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# Heart rate and blood pressure in soccer players differing in sports qualification

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#### ABSTRACT

Aim: To investigate the effects of exercise training on heart rate and blood pressure in soccer players of different skill levels.

**Materials and Methods:** 693 soccer players with different sports qualifications were studied. Heart rate (HR) and blood pressure (BP) were measured at rest at the beginning of the preparatory phase of the training cycle.

**Results:** HR in elite soccer players is 64.4±0.83 bpm, bradycardia occurs in 47.4%, tachycardia in 5.3%, hypotonic state of systolic (SBP) and diastolic (DBP) blood pressure in 9.0% and 8.3%, hypertensive state of SBP and DBP in 41.4% and 17.3%, respectively. HR in advanced soccer players is 67.5±0.5 bpm, bradycardia occurs in 36.0%, tachycardia in 8.6%, hypotonic state of SBP and DBP occurs in 11.1% and 32.9%, hypotonic state of DBP in 9.1%, and hypertensive state of DBP in 13.7%. The HR in intermediate soccer players is 71.3±0.73 bpm. Players with bradycardia in this group were found 21.3%, and with tachycardia 17.8%. Hypotonic state of SBP was found in 17.2% of players, and hypertonic state in 19.0%. Hypotonic state of DBP was found in 19.5% and hypertensive state in 8.6% of players. Bradycardia and hypertensive state of SBP are significantly more frequent in elite players than in intermediate players.

**Conclusions**: Considering the presence of 12.9% of athletes with BP  $\geq$  140/90 mmHg among advanced soccer players, it is recommended to perform additional examinations, including daily BP monitoring, as well as to make adjustments in the training and rehabilitation process.

KEY WORDS: soccer players, sports qualification, bradycardia, tachycardia, hypotonic and hypertensive states

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# INTRODUCTION

As physical culture and sports developed in Western Europe, medical control over the health of those involved in physical culture and sports began to develop. This task was carried out by doctors and paramedical staff. Their duties included, first and foremost, the medical examination of persons for the purpose of their admission to a particular type of sport or recreational physical training. At that time, in order to evaluate functional tests of the cardiovascular system, medical control specialists (sports physicians) used simple instrumental methods of heart rate (HR) and blood pressure (BP) measurement not only at rest, but also after dosed physical exertion in the form of the Martinet-Kushelevsky test (20 knee bends for 30 s).

At the time, the scientific interest was in comparing indicators of people involved in physical training and

sport with healthy people not involved in such activities to determine the effects of physical activity on the human body and to develop medical recommendations.

Nowadays, sports physicians and trainers are no longer satisfied with such comparisons. They need the results of an examination of an athlete of a particular sport, taking into account his qualification, age, gender, training experience, period of the training cycle, as well as the specifics of the influence of training and competitive loads on the functional state of the body systems, and first of all on the cardiovascular system [1].

The development of sports science allows the introduction of new research methods into the practice of sports medicine, expanding the practitioner's ability to assess the health and functional status of athletes. At the same time, the provision of complex portable instrumental research methods to the practicing sports physician is still inadequate. This motivates the continuation of the use of relatively simple, easily accessible research methods in medical control.

It is well known that various organs and systems of the athlete's body undergo functional and morphological changes as a result of sporting activity. Most of the changes in cardiovascular activity are related to the state of training. They are related to sympathoinhibitory and cholinergic mechanisms. In the first place, this refers to the reduction in the heart rate and the blood pressure. It is the decrease in heart rate and blood pressure that forms the concept of the so-called phenomenon of "economisation" of cardiac activity or training of a highly skilled athlete.

Regarding the heart rate, it is known that the average resting HR of healthy men who don't exercise varies between 60 and 80 beats min<sup>-1</sup>(bps) and is somewhat dependent on age, gender and body size. During regular exercise, the heart rate of athletes decreases due to the development of strong cholinergic responses at rest, one of the consequences of which are negative chronotropic effects and consequently a slowing of the heart rate. At the same time, there is a certain correlation between the intensity of negative chronotropic influences and the type and direction of the training process [2].

The results of almost all authors who have studied BP in athletes show that under the influence of systematic training BP decreases and corresponds to 100-110/60-70 mmHg [3]. These are average values obtained from a study of BP in a large number of athletes, without taking into account gender, age, sport specialization, years of experience and qualification, as all these factors influence BP in athletes.

Relatively reduced values of systolic (below 100 mmHg) and diastolic (below 60 mmHg) blood pressure are often observed in trained athletes, representing physiological hypotension, which is not always a sign of good training [4]. Sometimes hypotension is associated with circulatory dysregulation, in which case it is a syndrome of overtraining or an independent disease [5].

Based on the findings of Dembo [5], it has been observed that hypotension is more common in young athletes, with an incidence rate of 21.0% in masters and 2.6% in beginners. In addition, the incidence of hypotension in athletes tends to increase with more athletic experience. Specifically, up to 15-16 years of experience, the percentage of athletes with hypotension continues to increase. Beyond this point, however, the percentage begins to decrease due to the influence of the age factor. The prevalence of hypertension in athletes is reported to be between 9% and 13% [4]. It is noteworthy that an increase in blood pressure is observed from 3-4% to 10-15%, often reaching the upper threshold of the generally accepted range or entering the realm of potential danger. The improvement in cardiovascular regulatory mechanisms resulting from increased physical fitness contributes to the return of blood pressure to a normal range. Conversely, impaired fitness, characterized by conditions such as overfatigue, overtraining, or overexertion, often manifests as both an increase and a decrease in blood pressure levels [6].

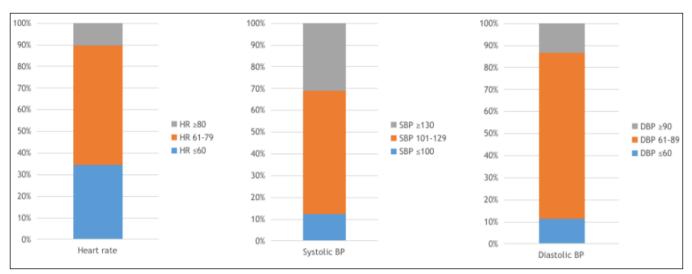
There is evidence that exercise and sports training are inversely related to the level of blood pressure and the prevalence of arterial hypertension, and this decrease can occur both in individuals with normal blood pressure numbers and in patients with arterial hypertension. There are studies in which the authors consider arterial hypertension in athletes as one of the forms of manifestation of overstrain of the cardiovascular system, which leads to pathological remodeling of the athlete's heart. According to the development of arterial hypertension, athletes whose training is dominated by static loads (weightlifting, athletic throwing, etc.) are at risk, since isometric loads are characterized by an increase in peripheral vascular resistance, causing transitional conditions with a potential risk of hypertension and an increase in overload with normal or slightly increased cardiac output. Significant influence on the increase in blood pressure also has the degree of emotional tension, gender, age. Thus, in men, increased blood pressure occurs 3 times more often than in women, and with increasing age of the athlete, the frequency of arterial hypertension increases. It should be taken into account that among athletes with hypertension there can be people with hereditary predisposition to hypertension [7].

The frequency of increase in blood pressure to some extent depends on the type of sports activity. Increased blood pressure in some athletes indicates the first manifestations of hypertension or is a symptom of other diseases. In some athletes the increase in blood pressure can be associated with improperly organized individual training process, as well as with the phenomena of fatigue, overstrain and mental overload [8, 9].

The importance of the issue of correct clinical assessment of changes in heart rate and blood pressure in athletes is not in doubt. It is not only about the possibility of doing sports for people with altered heart rate and blood pressure, but also about the frequency of detection and clinical evaluation of bradycardia and tachycardia, hypotensive and hypertensive conditions in athletes of different age and sports qualification.

# AIM

The aim of this study is to investigate the effects of exercise training on heart rate and blood pressure in soccer players of varying skill levels.





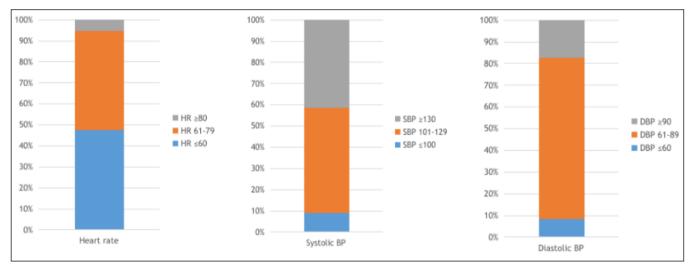


Fig. 2. Heart rate, systolic and diastolic blood pressure of elite soccer player.

# MATERIALS AND METHODS

# PARTICIPANTS

The study included 693 soccer players between the ages of 11 and 36 years (mean age  $19.9\pm0.18$  years), with a sports qualification from 3<sup>rd</sup> class athlete to Master of Sports of International Class. Included were 133 athletes with sports qualifications of Master of Sports and Master of Sports of International Class (elite soccer players), 386 athletes with sports qualifications of 1<sup>st</sup> class athlete and Candidate for Master of Sports (advanced soccer players), and 174 athletes with sports qualifications of 2<sup>nd</sup> or 3<sup>rd</sup> class athlete (Table 1).

The research was conducted in accordance with the main provisions of the Convention of the Council of Europe on Human Rights and Biomedicine (04.04.1997), Declaration of Helsinki of the World Medical Association on ethical principles of scientific medical research with human participation (2008-2013), Regulations of the Ministry of Health of Ukraine N<sup>o</sup>690 from 23.09.2009, N<sup>o</sup> 944 from 14.12.2009, N<sup>o</sup> 616 from 03.08.2012. All participants were informed about their rights and the possibility to leave the study at any time without explanation.

# PROCEDURE

The study was conducted during the preparatory phase of the training process. Heart rate was measured by an auscultatory method at rest in sitting position. Systolic and diastolic blood pressure were measured according to Korotkoff using the aneroid sphygmomanometer Romed (Netherlands) on the right hand. Measurements were performed in the sitting position, three times with an interval of 5 minutes, taking into account the minimum result [10].

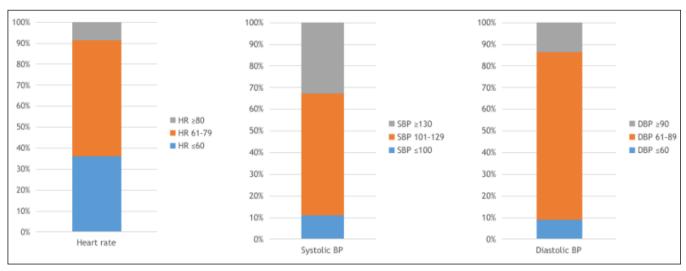


Fig. 3. Heart rate, systolic and diastolic blood pressure of advanced soccer player.

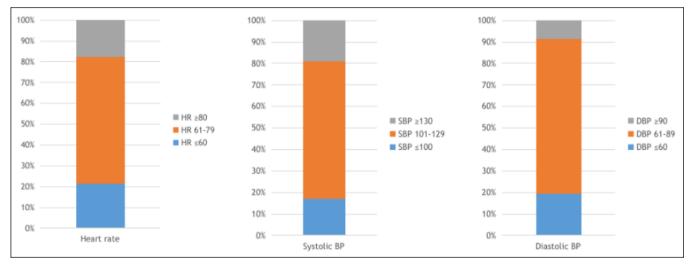


Fig. 4. Heart rate, systolic and diastolic blood pressure of intermediate soccer player.

# STATISTICAL ANALYSIS

Statistical analysis was performed using Statistica 13.0 software (StatSoft, USA)). Data are presented as mean (M)±standard error of the mean (SE). A two-tailed t-test was used to analyze independent samples. To determine a statistically significant association between two categorical variables, two-tailed Fisher's exact test was used. Differences between two subsets of data were considered statistically significant at p<0.05.

# RESULTS

Out of 693 players, 383 (55.3%) had a HR in the range of 61–79 bpm, which is considered normal. HR in the range of 60 bpm or less, i.e. bradycardia, was found in 239 (34.5%, p<0.001), and 80 bpm or more, i.e. tachycardia, occurred in 71 (10.2%, p<0.001). Systolic blood pressure (SBP) in the range of 101–129 mm

Hg, considered as normal, was found in 393 (56.7%) soccer players, with a value of 100 mm Hg or less, i.e. with a hypotensive state, in 85 (12.3%, p<0.001), and with systolic blood pressure 130 mm Hg or more, i.e. with a hypertensive state — in 215 (31.0%, p<0.001). Diastolic blood pressure (DBP) within normal values — 61–89 mm Hg was in 522 (75.3%) soccer players, diastolic blood pressure 60 mm Hg or less, i.e. with a hypotensive state — in 80 (11.5%, p<0.001) soccer players, and with a value of 90 mm Hg and more, i.e. with a hypertensive state — in 91 (13.1%, p<0.001) soccer players (Fig. 1).

Thus, in soccer players, who do not differ in sport qualification and age, HR, SBP and DBP are more often within normal values.

In order to obtain reliable information about the heart rate and the systolic and diastolic blood pressure, we have formed 3 groups of soccer players (elite,

Group	n	Age, years	Height, cm	Weight, cm
Elite soccer players (Master of Sports, International Class, Master of Sports)	133	25.6 ±0.37	182,9 ±0,52	77,4± 0,66
Advanced soccer players	386	19,8±	180,8±	73,0±
(Candidate for Masters of Sports, 1 <sup>st</sup> class athlete)		0,17	0,31	0,35
Intermediate soccer players	174	15,8±	174,8±	64,2±
(2 <sup>nd</sup> -3 <sup>rd</sup> class athlete)		0,15	0,68	0,85

#### Table 1. General characteristics of the examined soccer players

**Table 2.** Heart rate, systolic blood pressure and diastolic blood pressure of soccer players with different levels of athletic ability

Group	HR, bpm	SBP, mm Hg	DBP, mm Hg
Elite players	64,4±0,83 <sup>*‡</sup>	122,4±1,08 <sup>‡</sup>	76,9±0,9 <sup>‡</sup>
Advanced players	67,5±0,5	121,2±0,66 <sup>+</sup>	76,5±0,47 <sup>+</sup>
Intermediate players	71,3±0,73	116,3±0,97	72,1±0,68

Note: \* — elite vs advanced,  $p \le 0.001$ ; † — advanced vs intermediate,  $p \le 0.001$ ; ‡ — elite vs intermediate,  $p \le 0.001$ 

advanced, intermediate) according to their sport qualification and their age. The results of heart rate, systolic and diastolic blood pressure measurements are shown in Table 2.

Comparison of the studied indicators between groups showed that elite soccer players were older than advanced ( $25.6\pm0.37$  vs  $19.8\pm0.17$  years, p<0.001) and intermediate players ( $25.6\pm0.37$  vs  $15.8\pm0.15$ years, p<0.001). HR was lower in the elite group than in the advanced (p=0.001) and intermediate (p<0.001) groups. At the same time, elite players did not differ from advanced players in SBP and DBP. Statistically significant differences between SBP (p<0.001) and DBP (p<0.001) were found when comparing elite and intermediate soccer players, and between advanced and intermediate soccer players.

In the group of elite soccer players, HR in the normal range was found in 47.4%, bradycardia in 47.4%, tachycardia in 5.2% of athletes. Normal values of SBP and DBP were found in 49.6% and 74.4% of athletes, respectively. Hypotensive state of SBP and DBP was found in 9.0% and 8.3%, hypertensive state of SBP and DBP was found in 41.4% and 17.3%, respectively (Fig. 2).

In the group of advanced soccer players, HR in the normal range was found in 55.4% of the athletes studied, bradycardia in 36.0% and tachycardia in 8.6% of the athletes. SBP within reference values was found in 56.0% of athletes, with hypotensive state in 11.1% and with hypertensive state in 32.9%. DBP within normal limits was registered in 77.2% of athletes, with hypotension – in 13.7% of soccer players (Fig. 3).

In the group of intermediate soccer players, HR within normal limits was found in 60.9% of athletes.

21.3% and 17.8% of athletes had bradycardia and tachycardia, respectively. SBP within normal limits was found in 63.8% of soccer players, athletes with hypotensive state was found 17.2% and hypertensive state – 19.0%. DBP was within normal limits in 71.8% of athletes, hypotensive – in 19.5% and hypertensive – in 8.6% of athletes (Fig. 4).

The next stage of our work was to determine the relationship between HR and BP in soccer players according to sport qualification. Thus, in a group of elite soccer players, compared to a group of intermediate soccer players, bradycardia is more common – 47.4% vs 21.6% (p=0.009) and a hypertensive state of SBP – 41.35% vs 19.0% (p=0.030).

At the trend level, intermediate athletes had a higher prevalence of: normal HR – 60.9% vs 55.4% (p=0.351) in advanced athletes and 47.37% (p=0.086) in elite athletes; tachycardia – in 17.8% vs 8.6% (p=0.271) in advanced and 5.3% (p=0.407) in elite athletes; normal SBP - in 63.8% vs 56.0% (p=0.173) in advanced and 49.6% (p=0.064) in elite players; hypotonic state of SBP - in 17.2% vs 11.1% (p=0.455) in advanced and 9.0% (p=0.499) in elite players; hypotonic state of DBP - in 19.5% vs 9.1% (p=0.213) in advanced and 8.3% (p=0.384) in elite players. Hypertensive DBP was more common in the elite athletes group, 17.3% compared to the advanced group 13.7% (p=0.688) and intermediate athletes 8.6% (p=0.449). In terms of normal DBP values, advanced soccer players were 77.2% compared to elite (74.4%, p=0.574) and intermediate (71.8%, p=0.241) soccer players. Thus, the differences between the soccer player groups among HR and BP parameters were at the trend level except for bradycardia and hypertension, which were prevalent in elite athletes compared to younger intermediate soccer players.

# DISCUSSION

According to the classification of major sports according to Dembo et al. soccer is characterized by acyclic training and competitive work of variable power, developing qualities of agility, speed and strength [11]. Thus, it will be correct to compare the results of the study of heart rate and blood pressure obtained from soccer players or athletes in the training and competitive process of which such physical qualities prevail. In addition, it should be noted that this is a team sport where players have different roles [1].

It is known that as a result of systematic training the heart rate of athletes decreases. A certain value is the effect of increased tone of the vagus nerve on the automatism of the heart. In most trained athletes the HR is in the range of 44–66 bpm [3]. Deshin et al. [12] believed that the reduction of resting pulse in athletes is very favorable, and in well-trained athletes it can be reduced to 32–36 bpm. We assume that the authors of most studies use the term "trained" athletes to mean athletes who are in a high level of training during a competition period. "Untrained" athletes are those who do not participate in sports [1].

Among the studies can be given the results of medical examination of professional soccer players. First of all, sixty-three players from the 1<sup>st</sup> and 2<sup>nd</sup> divisions of the Spanish football championship, examined in the preparatory period, whose HR was 61.3±10.4 bpm [13], seven players of the Brazilian soccer club, examined in the competitive period (age 23±5 years, HR - 55±3 bpm) [14], twenty professional players of the Croatian team "Hajduk Split" (average age 22.0±2.9 years, and HR 59.6±5.9 bpm) [15], twenty-five elite players of the Italian soccer club "Fiorentino" (age 26±3.5 years, HR – 60±2 bpm) [16], as well as players of the Indian national soccer team (average age 27.1±1.5 years, HR – 57.8±0.6 bpm) [17] and seventeen professional soccer players from Brazil (average age 24±3 years, HR 57±3 bpm) [18].

Comparison of the average heart rate of elite soccer players of foreign teams, which amounted to 59.1 bpm, and the heart rate of elite Ukrainian soccer players showed that the latter had a slightly higher HR and amounted to 64.4±0.83 bpm.

We also present HR data obtained from soccer players of lower sports qualifications or younger age. These are mainly the data of 101 Ethiopian soccer players (mean age 24.06±3.46 years) without specifying the period of the survey whose HR was 62.45±13.31 bpm [19], 20 players under the age of 18 with a HR of 68.9±12.0 bpm [20], 35 Indian players aged 14-16 years with a HR of 71.5±6.4 bpm [21] and 30 Indian football players (mean age 21±3 years) with a HR

of  $69\pm4$  bpm [22]. The average HR of the less skilled players was 67.9 bpm, which is almost identical to our data obtained from advanced soccer players, which was  $67.5\pm0.5$  bpm.

We have already reported that, without taking into account sport qualifications, soccer players have normal HR values in 55.3% of cases. As far as the HR is concerned, there is a tendency to reduce the number of such players with increasing sport qualification, i.e. from 60.9% for intermediate players to 47.4% for elite players (p=0.086). Bradycardia without sport qualification occurred in 34.5% of cases and tachycardia in 10.3% of cases. At the same time, there was a significant increase in the number of players with bradycardia from the intermediate (21.3%) to the elite level – 47.4% (p=0.009), while the number of players with tachycardia tended to increase from 5.3% in elite athletes to 17.8% (p=0.407) in intermediate athletes.

Graevskaya and Shafeeva [23], having examined 500 soccer players in a state of good physical condition, obtained an average HR equal to 50.3±7.5 bpm (in the range from 39 to 68 bpm). Athletes with bradycardia were 96%, and in the range of 47–54 bpm there were 59.9% of athletes, and 55–60 bpm – 16.5% of athletes. The resulting low HR can be explained by the state of good training, which is possible for soccer players during the competition period. Our data obtained at the beginning of the preparation period differ significantly from the above results. HR in the range of 47-54 bpm was found in 79 (11.4%) athletes and in the range of 55–60 bpm in 235 (33.91%) athletes, which can also be explained by the training period in which the studies were conducted and the level of skill of the athletes.

According to our results, normal values of SBP were found in 56.7% of soccer players. Among them 12.3% were diagnosed with hypotensive state, and 31.0% with hypertensive state. According to Graevskaya and Shafeeva [23] 85.5% of soccer players in a good training condition had normal SBP, 11.7% had a hypotensive state and 2.8% had a hypertensive state, while SBP was in the range from 95 to 140 mm Hg. Volnov [24] found increased systolic blood pressure in soccer players in 16.6% of cases, and according to Levin – in 7.5% of cases [25].

As for normal values of DBP, they were found in 75.3%, hypotonic state in 11.5% and hypertension in 13.1% of soccer players. Graevskaya and Shafeeva [23] reported normal values of DBP in 69.6%, hypotension in 30% and hypertension in 0.4% of soccer players (in the range of 55-82 mm Hg). We believe that the existing discrepancies in the values of HR and blood pressure in soccer players can be associated with the

training periods in which the studies were conducted, as well as with the contingent of athletes studied, since Graevskaya and Shafeeva obtained these values from elite soccer players of the national team level. It should not be forgotten that football is a team sport, in which there are athletes who have a role from goalkeeper to striker, with training of different physical qualities, which naturally affects the average values of heart rate and blood pressure.

Studies conducted among foreign professional soccer players showed a significant variation in the average values of blood pressure. In 63 Spanish players, the values of SBP and DBP were 127.8±10.5 and 71.2±8.4 mm Hg [13], in 7 Brazilian players – 108.0±4,0 and 65.0±6.0 mm Hg [14], in 20 Croatian players -129.8±8.8 and 73.0±6.7 mm Hg [15], in 18 Indian players – 108.3±5.1 and 70.6±5.9 mm Hg [17], and in 17 professional Brazilian soccer players – 112.0±2.0 and 71.0±2.0 mm Hg [18]. That is, the SBP of foreign elite soccer players averaged 119.5 mm Hg, and the diastolic blood pressure - 71.45 mm Hg, which was slightly different from the values obtained by us from elite players – 122.4±1.08 and 76.9±0.9 mm Hg. In this case, the relatively low values of SBP (108±4 mm Hg) and diastolic blood pressure (65±6 mm Hg) in Brazilian football players can be explained by the fact that the pressure was measured during the competition period.

The SBP and DBP values of young or less skilled soccer players are presented in the results of the survey of 101 soccer players from Ethiopia and amounted to  $120.3\pm10.15 / 75.3\pm10.10$  mm Hg [19], 20 players under the age of  $18 - 118.0\pm11.0$  and  $69.5\pm8.2$  mm Hg [20], 95 Indian soccer players aged 14–16 years with blood pressure  $113.0\pm8.0$  and  $63.0\pm6.5$  mm Hg [21], as well as 30 football players of the Indian college with blood pressure  $- 120\pm3$  and  $78\pm3$  mm Hg [22]. The average value of blood pressure in low-skilled football players was 117.8/71.4 mm Hg, and compared to the advanced football players we studied showed slightly lower values  $- 121.2\pm0.66$  per  $76.5\pm0.47$  mm Hg, which does not exceed age norm.

The type of physical exercises used in training in certain sports has some influence on the percentage of athletes with hypertension, although the range is quite wide. Our results, obtained from football players without taking into account qualifications and age, indicate 215 (31.0%) individuals with increased systolic blood pressure and 91 (13.1%) with increased diastolic blood pressure.

Of interest is increased SBP in soccer players of different skill levels. Among 693 soccer players, 78 (11.3%) had systolic blood pressure ≥140/90 mm Hg. Among elite athletes, increased systolic pressure was found in 20 (25.6%) individuals, among advanced athletes in 48 (61.5%), and among intermediate athletes in 10 (12.8%). Thus, the number of athletes with stage I hypertension was significantly higher in advanced soccer players compared to elite (p=0.007) and intermediate soccer players (p=0.005). We came across a study of 594 soccer players (mean age 25 years) from two Norwegian elite divisions who recorded blood pressure 1 hour after exercise as the arithmetic mean of two measurements taken after 5 minutes in a sitting position. Hypertension was defined as ≥140/90 mm Hg. 38 (6.4%) soccer players were diagnosed with stage I hypertension [26]. Our results, obtained among 529 players from intermediate to elite level, without previous physical activity, showed the presence of 68 (12.85%) athletes blood pressure ≥140/90 mm Hg. This is 2 times more than indicated above, and considering that most of them were advanced soccer players, whose age was 19.8±0.17 years, attention should be paid to preventive measures against the development of hypertension and to adequate physical activity according to their functional state.

# CONCLUSIONS

- Elite soccer players have a heart rate of 64.4±0.8 bpm. Among them, 47.4% had bradycardia and 5.3% had tachycardia. The hypotensive state of the systolic and diastolic blood pressure was found in 9.0% and 8.3% of the studied athletes, respectively. The hypertensive state of the systolic and diastolic blood pressure was found in 41.3 % and 17.3 % of elite soccer players.
- 2. Advanced players have a heart rate of 67.5±0.5 bpm. Bradycardia occurs in 36.0%, tachycardia in 8.6% of players in this group. Persons with hypotonic state of systolic blood pressure were found in 11.1%, with hypertensive state – in 32.9%, with hypotonic state of diastolic blood pressure – in 9.1%, with hypertensive state – in 13.7%.
- 3. The heart rate of the intermediate soccer players was 71.3±0.7 bpm. Athletes with bradycardia were found in 21.3% and tachycardia in 17.8%. Hypotonic state of systolic blood pressure was found in 17.2%, hypertensive in 19.0%, hypotonic state of diastolic blood pressure in 19.5%, hypertensive in 8.6% of soccer players.
- 4. The main difference in sports qualification among the indicators studied is the frequency of bradycardia and hypertension, which are statistically more frequent in elite soccer players compared to intermediate soccer players.

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# **CONFLICT OF INTEREST**

The Authors declare no conflict of interest

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