwald and Bristow, 2000; Iemitsu et al., 2001).

Pathological Cardiac Hypertrophy

On the other hand, pathological cardiac hypertrophy is associated with high levels of neurohumoral mediators, hemodynamic overload, injury, and loss of cardiomyocytes. In the development of a pathological cardiac hypertrophy, cardiomyocyte growth exceeds the capacity of the capillaries to adequately supply nutrients and oxygen, leading to hypoxia and cardiac remodeling in rodents (Shimizu et al., 2010).

According to Shimizu and Minamino (2016), within physiological cardiac hypertrophy there is functional loss of cardiac tissue due to cell death, in addition to the presence of fibrosis in the cardiac tissue, which can lead to heart failure.

Physiological Cardiac Hypertrophy

Physiological cardiac hypertrophy demonstrates an increase in cardiomyocytes in response to exercise, and the enlarged cardiomyocytes receive adequate nutrition due to the expansion of the capillary network.

Structural or functional cardiac abnormalities do not occur in this scenario, and generally, physiological cardiac hypertrophy is not considered a risk factor for heart failure (Pinto, 2018).

Physiological stimuli can occur concentrically or eccentrically; however, chamber enlargement develops proportionally,

triggering an improvement in cardiac function without the presence of fibrosis (Bernardo et al., 2010).

In physiological hypertrophy, cardiac muscle growth can be concentric or eccentric depending on the type of stimulus applied (Pinto, 2018).

Physiological Hypertrophy Eccentric Cardiac

This hypertrophy occurs through cardiac remodeling, specifically of the left ventricle (LV). Remodeling in the form of eccentric hypertrophy occurs through the addition of sarcomeres in series and longitudinal growth of cardiomyocytes, which leads to increased dilation of the left ventricle (Fernandes et al., 2015).

Eccentric myocardial hypertrophy occurs due to an overload of blood volume, that is, an increase in preload, which raises diastolic tension, leading to the growth of myocytes.

In this type of hypertrophy, there is an increase in the number of sarcomeres, which contribute both to the length of the cells, thus generating a dilation in the diameter of the ventricular chamber, and to the thickness of the myocytes, causing mass thickening (Magalhães et al., 2008).

Physiological Hypertrophy Concentric Cardiac

In concentric myocardial hypertrophy, there is only an increase in the diameter of the muscle cells, thus only affecting the density of the ventricle. This is generated by pressure overload, that is, by an increase in afterload, which characterizes a peak in systolic pressure (Magalhães et al., 2008).

This hypertrophy generally leads to an increase in the thickness of the left ventricular (LV) wall without altering the chamber diameter, through the parallel addition of new sarcomeres and lateral growth of individual cardiomyocytes (Fernandes et al., 2015).

Dietary Parameters

According to Berg, Tymoczko, and Stryer (2014), physical exercise, combined with a healthy diet, constitutes one of the most effective treatments for various pathological conditions, such as diabetes, depression, a

variety of cancer types, hypertension, and coronary heart disease.

Food is a primary factor in humanity's daily routine, not only because it constitutes a basic need, but mainly because its use has become a public health problem, since its excess or lack can cause diseases (WHO, 2011).

For the National Health Surveillance Agency (Anvisa, 2008), a healthy diet must have qualitative characteristics, without needing to be expensive (since preparation can be done with natural foods, produced in the region where one lives), be tasty and composed of varied foods that need to be consumed in the correct quantity and free from contamination, that is, safe for consumption.

According to Flück and Hoppeler (2003), the availability of nutrients, as well as physical training, can be a stimulator for the modification of the morphological, metabolic and functional characteristics of striated muscle tissue; in addition, two aspects related to nutrition that need to be considered for the hypertrophy process stand out: the quantification of protein and calories ingested.

Protein Consumption and Supplementation

Among the organic functions of protein, we can mention the regulation of metabolism, nutrient transport, acting as natural catalysts, immune defense, acting as membrane receptors, and many others (Paiva, Alfenas and Bressan, 2007).

Protein energy needs are higher for those who practice physical activity and are influenced by the type, intensity, duration, and frequency of exercise (Maughan and Burke, 2004).

The American Dietetic Association (2012) places protein supplements as the most popular among those who practice physical activity, with the main purpose being to increase muscle mass.

In a systematic review study conducted by Nabuco, Rodrigues, and Ravagnani (2016), it was identified that the prevalence of the use of dietary supplements among Brazilian athletes can vary between 37% and 98%. This research also identified that 53% of the reviewed studies pointed to protein and amino acid supplements as the most used by this group of individuals.

Among gym-goers, through a systematic literature review, Nogueira, Souza

and Brito (2013) found that the prevalence of supplement use varies between 23.9% and 94%, depending on the region of Brazil and the age group investigated, motivated mainly by the improvement of physical fitness and health.

The indiscriminate use of these supplements without proper guidance is worrying, since inadequate consumption may lead to consequences for human health (Hirschbruch, et al., 2008), where excessively ingested protein will undergo conversion and storage in the form of glycogen and lipids (Alvarez, Brasioli and Nabholz, 2007).

Among the supplements derived from whey proteins, whey proteins (WP) have been widely used by people who practice physical activities and athletes, especially because they have high nutritional value and have a proven relationship with muscle hypertrophy (Carrilho, 2013).

Whey protein supplementation

The dietary supplement derived from soluble whey proteins, known as whey proteins, has been widely used by many people who practice physical exercise, due, among other reasons, to the presence of essential amino acids, mainly leucine, seen as one of the main amino acids capable of stimulating protein synthesis (Dickinson et al., 2014).

Whey protein (WP) is one of the components of milk protein and contains branched-chain amino acids (BCAAs), such as leucine, isoleucine, and valine, which have important health benefits, especially for skeletal muscle (Pal and Radavelli-Bagatini, 2013).

Whey protein is a protein whose beneficial properties for health, physical performance, and improvement of body composition are widely reported in the literature, as it favors anabolism and reduces muscle catabolism, reduces the action of oxidizing agents in skeletal muscles (Haraguchi, Abreu, Paula, 2006), and increases strength and lean mass (Morton et al., 2015).



Figure 5 - Bromatological Characterization and Amino Acid Profile of Whey Proteins. (Source: Laboratory of Physiology and Exercise Prescription of Maranhão).

Branched-chain amino acids make up 21.2% of its composition, and all essential amino acids constitute 42.7%. This particularity makes whey proteins a protein source concentrated in essential amino acids, specifically leucine, compared to other protein sources (Terada et al., 2009).

Thus, this amino acid profile makes its digestion and intestinal absorption faster, which promotes an increase in the concentration of amino acids in the plasma and stimulates protein synthesis in tissues (Haraguchi, Abreu and Paula, 2006).

It also has a high content of calcium and bicarbonate peptides from whey, providing possible effects on skeletal muscle protein synthesis, reduction of body fat, as well as in the modulation of adiposity, and improvement of physical performance. Among possible benefits, its hypotensive, antioxidant and hypocholesterolemic effects stand out (Terada et al., 2009).

In this way, protein intake favors muscle synthesis and recovery, as well as contributing to energy metabolism (Ormsbee et al., 2014).

Recommendations Regarding Daily Protein Intake

Recommendations regarding the ideal amount of protein to consume are still a subject of ongoing investigation.

Naderi et al., (2016), in their systematic review, suggest a dose of 0.20 to 0.25 g/kg of body mass for young individuals and 0.40 g/kg for elderly individuals in frequent meals throughout the day, or 20-25 g post-exercise for young athletes and 40 g/day post-exercise for adult athletes.

The American College of Sports Medicine (2016) states that a protein dose between 1.2 g/kg and 2.0 g/kg is necessary for metabolic adaptation and tissue repair.

The etiology of the ideal daily protein intake is under intense investigation, and several studies have been developed to resolve this question. Phillips and Van Loon (2011), in their work, set the ideal dose for sedentary individuals at 0.8 g/kg/day, and 1.2 to 2.0 g/kg/day for athletes.

Helms, Aragon, and Fitschen (2014) noted that dosages lower than 2.3 g/kg/day did not show efficiency in maintaining the amount of lean mass in bodybuilders, thus suggesting that higher dosages, between 2.3 and 3.1 g/kg/day, appear to be more efficient in maintaining the proportion of muscle mass in this population.

Another recent study by Macnaughton et al., (2016) observed that a dose of 40 g/kg/day was more efficient in the response of muscle protein synthesis, associated with resistance training in healthy, trained young men, when compared to a dosage of 20 g/kg/day used in the same study.

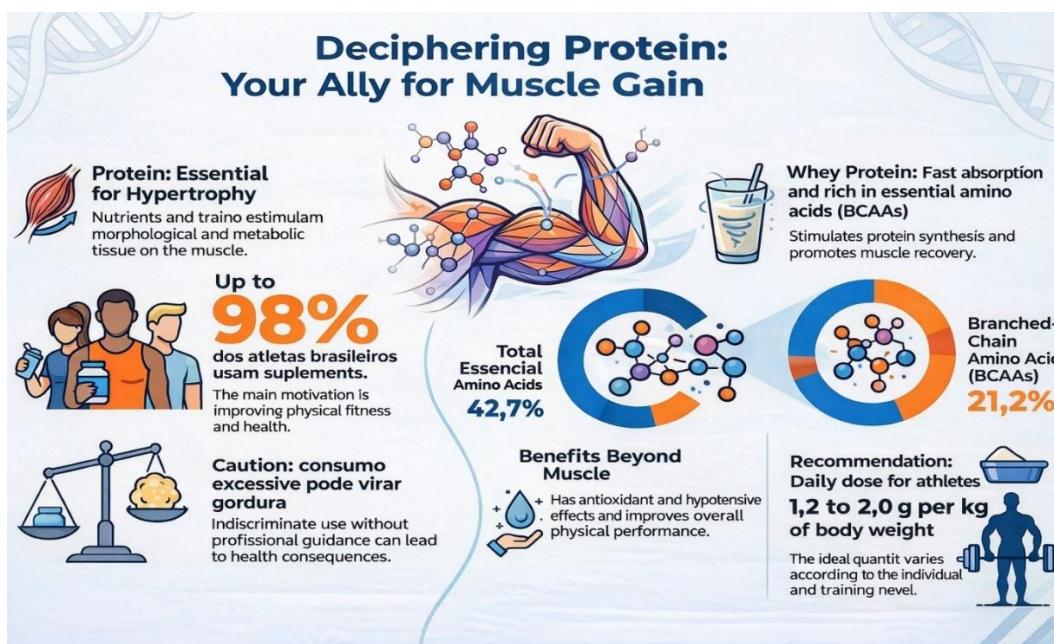


Figure 6 - Deciphering protein : your ally muscle gain.

Dunford (2012) states that one of the biggest problems in managing a diet with protein amounts above the recommended level is the disregard for the need for carbohydrates and lipids, leading to a possible nutritional deficit, which directly impairs performance in training and muscle hypertrophy.

It is possible to affirm that protein within a diet is essential for muscle hypertrophy and this need can be met by a balanced and appropriate diet for the individual (Zambão, Rocco and Heyde, 2015).

CONCLUSION

The combination of resistance training and whey protein supplementation represents an effective strategy to promote positive adaptations in both body composition and metabolic and cardiovascular function.

The available results indicate that this association enhances lean mass gain, improves physical performance, and contributes to the reduction of body fat, which reinforces its relevance as a tool for promoting health and preventing chronic diseases related to sedentary lifestyles.

In addition, evidence suggests that whey protein, due to its high nutritional quality and the presence of essential amino acids, has a direct effect on protein synthesis and energy metabolism.

When combined with resistance training, it favors muscle recovery, increases the contractile efficiency of the heart, and can help modulate metabolic parameters such as insulin sensitivity and glycemic control.

However, despite the observed benefits, there are still important gaps in the scientific literature.

It is necessary to investigate the molecular mechanisms involved in these adaptations, as well as to evaluate the effects of prolonged consumption and determine ideal supplementation protocols in different populations.

Therefore, further studies are essential to consolidate evidence and establish safe and effective recommendations to guide both clinical practice and sports prescription.

REFERENCES

- 1-ACSM. American College of Sports Medicine. Joint Position Statement: Nutrition and Athletic Performance. *Medicine & Science in Sports & Exercise*. Vol. 48. NNúm. 3. 2011. p. 543-568.
- 2-American Dietetic Association. Dietary fatty acids. *Journal of the American Dietetic Association*. Vol. 107. No. 9. 2012. p. 1599-1611.
- 3-Alvarez, T.; Brasioli, M.; Nabholz, T.V. Proteins and supplementation. In: Nabholz, T. V. *Sports nutrition: aspects related to nutritional supplementation*. 2007. p. 113-129.
- 4-Anversa, P.; Li, P.; Sonnenblick, E.H.; Olivetti, G. Effects of aging on quantitative structural properties of coronary vasculature and microvasculature in rats. *Am. J. Physiol.* Vol. 267. Núm. 3. 1994. p. 1062-1073.
- 5-ANVISA. National Health Surveillance Agency. *Healthy Eating: Stay Smart!* Brasília-DF. 2008. p. 4.
- 6-Berg, J.M.; Tymoczko, J.L.; Stryer, L. *Biochemistry*. 7th Edition. Rio de Janeiro: Guanabara Koogan. 2014.
- 7-Bergwerff, M.; Deruiter, M.C.; Groot, A.C.G. Comparative anatomy and ontogeny of the ductus arteriosus, a vascular outsider. *Anatomy and Embryology*. Vol. 200. 1999. p. 559-571.
- 8-Bernardo, B.C.; Weeks, K.L.; Pretorius, L.; McMullen, J.R. Molecular distinction between physiological and pathological cardiac hypertrophy: experimental findings and therapeutic strategies. *Pharmacology & therapeutics*. Vol. 128. Number 1. 2010. p. 191-227.
- 9-Bishopric, N. Evolution of the heart from bacteria to man. *Annals of the New York Academy of Sciences*. Vol. 1047. 2005. p. 13-29.
- 10-Braunwald, E.; Bristow, M.R. Congestive heart failure: fifty years of progress. *Circulation*. Vol. 102. Num. 20. 2000. p. IV14-23.
- 11-Burlew, B. S.; Weber, K.T. Connective tissue and the heart: functional significance and regulatory mechanisms. *Cardiol. Clinic.* Vol. 18. Num. 3. 2000. p. 435-442.
- 12-Câmara, L.C.; Bastos, C.C.; Volpe, E.F.T. Resistance exercise in frail elderly: a literature

review. *Fisioterapia em Movimento*. Vol. 25. Núm. 2. 2012. p. 435-443.

13-Carniatto, C.H.O.; Vidotti, A.P.; Bianchi, L.R.O.; Mello, J.M. Morphology and evolution of the heart in vertebrates: A Review. *Arquivos do MUDI*. Vol. 23. Núm. 3. 2019. p. 290-303.

14-Carriho, L.H. Benefits of using whey protein. *Revista Brasileira de Nutrição Esportiva*. São Paulo. Vol. 7. Núm. 40. 2013. p. 195-203.

15-Dickinson, J.M.; Gundermann, D.M.; Walker, D.K.; Reidy, P.T.; Borack, M.S.; Drummond, M.J.; Arora, M.; Volpi, E.; Rasmussen, B.B. Leucine-enriched amino acid ingestion after resistance exercise prolongs myofibrillar protein synthesis and amino acid transponer expression in older men. *The Journal of Nutrition*. Vol. 144. Núm. 11. 2014. p. 1694-1702.

16-Droge, W. Free radicals in the physiological control of cell function. *Physiological Review*. Vol. 82. No. 1. 2002. p. 47-95.

17-Dunford, M. *Fundamentals of nutrition in sport and exercise*. Manole. 2012.

18-Fernandes, T.; Baraúna, V.G.; Negrão, C.E.; Phillips, M.I.; Oliveira, E.M. Aerobic exercise training promotes physiological cardiac remodeling involving a set of microRNAs. *American Journal of Physiology-Heart and Circulatory Physiology*. Vol. 309. Núm. 4. 2015. p. 543-552.

19-Flück, M.; Hoppeler, H. Molecular Basis of Skeletal Muscle Plasticity-from Gene to Form and Function. *Reviews of physiology, biochemistry, and pharmacology*. Vol. 146. 2003. p. 159-216.

20-Gianolla, F. *Bodybuilding: basic concepts*. Manole. 2003.

21-Gonçalves, M.P.; Alchieri, J.C. Motivation for physical activity: a study with non-athlete practitioners. *Psico-USF*. Vol. 15. Núm. 1. 2010. p. 125-134.

22-Gupta, M.P. Factors controlling cardiac myosin-isoform shift during hypertrophy and heart failure. *Journal of molecular and cellular cardiology*. Vol. 43. Núm. 4. 2007. p. 388-403.

23-Haraguchi, F.K.; Abreu, W.C.; Paula, H. Whey proteins: composition, nutritional properties, applications in sports and benefits for human health. *Revista de Nutrição*. Vol. 19. Núm. 4. 2006. p. 479-488.

24-Helms, E. R.; Aragon, A.; Fitschen, P.J. Evidence-based recommendations for natural bodybuilding contest preparation: nutrition and supplementation. *Journal of The International Society of Sports Nutrition*. Vol. 11. Núm. 1. 2014. p. 2-20.

25-Hickman, C. P.; Roberts, L. S.; Keen, S. L.; Eisenhour, D.J.; Larson, A.; L Anson, H. *Integrated principles of zoology*. 16th Edition. Guanabara Koogan. 2016. p. 937.

26-Hirschbruch, M.D.; Fisberg, M.; Mochizuki, L. Supplement use among young gym-goers in São Paulo. *Brazilian Journal of Sports Medicine*. Vol. 14. Núm. 6. 2008. p. 539-543.

27-Iemitsu, M.; Miyauchi, T.; Maeda, S.; Sakai, S.; Kobayashi, T.; Fujii, N.; Miyazaki, H.; Matsuda, M.; Yamaguchi, I. Physiological and pathological cardiac hypertrophy induce different molecular phenotypes in the rat. *American Journal of Physiology. Regulatory, Integrative, and Comparative Physiology*. Vol. 281. Núm. 6. 2001. p. R2029-2036.

28-Jaenisch, R.B.; Faralozzo, F. Effect of resistance training in patients with heart failure. *Revista Perspectiva: Ciência e Saúde*. Vol. 2. Núm. 1. 2017. p. 124-136.

29-Junqueira, L.C.; Carneiro, J. *Basic Histology*. 7th Edition. Guanabara Koogan. 2000.

30-Kardong, K.V. *Vertebrates: comparative anatomy, function and evolution*. 7th Edition. Guanabara Koogan. 2016. p. 788.

31-Kemi, O.J.; Haram, M.; Wisløff, U.; Ellingsen, Ø. Aerobic fitness is associated with cardiomyocyte contractile capacity and endothelial function in exercise training and detraining. *Circulation*. Vol. 109. Num. 23. 2004. p. 2897-2904.

32-Kemi, O.J.; Haram, P. M.; Loennechen, J.P.; Osnes, J-B.; Skomedal, T.; Wisløff, U.; Ellingsen, Ø. Moderate vs. high exercise intensity: differential effects on aerobic fitness,

cardiomyocyte contractility, and endothelial function. *Cardiovasc. Res.* Vol. 67. Num. 1. 2005. p. 161-172.

33-Kemi, O.J.; Ellingsen, Ø.; Ceci, M.; Grimaldi, S.; Smith, G. L.; Condorelli, G.; Wisloff, U. Aerobic interval training enhances cardiomyocyte contractility and Ca²⁺ cycling by phosphorylation of CaMKII and Thr-17 of phospholamban. *J. Mol. Cell. Cardiol.* Vol. 43. Num. 3. 2007. p. 354-361.

34-Lima, F.V.S. Effects of resistance training in patients with heart failure with reduced ejection fraction: systematic review and meta-analysis. Master's Dissertation in Health Sciences and Technologies. University of Brasília. 2016.

35-Macnaughton, L.S.; Wardle, S.L.; Witard, O.E.; McGlory, C.; Hamilton, D.L.; Jeromson, S.; Lawrence, C.E.; Wallis, G.A.; Tipton, K.D. The response of muscle protein synthesis following whole-body resistance exercise is greater following 40 g than 20 g of ingested whey protein. *Physiological Reports.* Vol. 4. Núm. 15. 2016. p. 1-16.

36-Magalhães, F.C.; Barretti, D.; Hashimoto, N.; Melo, F.S.F.; Roque, F.R.; Oliveira, E.M. Cardiac hypertrophy induced by physical training: molecular and cellular events that modify the phenotype. *Revista Mackenzie de Educação Física e Esporte.* Vol. 7. Núm. 1. 2008. p. 189-193.

37-Maron, B.J.; Pelliccia, A. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. *Circulation.* Vol. 114. Núm. 15. 2006. p. 1633-1644.

38-Marques, R.F. Resistance training and regulation of muscle mass. *Brazilian Journal of Exercise Prescription and Physiology.* Vol. 10. Núm. 62. 2016. p. 438-440.

39-Maughan, R.J.; Burke, L.M. *Sports Nutrition.* Artmed. 2004. p. 27-37.

40-McArdle, W.D.; Katch, F.I.; Katch, V.L. *Exercise Physiology.* 5th Edition. Rio de Janeiro: Guanabara Koogan. 2003.

41-Monahan-Earley, R.; Dvorak, A. M.; Aird, W. C. Evolutionary origins of the blood vascular system and endothelium. *Journal of Thrombosis and Haemostasis.* Vol. 11. Num. s1. 2013. p. 46-66.

42-Morton, R.W.; McGlory, C.; Phillips, S.M. Nutritional interventions to augment resistance training-induced skeletal muscle hypertrophy. *Frontiers in Physiology.* Vol. 6. 2015. p. 245.

43-Nabuco, H.C.G.; Rodrigues, V.B.; Ravagnani, C.F.C. Factors associated with the use of dietary supplements among athletes: A systematic review. *Brazilian Journal of Sports Medicine.* Vol. 22. Núm. 5. 2016. p. 4.

44-Naderi, A.; Oliveira, E.P.; Ziegenfuss, T.N.; Willem, M.T. Timing, Optimal Dose and Intake Duration of Dietary Supplements with Evidence-Based Use in Sports Nutrition. *Journal of Exercise Nutrition & Biochemistry.* Vol. 20. Núm. 4. 2016. p. 1-12.

45-Nogueira, F.R.S.; Souza, A.; Brito, A. Prevalence of the use and effects of ergogenic aids by bodybuilding practitioners in Brazilian gyms: a systematic review. *Revista Brasileira de Atividade Física e Saúde.* Vol. 18. Núm. 1. 2013. p. 16-30.

46-NSCA. National Strength and Conditioning Association. Youth resistance training: update position statement paper from the National Strength and Conditioning Association. *The Journal of Strength & Conditioning Research.* Vol. 23. Núm. 5. 2009. p. 560-579.

47-Ormsbee, M.J.; Bach, C.W.; Baur, D. A. Pre-exercise nutrition: the role of macronutrients, modified starches and supplements on metabolism and endurance performance. *Nutrients.* Vol. 6. Núm. 5. 2014. p. 1782-1808.

48-Paiva, A.C.; Alfenas, R.C.G.; Bressan, J. Effects of high protein intake in the metabolism. *Brazilian Journal of Clinical Nutrition.* Vol. 22. Núm. 1. 2007. p. 83-84.

49-Pal, S.; Radavelli-Bagatini, S. The effects of whey protein on cardiometabolic risk factors. *Obesity Reviews.* Vol. 14. Núm. 4. 2013. p. 324-343.

50-Pelster, B.; Bemis, W. E. Ontogeny of heart function in the little skate *Raja erinacea*. *The Journal of Experimental Biology.* Vol. 156. 1991. p. 387-398.

51-Phillips, S. M. Physiologic and molecular bases of muscle hypertrophy and atrophy: impact of resistance exercise on human skeletal muscle. *Applied Physiology, Nutrition, And Metabolism*. Vol. 34. Núm. 3. 2009. p. 403-410.

52-Phillips, S. M.; Van Loon, L.J. Dietary proteins for athletes: From requirements to optimum adaptation. *Journal of Sports Sciences*. Vol. 29. Núm. 1. 2011. p. 29-38.

53-Pinto, G.H. Analysis of miRNA profile and related signaling pathways in an animal model of physiological cardiac hypertrophy induced by swimming. Doctoral Thesis. Postgraduate Program in Health Sciences: Cardiology and Cardiovascular Sciences. Federal University of Rio Grande do Sul. 2018.

54-Pinho, R.A.; Araújo, M.C.; Ghisi, G.L.M.; Benetti, M. Coronary artery disease, physical exercise and oxidative stress. *Arq Bras Cardiol*. Vol. 94. Núm. 4. 2010. p. 549-555.

55-Rios, E.T.; Rodrigues, F.C.; Rocha, L.F.; Salemi, V.M.C.; Miranda, D.P. Influence of weekly volume and resistance training on the incidence of injury in street runners. *Brazilian Journal of Exercise Prescription and Physiology*. Vol. 11. Núm. 64. 2017. p. 104-109.

56-Robergs, R.A.; Roberts, S.O. *Fundamental Principles of Exercise Physiology for Fitness, Performance and Health*. Phorte. 2002.

57-Shimizu, I.; Minamino, T.; Toko, H.; Okada, S.; Ikeda, H.; Yasuda, N.; Tateno, K.; Moriya, J.; Yokoyama, M.; Nojima, A.; Koh, G.Y.; Akazawa, H.; Shiojima, I.; Kahn, C.R.; Abel, E.D.; Komuro, I. Excessive cardiac insulin signaling exacerbates systolic dysfunction induced by pressure overload in rodents. *The Journal of Clinical Investigation*. Vol. 120. Núm. 5. 2010. p. 1506-1514.

58-Shimizu, I.; Minamino, T. Physiological and pathological cardiac hypertrophy. *Journal of Molecular and Cellular Cardiology*. Vol. 97. 2016. p. 245-262.

59-Silverthorn, D.U. *Human Physiology: An Integrated Approach*. 7th Edition. Artmed Editora. 2017.

60-Terada, L.C.; Godoi, M.R.; Silva, T.C.V.; Monteiro, T.L. Metabolic effects of whey protein supplementation in weight training practitioners. *Brazilian Journal of Sports Nutrition*. Vol. 3. Núm. 16. 2009. p. 295-305.

61-Van Berlo, J.H.; Pandya, K.; Molkentin, J.D. Signaling effectors underlying pathologic growth and remodeling of the heart. *The Journal of Clinical Investigation*. Vol. 123. Núm. 1. 2013. p. 37-45.

62-Wang, S.; Ma, J.Z.; Zhu, S.S.; Xu, D.J.; Zou, J.G.; Cao, K.J. Swimming training can affect intrinsic calcium current characteristics in rat myocardium. *Eur. J. Appl. Physiol.* Vol. 104. Núm. 3. 2008. p. 549-555.

63-WHO. World Health Organization. *Nutrition. Global Strategy on Diet, Physical Activity and Health*. 2011.

64-Zambão, J.E.; Rocco, C.S.; Heyde, M.E.D. Relationship between whey protein supplementation and muscle hypertrophy: a review. *Revista Brasileira de Nutrição Esportiva*. Vol. 9. Núm. 50. 2015. p. 179-192.

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Received for publication on 25/10/2025
 Accepted on 30/01/2026