

Clinical and mathematical prediction of the physiotherapy results in adolescents with primary hypertension training on a stationary bike

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Abstract. Background. The aim of the research is to clarify the indications for physical rehabilitation of adolescents with primary hypertension based on the individual clinical and mathematical prediction of long-term treatment outcomes. **Materials and methods.** There were observed 82 adolescents, 44 boys and 38 girls, aged 17.10 ± 0.05 years with a newly diagnosed primary hypertension. Physical rehabilitation for 7 months in the form of exercises on a stationary bike was prescribed to 44 patients who formed the main group. The rest of 38 adolescents who did not complete the stationary bike course and adhered to the recommendations for a healthy lifestyle formed the control group. **Results.** According to the ROC analysis, predictors of an adverse outcome of an attempt at physical rehabilitation were as follows: the average systolic blood pressure above 130 mm Hg at the start of a program, pulse rate variability index pNN50 of more than 16.6 % and body mass index above 25 kg/m². Also, for the development of stable hypertension and an increase in the left ventricular posterior wall thickness in diastole above 8.0 mm, the average heart rate at night more than 68 bpm according to the Holter monitoring and the daily pulse pressure for 24-h monitoring more than 57 mm Hg were unfavorable. **Conclusions.** Adolescents with primary hypertension should train at stationary bike in conditions of waiting for an effect of treatment. If an unfavorable course of the disease is predicted, physical rehabilitation must be combined with drug treatment.

Keywords: adolescents; hypertension; left ventricular hypertrophy; physiotherapy; physical rehabilitation; stationary bike; prognostic factors

Introduction

Hypertension is a medical and social problem of the present not only in Ukraine but also in the entire world. This is one of the most common chronic diseases, which should be considered as a major factor in the development of cardiovascular events that significantly affect the life expectancy of the population [1, 2]. The origins of hypertension should be sought in childhood and adolescence, when the neurogenic and humeral mechanisms of the cardiovascular system dysregulation are formed. It has been repeatedly determined that hypertension is not always diagnosed in a timely manner, since it has an asymptomatic course [3, 4]. The incidence of hypertension in children and adolescents with excess body weight and obesity is partially a consequence of hypodynamia [5, 6]. After detecting an in-

crease in blood pressure (BP) in children, hypertension has a progressive nature over the next 2–7 years. In 17–26 % of adolescents [7, 8], body mass normalization, systematic aerobic dynamic exercises and dietary modifications can significantly reduce blood pressure [9, 10].

Therefore, experts from leading pediatric doctors' associations argue that the treatment of hypertension in children and adolescents should begin with non-drug therapy. Aerobic exercise is low-intensity exercise that uses oxygen as the primary source of energy to support muscle movement. Aerobic exercises include walking, running, swimming, climbing stairs, roller skating, dancing and tennis. Regular aerobic training strengthens the heart muscle, increases its efficiency, reduces the heart rate at rest, strengthens the skeletal muscles of the whole body, improves



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blood circulation, lowers blood pressure, and improves mental state [11, 12].

Performing cyclic aerobic exercises on a stationary bike (SB) leads to a decrease in systolic blood pressure (SBP), a positive effect on muscle oxygen saturation, and increases cardiorespiratory endurance. There are positive effects of aerobic dynamic training, which are manifested themselves in a gradual decrease in heart rate at rest and a restructuring of circadian rhythms of BP with an increase in the proportion of individuals demonstrating a prognostically favorable type of blood pressure [13, 14].

That is why the studies of a physiotherapy effectiveness in young individuals with hypertensive predictors, taking into account a risk of complications of primary hypertension in the early stages of its development, are actual in preventing the disease.

The purpose of the study was to determine the possibility of using the clinical and mathematical parameters to predict the results of physiotherapy in adolescents with primary hypertension.

Materials and methods

Based on the office BP measurements with intervals of one to two weeks, 82 patients were selected: 42 (51.2 %) males and 38 (48.8 %) females with an average age of 17.10 ± 0.05 years; all of them were observed repeatedly with $BP \geq 120/80$ mm Hg. These adolescents formed the main group with a possible hypertension diagnosis. All the examinees have been recommended to modify their lifestyle, which included a diet with restrictions on the use of cook salt, an increase in overall motor activity, and cessation of smoking and energy drinks. After signing the informed consent to participate in the study, all adolescents were involved in an in-depth clinical examination. It included the use of physical, laboratory and instrumental methods to exclude symptomatic hypertension. To verify primary hypertension, 24-hour ambulatory blood pressure monitoring (ABPM) was also performed using the CardioTens device (Meditech Ltd., Hungary) in accordance with current recommendations. Meanwhile, with the same device which served as a Holter monitor, the daily heart rate (HR) and heart rate variability were investigated on the basis of 24-h electrocardiography. The morphofunctional state of the left ventricular (LV) myocardium was examined through echocardiography according to the generally accepted method with ALOKA SSD-500 device (Japan). To examine the general physical condition of adolescents, physical performance was evaluated by the classic physical work capacity (PWC170) test.

The methodology for developing algorithms to predict the course of primary hypertension in condition of the physical rehabilitation was based on the results of an 8-month prospective study of the BP dynamics and parameters of the left ventricular hypertrophy (LVH).

Forty-four adolescents (26 boys and 18 girls) took part in a program of physical rehabilitation. In a medical center, they have been training on the Progress VK-1061 stationary bike. The course lasted 7 months (2 months of introductory period and 5 months of main training period). The 30-min sessions were held twice a week. The intensity of the train-

ing was controlled by the pulse value. During exercises, the pulse rate was maintained at a level close to 65–75 % of the maximum age pulse. It was calculated according to the following equation: 220 minus age of the test subject (in years). In general, the pulse rate during the introductory period was 120–140 bpm and 150–170 bpm in the main period. The speed of the virtual bicycle race was 12–15 km/h with summary energy expenditure of 280 to 400 kcal. Additional physical training sessions and self-organized moderate-intensity isometric exercises were not limited for some male adolescents. At the end of the SB training course, adolescents repeatedly underwent office BP and ABPM measurements, physical performance evaluation according to the PWC170 test, echocardiography and calculation of the body mass index (BMI), which allowed obtaining data on the therapeutic effects of exercises.

Thirty-six adolescents (18 males and 18 females) with primary hypertension from control group did not undergo SB exercises but followed the recommendations for a healthy lifestyle.

The objective of the rehabilitation program was to reach a steady decrease in BP to the target levels as a systolic/diastolic BP below 120/80 mm Hg according to the ABPM.

The follow-up, which made it possible to assess the development of LV lesions, has been conducted 8–10 months after the start of the observation program. At this stage, the dynamics of echocardiography indicators of the morphofunctional status of the LV has been evaluated for all studied adolescents, regardless of their participation in SB exercises.

Statistical processing of the results has been conducted using the Statistica 6.0 software package (StatSoft Inc., USA, AXXR712D833214FAN5). The sample data have been checked for compliance with a normal distribution using the Shapiro criterion. The reliability of the differences has been evaluated using the Student's t-test or the non-parametric Mann-Whitney U test for unlinked samples and the Wilcoxon criterion for the linked samples. To evaluate the relationship between the indicators, a correlation-regression analysis has been used with calculation of the Pearson correlation coefficient. The risk ratios have been calculated with a 95% confidence interval (CI) to determine the influence of factors aggravating hypertension course. In the development of predictive equations, a correlation-regression analysis with the receiver operating characteristic (ROC) curves building and logistic regression with calculation of the determination coefficient have been used.

Results and discussion

It has been found that in the early stages of hypertension in adolescents, the use of physical rehabilitation methods is completely justified. Indeed, adolescents often showed a low physical performance level. For instance, low PWC170 test results (less than 850 and 500 kg/min) have been observed in 11 % of male and 37 % of female subjects, which is explained by a sedentary lifestyle and a reluctance to participate in physical activities.

During the SB exercise period, the boys increased their physical performance according to the PWC170 test from 12.2 ± 1.8 to 15.9 ± 1.7 kg/min per 1 kg of body weight

($p < 0.05$) and the girls from 8.2 ± 2.4 to 13.2 ± 1.6 kg/min per 1 kg of body weight ($p < 0.05$).

At the same time, against the background of physical rehabilitation program, the daily BP indicators showed positive changes: 26 (56.5 %) hypertensive children achieved the target level $\leq 120/80$ mm Hg, while in the control group, the indicators remained unstable and almost unchanged (Table 1).

It must be added that the advised physical program had not changed the BMI in all observation groups.

When analyzing the state of the program participants who did not achieve a reliable reduction of high BP, a direct correlation was found between SBP level at the beginning of the exercise program and after its completion, as well as between the average daily SBP in adolescents who completed the full SB exercise course and the pNN50 and BMI before its start.

The obtained data allowed determining the prognostic value of the defined predictors of a positive or adverse outcome in case of dynamic aerobic exercises in the physical rehabilitation of adolescents with hypertension, i.e. not achieving the SBP target level ≤ 120 mm Hg.

When building the ROC curve (Fig. 1), the corresponding cutoff points have been determined for the sensitivity and informativity of the values for SBP of 131 mm Hg, pNN50 of 16.6 %, and BMI of 25 kg/m² as prognostic ones. The area under the ROC curve [95% CI] was 0.928 [0.824–0.980; $p < 0.0001$], with a sensitivity level of 80.0 % and a specificity level of 94.1 %. The binary logistic regression equation (1) has been developed, with Fisher's criterion of 39.9 and a determination coefficient of 88.9 % ($p < 0.0001$), which allows calculating the β determinant:

$$\beta = -45.419 + 0.158 \times P_1 + 0.304 \times P_2 + 0.742 \times P_3 \quad (1)$$

where β is a coefficient for the equation (2);

–45.419 is a constant term of the equation;

P_1 is average daily SBP (mm Hg) according to the ABPM;

P_2 is pNN50 (%);

P_3 is BMI (kg/m²).

The confidence in the event is determined by the probability of a statistical error (\leq or $>$ 0.05). Individual risk of the expected future positive or adverse result of SB exercise (P) as reaching the target BP of 120/80 mm Hg in adolescents with hypertension can be calculated by the following equation (2):

$$P = 1 / (1 + \exp(-\beta)), \quad (2)$$

where P is the probability of conclusion statistical error.

For example:

1) corresponding to the SBP of 110 mm Hg, pNN50 of 8% and BMI of 21 kg/m², the final expectant result of the SB training waiting to be positive and is confirmed with probability of mistake of 0.033;

2) corresponding to the SBP of 136 mm Hg, pNN50 of 60 % and BMI of 28 kg/m², the final expectant result of the SB training suspected to be negative and is confirmed with probability of mistake of 0.05;

3) corresponding to the SBP of 130 mm Hg, pNN50 of 20 % and BMI of 25 kg/m², the final expectant result of the SB training is not clear because the probability of conclusion mistake is high (0.25).

In 70 (85 %) adolescents with hypertension from both main and control groups, a LV geometry close to normal has been observed at the time of the program beginning. However, after 10 months, the processes of LV myocardial remodeling have been noted in 31 (38 %) of hypertensive children (15 of them showed concentric and 16 eccentric LVH). This fact indicates the necessity of individualizing the applications to control the physical rehabilitation and possibly signals about the use of medical treatment.

Based on a correlation analysis, the associations of possible predictors with the development of a stable increase in BP resistant to non-drug and SB treatment have been defined. The following prognostic signs have been selected:

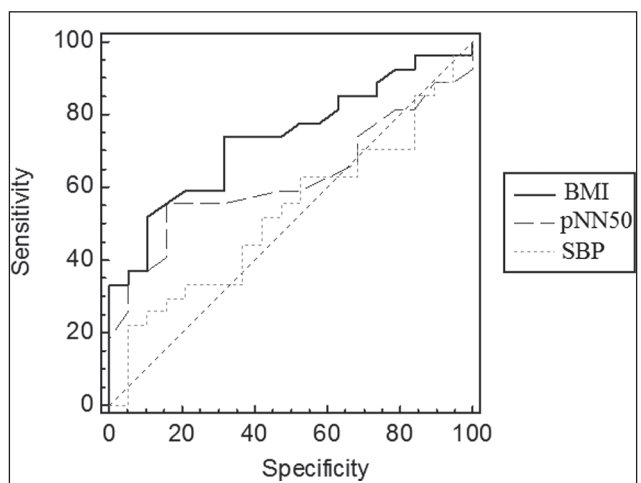


Figure 1. ROC curves showing the relationship between the sensitivity and specificity of the average daily SBP, BMI and pNN50 values for predicting the remote outcome of the SB exercise course

Table 1. BP dynamics in adolescents with hypertension who completed the hypertension physical rehabilitation program and in controls

Observation groups	n	Average daily BP (M ± m), mm Hg			
		Start of observation		End of observation	
		Systolic	Diastolic	Systolic	Diastolic
Males trained on SB	26	129.9 ± 1.7	75.5 ± 0.9*	127.0 ± 1.3	72.0 ± 1.1*
Males, control group	18	127.9 ± 2.2	74.7 ± 2.0	131.5 ± 2.8	75.1 ± 2.1
Females trained on SB	20	128.9 ± 1.3*	72.6 ± 0.8	117.9 ± 1.2*	71.3 ± 1.0
Females, control group	18	131.1 ± 3.8	72.4 ± 1.1	129.9 ± 3.0	72.5 ± 1.2

Note: * – probability of error when detecting discrepancies in statistical indicators < 0.05.

average night HR per minute according to Holter monitoring, BMI, and daily pulse pressure (PP) according to the ABPM. Having obtained possible predictors based on reliable correlation coefficients ($r \geq 0.5$), ROC curves have been built with corresponding sensitivity and informativity cut-off points for the selected symptoms and areas under the curves to confirm the reliability of the selected prognostic model (Fig. 2).

According to the resulting ROC curve, the prediction of a stable hypertension resistant to non-drug and SB treatment in adolescents with primary hypertension can be conducted by the following logistic regression equation (3), which has a determination coefficient of 46 % and Fisher's criterion of 14.24 at $p < 0.01$:

$$\beta = -3.78 + 0.01 \times P_4 + 0.06 \times P_5 + 0.02 \times P_6, \quad (3)$$

where β is a coefficient for the equation (2);
 -3.78 is a constant term of the equation;
 P_4 is average night HR per minute according to the Holter's method;
 P_5 is BMI (kg/m^2);
 P_6 is average daily PP (mm Hg) according to the ABPM.

Further, the probability of expecting the resistant BP in adolescents with primary hypertension is calculated by the above equation (2).

Similarly, an appropriate ROC curve has been built with the values of defined predictors that contribute to the LV remodeling (Fig. 3): posterior wall thickness in diastole (LVPWd) of more than 8.0 mm at the time of the first patient's visit due to hypertension, BMI above 25 kg/m^2 and average daily PP higher than 57 mm Hg.

The prediction of LVH development in adolescents with primary hypertension can be conducted by the following logistic regression equation (4), which has a determination coefficient of 49 % and Fisher's criterion of 9.16 at $p < 0.0001$:

$$\beta = -3.13 + 0.03 \times P_7 + 0.18 \times P_8 + 0.02 \times P_9, \quad (4)$$

where β is a coefficient for the equation (2) of the expectation of LVH development;

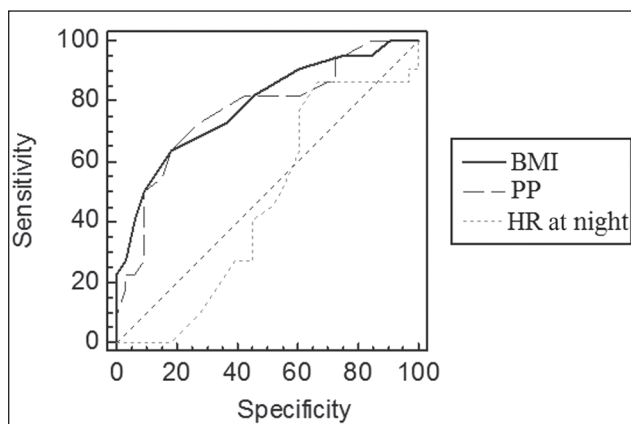


Figure 2. ROC curve showing the relationship between the sensitivity and specificity of the average night HR, BMI, and average daily PP for predicting the development of stable elevated BP in adolescents with newly diagnosed hypertension

-3.13 is a constant term of the equation;
 P_7 is BMI (kg/m^2);
 P_8 is LVPWd (mm) at the time of the patient's first visit;
 P_9 is average daily PP according to the ABPM (mm Hg).

Further, the risk of developing LVH in the future in adolescents with primary hypertension is calculated by the above equation (2).

Observing the adolescents directly during exercise revealed the natural impact of dynamic aerobic SB load on the BP, which did not significantly depend on sex and BP values before exercise. It is important to note that these positive effects have been observed since the first sessions, even during the introductory period, which lasted 2 months. Exercise period of 7 months resulted in a confirmed increase in physical performance as per PWC170 test but did not significantly affect BMI. During exercises, a decrease in SBP after 5 minutes of the recovery period has been observed in both male and female subjects with primary hypertension (by 9.3 and 7.9 %, respectively, compared to baseline at $p < 0.05$), which should be attributed to direct positive effects of SB training. At the same time, the diastolic BP remained constant within the normal age limits. Achievement of the target SBP level occurred in 56.5 % of adolescents and was maintained for at least 7 months. Based on individual prediction, the stable positive effect of physical rehabilitation in hypertensive adolescents could be expected by 3 predictors: average daily SBP at the beginning of the exercise course, which does not exceed 130 mm Hg, pNN50 less than 16.6 % and BMI below 25 kg/m^2 .

In contrast in the rest of the patients (43.5 %), there was an insufficient effect of physical rehabilitation. Hypertension has continued and damaging processes in the target organ (LV) have progressed. The development of stable hypertension, exceeding 95th percentile by sex, age and height, with a daily pressure loading of more than 50 % of time, can be predicted based on an individual clinical and mathematical approach using the average daily PP (cut-off point of more than 57 mm Hg), the average night HR (cut-off point above 68 per minute) and BMI value over 25 kg/m^2 . At the

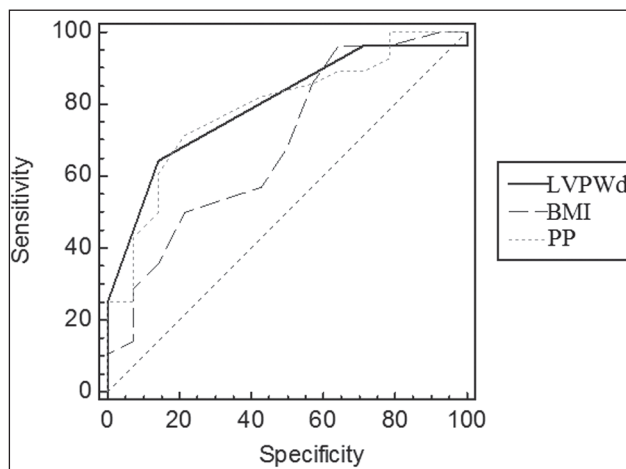


Figure 3. ROC curve showing the relationship between the sensitivity and specificity of the LVPWd, BMI and average daily PP values for predicting the development of LVH in adolescents with onset of hypertension

same time, in this category of patients, the LV remodeling processes can progress. This adverse event can be predicted with the help of a mathematical equation that contains the initial values of LVPWd (cut-off point of 8.0 mm), mean daily PP (cut-off point above 57 mm Hg) and BMI (cut-off point equal or more than 25 kg/m²).

Conclusions

1. Adolescents aged 16–17 years who are prone to hypertension can achieve arterial blood pressure stabilization at a level of $\leq 120/80$ mm Hg without medical treatment, with long-term SB training only. The group with favorable prognosis for the SB exercises are children with pNN50 values less than 16.6 %, BMI below 25 kg/m² and average daily SBP of not more than 130 mm Hg.

2. Prognostically unfavorable signs of stable persistence of elevated BP are the average HR at night above 68 bpm by the Holter monitoring method, average PP of more than 57 mm Hg by daily monitoring and BMI higher than 25 kg/m².

3. LVPWd over 8.0 mm at the time of hypertension diagnosis, BMI higher than 25 kg/m² and the average daily PP above 57 mm Hg according to the daily monitoring should be considered as predictors for the development of LV remodeling within next 10 months.

4. For adolescents with primary hypertension, SB exercises in aerobic mode and adherence to lifestyle modification should be recommended to delay the manifestations of cardiovascular complications of hypertension. If based on clinical and mathematical prediction, adolescents with hypertension might have its unfavorable course (persistence of elevated BP and/or the risk of LV damage), antihypertensive medical treatment should be considered in addition to physical rehabilitation.

Prospects for further research. Based on the application of prediction algorithms, it is planned to determine their impact on the final long-term results of treatment of adolescents with primary hypertension.

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Клініко-математичне прогнозування результатів лікувальної фізкультури в підлітків із первинною артеріальною гіпертензією при заняттях на велотренажері

Резюме. Актуальність. Мета роботи: клініко-математичне прогнозування віддалених результатів фізичної реабілітації підлітків із первинною артеріальною гіпертензією (АГ), які пройшли курс тренувань на велотренажері. **Матеріали та методи.** Обстежили 82 підлітків (44 юнаки та 38 дівчат) середнім віком $17,10 \pm 0,05$ року із первинною АГ. Фізична реабілітація протягом 7 місяців у вигляді занять на велотренажері була призначена 44 підліткам основної групи, інші 38, які не проходили курс тренувань і дотримувались рекомендацій щодо здорового способу життя, увійшли в контрольну групу. **Результати.** За даними ROC-аналізу були виявлені предиктори несприятливого результату спроби фізичної реабілітації: середній добовий систолічний артеріальний тиск вище 130 мм рт.ст. перед початком програми, індекс варіабельності пульсу рNN50 більше 16,6% та індекс маси тіла понад 25 кг/м^2 . Несприятливими щодо розвитку стабільної АГ були: середня частота серцевих скорочень вночі $> 68 \text{ уд/хв}$

за даними холтерівського моніторингу, середньодобовий пульсовий артеріальний тиск більше ніж 57 мм рт.ст. за результатами добового моніторингу та індекс маси тіла понад 25 кг/м^2 . Товщина задньої стінки лівого шлуночка $> 8,0 \text{ мм}$ на момент встановлення діагнозу АГ, індекс маси тіла більше ніж 25 кг/м^2 та середньодобовий пульсовий артеріальний тиск понад 57 мм рт.ст. за даними добового моніторингу є предикторами швидкої гіпертрофії лівого шлуночка. **Висновки.** Підліткам із первинною АГ за умов очікування позитивного ефекту лікування слід призначати фізичну реабілітацію у вигляді занять на велотренажері. Якщо передбачається несприятливий перебіг хвороби, фізичну реабілітацію слід поєднувати з медикаментозними засобами лікування.

Ключові слова: підлітки; артеріальна гіпертензія; гіпертрофія лівого шлуночка; фізіотерапія; фізична реабілітація; велотренажер; прогностичні фактори