Post-sports career healthy ageing: The Janus-faced, high-performance sport

A. LELBACH\textsuperscript{1,2,3,4,5}, G. DÖRNYEI\textsuperscript{6}, F. IHÁSZ\textsuperscript{7} and A. KOLLER\textsuperscript{4,5,6,7,8}\* 

\textsuperscript{1} Dr Rose Private Hospital, Budapest, Hungary 
\textsuperscript{2} Departmental Group of Geriatrics, 2nd Department of Internal Medicine, Faculty of Medicine, Semmelweis University, Budapest, Hungary 
\textsuperscript{3} Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary 
\textsuperscript{4} Department of Translational Medicine, Faculty of Medicine, Semmelweis University, Budapest, Hungary 
\textsuperscript{5} Sport-physiology Research Center, Institute for Sports and Health Sciences, University of Physical Education, Budapest, Hungary 
\textsuperscript{6} Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary 
\textsuperscript{7} Faculty of Education and Psychology, Eötvös Loránd University, Budapest, Hungary 
\textsuperscript{8} Department of Physiology, New York Medical College, Valhalla, NY, USA 

ABSTRACT
By now, there is no doubt that regular physical exercise has an overall beneficial effect on each organ of the body. However, the effects of highly competitive sports (HCS) are more complex, as they exert greater demands on the cardiovascular and metabolic systems, among others. Strength, athletic, and aesthetic sport types each has a different exercise intensity and nutritional loading, as well as a different prevalence of cardiometabolic diseases at a later age. HCS athletes experience hypertension and mental stress during competitions and high nutritional loads between them. The post-career effects of this behaviour on the heart, arteries, cellular metabolism, and risk of obesity, are not well known and are not often the focus of research. In this review, we aimed to summarize the post-career effects of HCS. Based on data in the literature, we propose that athletes involved in highly competitive strength sports progressively develop metabolic syndrome and sustained elevated blood pressure.

KEYWORDS
physical activity, sport, metabolism, cardiovascular system, hypertension

THE SAD FACE OF JANUS

Post-sports career hypertension

Cardiovascular diseases have a high incidence in the developed world, and one of the most important risk factors is hypertension [1]. Its development is associated with genetic predisposition [4], sodium consumption, and other factors [2, 3]. The great demands highly competitive sports (HCS) place on the cardiovascular system and the metabolism have been well studied [5–8]. Less is known about the delayed effects, especially after a sports career is over. Exercise intensity, nutritional loading, and the risk of cardiometabolic diseases such as diabetes, dyslipidemia, non-alcoholic fatty liver, cardiovascular, and cerebrovascular diseases – all these factors vary depending on whether the sport is of the strength, athletic, or aesthetic type. It is well known that hypertension is a significant pathogenic factor in the development
of cardiometabolic diseases [1]. Its pathomechanisms, including a reduction in the elasticity of medium and large vessels, follow numerous parallel pathways. It has also been shown that regular, but non-competitive physical training with dynamic activities is one of the most important factors in the prevention of hypertension [9]. Previous studies have shown, however, that hypertension can develop in competitive athletes [5]. Berge et al. [6] measured significantly higher systolic and diastolic blood pressures in athletes of strength sports compared to athletes of endurance sports (131.3 ± 5.3/77.3 ± 1.4 vs. 118.6 ± 2.8/71.8 ± 1.2 mmHg, P < 0.05). Strength sports can increase arterial stiffness [10], but combined with moderate-load, individualized exercises, they can also have beneficial effects. Although the post-career effects of HCS are less well investigated, we propose that hypertension and metabolic syndrome progressively develop in athletes involved in strength sports.

**Post-sports career metabolic syndrome**

In the study of Tucker et al., overweight American football players suffered from dyslipidemia and related cardiometabolic diseases [7]. Guo et al. found a significantly increased cardiometabolic risk in strength athletes in the heaviest weight class, compared to all other weight classes [8]. Also, in strength athletes who have finished a competitive sports career, the prevalence of diabetes and metabolic syndrome were found to be significantly higher than in any other sport type [11–13]. Based on the results of Guo et al., moderately intensive aerobic exercise effectively improved the cardiometabolic risk factors in overweight athletes with metabolic syndrome [14]. Although regular exercise is essential to delay the ageing of the cardiovascular and skeletal muscle systems and to maintain normal hemorheological properties and metabolism, the beneficial effects of competitive sports – especially strength sports – on the ageing process are highly questionable. Pathological changes become more evident after the sports career is over, when hypertension, metabolic syndrome, and other risk factors can develop.

**Post-sports career hypertension and obesity**

In developed countries, increasing prevalence of obesity has been observed in recent decades, and it is correlated with an increasing prevalence of hypertension and cardiac disease [15]. People suffering from obesity and hypertension have pathological changes such as sympathetic nervous system activation [16], renin-angiotensin system activation (resulting in sodium retention), and increased glucose tolerance [17].

**Ageing**

In the developed world, life expectancy has increased significantly, but so has the prevalence of hypertension. Accelerated ageing must be differentiated from normal ageing and ageing with various diseases [18]. Hypertension induced by obesity or ageing, or both, increases myocardium tension and thickness and causes cardiac remodelling, mostly in the left ventricle. At the same time, loss of elasticity in the large arteries causes structural and functional changes of the arterial walls. The results are remodelling and stiffening of the vascular walls and isolated high systolic blood pressure through the reduction of the “windkessel” function of the aorta and the large arteries. An increase of systolic pressure above 150 mmHg, as well as a reduction of diastolic pressure below 95 mmHg can be observed [19–20]. The increased basal tone and reduced vasodilation capacity of the small arteries and arterioles cause increased peripheral resistance and diastolic pressure. Since these pathological modifications of the vascular system need long years to develop, regular blood pressure measurement has high importance in the prevention of high-blood-pressure disease (borderline RR 140/90 mmHg) [21]. Regular physical exercise can help prevent the development of cardiac and vascular remodelling [22], especially if it reduces the need for medicine in the early stage of the development of hypertension [23]. The ageing process influences molecular biological mechanisms such as oxidative stress and chronic inflammation, which can have significant effects on the immune and endocrine systems (cytokine production, IGF system) [20, 24]. Other organs, e.g. the kidney (salt excretion, as well as volume overload), also affect blood pressure, both systolic and diastolic. The above-mentioned changes can have positive effects on the cardiovascular system through the improvement of its oxygen and nutritional supply [25–27]. Different exercise modalities could delay or prevent the development of hypertension by having a beneficial influence on the cardiovascular system.

**THE HAPPY FACE OF JANUS**

Effects of regular, mild-intensity exercise on hemorheological characteristics of the cardiovascular system and skeletal muscle

The influence of physical activity on the hemorheological status. The importance of mild-intensity exercise has been proven to have beneficial effects on hemorheological status in older age [28]. Better flow quality and tissue perfusion, as well as decreased blood viscosity and red blood cell aggregation [30] protect against the well documented proinflammatory conditions and elevated plasma fibrinogen levels in older adults [28]. In the paracrine effect, blood flow dynamics during physical exercise are also influenced by the release of adenosine triphosphate (ATP) and Nitric oxide (NO) from red blood cells [29].

The influence of physical activity on the heart – haemodynamic and molecular aspects. Physical training consumes and requires a lot of energy, produced mostly by the oxidation of glucose [30], and circulation is the main player in delivering oxygen and glucose to the different organs. During physical stress, the heart has more significant work
than in rest. To supply sufficient blood to the tissues, there must be an increased number of heartbeats, since heart rate x stroke volume = cardiac output [31]. Physical exercise prevents cardiovascular damage by increasing the level of antioxidants [32]. This is one of its most important positive effects at the molecular and cell-physiology level. Heat shock proteins, which are proven to have a role in cell survival and ischaemic damage protection, have an increased gene expression during physical exercise [33]. Another beneficial effect of physical exercise is a mitochondrial adaptation, which has a cardioprotective effect through opening potassium channels of the sarcolemma.

The influence of mild-intensity physical activity on the arterial system – haemodynamic and molecular aspects. Changes in the diameter of the arterioles and venules have a significant influence on blood flow [34]. That is why the vessels of organs which need a smaller amount of oxygen during physical exercise are vasoconstrictive, but those which need a larger amount are dilated to generate an increased blood flow [35]. The result is a good supply of oxygen and glucose to those organs for which it is the most essential. Vascular remodelling and the positive alteration of endothelial function through exercise are also beneficial [36]. NO and prostacyclin (PGI2) have a vasodilator effect; endothelin-1 (ET-1) and platelet-activation factor (PAF) are vasoconstrictor molecules. All of them are important regulatory modulators of the endothelium and have a very important role in vasoconstrictor and vasodilator mechanisms [37, 38]. Physical exercise increases the presence of endothelial nitric oxide synthase (eNOS) through increased gene expression, which is the result of increased wall shear stress [39]. Increased eNOS function results in increased NO production, which has significant vasodilator effect. Increased prostaglandins also lead to vasodilation and have a cardioprotective effect through anti-inflammatory and platelet inhibition [34, 40].

The influence of physical activity on skeletal muscle metabolism. The main energy source of skeletal muscle during low to moderate physical exercise is glucose. The origin of glucose is the oral intake, hepatic glycogenolysis and gluconeogenesis, and the release of free fatty acids (FFAs) from adipose tissues through lipolysis [41]. Power output and energy consumption determine the need for ATP. On the other hand, relative exercise intensity determines the carbohydrate and lipid contribution to energy supply [41]. In case of progressively increasing exercise and an insufficient oxygen level, or when blood flow is inefficient because of “muscle pump,” e.g. during isometric exercise, the development of anaerobic energy production and lactate synthesis is accelerated [42]. Ischaemia or hypoxaemia causes an elevated lactate level in various organs, but it is also detectable as a normal response to vigorous physical activity.

Exercise types for health promotion: aerobic – anaerobic – flexibility exercises

The cardiovascular and metabolic effects of intensive physical activity were discussed in the previous section. For different types of hypertension, a different type of exercise can have the optimal therapeutic effect.

Exercise types can be classified into three major forms:

1. **aerobic exercise**: physical activity with a low-to-moderate intensity. The main energy sources are glucose and FFAs (with no significant elevation of lactate level in the plasma). Cylcical movements like walking, running, and cycling, and non-cylcical movements like soccer, handball, and tennis, are the most usual aerobic exercises [43].

2. **anaerobic exercise**: usually short-duration muscle strength activities (e.g. weightlifting) [42], causing insufficient oxygen supply and anaerobic energy production with significant lactate synthesis [42]. During this type of exercise, metabolism progressively switches from major aerobic metabolism at the beginning to anaerobic metabolism thereafter [42].

3. **stretching/flexibility exercise**: a range of motion of both muscles and joints can be improved through these exercises. Because stretching is performed with low intensity, aerobic mechanisms are the most usual energy supply.

The American College of Sports Medicine (ACSM) states that the most effective and recommended treatment of hypertension is aerobic dynamic exercise training [45].

Regular, mild physical activity as an effective rehabilitation for post-sport career syndrome

Regular physical activity modalities, as well as fitness programs, are proven to have a blood pressure-lowering effect and a positive influence on metabolic syndrome through several physiological processes.

Neuro-humoural effects of physical activity. Physical activity increases serum catecholamine levels, which increase the total peripheral resistance [46]. When circulating catecholamines are at a low-to-moderate level, increased cardiac output causes a redistribution of blood flow, with an increased circulation in the musculature and the liver, but a significantly unchanged mean arterial pressure [47]. The unchanged arterial pressure is explained by the activation of vascular β2-adrenoceptors, the result of which is the decrease of systemic vascular resistance (despite increased cardiac output). With higher catecholamine levels in the plasma, more catecholamine binds to α-adrenoceptors in the vasculature, and arterial pressure is increased. This is in compensation for the vasodilation mediated by β2-adrenoceptors [47]. General physical condition (whether trained or untrained), emotional or other psychic stress, nutritional state, and age also influence the effect of catecholamines [46]. Endurance training (e.g. running, rowing, or cycling) has a positive effect on the function of the autonomic
nervous system. The mechanism of this improvement is the increase of parasympathetic activity, while sympathetic activity is decreased [48].

**Vasomotor effects of physical activity.** Modulation of vasodilator and vasoconstrictor mechanisms [49] and vasculature structural adaptations are both important effects of exercise on vascular function [50] and coronary and skeletal muscle microcirculation. As previously discussed, the endothelium of the different vessels (including lymphatic vessels) has a significant role – through the production of vasoactive mediators – in controlling vasoconstrictor and vasodilator mechanisms [38]. Not only the gene for eNOS, which synthesizes the vasodilator, NO, but also the gene for the antioxidant enzyme superoxide dismutase is upregulated by physical training [39]. Exercise-induced cardiac remodelling (EICR) is a structural cardiac adaptation resulting in left-ventricular hypertrophy with a well-known sport-specific appearance referred to as eccentric hypertrophy. According to the results of international research groups, a gain of VO2 max is in connection with this myocardial adaptation [51].

**The effects of long-term exercise training programs on gene expression.** Regular physical activity generates alterations in the expression of various genes influencing blood pressure (e.g. APOE (Apolipoprotein E), ACE (Angiotensin I converting enzyme), NOS3 (Nitric oxide synthase 3), EDN1 (Endothelin 1), LPL (Lipoprotein lipase), PPARα ( Peroxisome proliferator-activated receptor alpha), NFκB1 (Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1)). It also influences lipid metabolism, endothelial function, and oxidative and glucose homoeostasis, all of which are significant factors in the blood pressure-lowering mechanisms of exercise programs [52].

The reduced or increased synthesis of the above-discussed molecules through their gene expression regulation can be a consequence of different types of exercise training. Other post-exercise changes such as the activation of immediate early genes can be stimulated, as well. These molecular biological changes are regulated through the modulation of different signal transduction pathways, as in the interaction of molecules of chronic inflammation and oxidative stress (interfering also with obesity and ageing) [20, 27].

**The influence of different types of physical training on serum lipid levels.** Dyslipidemia is an important risk factor for cardiovascular diseases. Physical activity plays an important role in the improvement of serum lipid parameters, as do the diet, weight loss and lipid-lowering medications. Based on the results of meta-analyses of randomized controlled trials, aerobic training raises serum high-density lipoprotein cholesterol (HDL-C) [53], while anaerobic training lowers serum low-density lipoprotein cholesterol (LDL-C) levels [54]. The combination of aerobic and anaerobic training (simultaneously performed) has the beneficial effect of increasing serum HDL-C and lowering serum LDL-C levels [54]. Whereas aerobic and anaerobic training should have a beneficial role in the reduction of serum triglycerides (TG), the optimal exercise intensity and dosage still cannot be clearly defined [54]. Recent meta-analyses of large databases have revealed the so-called obesity paradox (OP) [55]. In the OP, being overweight increases the risk of cardiovascular disease; at the same time, people who are moderately overweight have lower mortality than those with normal body weight [56]. The possible explanation could be the better survival rate in serious life-threatening conditions (stroke or myocardial infarction).

**The FITT (Frequency, Intensity, Type, and Time) principle of exercise prescription**

The Frequency, Intensity, Type, and Time (FITT) principle is used to apply the results of basic cardiovascular research into hypertension treatment with a personalized physical activity program, according to the medical needs of patients. It provides medical professionals with a new possibility in hypertension treatment (Fig. 1). The three main exercise types are aerobic, anaerobic, and flexibility exercises. Simultaneously performed aerobic and anaerobic training during the same physical exercise or within the next few hours [57] is a typical training method and could have a beneficial effect on hypertension and numerous connected cardiovascular risk factors [57, 58]. The Borg Rating of Perceived Exertion (RPE) is a perceived exertion scale to measure physical activity intensity level, according to a participant’s self-reporting of exertion. It approximately correlates with parameters such as heart and respiration rate, sweating, and muscle fatigue. The perceived exertion intensity ranges from 6 (no exertion at all) to 20 (maximum exertion) [58]. The energy cost of physical activities can be expressed by the Metabolic Equivalent of Task (MET). The Resting Metabolic Rate (RMR) used in sitting (without any motion) originally equals 1 MET (3.5 mL/kg/min). MET values of activities range from 0.9 (sleeping) to 23 (running at 22.5 km/h) [58]. According to the ACSM, aerobic

Unauthenticated | Downloaded 07/15/21 08:26 AM UTC
dynamic exercise training for hypertensive individuals is recommended as follows [45]:

- **Frequency** – daily aerobic exercise with an additional resistance exercise three days per week [45].

- **Intensity** – moderate-intensity aerobic exercise with a 40–60% oxygen consumption reserve (VO₂ reserve) or HR (heart rate) reserve (R). The so-called Karvonen formula: Target Heart Rate = [(max HR – resting HR) × % Intensity] + resting HR, as well as 11-13 RPE rate (Level 11 is “Light”, and 13 is “Somewhat hard”) on the Borg scale (a subjective reinforcement) [45].

- **Time** – the recommendation is to perform 45–80 min of concurrent exercise per training, divided into 30 min of aerobic training and 15–40 min of dynamic resistance exercise [43].

- **Type** – simultaneously performed aerobic exercise activities (walking, jogging, or cycling) and dynamic resistance exercises (free weights or machine weights), and circuit resistance training, without a specially recommended modality, is effective [60, 61]. These exercise prescriptions (FITT) also contain the MET value (Volume) and training progression (Progression) of the exercise protocols (FITT-VP). Based on the ACSM, a volume between 500 and 1000 MET-min per week could provide the most antihypertensive benefits. Furthermore, the progression of exercises should be increased gradually in intensity and volume [62].

**CONCLUSIONS**

HCS are frequently associated with post-career development of hypertension and metabolic syndrome. Importantly, these unwanted effects can be reduced by light-intensity regular daily exercise programs, as opposed to a sedentary lifestyle. Our previous studies and the recent literature highlight the fact that post-career exercise programs have a beneficial effect on the modulation of hypertension and related diseases. According to the ACSM [45] and The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC8), the most effective and recommended physical activity to treat hypertension is aerobic dynamic exercise training [63]. Although anaerobic training is also preventative for hypertension and connected chronic diseases [44], it should be carefully practised by patients with these diseases (e.g. Valsalva manoeuvre). Simultaneously performed aerobic and anaerobic training by hypertension patients has the same effect as aerobic training [57, 58]. After careful consideration of individual needs and conditions – with the help of the FITT principle – personalized exercise programs should be designed (Fig. 1); their success, however, is certainly based on the involvement of patients in the decision-making process.

**Ethical approval:** NA.

**Funding:** National Research, Development and Innovation Fund, OTKA K 10844, K 132596, Higher Education Institutional Excellence Program at Semmelweis University and the National Bionika Program ED_17-1-2017-0009, Hungary and Scientific Excellence Program 2019, at the University of Physical Education, Innovation and Technology Ministry, Hungary TUDFO/51757/2019-ITM.

**Authors’ contribution:** AL: conceptualization, original draft preparation, review editing, GD: review editing, FI: review editing, AK: conceptualization, revising it critically for important intellectual content.

**Conflicts of interest/Funding:** National Research, Development and Innovation Fund, OTKA K 10844, K 132596, Higher Education Institutional Excellence Program at Semmelweis University and the National Bionika Program ED_17-1-2017-0009, Hungary and Scientific Excellence Program 2019, at the University of Physical Education, Innovation and Technology Ministry, Hungary TUDFO/51757/2019-ITM. The authors declare no conflicts of interest.

**REFERENCES**

1. Writing Group Members, Mozaffarian D, Benjamin EJ, et al. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation 2016;133(4):e38–360. https://doi.org/10.1161/CIR.0000000000000350.

2. Leibach A, Koller A. Mechanisms underlying exercise-induced modulation of hypertension. J Hypertens Res 2017;3(2):35–43.

3. Peters SAE, Dunford E, Ware IJ, et al. The sodium content of processed foods in South Africa during the introduction of mandatory sodium limits. Nutrients 2017;9(4):404. https://doi.org/10.3390/nu9040404.

4. Dodoo SN, Benjamin IJ. Genomic approaches to hypertension. Cardiol Clin 2017;35(2):185–96. https://doi.org/10.1016/j.ccl.2016.12.001.

5. Weiner RB, Wang F, Isaacs SK, et al. Blood pressure and left ventricular hypertrophy during American-style football participation. Circulation 2013;128(5):524–31. https://doi.org/10.1161/CIRCULATIONAHA.113.03522.

6. Berge HM, Isern CB, Berge E. Blood pressure and hypertension in athletes: a systematic review. Br J Sports Med 2015;49(11):716–23. https://doi.org/10.1136/bjsports-2014-093976.

7. Tucker AM, Vogel RA, Lincoln AE. Prevalence of cardiovascular disease risk factors among National Football League players. JAMA 2009;301(20):2111–9. https://doi.org/10.1001/jama.2009.716.

8. Guo J, Zhang X, Wang L. Prevalence of metabolic syndrome and its components among Chinese professional athletes of strength sports with different body weight categories. PLoS One 2013;8(11):e79758. https://doi.org/10.1371/journal.pone.0079758.

9. Pedersen BK, Saltin B. Exercise as medicine – evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports 2015;25(Suppl. 3):1–72. https://doi.org/10.1111/sms.12581.

10. Gojanovic B. Fitness, sports and blood pressure. Praxis (Bern 1994) 2010;99(25):1551–7.
11. Buell JL, Calland D, Hanks F, et al. Presence of metabolic syndrome in football linemen. J Athl Train 2008;43(6):608–16. https://doi.org/10.4085/1062-6050-43.6.608.

12. Kujala UM, Kaprio J, Taimela S. Prevalence of diabetes, hypertension, and ischemic heart disease in former elite athletes. Metabolism 1994;43(10):1255–60.

13. Miller MA, Croft LB, Belanger AR, Somers VK, Roberts AJ, et al. Prevalence of metabolic syndrome in retired National Football League players. Am J Cardiol 2008;101(9):1281–4. https://doi.org/10.1016/j.amjcard.2007.12.029.

14. Guo J, Lou Y, Zhang X, et al. Effect of aerobic exercise training on cardiometabolic risk factors among professional athletes in the heaviest-weight class. Diabetol Metab Syndr 2015;7:78. https://doi.org/10.1186/s13098-015-0071-y.

15. Karimian S, Stein J, Bauer B, et al. Impact of severe obesity and adipose tissue renin-angiotensin-aldosterone system signaling and obesity-associated hypertension. Physiology 2017;32(3):197–209. https://doi.org/10.1152/physiol.00037.2016.

16. Hurr C, Young CN. Neural control of non-vasomotor organs in hypertension. Curr Hypertens Rep 2016;18(4):30. https://doi.org/10.1007/s11906-016-0635-8.

17. Schüttén MT, Houben AJL, de Leeuw PW, et al. The link between adipose tissue remodelling and obesity. Arterioscler Thromb Vasc Biol 2019;39(3):603–15. https://doi.org/10.1161/ATVBAHA.118.310637.

18. Aiello A, Accardi G, Candore G, et al. Nutrigerontology: a key for achieving successful aging and longevity. Immun Ageing 2016;13:17. https://doi.org/10.1186/s12979-016-0071-2.

19. Thijsen DH, Carter SE, Green DJ. Arterial structure and function in vascular ageing: are you as old as your arteries? J Physiol 2016;594(8):2275–84. https://doi.org/10.1113/JP270597.

20. Szkabs B, Lehbach A, Kiss I, et al. Obesity in the elderly. In: Bedros RJ, editor. Clinical obesityology (University Textbook). Budapest: Semmelweis Kiadó; 2017. pp. 547–62.

21. Melgarejo JD, Maestre GE, Thiss L, et al. Prevalence, treatment, and control rates of conventional and ambulatory hypertension across 10 populations in 3 continents. Hypertension 2017;70:50–8. https://doi.org/10.1161/HYPERTENSIONAHA.117.09188.

22. Zeppilli P, Vannicelli R, Santini C, et al. Echocardiographic size of ventricular function and morphology: assessment by 2-dimensional speckle-tracking echocardiography. J Obes 2016;2016:2732613. https://doi.org/10.1155/2016/2732613.

23. Miller MA, Croft LB, Belanger AR, Romero-Corral A, Somers VK, Roberts AJ, et al. Prevalence of metabolic syndrome in retired National Football League players. Am J Cardiol 2008;101(9):1281–4. https://doi.org/10.1016/j.amjcard.2007.12.029.

24. Guo J, Lou Y, Zhang X, et al. Effect of aerobic exercise training on cardiometabolic risk factors among professional athletes in the heaviest-weight class. Diabetol Metab Syndr 2015;7:78. https://doi.org/10.1186/s13098-015-0071-y.

25. Karimian S, Stein J, Bauer B, et al. Impact of severe obesity and adipose tissue renin-angiotensin-aldosterone system signaling and obesity-associated hypertension. Physiology 2017;32(3):197–209. https://doi.org/10.1152/physiol.00037.2016.

26. Aiello A, Accardi G, Candore G, et al. Nutrigerontology: a key for achieving successful aging and longevity. Immun Ageing 2016;13:17. https://doi.org/10.1186/s12979-016-0071-2.

27. Thijsen DH, Carter SE, Green DJ. Arterial structure and function in vascular ageing: are you as old as your arteries? J Physiol 2016;594(8):2275–84. https://doi.org/10.1113/JP270597.

28. Aiello A, Accardi G, Candore G, et al. Nutrigerontology: a key for achieving successful aging and longevity. Immun Ageing 2016;13:17. https://doi.org/10.1186/s12979-016-0071-2.
46. Zouhal H, Jacob C, Delamarche P, et al. Catecholamines and the effects of exercise, training and gender. Sports Med 2008;38(5):401–23.
47. Klabunde RE. Cardiovascular physiology concepts. 2nd ed. Baltimore: Lippincott Williams & Wilkins; 2012.
48. White D, Fernhall B. Effects of exercise on blood pressure and autonomic function and other hemodynamic regulatory factors. In: Pescatello LS, editor. Effects of exercise on hypertension. Switzerland: Springer International Publishing, Humana Press; 2015. p. 203–27.
49. Winterfeld HJ, Siewert H, Bohm J, Möbes R, et al. Hemodynamics in arterial hypertension treated with running endurance training or nifedipine therapy. Z Kardiol 1996;85(3):171–7.
50. Black JM, Stöhr EJ, Shave R, et al. Influence of exercise training mode on arterial diameter: a systematic review and metaanalysis. J Sci Med Sport 2016 Jan;19(1):74–80. https://doi.org/10.1016/j.jsams.2014.12.007.
51. Cavalcante PAM, Perilhao MS, da Silva AA, et al. Cardiac remodeling and physical exercise: a brief review about concepts and adaptations. Int J Sports Sci 2016;6(2):52–61. https://doi.org/10.5923/j.sports.20160602.06.
52. Bray MS, Hagberg JM, Pérusse L, et al. The human gene map for performance and health-related fitness phenotypes: the 2006–2007 update. Med Sci Sports Exerc 2009;41(1):35–73.
53. Durstine JL, Grandjean PW, Davis PG, et al. Blood lipid and lipoprotein adaptations to exercise: a quantitative analysis. Sports Med 2001;31(15):1033–62.
54. Tambalis K, Panagiotakos DB, Kavouras SA et al. Responses of blood lipids to aerobic, resistance, and combined aerobic with resistance exercise training: a systematic review of current evidence. Angiology 2009;60(5):614–32. https://doi.org/10.1177/0003319708324927.
55. Antonopoulos AS, Oikonomou EK, Antoniades C, et al. From the BMI paradox to the obesity paradox: the obesity-mortality association in coronary heart disease. Obes Rev 2016;17(10):989–1000. https://doi.org/10.1111/obr.12440.
56. McAuley PA, Blair SN. Obesity paradoxes. J Sports Sci 2011;29(8):773–82. https://doi.org/10.1080/02640414.2011.553965.
57. Corso LM, Macdonald HV, Johnson BT, et al. Is concurrent training efficacious antihypertensive therapy? a meta-analysis. Med Sci Sports Exerc 2016;48(12):2398–406.
58. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc 2013;2(1):e004473. https://doi.org/10.1161/JAHA.112.004473.
59. Borg G. Perceived exertion and pain scales. Champaign: Human Kinetics; 1998.
60. Dos Santos ES, Asano RY, Filho IG, Lopes NL, Panelli P, Nascimento DD, et al. Acute and chronic cardiovascular response to 16 weeks of combined eccentric or traditional resistance and aerobic training in elderly hypertensive women: a randomized controlled trial. J Strength Cond Res 2014;28(11):3073–84. https://doi.org/10.1519/JSC.0b013e31829a68cf.
61. Laterza MC, de Matos LD, Trombetta IC, et al. Exercise training restores baroreflex sensitivity in never-treated hypertensive patients. Hypertension 2007;49(6):1298–306.
62. Thompson PD, Arena R, Riebe D, Pescatello LS. ACSM’s new preparticipation health screening recommendations from ACSM’s guidelines for exercise testing and prescription, ninth edition. Curr Sports Med Rep 2013;12(4):215–7. https://doi.org/10.1249/JSR.0b013e31829a68cf.
63. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014;311(5):507–20. https://doi.org/10.1001/jama.2013.284427.