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EVALUATION OF THE POST-COVID PROGRAMME EFFECTS IN THE ENSANA REHABILITATION AND HEALTH FACILITY, MARIÁNSKÉ LÁZNĚ

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Introduction

In the last year, medical fields have noticed a new nosological unit called Post - COVID-19 Syndrome [1]. Every second patient after experiencing COVID-19 disease states persisting problems. We talk about Post - COVID-19, if the problems persist after the fifth week from the beginning of disease. One of the terms given in the work of Mayo Clinic in the USA is Long Haul Syndrome [13]. In one of its studies performed by this clinic on 100 patients during the period from 01/06/2021 to 31/12/2020 states that 59% of patients complain about respiratory difficulties, mainly about the decrease in aerobic tolerance, 59% of patients have neurological difficulties and cognitive function disorder, sleep disorder, 34% have depression, anxiety, disturbed balance of mind. Most of them, up to 80%, complain about increased fatigue. With respect to the multidisciplinary affection, the indication of Post-COVID Disorders Syndrome (PCDS) is also correct and we can include into it the entire complex of persisting symptoms. Only 1 of 3 patients returned to his/her original job during 7 months of observation. The symptoms, including mood, fatigue disorder and cognitive impairment led to the serious negative impacts on the restoration of functional and work activities [6; 7; 8; 9].

There are three possibilities of treating Post-COVID19 Syndromes.

1. Outpatient treatment in the rehabilitation clinics, departments and outpatient's departments - there is an advantage consisting in regular visits to get treatment and the possibility of everyday therapy is not mostly provided [2;4].
2. Therapy during hospitalization takes usually place in the pulmonary clinic or departments - therapy is provided on bed, the possibility of sufficient movement is not largely provided as well as the provision of conditions for fast return to everyday activities [3; 10; 12].
3. Spa rehabilitation therapy - the most effective approach to reach physical conditions of the period before COVID-19, concurrent therapy accompanying diseases, dietetic therapy and education, the use of field treatment and climatic therapy, positive impact on mental health [11].

Spa rehabilitation therapy is an integral part of therapeutic and preventive care with its irreplaceable place in the treatment of Post-COVID syndrome as well. However, based on the Indication List, it is possible to treat the patients after COVID-19 in the spa for 3 weeks within 4 months from pneumonia treatment on the basis of the physician or pulmonary specialist recommendation and these patients must have medical insurance.

In the spa sanatoriums of the ENSANA company, the observation of 100 patients undertaking therapy in the post-COVID-19 programme was carried out. These were the patients going through COVID-19 with a more serious course and were entitled to get full-scale spa therapy aimed at the indication of V/3 - conditions after complicated lung inflammation, or private patients whose spa stay corresponded to the full-scale care in its full extent. The all patients observed went through the unified intensive rehabilitation aimed at the improvement of breathing functions and body performance.

In particular, spa therapeutic rehabilitation was concentrated mainly on the ventilation functions of airways, restoration of a proper technique of breathing (ribs mobility, breathing muscles), the renewal of airway patency, the improvement of overall conditions and resistance of the organism, positive influence on accompanying diseases (cardiac and vascular, sugar diabetes, obesity...), removal of pollutants from the external environment (allergens, dust, emotional strain,...), reduction of inability to work and fast return to the original job and regular life.

The aim of this study was to verify the effects of spa rehabilitation care provided in the Ensana spa sanatoriums on several factors under observation, particularly on physical fitness, breathlessness, oxymetry and spirometry values. The measurement methods will be described in the following chapter. Based on the results, a selection of patients will be performed as well as some quantities for the subsequent clinical study.

Health Programme Methods

The observed patients went through 3 therapeutic procedures a day; of this, group physiotherapy 4 times a week, individual therapeutic physical education up to the total number of 21 procedures a week based on the initial medical examination. They went through classical and reflexology massages, baths in mineral water, electrotherapeutic and thermal therapeutic procedures, including the inhalation of mineral water of Mariánské Lázně and vertical walking once a day.

During the first week, the programme started with the examination by a specialist in the area of physical and rehabilitation medicine, including a kinesiologic analysis and education of each patient. Then, a group education followed with a load examination of body fitness by 6MWT test (6-minute walk test), including spirometry examination - SpO_2 (blood oxygen saturation), spirometry examination - determination of FVC (forced vital capacity), determination of a level of breathlessness by Borg scale.

Physiotherapeutic intervention of strengthening breathing functions was carried out individually and in groups. It was oriented on the drill of upright sitting position, strengthening biceps brachii, pectoral muscles stretching, the drill of diaphragmatic breathing in the position on abdomen, exercised developing the chest and side diaphragmatic breathing, the drill of prolonged expiration through pursed lips and huffing - expectoration, weakened muscles strengthening and stretching of shortened muscles, vertical walking with sticks. Once a week, therapeutic physical education was carried out individually to remove wrong individual habits, and in groups next days.

During three-week rehabilitation therapy, the patients were checked by an attending doctor and physiotherapist.

At the end of the third week, the rehabilitation therapeutic stay was evaluated with the performance of kinesiologic analysis, 6MWT load-test, oxymetry examination, determination of a level of breathlessness and spirometry examination. A patient received a discharge report with the recommendation of subsequent therapeutic procedure.

Individual examinations, on which the results of this study are based are described in following chapters. It is about spirometry, examination by pulse oxymeter and 6MWT load-test, including the evaluation of a level of breathlessness during maximum exertion.

Spirometry

Spirometry is a non-demanding and painless physiological test belonging to the basic internal examination methods and investigates lung functionality. The examination takes place in sitting position and a patient attaches a small peg on his/her nose, inserts a special mouthpiece into his/her mouth through which he/she inhales and exhales. During examination, a patient cooperates and breaths in the spirometer according to the instructions of a doctor or nurse. This is the way, how we record a volume of exhaled air, expiratory speed and other parameters. The examination output is a diagram with a curve and recorded values. For the needs of presented observation, we used the **FVC** value (forced vital capacity) - a maximum volume of air which can be exhaled sharply with a maximum forced exhalation after a maximum inspiration. There is no need for a patient to prepare for this examination. Shortly before examination, he/she must avoid food and cigarettes. We performed the examination at the beginning of spa rehabilitation and then after 3-week therapy.

Examination by Pulse Oxymeter

The examination is used for non-invasive measurement of oxygen in blood (**SpO2** - blood oxygen saturation). It is a simple device, which is fastened on a place well perfused with blood, most often on a finger or earlobe. It includes a source of light going through tissue and falling on a detector measuring its intensity. We measure the amount of light absorbed by arterial blood. The examination is used as one of the basic instruments for monitoring vital functions.

The examination was performed at the beginning and at the end of spa rehabilitation in the scope of the 6MWT load-test (see below), always before and after the test.

6MWT Load Test

6MWT (six-minute walking test) is a 6-minute walking test, simple, undemanding test using a sub-maximum load to evaluate physical fitness of a patient. Before starting the test, there was carried out ECG examination in each patient, pulse rate and blood pressure measurement. The test was performed on the covered colonnade of Mariánské Lázně in the corridor of 30 m in length; a patient walked along the specified route as fast as possible for a period of 6 minutes. He/she could interrupt walking at any time. The test measures in meters a distance, which a patient can walk for 6 minutes and we call it 6MWD (distance walked in 6 minutes).

In the scope of the load-test, after its ending, a level of breathlessness with maximum exertion was recorded - so-called **Borg scale.** It is a simple breathlessness test used very often which describes in words different levels of breathlessness on the scale from 0 (no breathlessness) to 1 (maximum breathlessness). [14]

Statistical Evaluation Methods

To make a statistical evaluation, the programmable language R was used. In the following subchapters, individual methods are briefly described; they were used in the statistical evaluation, see more [15, 16]. In the last subchapter, a procedure of the analysis itself is described.

Hypothesis Testing

In hypothesis testing, we always test a zero hypothesis against the alternative one (see below Anderson-Darling Test, Wilcoxon Test, etc.).

To decide on the validity of the zero hypothesis, we use a so-called p-value, so the smallest level of significance when we refuse the zero hypothesis. The level of significance presents the probability of the fact that the zero hypothesis will be rejected without authorization (we say that therapy has some effect, even though it is not true), we set it at 5% because we want it to be as small as possible. If the p-value is smaller than 5%, we reject the zero hypothesis because it has a very small support in data - we reject it with the smaller probability of an error than we set it ourselves. In other words, the smaller the p-value of the test is, the less the test says that the zero hypothesis is valid.

Anderson-Darling Test

To test the data normality, we chose Anderson-Darling Test of normality. In this case we test the zero hypothesis

H_0: *Data are managed by standard distribution*

against the alternative hypothesis.

H_0: *Data are managed by standard distribution.*

If the p-value is lower than the significance level of 5%, we reject the data normality zero hypothesis and in the next testing, we will use so-called non-parametric tests, which are suitable for abnormal data. On the contrary, if the test confirms data normality, we will work with parametric tests of which use is conditioned just by normality.

Wilcoxon Paired Test

It is used to compare two dependent samples (paired samples) when the samples are not managed by standard distribution, so it is the non-parametric test. In our case, it was used for comparing the values of 6MWT test, Borg scale and SpO2 at the beginning and at the end of the spa stay. We test the zero hypothesis against the alternative one:

H_0: *median of differences between two samples is zero*

i.e. there is no difference between the values at the beginning and at the end of staying in the spa, against the alternative hypothesis.

H_a: *median of differences between two samples differs from zero*

i.e. there is a difference between the values at the beginning and at the end of staying in the spa.

In case that p-value is smaller than the significance level of 5%, we reject the zero hypothesis and we can say that there is a difference between the values before and after stay in the spa (therapy is effective).

Paired T-Test

It is used for the same purpose as Wilcoxon Paired Test, so to compare two paired samples. The difference is that *t*-test requires data to be managed by standard distribution. We test the zero hypothesis

H_0: *mean value of differences between two samples is zero*

i.e. there is no difference between the values at the beginning and at the end of staying in the spa

H_a: *mean value of differences between two samples differs from zero*

i.e. there is a difference between the values at the beginning and at the end of staying in the spa.

In case that p-value is smaller than the significance level of 5%, we reject the zero hypothesis and we can say that there is a difference between the data before and after the spa stay (therapy is effective).

Mann-Whitney Test

It is a non-parametric test used to verify, if two independent random samples come from the same distribution. We use it to compare a change in the measured parameter depending on gender, so when calculating, if the parameter value changes more or less according to whether a proband is a man or a woman. We test the zero hypothesis

H_0: *samples come from the same distribution*

i.e. the change of the measured parameter does not depend on gender of probands, compared to the alternative hypothesis

H_a: *samples do not come from the same distribution*

i.e. the change in the measured parameter depends on probands gender.

In case that p-value is smaller than the level of significance of 5%, we reject the zero hypothesis and we can say that the therapeutic effect is larger in one gender than in the other one.

Two Independent Samples T-Test

Unpaired test is used for the same purpose as the Mann-Whitney Test; however, it is parametric test, so it is conditioned by using data. Another condition is equality of dispersions measured according to F-test, see more [15, 16]. We test the zero hypothesis here

H_0: *mean values of two independent samples are identical*

i.e. the change of the measured parameter does not depend on gender of probands

H_a: *mean values of two independent samples differ from each other*

i.e. the change in the measured parameter depends on gender of probands.

In case that p-value is smaller than the level of significance of 5%, we reject the zero hypothesis and we can say that the therapeutic effect is larger in one gender than in the other one.

ANOVA

The analysis of variance, shortly ANOVA is a statistical method helping to verify, whether one or more factors, or their combination, have a provable influence on one quantity observed. In our case, the factors are individual comorbidities which acquire two values: 0 - a proband does not suffer from given comorbidity, 1 - a proband suffers from given comorbidity. The quantities under observation are all the measured quantities, so 6MWT test, Borg scale, SpO2 and FVC.

The zero hypothesis tested for each factor or their combination is

H_0: *mean values of random samples are identical independently on the factor value*

i.e. the change in the factor value does not impact on the measured quantity, so the given comorbidity or their combination does not affect therapeutic effect compared to the alternative hypothesis

H_a: *mean values of random samples differ depending on the factor value*

i.e. the change in the factor value impacts on the measured quantity, so the given comorbidity or their combination affects therapeutic effect.

The ANOVA results are recorded in so-called ANOVA tables, see more [15, 16]. With regard to the interpretation of results, we are mostly interested in the first and last column, where in the first one, we see the tested factor or their combination marked with the colon between the factors, and in the last one, we see the *p*-value of the test. If the *p*-value with some of factors is smaller than the significance level of 5%, we reject the zero hypothesis and can say that the given factor or their combination affects the measured quantity, so the therapy effect.

Correlation Coefficient, Significance Test

To express a degree of dependency of the changes in individual indicators on age, we used the Pearson's correlation coefficient. It measures the strength of dependency between two quantities and can acquire the value from -1 to 1. The closer to the value -1 or to 1 the coefficient is, the larger the negative positive dependency is, so when it is going down one variable is growing, the second one is going down as well. If the correlation coefficient value is close to 0, it means that the variables are linearly independent.

In case of the correlation coefficient we can test, if its value is significant - differs or does not differ from 0 significantly. So the zero hypothesis is tested H_0: $r = 0$, *correlation coefficient is insignificant compared to the alternative*: H_a:$r \neq 0$, *correlation coefficient is significant, namely at the significance level* $\alpha = 0.05$

A decision on rejection / no rejection of the zero hypothesis is performed using the *p*-value. If it is smaller than the significance level, the correlation coefficient significantly differs from 0.

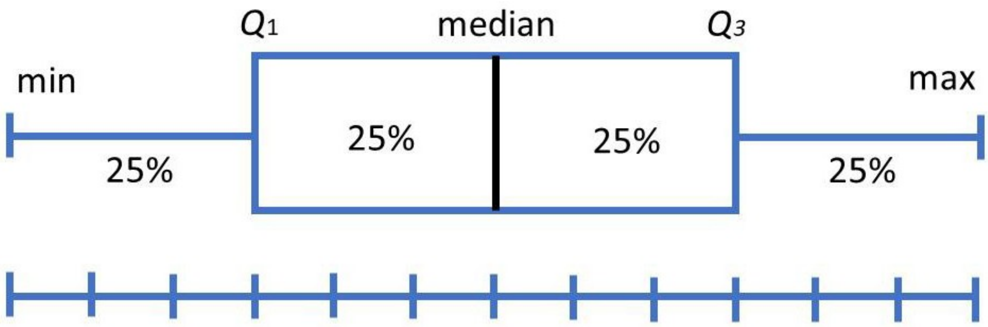
Diagrams

Histograms

The histogram represents a graphical illustration of data distribution by the column graph. Each column represents the interval of the given indicator values, its height shows then a number of the patients with the indicator at the level of the given interval. We used this diagram mainly as a complement to Anderson-Darling test in deciding on normality. If the data are managed by standard distribution, the histogram is similar with its shape with the density of probability of standard distribution (Gauss curve).

Boxplot

To visualise the differences between data distribution we used boxplots. It is another graphical illustration of data distribution – in this case by quartiles. A box, which creates the main part of the boxplot shows 50% of all data (from - to). The boxplot edges represent the first and second quartiles, limit values - maximum and minimum. Apart from minimum and maximum values, the boxplot can show the unrelated values (dots).



Difference Calculation

To make a decision on the impact of age or gender on the value changes at the beginning and at the end of therapy, we used a percentage change of the given indicator values. It was calculated as follows

$$R = \frac{U_t - U_{t-1}}{U_t} \cdot 100,$$

where U_t is the value at the end of therapy and

U_{t-1} is the indicator value at the beginning of therapy.

It results in the percentage expression of how much the indicator decreased/increased after treatment.

Analysis Process

1. **Normality test** - we verify normality with data by the Anderson-Darling test and based on it, we will chose parametric or non-parametric tests.

   Testing of a difference between the values at the beginning and at the end of the spa stay (paired tests) - we will find whether there is a difference between the values before and after therapy.

3. **Testing of conformity with the theoretic value** (only in case of the 6MWT test, paired test) – we will find out, whether the values before and after treatment are conformed with the physiological value.
4. **Testing of the impact of age on the change rate** (calculated from the difference in the values, correlation coefficient, significance test of the correlation coefficient - we will find, whether the improvement or worsening in the patients is caused by their age.
5. **Testing of the impact of age on change rate** (calculated from the differences in the values, Mann-Whitney test / t-test)
   - we will find whether the improvement or worsening in the patients is caused by their gender.
6. **Testing of the impact of a period elapsed between COVID-19 disease and the beginning of the spa stay** (calculated from the differences in the values, correlation coefficient, significance test of the correlation coefficient) - we will find whether the improvement or worsening in the patients is caused by the length of a period elapsed between COVID-19 disease and the beginning of the spa stay.

   Testing of the impact of comorbidities and their interaction (calculated from the differences in the values, Mann-Whitney test, ANOVA) – we will find out whether the resulting improvement or worsening of any of the analysed quantities is affected by the presence of comorbidity or their mutual interactions.

When, during the analysis, unrelated observation was revealed, it was excluded from the given indicator valuation.

Information on the Research Group

The research group is created by 100 probands, 50 women and 50 men who participated in the 3-week post-COVID-19 programme with so-called post COVID syndrome. These are the patients with indication of V/3 - the conditions after complicated pneumonia.

Apart from this indication, the 85 of them suffered from other comorbidities (85%); most often, cardiovascular system disease and diabetes mellitus. More details in Table 1.

	Men	**Women**	**Total**
With comorbidity	**43**	**42**	**85**
Diabetes mellitus	14	14	28
Obesity	11	18	29
High blood pressure, cardiological diseases	35	18	54
COPD, bronchitis, asthma	6	14	20
Without comorbidity	**7**	**8**	**15**
Total	**50**	**50**	**100**

Table 1: Information on the research group

The youngest patient was 24 years old, the oldest one 78, half of the patients was older than 61 years. More detailed information about the patient structure is given in the histogram, see Figure 1 and Table 2.

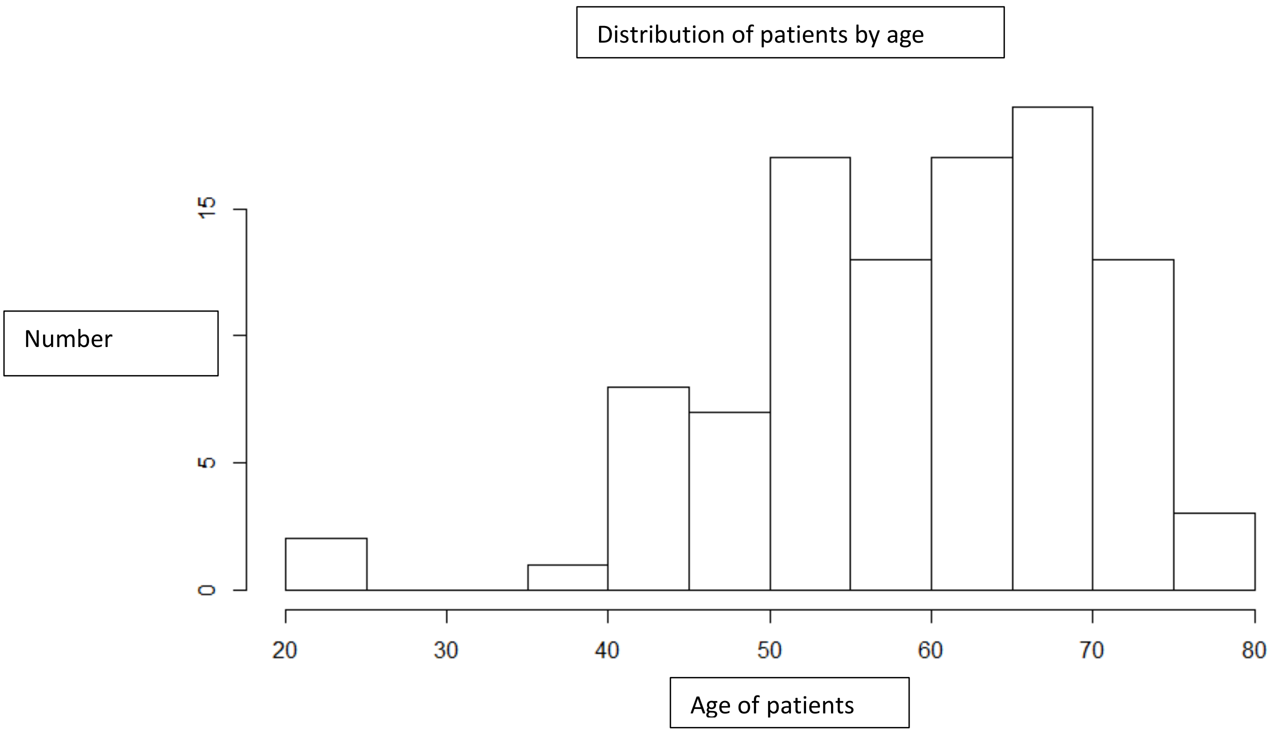


Figure 1: Histogram - age structure of patients

	Min	Max	Mean	Median
Age structure	24	78	59.63	61

Table 2: The research group according to the age structure of patients

On average, 93 days or about 3 months elapsed between experiencing Covid-19 disease (i.e. from the last day of disease according to the patient's medical records) and entering spa rehabilitation care. A patient started treatment 6 days after experiencing Covid-19 at the earliest; the latest time of starting treatment was 198 days after disease. Details are given in the histogram in Figure 2 and Table 3.

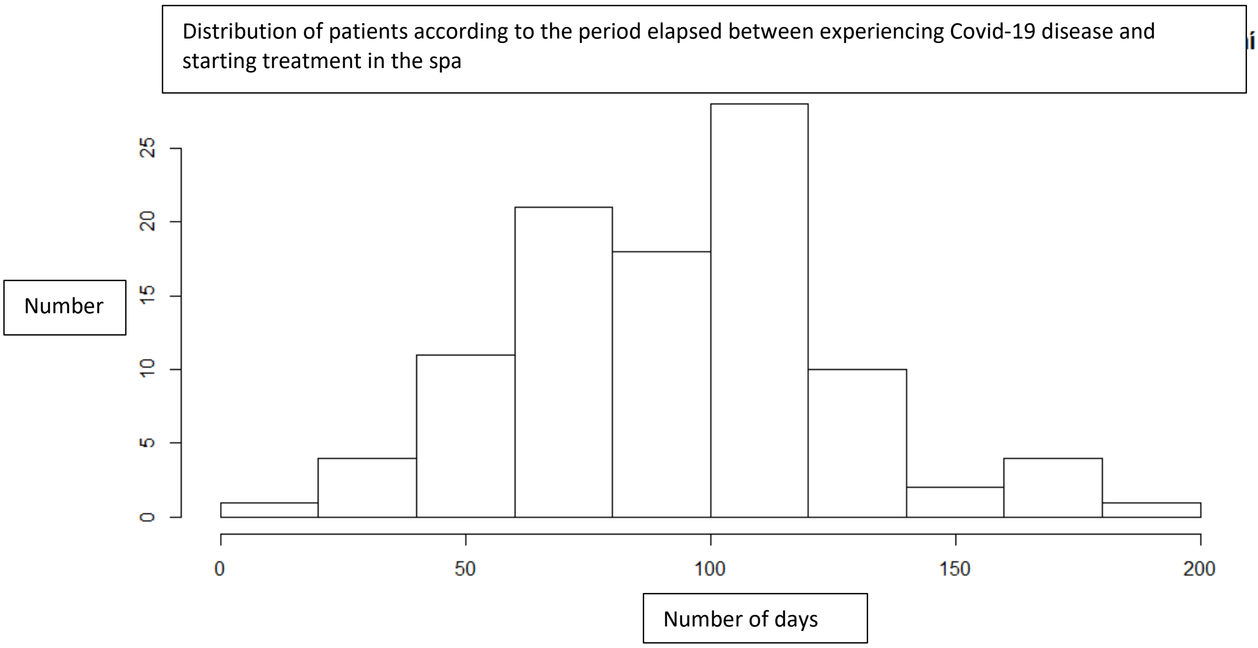


Figure 2: Histogram - a period between experiencing Covid-19 disease and starting treatment in the spa

	Min	Max	Mean	Median	Standard deviation
Number of days	6	198	93	94	34.56

Table 3: The research group according to a number of days elapsed between experiencing Covid-19 disease and starting treatment in the spa

6MWT Test

To assess physical fitness the 6MWT test was used (the six-minute walk test). This load test was carried out in the environment of the colonnade in Mariánské Lázně at the beginning and at the end of stay in the spa.

In case of this variable, we will compare not only the values at the beginning and at the end of stay, but also the measured values with a theoretical value considered optimum when taking into account age. Calculation of this 6MWD value (the distance walked in 6 minutes) takes into account a patient's age and is calculated as follows: $6 = 800 - 5.4 \cdot$, when is a patient's age.

Data Normality

According to the given histograms (Figure 3) and a result of normality test (see Table 4) it can be stated that the data are not managed by standard distribution. Because the p-value is smaller than the significance level of 5%, we reject the zero hypothesis of standard distribution and further, non-parametric test will be used for the analysis of this variable.

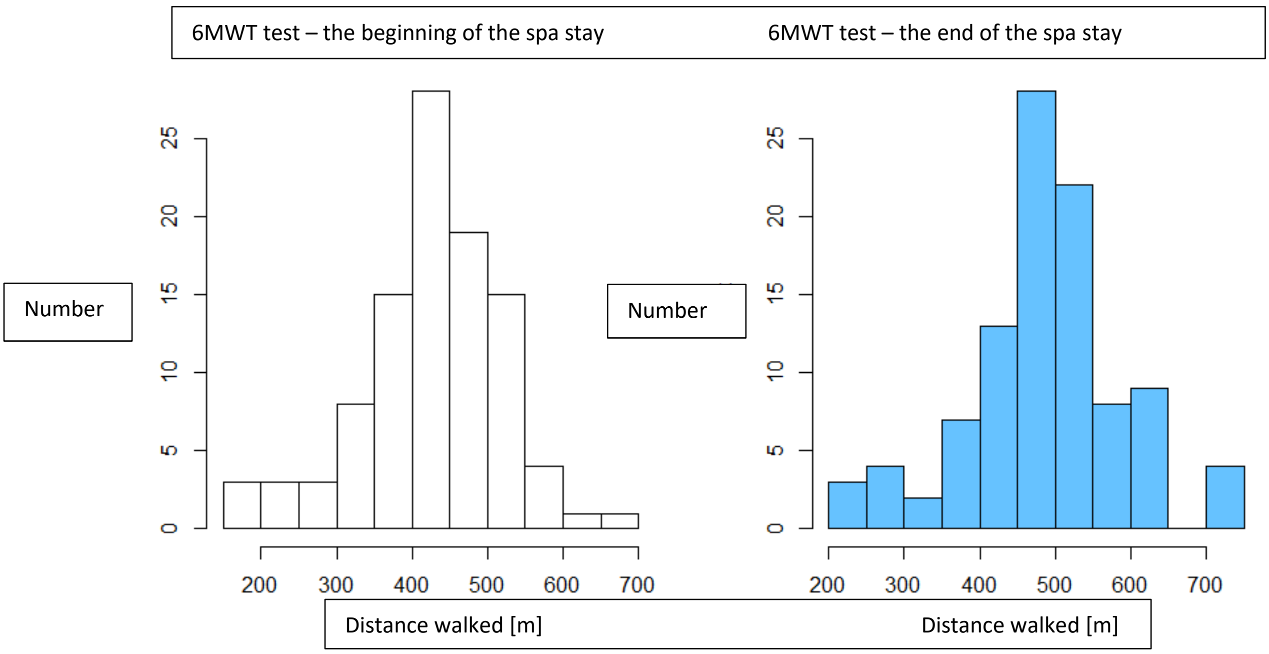


Figure 3: 6MWT - histograms: the beginning and the end of the spa stay

Anderson-Darling Normality Test	**Beginning of stay**	**End of stay**
***p*-value**	0.014	0.001

Table 4: 6MWT - normality test

Change in the Values after Spa Stay

Calculated characteristics of the 6MWT value, including the data corresponding with the standard value according to the formula above are given in Table 5. These data show that the average number of meters walked was 427.47 at the beginning of stay, whereas at the end, it increased by more than 57 meters. At the same time, the mean of theoretically standard values is 478 meters; this mean was even broken after stay. On average, the 6MWT values improved by 11.6% after spa stay.

	Min	**Max**	**Mean**	**Median**	***p*-value**
Beginning of stay	173	662	427.47	438.5	<0.001
End of stay	205	746	484.68	480.5	
Change [%]	-8.0 %	34.1 %	11.6 %	9.8 %	
Standard value	378.8	670.4	478	470.6	

Table 5: 6MWT - basic characteristics of measured values and the % of changes, p-value of Wilcoxon test, standard values

The boxplot given in Figure 4 shows that at the end of stay, a number of meters a patient was able to make in 6 minutes significantly increased. Even the Wilcoxon paired test confirmed that there is a difference between the test values before and after stay, p-value is smaller than 5% (see Table 6), so we reject the zero hypothesis

We can say about their conformity that patients' physical fitness significantly improved after staying in the spa.

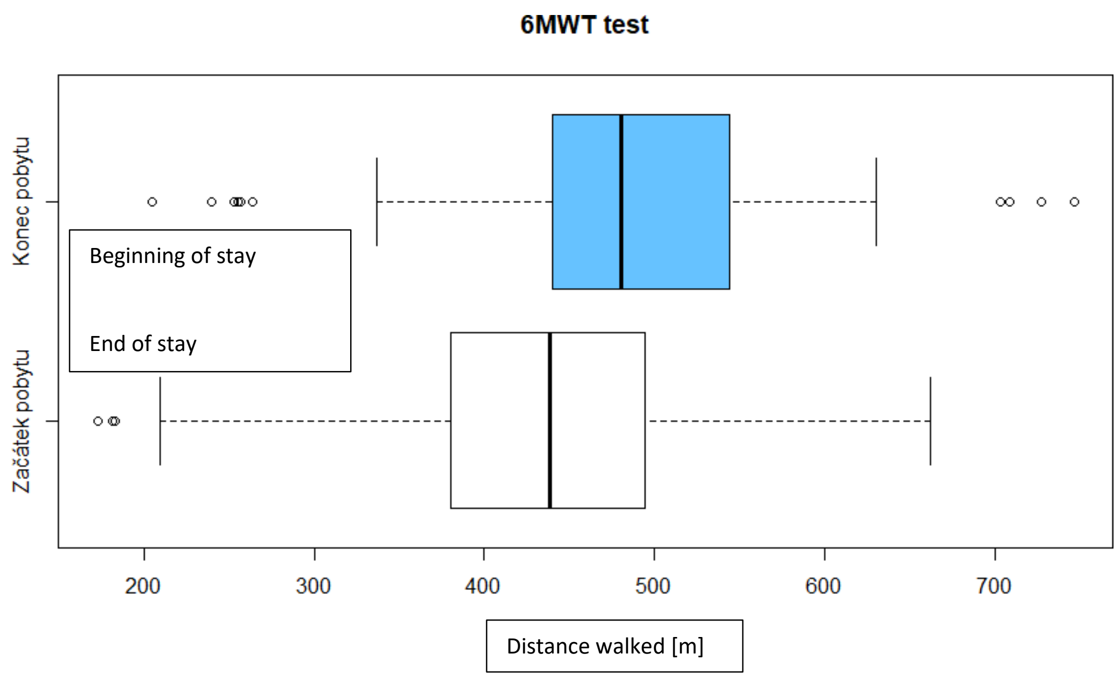


Figure 4: Boxplot - 6MWT test at the beginning and at the end of hospitalization

The same is proved by another Wilcoxon test performed, which showed that after the spa staying, a distribution of 6MWT values corresponds to standard values (see 6MWT formula) which the patients, depending on their age should achieve optimally, whereas it was not like that at the beginning. You can see in the following Table 6 that in case of comparing theoretical values with the values measured at the beginning of stay, *p*-value is smaller than the significance level of 5%, we thus reject the zero hypothesis of conformity and can say that the measured values do not correspond to the theoretical ones. When comparing with the values measured at the end of stay, *p*-value is larger than 5%, which means in this case that the distribution of theoretical values and the values after stay is identical. Thus, we can say that after the spa stay, patients' physical fitness corresponds to the given standard.

	Beginning of stay	End of stay
***p*-value**	<0.001	0.301

Table 6: Wilcoxon test - the conformity of the measured values with the theoretical once at the beginning and at the end of stay

Dependence on Age

You can see in Figure 5, that the difference between the values at the beginning and at the end of the stay does not depend on age. The correlation coefficient value shows the same - in this case, it gains the value of **-0.0214** and its significance test *p*-value was **0.832.** So, the correlation coefficient is statistically insignificant which means that the patients' values improve equally in all patients in the scope of 6MWT test independently of their age.

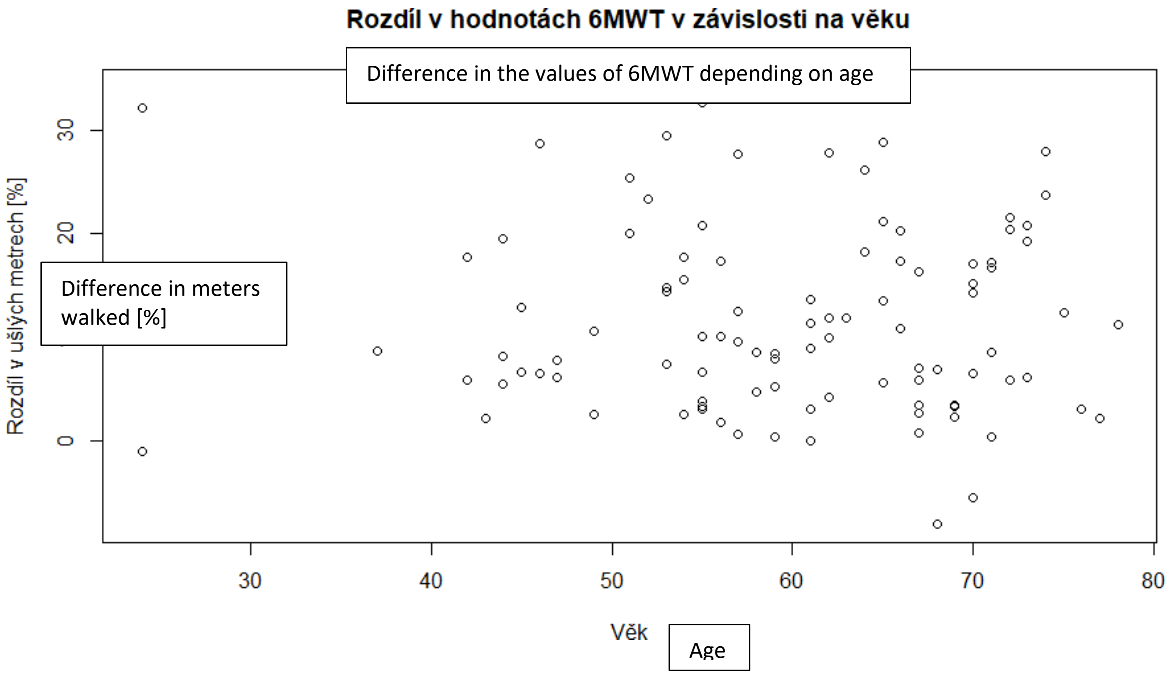


Figure 5: 6MWT - Scatter chart, dependence of change in values on age

Dependence on Gender

We see in the following table that men improved their fitness by 12.5% and women by 10.7% on average. The man, who improved in his physical fitness test the least walked even by 8% of meters less at the end of his stay compared to the beginning.

	Min	Max	Mean	Median	p-value
Men	-8 %	34.1 %	12.5 %	11.3 %	0.365
Women	-5.4 %	32.1 %	10.7 %	8.5 %	

Table 7: 6MWT - Basic characteristics of the changes in the % according to gender and the resulting p-value of the Mann-Whitney test

In Figure 6, you can see the boxplot showing the distribution of changes in the values before and after the boxplot showing the distribution of changes the spa stay. You can see that women improved slightly less than men but the difference in medians is not significant. This is also confirmed by the Mann-Whitney Test; on its base we do not reject the zero hypothesis of the coincidence of data distribution in individual categories (Man, Woman), *p*-value was not smaller than the level of significance of 5%. The values of the 6MWT test change independently of gender.

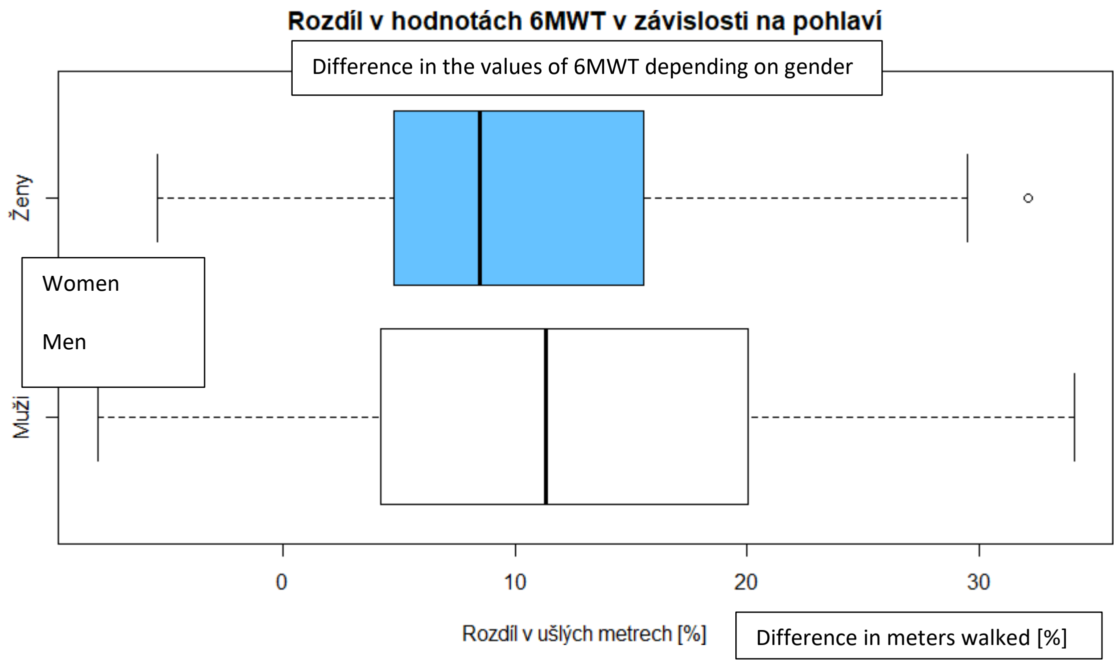


Figure 6: 6MWT - Boxplots: a difference between the values depending on gender

Influence of a Period between COVID-19 Disease and Spa Admission

You can see in the scatter diagram in Figure 7 that the changes in the resulting values of the 6MWT test slightly decrease, if more days (about 135) elapsed after experiencing Covid-19 disease. This partially confirms that even the calculated correlation coefficient with negative sign **-0.362**. p-value of significance test is **0.077**, so larger than the level of significance of 5% and we do not reject the zero hypothesis of the insignificance of correlation coefficient. Since the p-value does not differ significantly from the significance level and we do not have enough probands in the study group for whom the time between passing Covid-19 and entering spa treatment was longer than 135 days (13 probands out of 100), this result cannot be interpreted unambiguously. **After confirming or disproving the influence of this quantity it would be suitable to have in the research group more of such probands.**

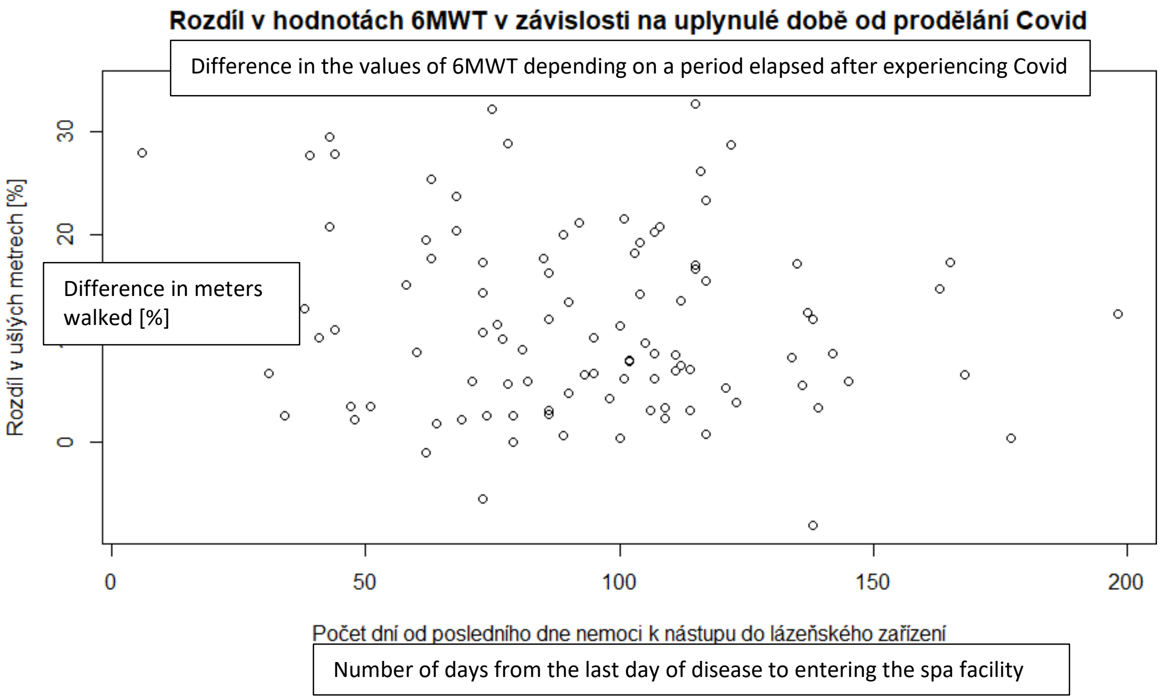


Figure 7: 6MWT - Scatter diagram, the dependence of value change on the time elapsed from experiencing Covid-19.

Impact of Comorbidities

At first, the influence of any comorbity was assessed, so we were interested in the difference between the probands who have no comorbidity compared with those who suffered from any of monitored comorbidities, see Table 1. You can see in the boxplot that the probands without comorbidities showed slightly higher differences between the 6MWT values at the beginning and at the end of the spa stay.

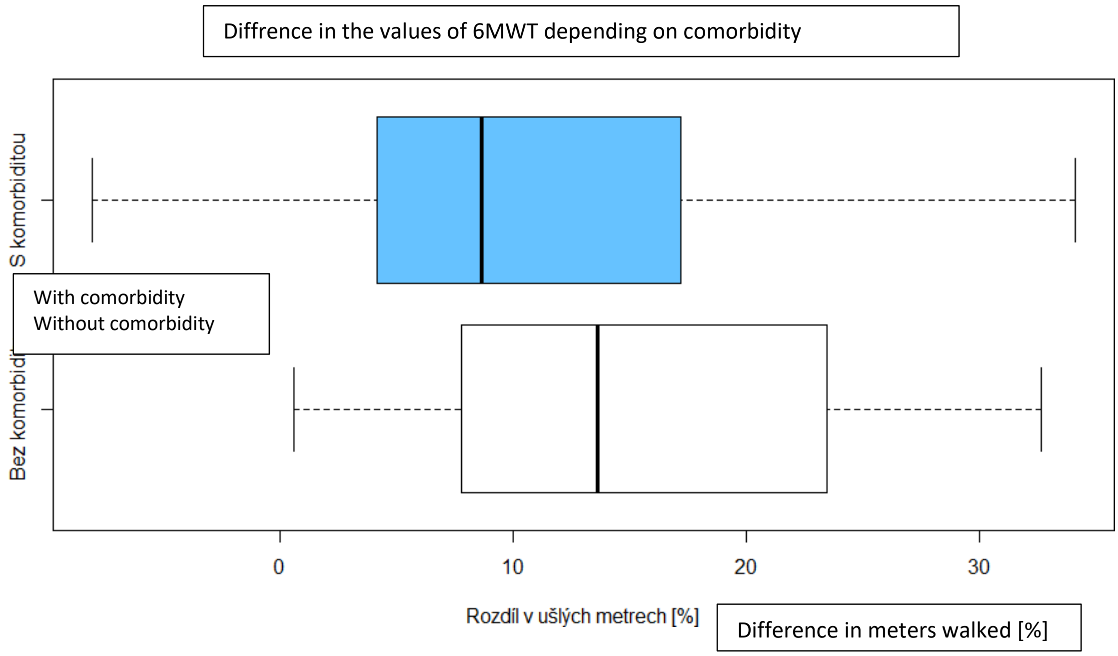


Figure 8: 6MWT - Boxplots, differences in the 6MWT values depending on the existence of comorbidity

On average, the 6MWT test values in the probands without comorbidity improved by 15% and in a half of them, they improved by at least 14%. On average, the values in the probands with comorbidity improved by 10.9% and a half of them, they improved by at least 8.6%, see Table 8. The Mann-Whitney test resulted in the **p-value of 0.146,** so higher than the level of significance of 5%; thus, we do not reject the zero hypothesis that the distributions of probability are identical in both sample groups. In general, it cannot be stated that a difference between the 6MWT test values is statistically and significantly affected by the fact that a given patient suffers or does not suffer from another comorbidity. However, the resulting p-value and test result itself can be distorted by the fact that there are only 15 patients in the study without comorbidity and, conversely, 85 people with at least one comorbidity. For this reason, we continued with a more detailed analysis where we differentiated individual comorbidities.

	Min	**Max**	**Mean**	**Median**	**p-value**
Comorbidity	-8 %	34.1 %	10.9 %	8.6 %	0.1463
Without comorbidity	1 %	33 %	15 %	14 %	

Table 8: 6MWT - Basic characteristics of the changes in the % according to the existence of comorbidity and the resulting p-value of the Mann-Whitney test

Following ANOVA table, see Table 9, shows the results of the more detailed analysis. It is obvious that the p-value is smaller than the significance level of 5% only in case of one factor, namely obesity. It means that this factor statistically and significantly affects the value of change in 6MWT test values after stay. Other comorbidities do not have such a large influence on this change.

6MWT	**Df**	**Sum of Squares**	**Mean of Squares**	**F-value**	**P-value**
Diabetes mell	1	0.000	0.000	0.001	0.979
Obesity	1	0.034	0.034	4.025	**0.048**
High blood pressure, cardio	1	0.013	0.013	1.574	0.213
Bronchitis, COPD, asthma	1	0.004	0.004	0.513	0.476
Without comorbidity	1	0.002	0.002	0.228	0.634
Diabetes mell: Obesity	1	0.004	0.004	0.438	0.510
Diabetes mell : High blood pressure, cardio	1	0.002	0.002	0.204	0.653
Obesity: High blood pressure, cardio	1	0.002	0.002	0.279	0.598
Diabetes: Bronchitis, COPD, asthma	1	0.000	0.000	0.016	0.901
Obesity: Bronchitis, COPD, asthma	1	0.000	0.000	0.043	0.837
High blood pressure, cardio: Bronchitis, COPD, asthma	1	0.016	0.016	1.949	0.166
Diabetes mell : Obesity: High blood pressure, cardio	1	0.011	0.011	1.346	0.249
Diabetes mell : High blood pressure, cardio: COPD, bronchitis, asthma	1	0.003	0.003	0.337	0.563
Obesity: High blood pressure, cardio: Bronchitis, COPD, asthma	1	0.001	0.001	0.099	0.754
Residuals	85	0.718	0.008		

Table 9: 6MWT – ANOVA, influence of comorbidities

You can see in Figure 9, in the right upper corner, that this influence consists in the fact, that non obese probands achieve larger differences between the meters walked during the spa stay compared with the probands with obesity. The ANOVA table also shows that a combination of individual comorbidities does not matter but obesity does. **In the scope of subsequent studies, it would be necessary to analyse this factor in more details, e.g. to test the dependence of results on the BMI of a given proband.**

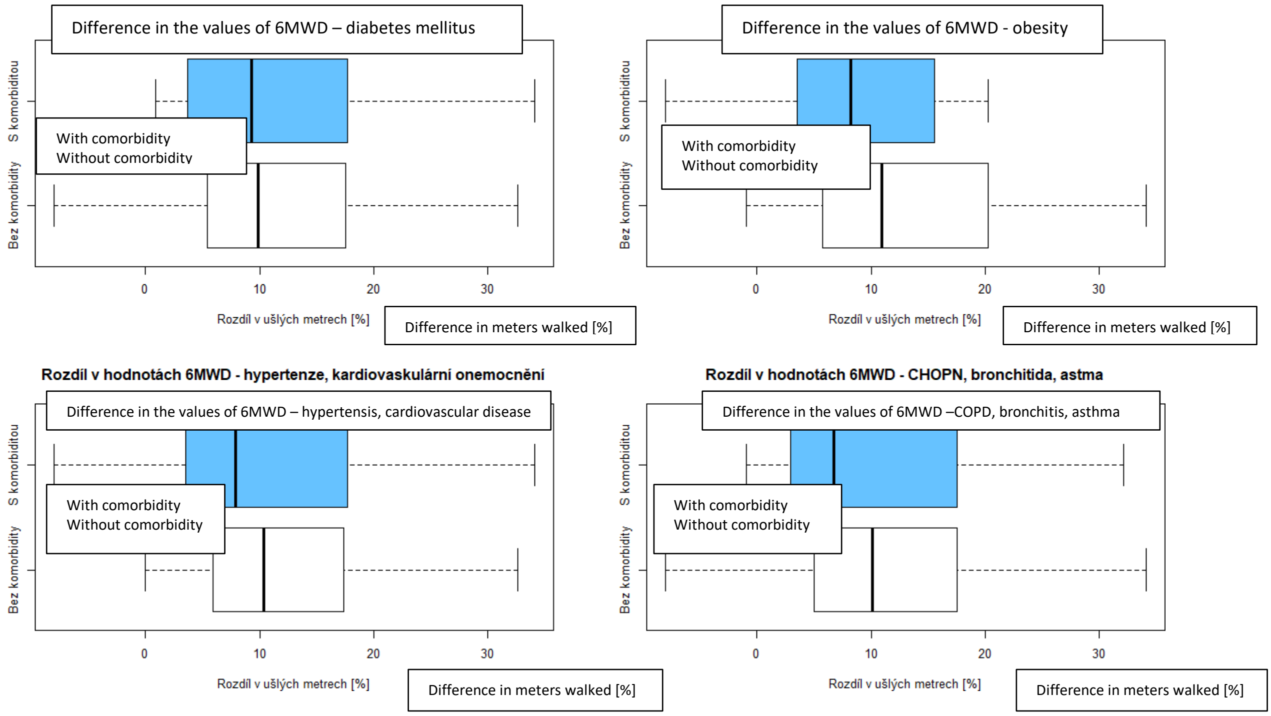


Figure 9: 6MWT - Boxplots, the influence of individual comorbidities

Summary

There was confirmed the statistically significant change in 6WMT test values after experiencing the spa stay. On average, the distance walked increased by 11.6%. At the same time, it was confirmed that the test values after the stay are identical with the theoretical values, which the probands should achieve according to their age. This confirmed a positive influence of the spa treatment on the probands' physical fitness.

This influence appears independently on the probands' age and gender. The influence of the number of days elapsed between the onset of Covid-19 disease and admission to the spa facility could not be clearly demonstrated. Of all the comorbidities analysed, only obesity was found to be significant, in the sense that non-obese probands achieved higher changes in the number of meters walked, i.e. better post-stay outcomes than obese probands.

Borg Scale

The Borg scale, thus the level of breathlessness at maximum effort was recorded after finishing the 6MWT test, so at the beginning and at the end of the spa stay. It can gain the values from 0 (without breathlessness) to 10 (maximum breathlessness, walking cannot be made without breaks).

Outlier Observations

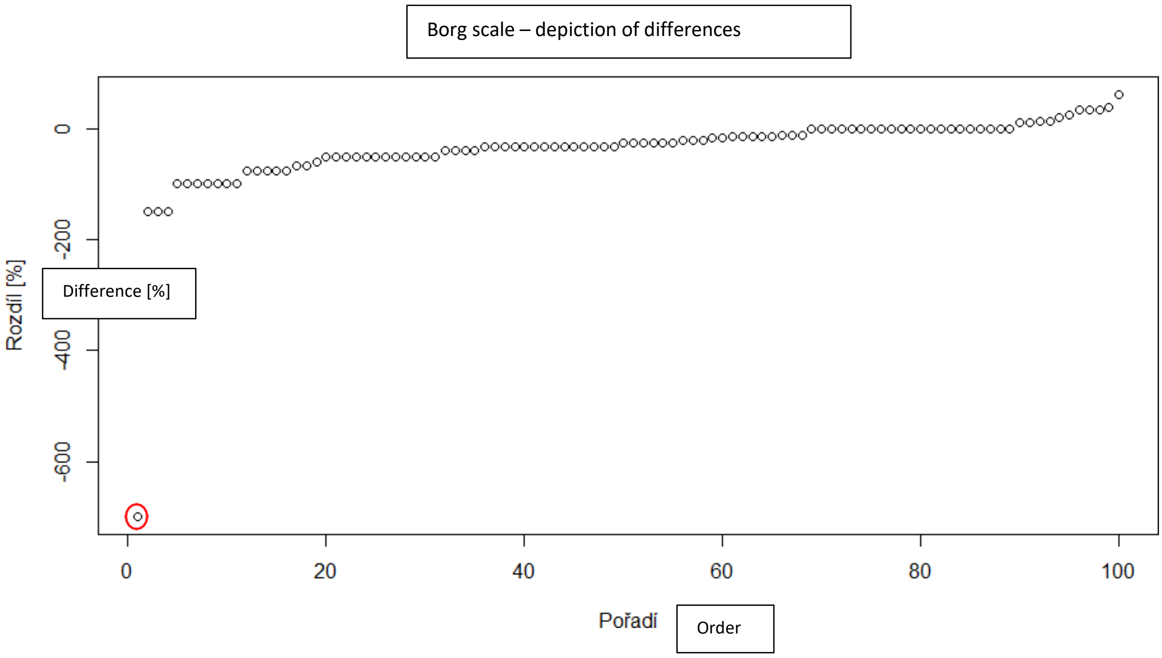


Figure 10: Borg scale - Scatter diagram of the % of changes, outlier observation identification

During the analysis, outlier observation was found out - the proband no. 24, see Figure 10. The change in Borg scale was -700% (his score dropped from 8 to 1). To avoid any distortion of the evaluation results, the proband was excluded from this analysis.

Data Normality

It is clear in the histograms in Figure 11 that the data are not managed by standard distribution. The same is confirmed by the normality test, see Table 10. In both cases, the *p*-value is smaller than the significance level of 5%, thus we reject the zero hypothesis of data normality, and further, we will further use non-parametric tests in the analysis.

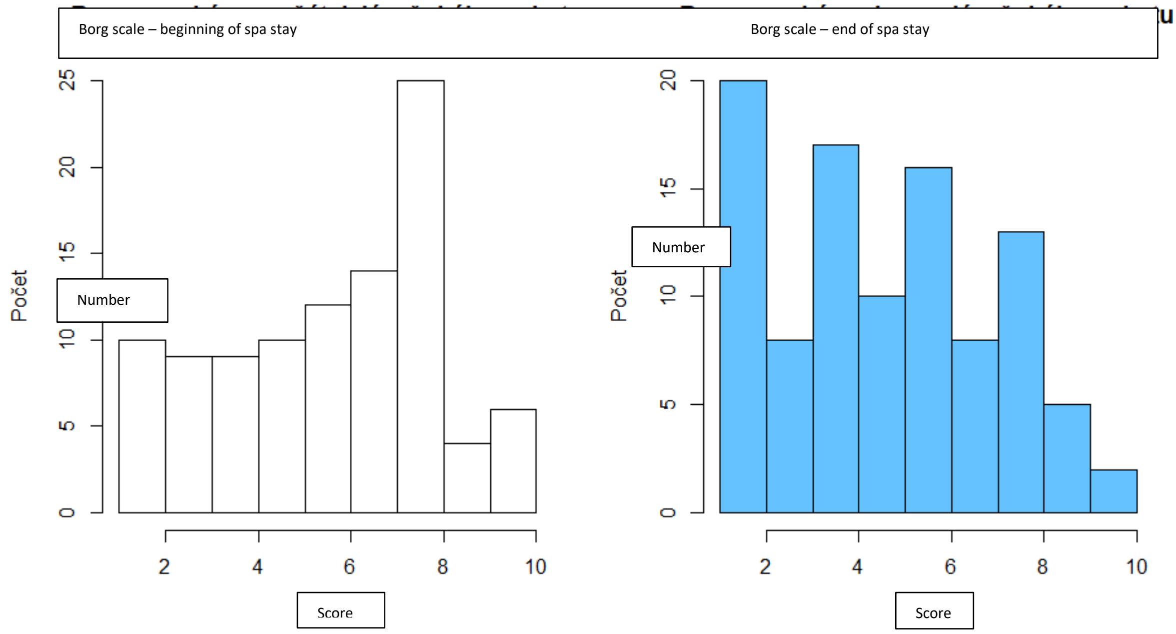


Figure 11: Borg scale - histograms: the beginning and the end of the spa stay

Anderson-Darling Normality Test	Beginning of stay	End of stay
***p*-value**	<0.001	< 0.001

Table 10: Borg scale - normality test

Change in the Values after Spa Stay

In Table 11, you can see the basic characteristics calculated from the values recorded. Although the minimum and maximum valued were identical at the end of stay as well, mean values and median improved (dropped by one degree on the Borg scale). On average, the value of breathlessness dropped by 30.3%.

	Min	Max	Mean	Median	p-value
Beginning of stay	1	10	6.04	6	<0.001
End of stay	1	10	5.04	5	
Change [%]	-150,0 %	62,5 %	-30,3 %	-25,0 %	

Table 11: Borg scale - Basic characteristics of measured values and the % of changes, p-value of the Wilcoxon test

The boxplots in Figure 12 show that the first and third data quartile also moved, so it is clear that breathlessness dropped after the stay. The Wilcoxon test proved the same and on its basis, we reject the zero hypothesis of the coincidence of medians before and after the spa stay, and we can say that after the spa stay, the level of breathlessness is statistically significantly lower.

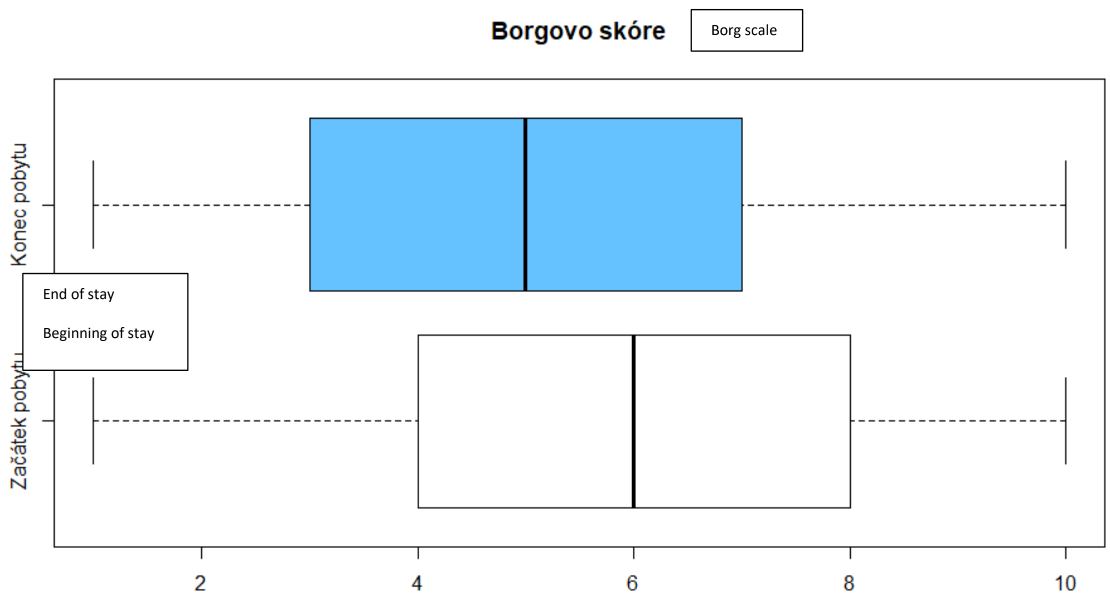


Figure 12: Borg scale - Boxplots: the values at the beginning and at the end of hospitalizations

Dependence on Age

You can see in the scatter diagram in Figure 13 that the values of a difference between Borg scale at the beginning and at the end of stay does not depend on age. This is also confirmed by the calculated correlation coefficient which is in this case **0.030**, p-value of the significance test was **0.768.** Thus, we do not reject the zero hypothesis of the significance of correlation coefficient and we can state that the change in the evaluation of the breathlessness level does not depend on age.

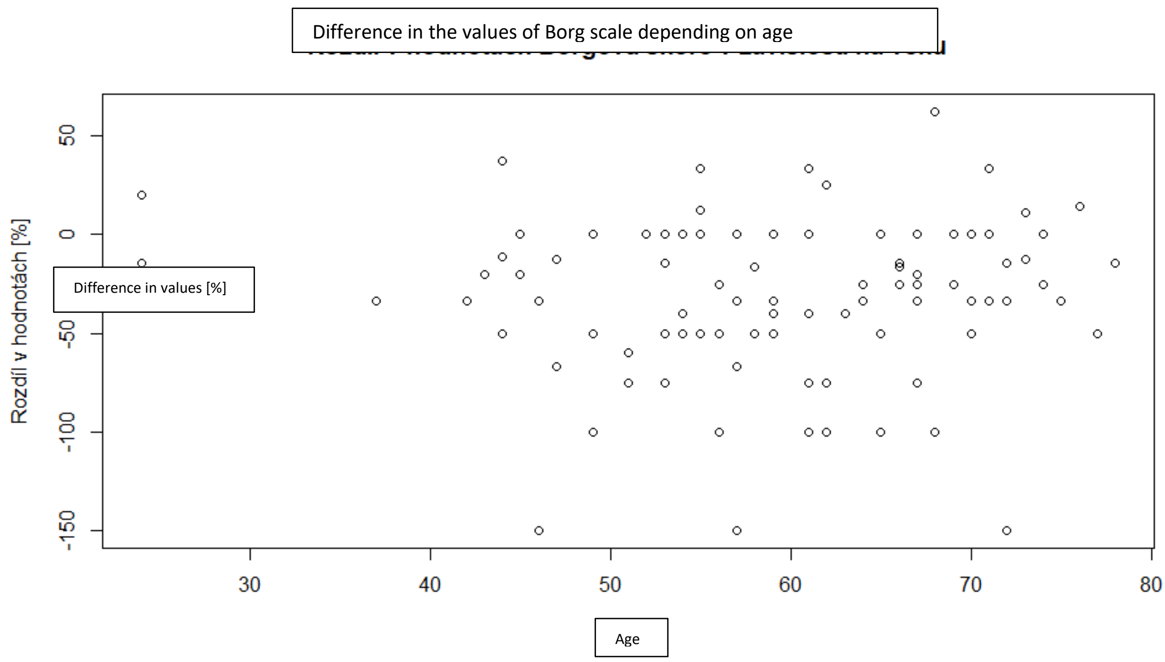


Figure 13: Borg scale - Scatter diagram, dependence of change in the score values on age

Dependence on Gender

The basic characteristics showed in Table 12 were calculated from the percentage change in a patient's evaluation by the Borg scale depending on gender. We can see that medians of the change, in both men and women fluctuate in a similar rate, so there is no difference between genders. We can see the same in the boxplot in Figure 14. Although the groups differ in the minimum and maximum values, the calculated median an Q1 and Q3 are almost identical for both men and women. The Mann-Whitney Test confirmed the same, see *p*-value in Table 9. Since it is greater than the significance level of 5%, we do not reject the coincidence of data distribution and can say that the change in breathlessness score is not gender dependent, i.e. it changes equally in both men and women.

	Min	Max	Mean	Median	p-value
Men	-100 %	62.5 %	-25.1 %	-25 %	0.350
Women	-150 %	37.5 %	-35.4 %	-29.2 %	

Table 12: Borg scale - Basic characteristics of the changes in the % according to gender and the resulting p-value of the Mann-Whitney test

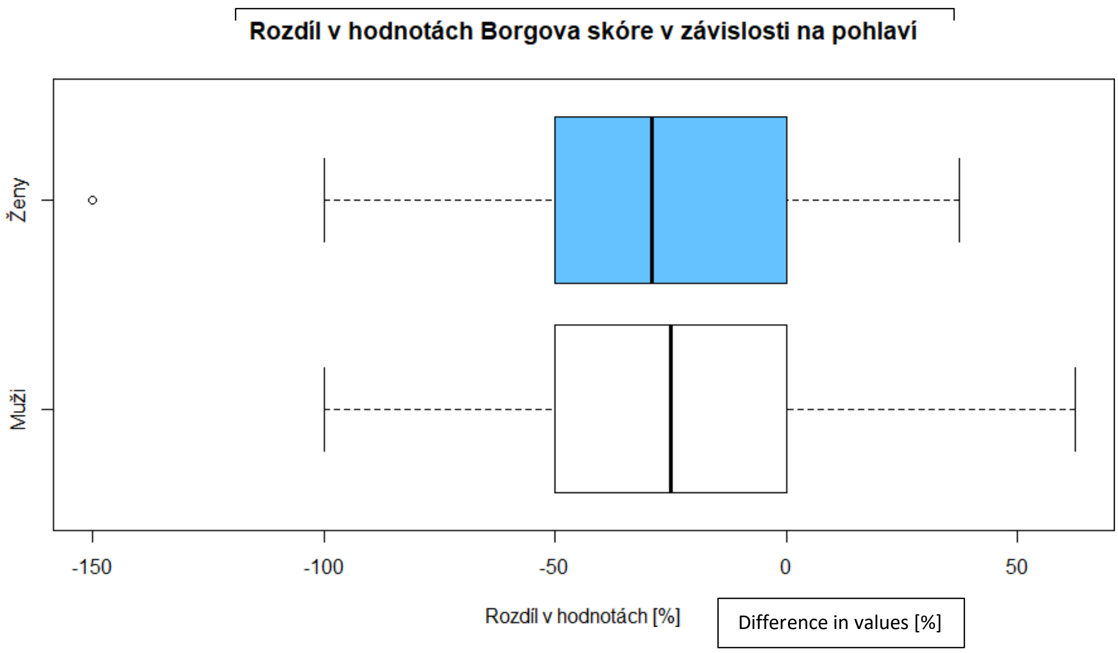


Figure 14: Borg scale - Boxplots: a difference between the values depending on gender

Influence of a Period between COVID-19 Disease and Spa Admission

It is obvious in the scatter diagram in Figure 15 that a period between experiencing Covid-19 and the beginning of spa treatment has no influence on the changes in the Borg scale values after finishing the stay. This also confirms the calculated correlation coefficient with the value of 0.047 and the p-value of significance test value of 0.642. Thus, we do not reject the zero hypothesis of its insignificance and can say that this factor has no influence on the change of the Borg scale after finishing the stay.

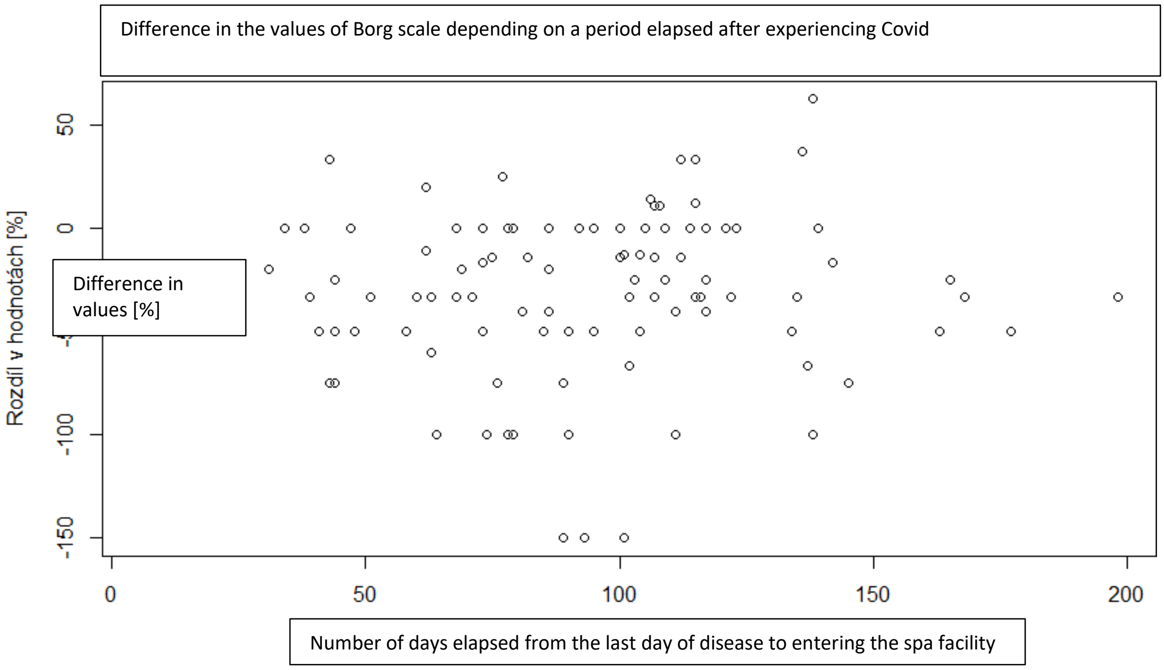


Figure 15: Borg scale - Scatter diagram, the dependence of value change on the time elapsed from experiencing Covid-19.

Impact of Comorbidities

To assess the difference between the probands with any comorbidity and the probands without it, you can see in Figure 16 that no significant differences are visible.

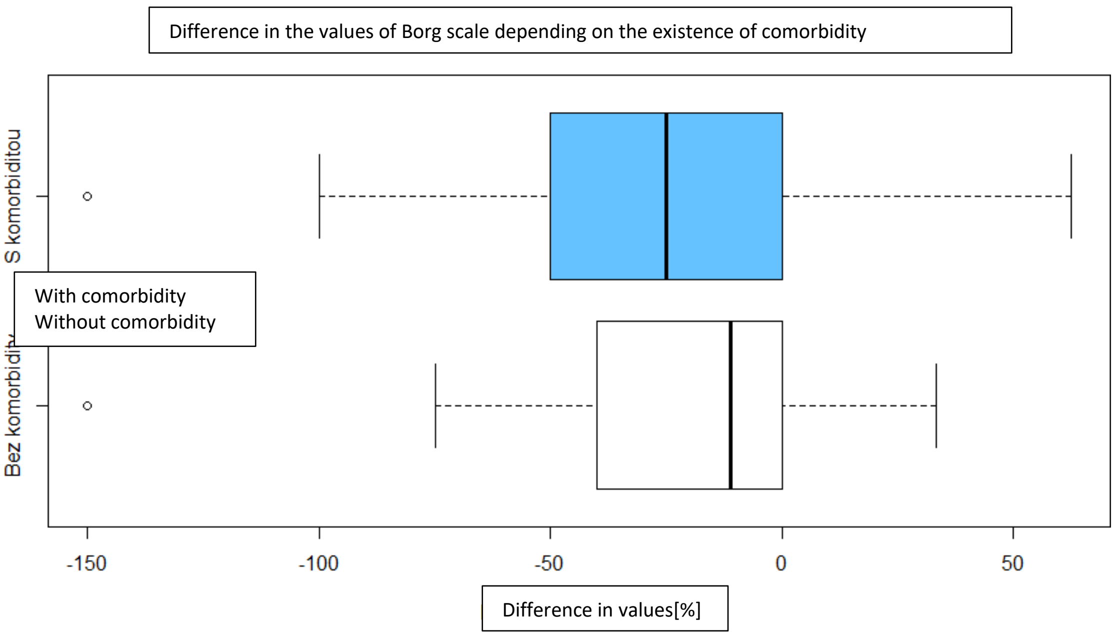


Figure 16: Borg scale - Boxplots, differences between the 6MWT values depending on the existence of comorbidity

Average change was in the probands with comorbidity - 31.5%, whereas in the probands without comorbidity only - 23.6%. This suggests that the probands without other comorbidities did not improve dyspnoea values as significantly as those with comorbidities. However, this difference is not statistically significant, see the *p*-value in the Mann-Whitney test in Table 13 which is higher than the significance level of 5%. We do not reject the zero hypothesis of the conformity of probability distribution. However, the result can again be distorted by a number of the probands without comorbidities.

	Min	Max	Mean	Median	p-value

Comorbidity	-150 %	62.5 %	-31.5 %	-25 %	0.330
Without comorbidity	-150 %	33.3 %	-23.6 %	-11.1 %	

Table 13: Borg scale - Basic characteristics of the changes in the % depending on the existence of comorbidity and the resulting p-value of the Mann-Whitney test

For this reason, we have performed a more detailed analysis, where we already categorize the probands with comorbidities according to the specific comorbidity. In the ANOVA table below, we see that with none of the factors analysed the *p*-value is smaller than the significance level of 5%, so none of the comorbidities or their combination has a statistically significant effect on the rate of change in Borg score p-values of completing the therapy stay. We can see the same in the boxplot in Figure 18.

Borg score	**Df**	**Sum of Squares**	**Mean of Squares**	**F-value**	**P-value**
Diabetes mell	1	0.085	0.085	0.516	0.475
Obesity	1	0.461	0.461	2.794	0.098
High blood pressure, cardio	1	0.014	0.014	0.085	0.771
Bronchitis, COPD, asthma	1	0.531	0.531	3.215	0.077
Without comorbidity	1	0.002	0.002	0.014	0.905
Diabetes mell: Obesity	1	0.002	0.002	0.012	0.914
Diabetes mell : High blood pressure, cardio	1	0.014	0.014	0.088	0.768
Obesity: High blood pressure, cardio	1	0.009	0.009	0.052	0.820
Diabetes: Bronchitis, COPD, asthma	1	0.043	0.043	0.260	0.612
Obesity: Bronchitis, COPD, asthma	1	0.020	0.020	0.118	0.732
High blood pressure, cardio: Bronchitis, COPD, asthma	1	0.209	0.209	1.265	0.264
Diabetes mell : Obesity: High blood pressure, cardio	1	0.080	0.080	0.487	0.487
Diabetes mell : High blood pressure, cardio: COPD, bronchitis, asthma	1	0.076	0.076	0.458	0.501
Obesity: High blood pressure, cardio: Bronchitis, COPD, asthma	1	0.220	0.220	1.331	0.252
Residuals	84	13.864	0.165		

Table 14: Borg scale – ANOVA, influence of comorbidities

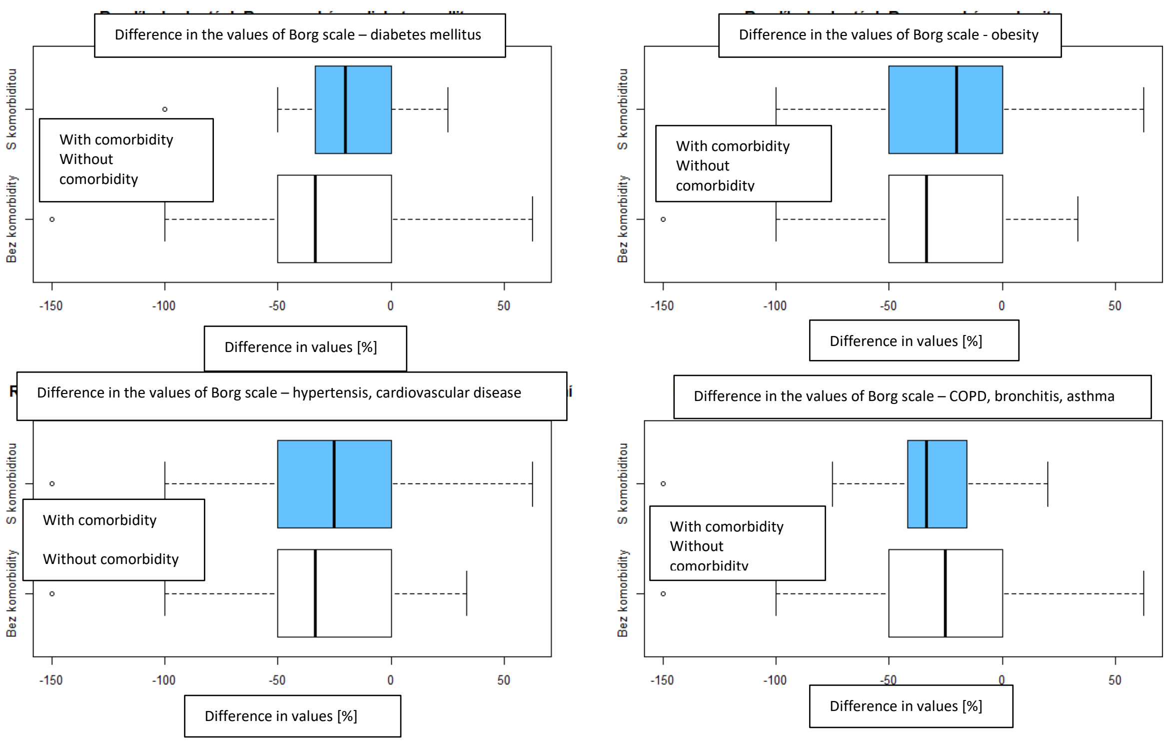


Figure 17: Borg scale – ANOVA, influence of individual comorbidities

Summary

There was confirmed the statistically significant change in the Borg score values after experiencing the spa stay. On average, the value of dyspnoea dropped by 30.3%. Overall, we can get to the conclusion that the spa stay has a positive effect on the breathlessness of the proband, which decreases after the spa stay.

This effect is independent on gender, age of the probands or the time elapsed between the onset of Covid-19 and admission to the spa. None of the comorbidities analysed had an effect on the change in dyspnoea values after the spa stay.

SpO2

The SpO2 value was measured within the 6MWT test, namely always before performing the test and then after it. For this reason, we evaluated the change in the value after the spa stay for two variables - SpO2 before the 6MWT test and SpO2 after the 6MWT test.

Data Normality

As we can see in the histograms in Figures 18 and 19, as well as in Result Table 15, the data do not follow a standard distribution (the *p*-value is less than 5% in both cases). Thus, we will further use non-parametric tests.

Anderson-Darling Normality Test	Beginning of stay	End of stay
***p*-value, before the test**	< 0.001	< 0.001
***p*-value, after the test**	< 0.001	< 0.001

Table 15: SpO2 - Normality test

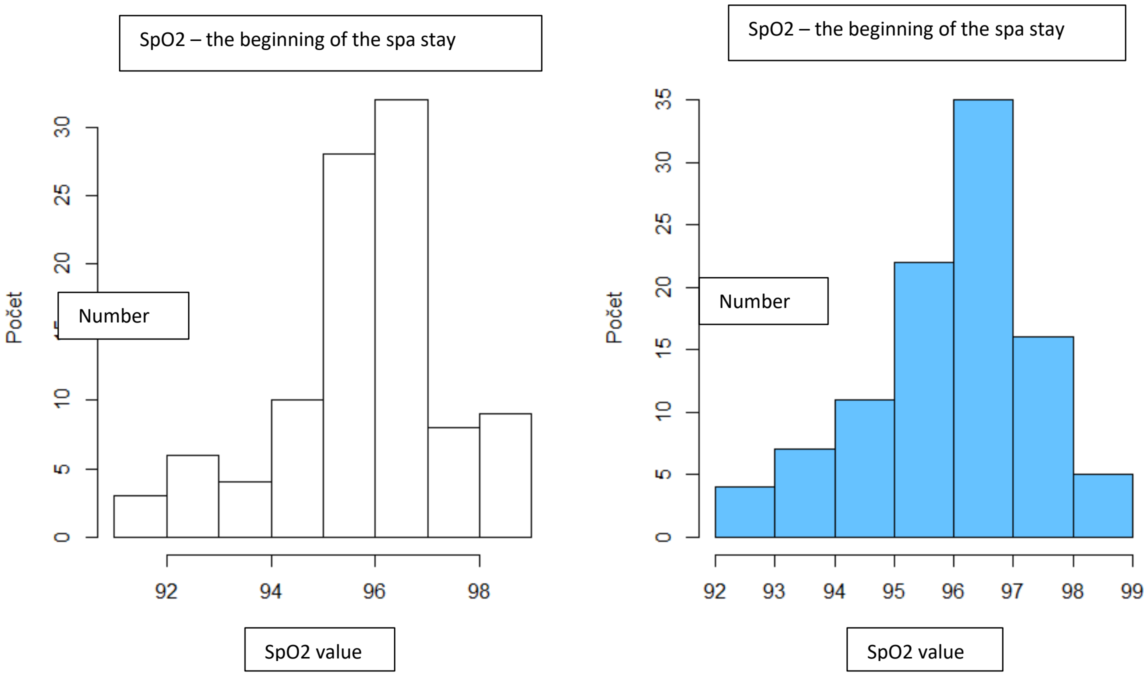


Figure 18: SpO2 before the 6MWT test - Histograms: the beginning and the end of stay in spa

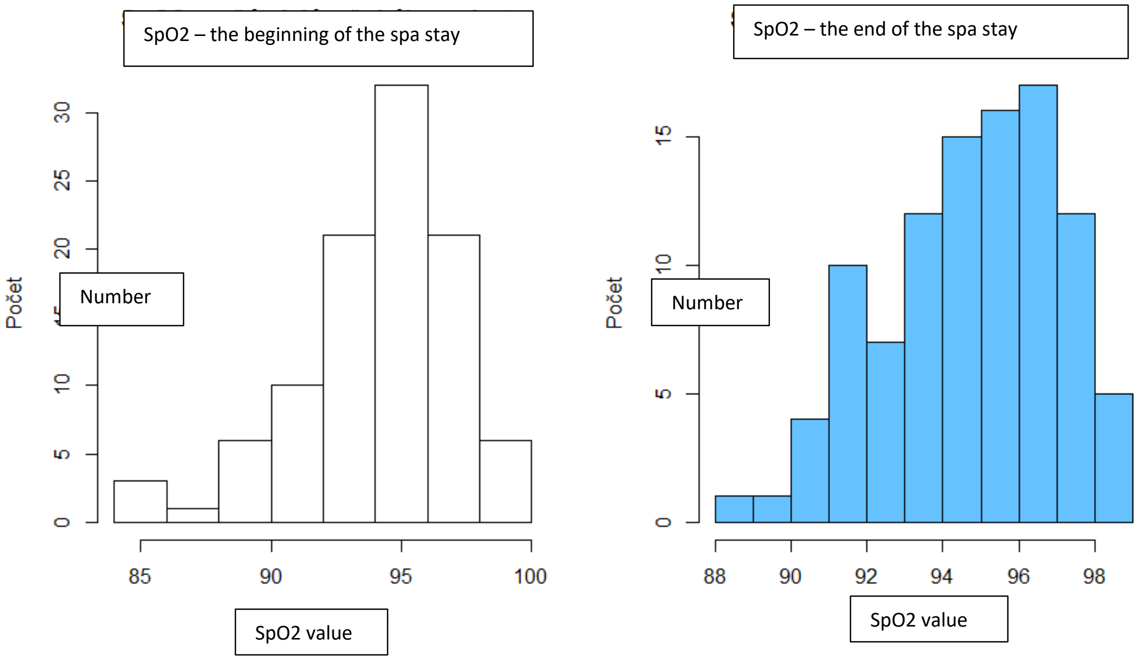


Figure 19: SpO2 after the 6MWT test - Histograms: the beginning and the end of stay in spa

Change in the Values after Spa Stay

We first evaluated SpO2 values before performing the 6MWT test. In the following Figure, you can see the boxplots, which show that although the median value increased at the end of the stay, the values distribution as such remains almost the same. The same is confirmed by the values in Table 16, where we can see that all the calculated characteristics are similar at the beginning and at the end of the spa stay. The average change in SpO2 was 0.16%.

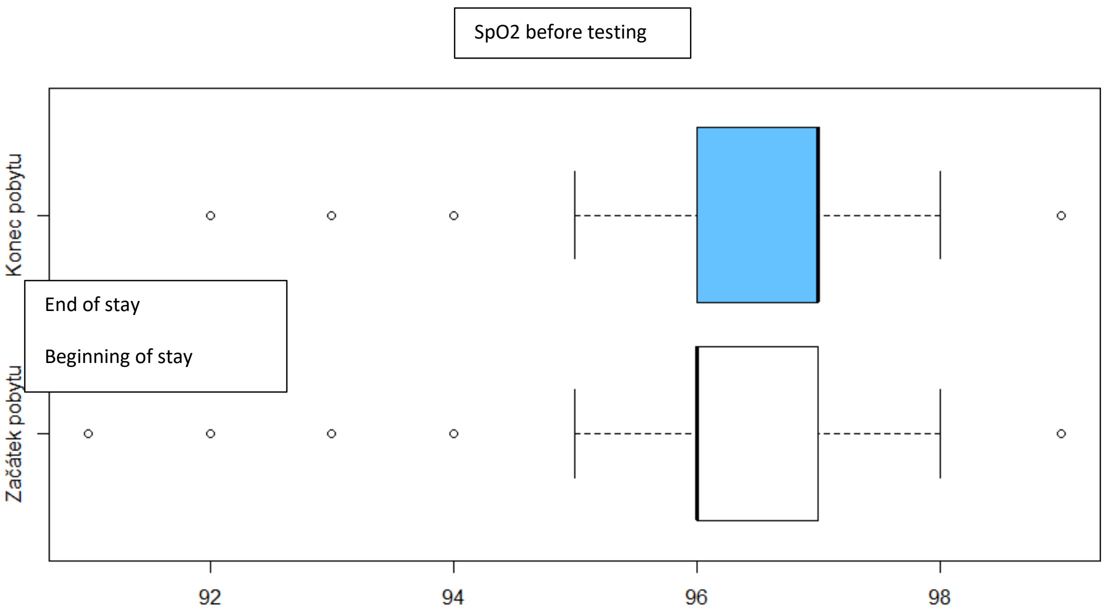


Figure 20: SpO2 before the 6MWT test - boxplots

The same is confirmed by the Wilcoxon test of which the *p*-value was greater than 5%, so we do not reject the hypothesis due to the difference of medians is zero, i.e. that there is no difference between the values before and after the spa stay.

	Min	Max	Mean	Median	p-value
Beginning of stay	91	99	96.26	96	0.360
End of stay	92	99	96.43	97	
Change [%]	-6.45 %	4.21 %	0.16 %	0 %	

Table 16: SpO2 before the MWT test - Basic characteristics of measured values and the % of changes, p-value of the Wilcox test

We further evaluated the same for the difference between the measured SpO2 values after the 6MWT test. Below, we can see again the boxplots plotted and Table 17 with the basic characteristics and also the *p*-value of the Wilcoxon test From the boxplots we can see that at the beginning of stay the SpO2 values were slightly lower than at the end of the stay. However, the values of the characteristics are very similar, only the mean and median slightly increased. On average, the SpO_2value measured after the test increased by 0.66%.

The *p*-value of the Wilcoxon test is in this case 6.7% which is greater than the significance level of 5%, so we do not reject the hypothesis, that the median values remain the same at the beginning and at the end of the spa stay. On the other hand, we can perceive that the *p*-value is not significantly different from the significance level in the previous cases and therefore, the result cannot be taken as unequivocal. **We recommend this variable to be monitored in follow-up studies for a clear rejection / no-rejection of the zero hypothesis with a higher number of patients.**

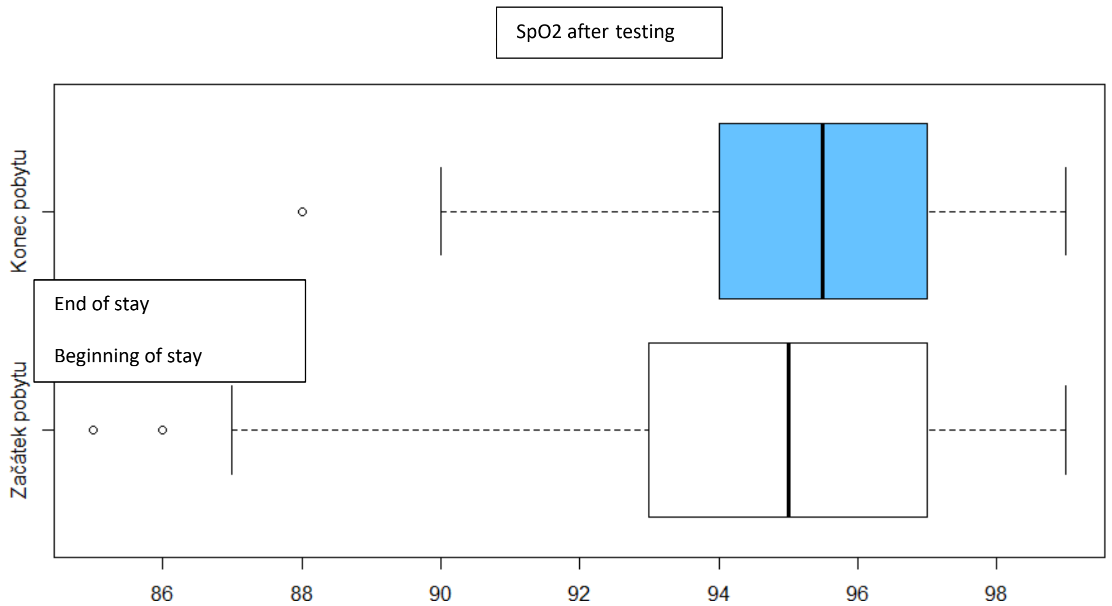


Figure 21: SpO2 after the 6MWT test - boxplots

	Min	Max	Mean	Median	p-value
Beginning of stay	85	99	94.56	95	0.067
End of stay	88	99	95.22	95.5	
Change [%]	-7.61 %	11.22 %	0.66 %	0.00 %	

Table 17: SpO2 after the MWT test - Basic characteristics of measured values and the % of changes, p-value of the Wilcoxon test

Dependence on Age

The scatter diagram in Figure 22 shows the percentage changes in the SpO2 values before performing the 6MWT test depending on age. We can see that the values changes according to the age do not differ too much, only with the age of 65+, several cases appear with the SpO2 value worsening by more than 4%. Correlation between the percentage differences of the values and a patient's age is -**0.19**; this correlation coefficient is statistically significant from 0 because the *p*-value of the significance test is **0.047**; thus, these differences in the SpO2 values are slightly lower with increasing age (i.e. older people do not improve as much as the younger). However, here again it should be noticed that the *p*-value of 4.7% is not too far from the significance level of 5% and the correlation coefficient is still very close to 0, therefore we should investigate this dependence further.

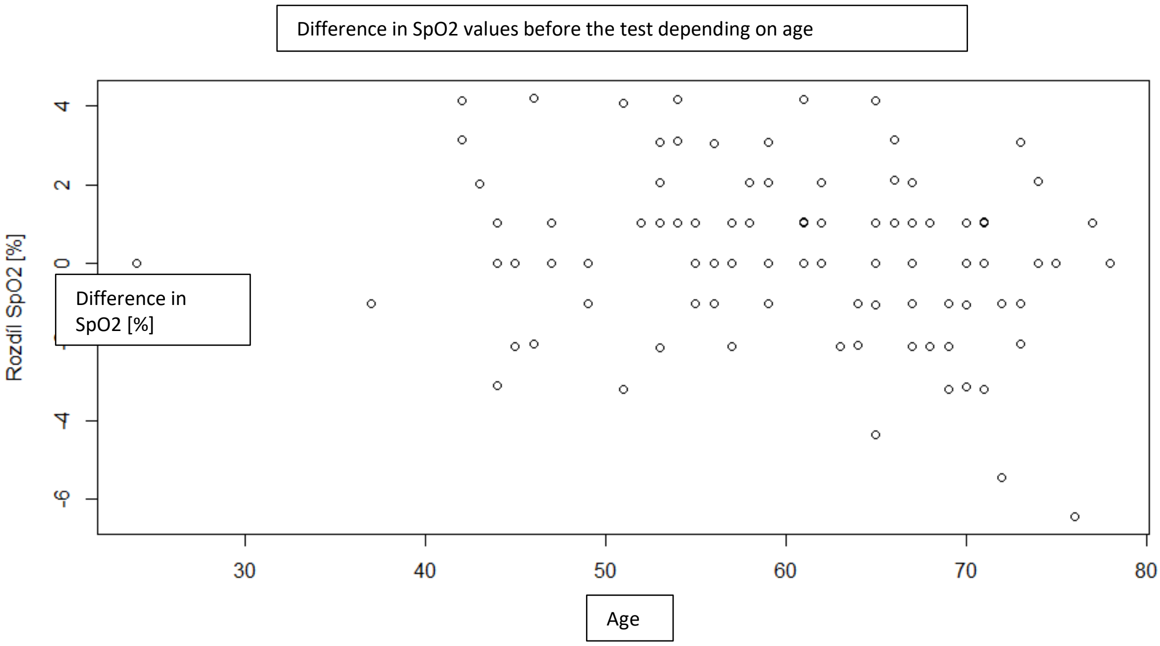


Figure 22: SpO2 before the test - Scatter diagram, dependence of change in the score values on age

In case of the differences in 2 values after the 6MWT test, Figure 23 shows that there is no dependence between the differences in the rate of improvement/deterioration of results and the age of a patient. This was confirmed by the calculated correlation coefficient with a value of **-0.02** for which the significance test showed that it was not statistically significantly different from 0 (*p*-value **0.799)**.

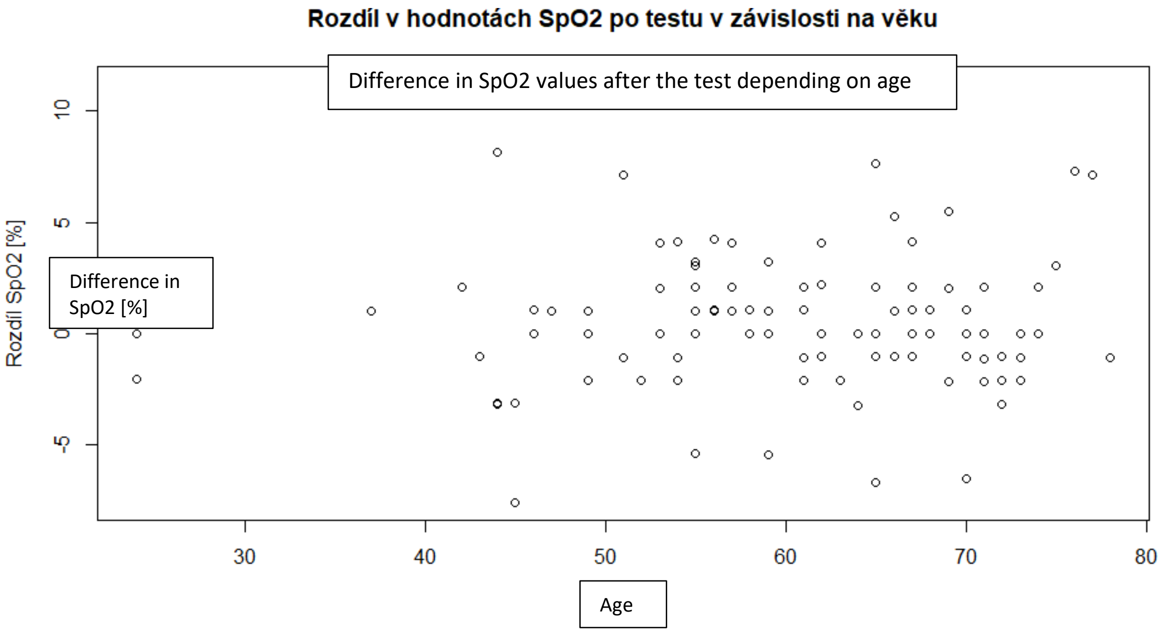


Figure 23: SpO2 after the test - Scatter diagram, dependence of change in the score values on age

Dependence on Gender

In this case too, there was no gender dependence of the differences in the values before and after the spa stay, see Figures 24 and 25 with the boxplots depending on gender and Tables 18 and 19 with the calculated basic characteristics for women and men. The *p*-values of the Mann-Whitney test are greater than 5% in both cases, so we do not reject the zero hypothesis of a coincidence of data distribution in both groups.

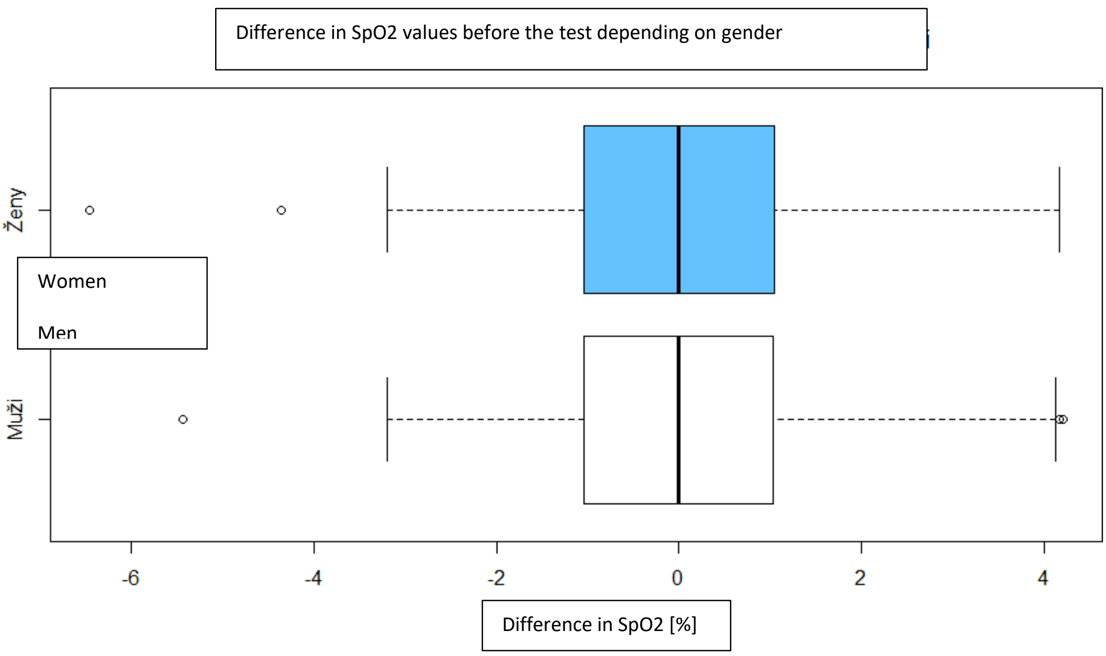


Figure 24: SpO2 before the 6MWT test - Boxplots: a difference in the values depending on gender

	Min	Max	Mean	Median	p-value
Men	-54.3 %	42.1 %	0.132 %	0	0.631
Women	-64.5 %	41.7 %	0.185 %	0	

Table 18: SpO2 before the 6MWT test - Basic characteristics of the changes in the % according to gender and the resulting p-value of the Mann-Whitney test

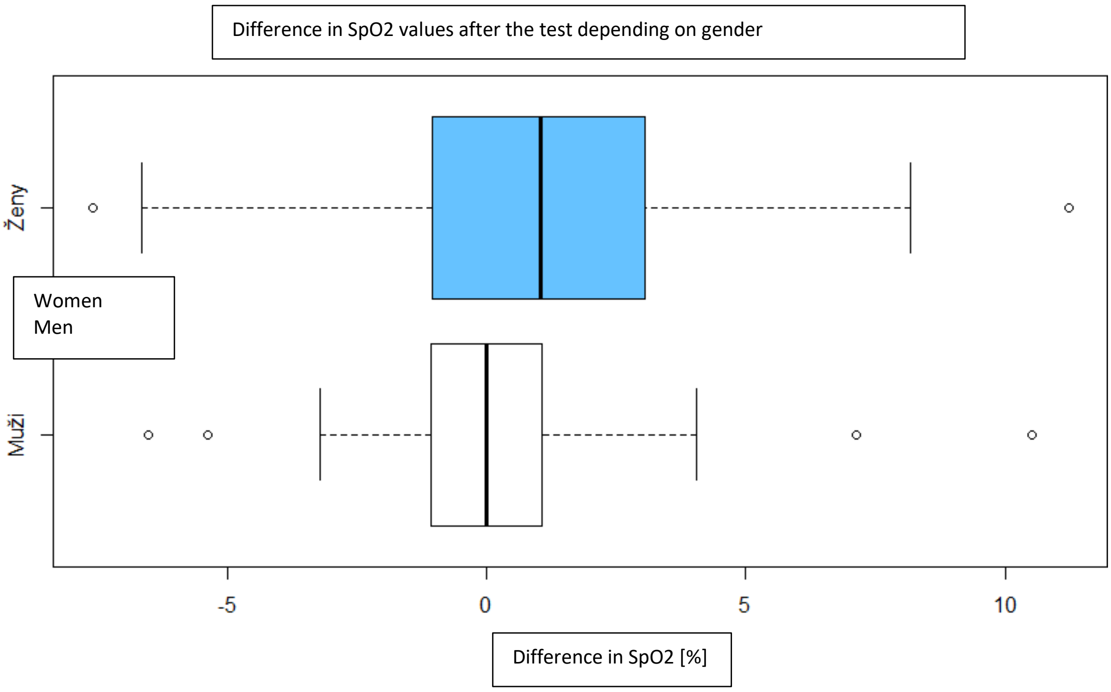


Figure 25: SpO2 after the 6MWT test - Boxplots: a difference between the values depending on gender

	Min	Max	Mean	Median	p-value
Men	-6.5 %	10.5 %	0.3 %	0 %	0.148
Women	-7.6 %	11.2 %	1.0 %	1 %	

Table 19: SpO2 after the 6MWT test - Basic characteristics of the changes in the % according to gender and the resulting p-value of the Mann-Whitney test

Influence of a Period between COVID-19 Disease and Spa Admission

In both cases, i.e. SpO2 values before and after the 6MWT test, there is not apparent dependence on the time between experiencing Covid-19 disease and the admission to the spa treatment, see scatter diagrams in Figures 26 and 27. This is confirmed by the calculated values of the correlation coefficients where in case of the change in values before the test, the correlation coefficient was **-0.054** and the *p*-value of the significance test was **0.595**, in case of the changes after the test, the correlation coefficient was **0.022** with the p-value of the significance test **0.8242**. In both cases, the *p*-value is higher than the significance level of 5%, therefore, we do not reject the zero hypothesis of the insignificance of correlation coefficients and we can say, that the change in SpO2 values before and after the 6MWT test does not depend on a number of days elapsed between experiencing the Covid-19 disease and the admission to the spa treatment.

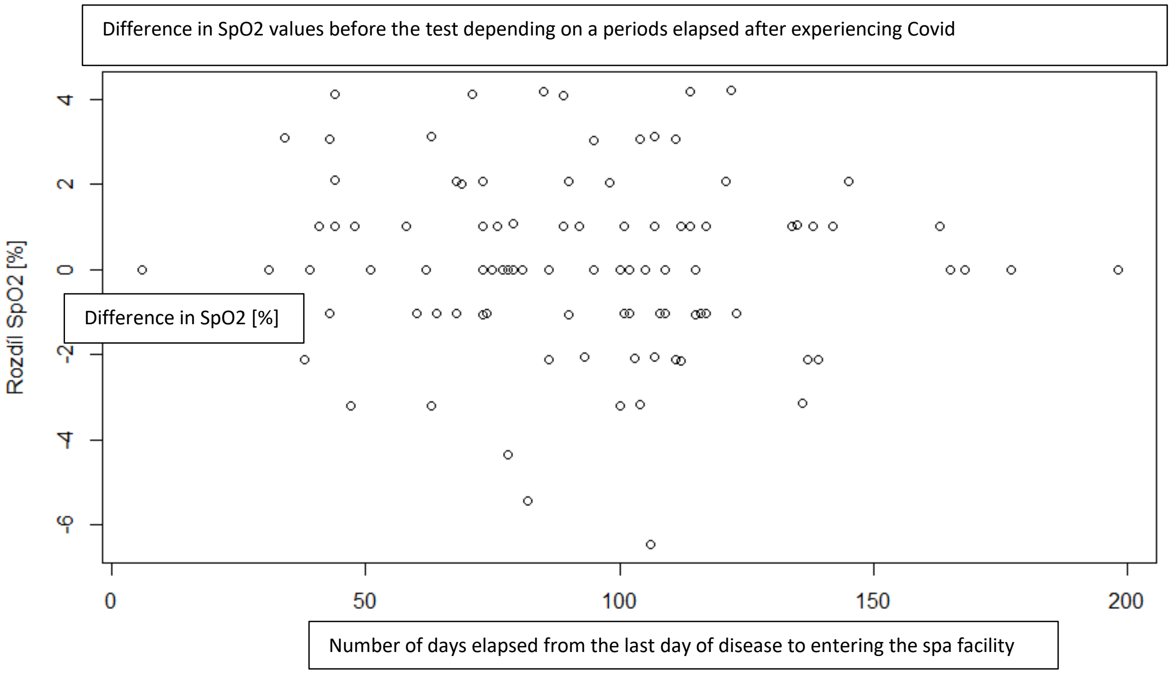


Figure 26: SpO2 before the test - Scatter diagram, the dependence of value change on the time elapsed from experiencing Covid-19.

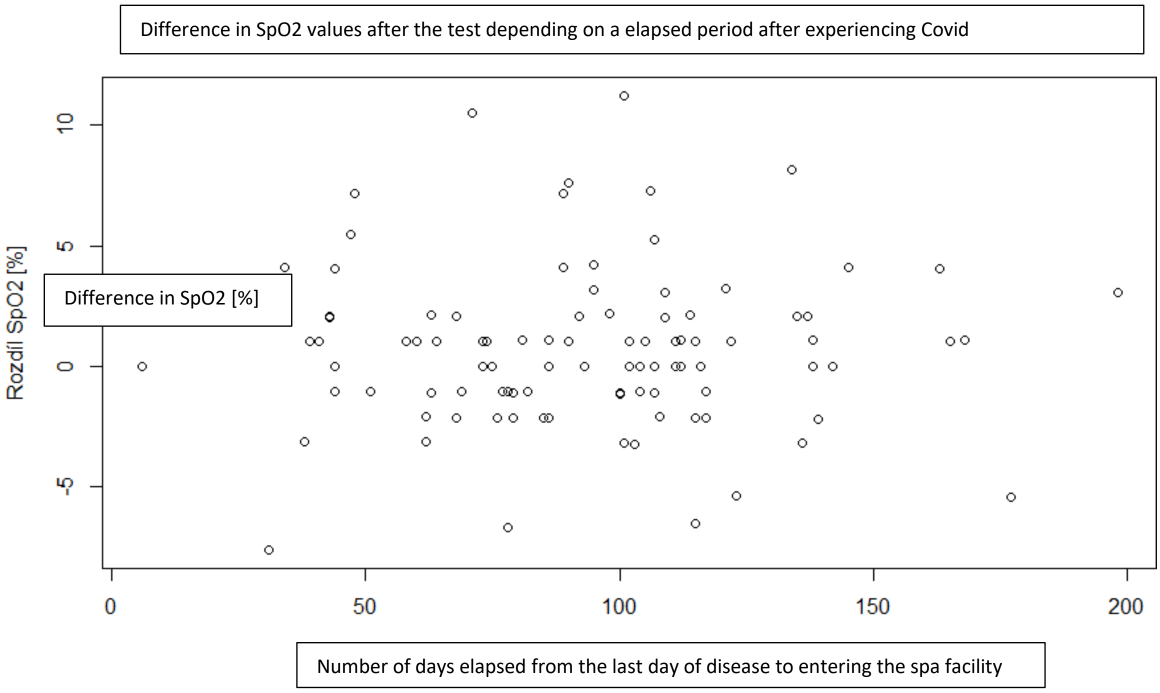


Figure 27: SpO2 after the test - Scatter diagram, the dependence of value change on the time elapsed from experiencing Covid-19.

Impact of Comorbidities

To assess the difference between the probands with any comorbidity and the probands without them, and Figures 28 a 29 show that no significant differences are visible. Even the values in Tables 20 and 21 show mainly the fact that there was no significant change in this parameter, whether in the patients with other comorbidities or without them. In both cases, the *p*-value of the Mann-Whitney test was greater than the significance level of 5%; so we do not reject the zero hypothesis of the coincidence of probability distribution.

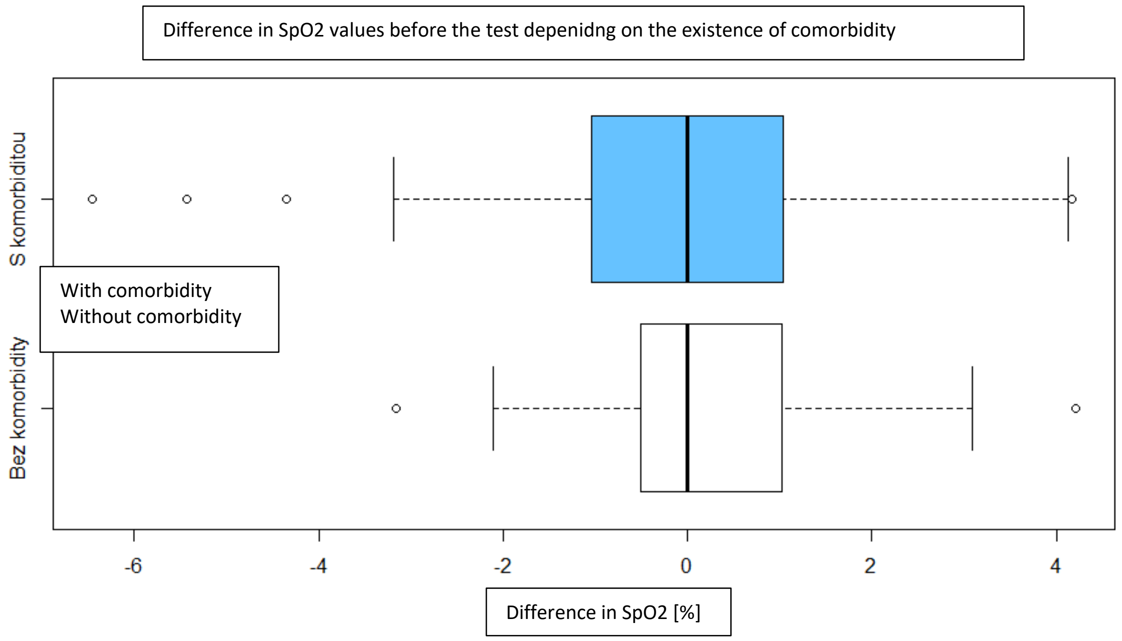


Figure 28: SpO2 -before the test - Boxplots, differences between the 6MWT values depending on the existence of comorbidity

	Min	Max	Mean	Median	p-value
Comorbidity	-6.5 %	4.2 %	0.1 %	0 %	0.880
Without comorbidity	-3 %	4 %	0 %	0 %	

Table 20 - SpO2 before the test - Basic characteristics of the changes in the % depending on the existence of comorbidity and the resulting p-value of the Mann-Whitney test

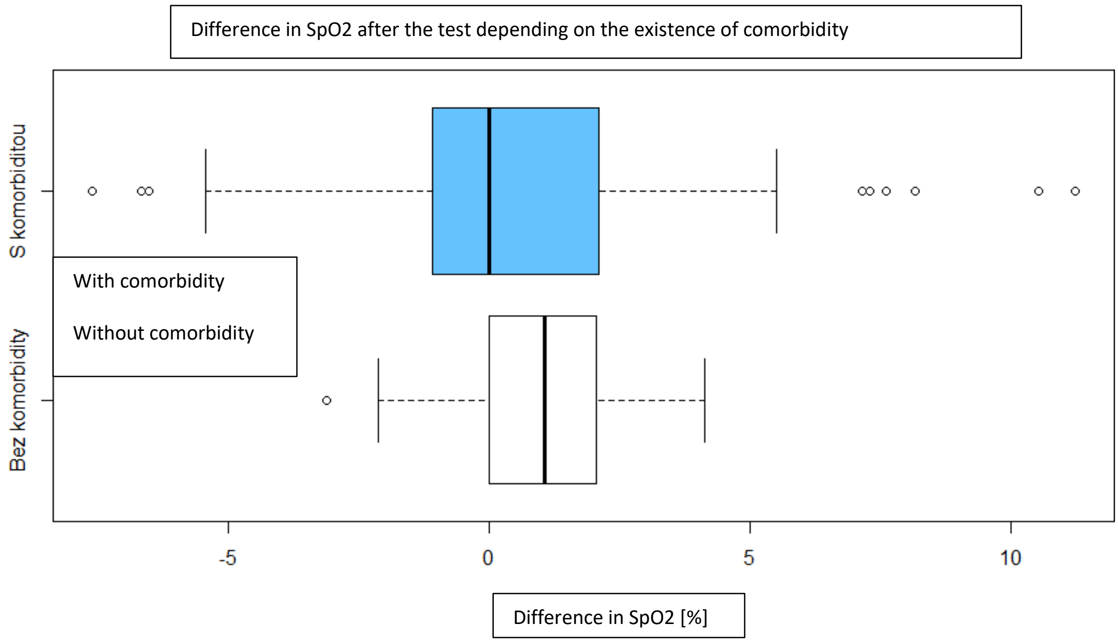


Figure 29: SpO2 after the test - Boxplots, differences between the 6MWT values depending on the existence of comorbidity

	Min	Max	Mean	Median	p-value
Comorbidity	-7.6 %	11.2 %	0.6 %	0 %	0.314
Without comorbidity	-3 %	4 %	1 %	1 %	

Table 21: SpO2 after the test - Basic characteristics of the changes in the % according to the existence of comorbidity and the resulting p-value of the Mann-Whitney test

Since no change in SpO0 values was proved before and after the spa stay, we will not discuss the detailed results. According to the ANOVA results, there was not proved any significant influence of the existence of some comorbidities in the patients on the change in SpO1 values before or after the 6MWT test.

Summary

SpO2 value was always measured twice - before and after the 6MWT physical fitness test. In case of the values before this test, no statistically significant change was proved after the spa stay, neither in relation to gender, age of the probands, the time elapsed between experiencing Covid-19 disease and the admission to the spa nor the existence of comorbidities. On average, this value changed by 0.16% only.

In case of SpO2 values after the fitness test, it is not possible to clearly decide, whether such a significant change occurred and this variable needs to be further monitored. On average, the values in the probands increased by 0.66%. However, not even in this case no effect on gender and age of probands was proven, on the time elapsed between experiencing Covid-19 disease and the admission to the spa facility or on the existence of comorbidities studied.

FVC

In scope of the spirometric examination at the initial and final check (so before and after the spa stay), FVC value was recorded - the maximum volume of air which can be exhaled sharply after the maximum inspiration.

Outlying Observations

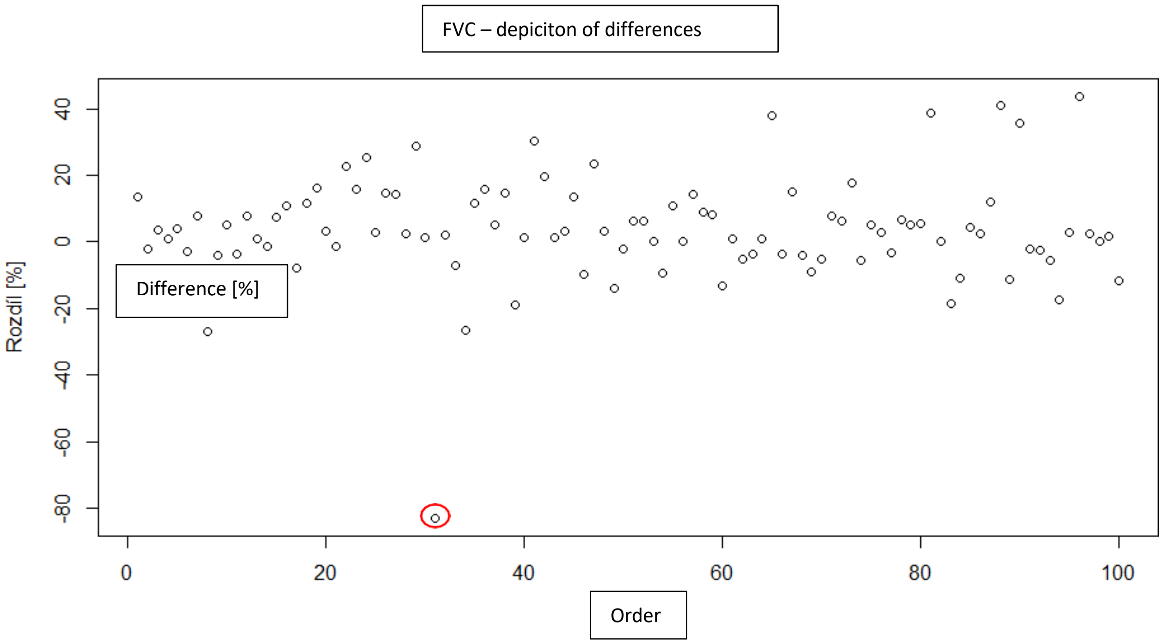


Figure 30: FVC - Scatter diagram, outlier observation

During the analysis, outlier observation was found out - the patient no. 96, whose FVC value dropped after therapy by 80%, see Figure 30. To protect the results from distortion, this patient was excluded from the FVC evaluation.

Normality

3

5

We see in the histograms in Figure 31 that the data look like the Gauss curve. Normality was proved even by the Anderson-Darling normality test, see Table 22, p-value is greater than the significance level of 5%, so we do not reject the zero hypothesis of data normality. In this case, we use parametric tests for the analysis.

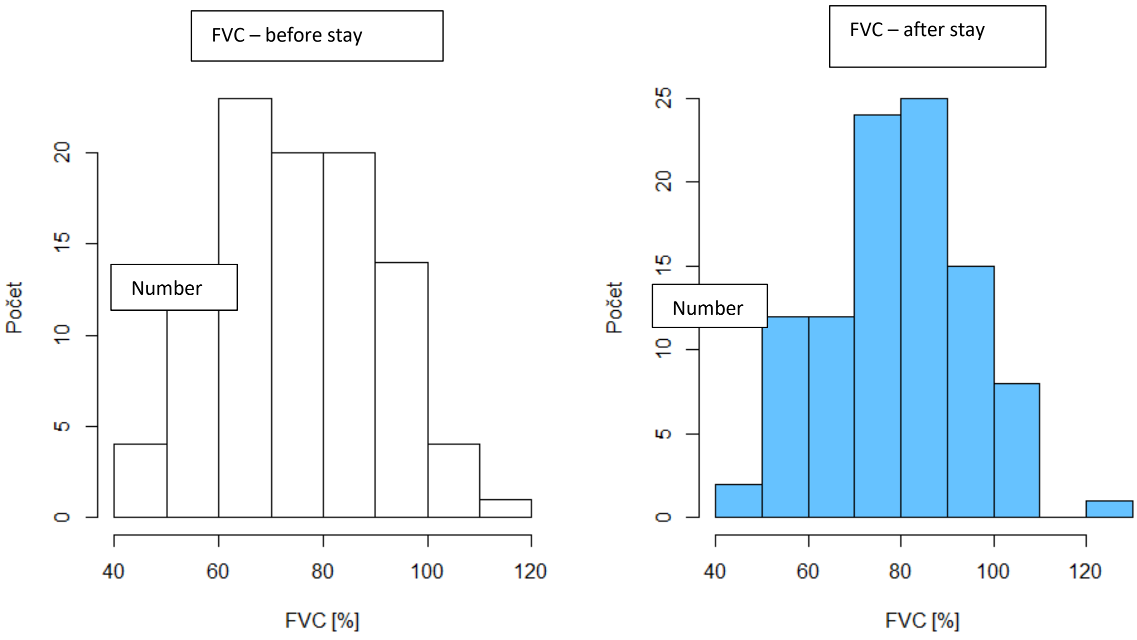


Figure 31: FVC - histograms: the beginning and the end of the spa stay

	Beginning of stay	**End of stay**
***p*-value**	0.126	0.142

Table 22: FVC - Normality test

Change in the Values after Spa Stay

In Figure 32, you can see the boxplots of the FVC value before and after the spa stay. We see that the median of values after the stay is greater than before the stay and the values of the 1st and 3rd quarter moved as well.

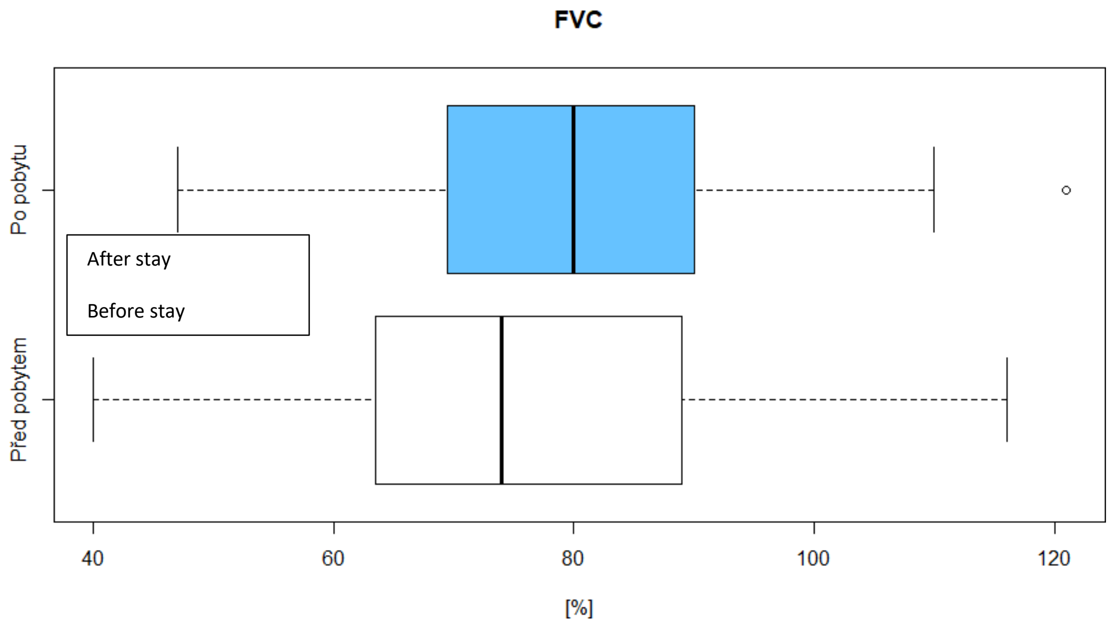


Figure 32: FVC - boxplots: the values before and after the stay

In Table 23, we can see the calculated basic characteristics for the measured SpO2 values before and after the stay. We see that all 4 calculated characteristics increased after the stay. On average, the values increased by 4.5

% The increase in SpO2 values after the spa stay was also confirmed by the paired *t*-test, see the *p*-value in Table 23 which is lower than the significance level of 5%, so we reject the zero hypothesis of the conformity of mean values. We can say based on it that the SpO2 values are statistically significantly greater after the stay than before the stay.

	Min	Max	Mean	Median	p-value
Before stay	40.0 %	116.0 %	75.7 %	74 %	<0.001
After stay	47 %	121 %	79.9 %	80 %	
Difference [%]	-26.8 %	43.8 %	4.5 %	3 %	

Table 23: FVC - Basic characteristics of measured values and the % of changes, p-value of the paired t-test

Dependence on Age

You can see in Figure 33, that the difference between the values at the beginning and at the end stay does not depend on age. The correlation coefficient value shows the same - in this case, it gains the value of **-0.044** and its significance test *p*-value was **0.832, so it is statistically insignificant.** Thus, the patients' FVC values change equally for all of them irrespective of their age.

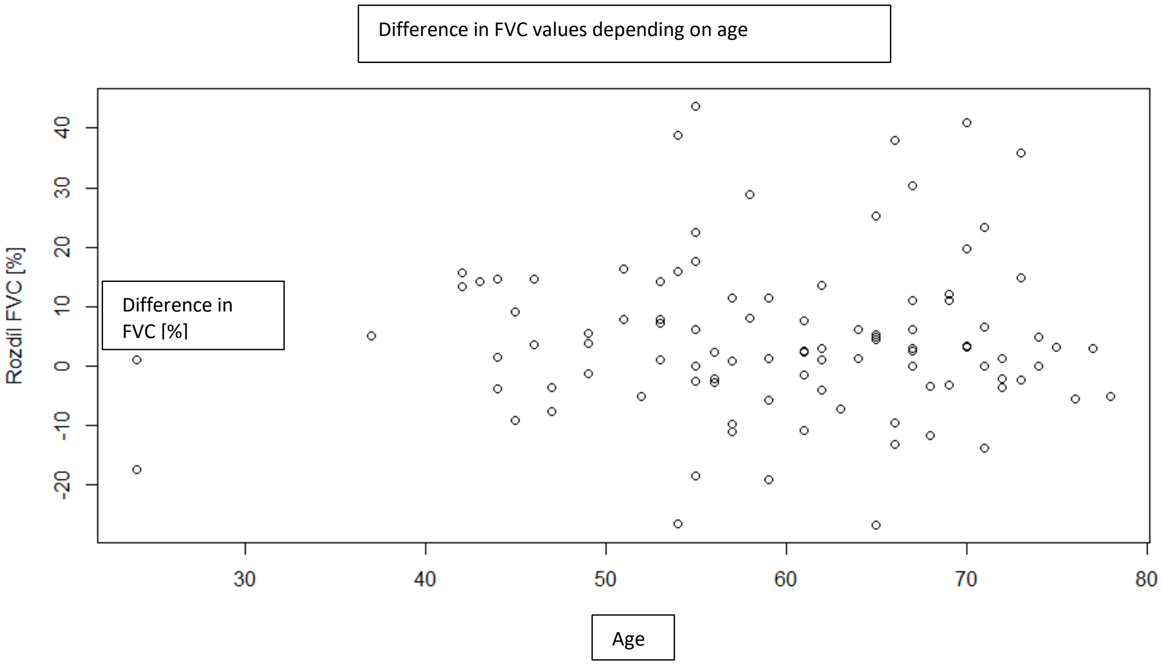


Figure 33: FVC - Scatter diagram, dependence of the difference in the scores on age

Dependence on Gender

In Table 24 below, we see that men improved by an average of 4.86% and women by 4.21%, so almost identically. We can see the same in Figure 34 which shows the boxplosts for the percentage differences between the FVC values before and after the spay stay depending on gender.

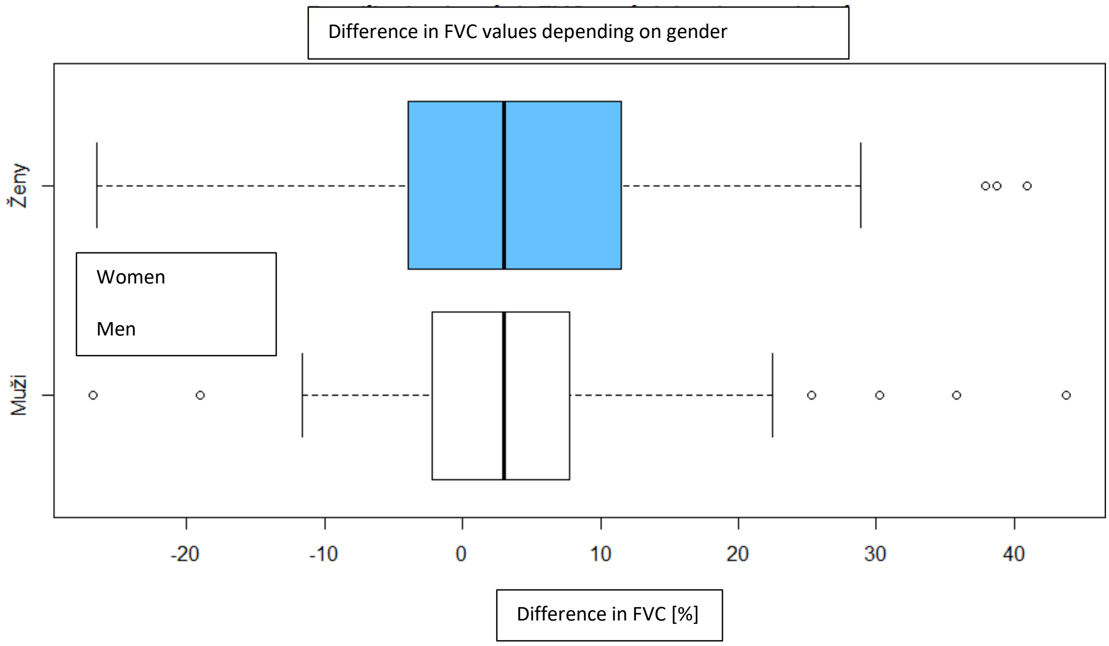


Figure 34: FVC - Boxplots: difference between the values depending on gender

To test the conformity between two means, we used the t-test for two independent samples with identical variances, the p-value of the two-sample F-tests for variance was 0.14, so we do not reject the zero hypothesis of the equality of variances. In this case the test proved that there is no difference in the rate of improvement in FVC depending on gender, see *p*-value in Table 24. Men and women achieve identical changes after experiencing the spa stay.

	Min	**Max**	**Mean**	**Median**	**p-value**
Men	-0.268	0.438	0.0486	0.0296	0.548
Women	-0.265	0.409	0.0421	0.0297	

Table 24: FVC - Basic characteristics of the changes in the % according to gender and the resulting p-value of the ANOVA test

Influence of a Period between experiencing COVID-19 Disease and Spa Admission

It is obvious in the scatter diagram, see Figure 35, that the change in FVC after the spa stay does not depend on a number of days elapsed after experiencing Covid-19 disease and the admission to the treatment programme. This is also confirmed by the calculated correlation coefficient with the value of **-0.12** and the *p*-value of significance test **0.236**. Since the *p*-value is higher than the significance level of 5%, we do not reject the zero hypothesis of the insignificance of the correlation coefficient and we can conclude that a period between experiencing Covid-19 disease and the admission to the therapy does not affect treatment outcomes.

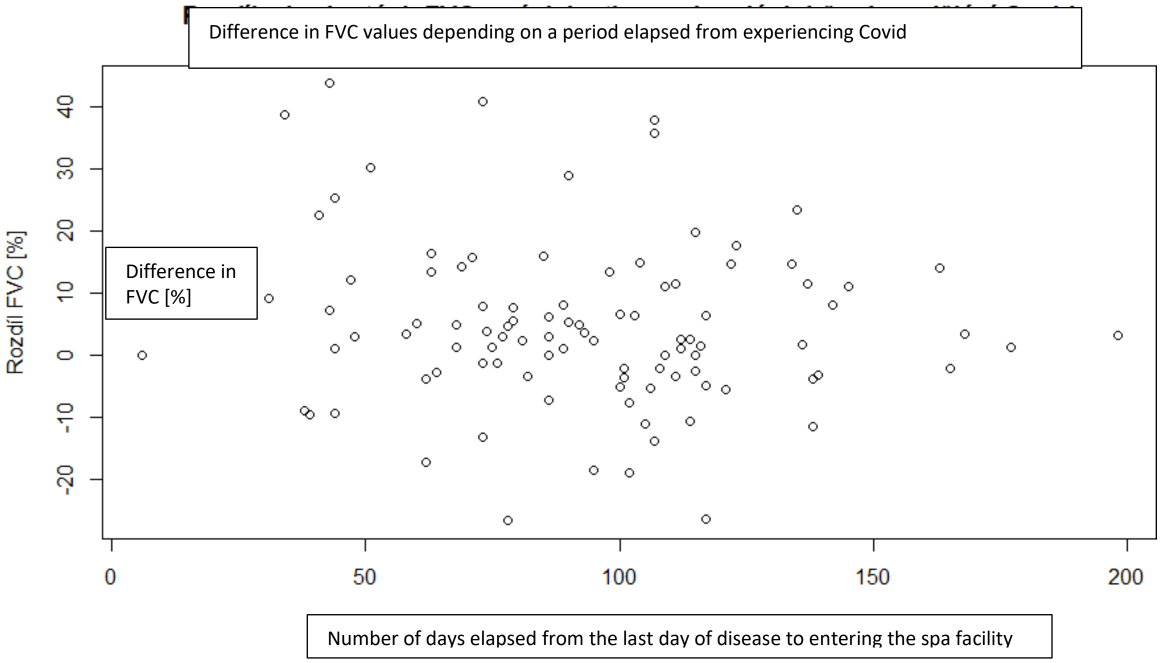


Figure 35: FVC - Scatter diagram, the dependence of value change on the time elapsed from experiencing Covid-19.

Impact of Comorbidities

In Figure 36, we can see the boxplots of the differences between the FVC values before and after the spa stay. At first glance, there is no significant difference in the values of probands with and without other comorbidities. This is confirmed by the Mann-Whitney test, see Table 25 of which the *p*-value is higher than the significance level of 5%. We do not reject the zero hypothesis of the conformity of probability distribution. As in all previous cases, these results may be biased by the fact that the probands without comorbidities are significantly less represented than the probands with comorbidities.

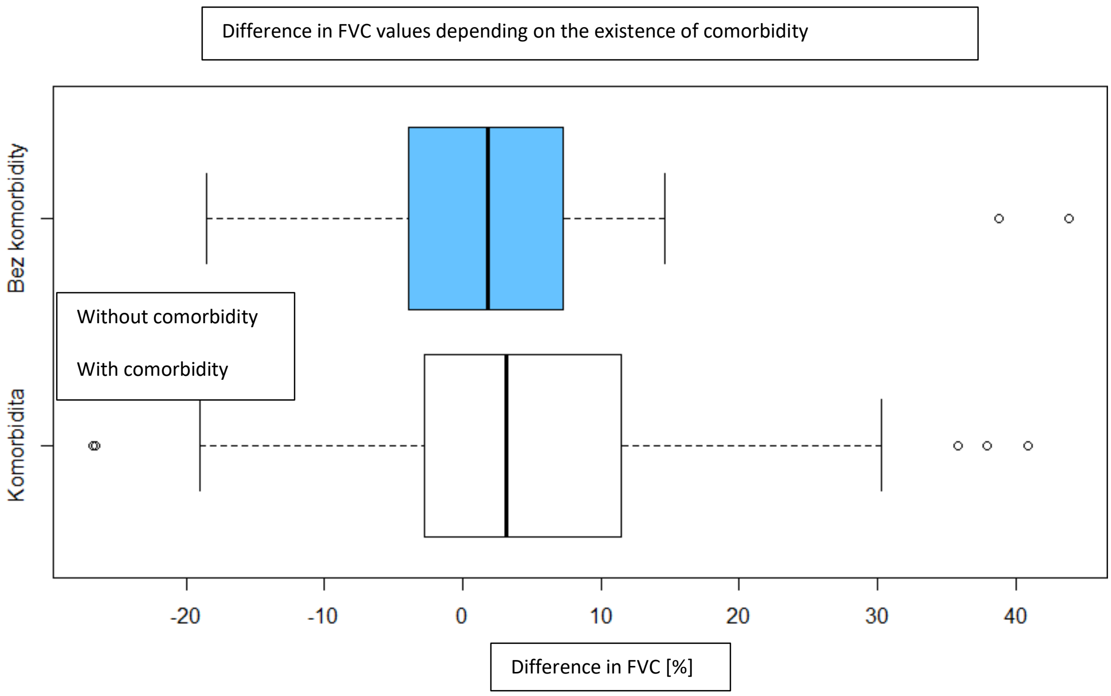


Figure 36: FVC - Boxplots, differences in the 6MWT values depending on the existence of comorbidity

	Min	Max	Mean	Median	p-value
Comorbidity	-27 %	41 %	4 %	3 %	0.6695
Without comorbidity	-19 %	44 %	5 %	2 %	

Table 25: FVC - Basic characteristics of the changes in the % according to the existence of comorbidity and the resulting p-value of the Mann-Whitney test

Therefore, we performed a more detailed analysis using ANOVA. The results are presented in Table 26. As we can see, in neither case the *p*-value is lower than the significance level, none of the factors analysed, so individual comorbidities, have significant effect on the value of the change in FVC after the spa stay.

FVC	Df	Sum of Squares	Mean of squares	F-value	p-value
Diabetes mell	1	0.019	0.019	1.071	0.304
Obesity	1	0.035	0.035	1.948	0.167
High blood pressure, cardio	1	0.004	0.004	0.240	0.626
Bronchitis, COPD, asthma	1	0.000	0.000	0.008	0.929
Without comorbidity	1	0.036	0.036	2.022	0.159
Diabetes mell: Obesity	1	0.038	0.038	2.140	0.147
Diabetes mell : High blood pressure, cardio	1	0.028	0.028	1.563	0.215
Obesity: High blood pressure, cardio	1	0.007	0.007	0.371	0.544
Diabetes: Bronchitis, COPD, asthma	1	0.000	0.000	0.023	0.879
Obesity: Bronchitis, COPD, asthma	1	0.001	0.001	0.050	0.824
High blood pressure, cardio: Bronchitis, COPD, asthma	1	0.033	0.033	1.872	0.175
Diabetes mell : Obesity: High blood pressure, cardio	1	0.016	0.016	0.902	0.345
Diabetes mell : High blood pressure, cardio: COPD, bronchitis asthma	1	0.015	0.015	0.832	0.364
Obesity: High blood pressure, cardio: bronchitis, COPD, asthma	1	0.010	0.010	0.546	0.462
Residuals	84	1.493	0.018		

Table 26: FVC – ANOVA, influence of comorbidities

Graphical results are presented in the boxplots, see Figure 37.

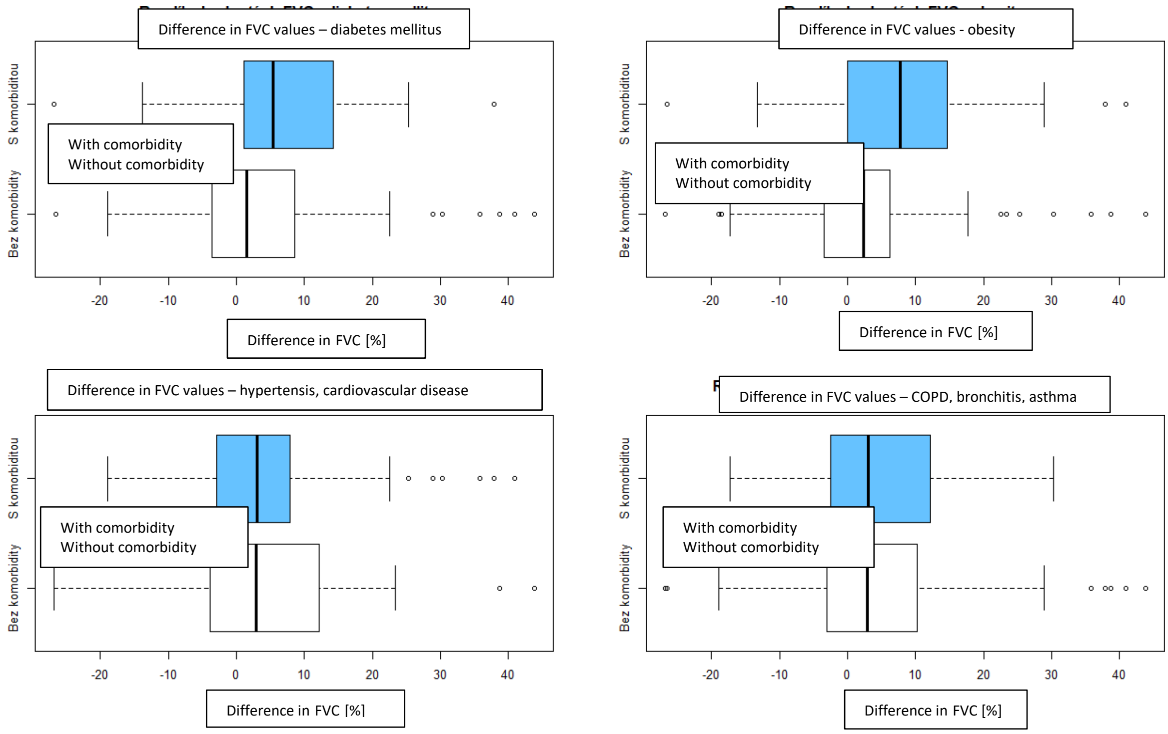


Figure 37: FVC– Boxplots, the influence of individual comorbidities

Summary

There was confirmed the statistically significant change in the FVC values after experiencing the spa stay. On average, this value in the probands increased by 4.5%. Thus we can say that after experiencing the spa stay, the maximum value of air which can be sharply exhaled after maximum inspiration significantly increased, so the treatment had a positive effect.

This effect is independent on gender, age of the probands or the time elapsed between experiencing Covid-19 and the admission to the spa. None of the comorbidities analysed had an effect on the change in FVC values after the spa stay.

Conclusion and Recommendations

The physical fitness test (6MWT) proved a positive change after the spa stay. Based on the evaluation, we concluded that the patients walked statistically more meters after the spa therapy than before the stay, thus their physical fitness demonstrably improved. At the same time, we proved that the distance walked was close to the standard, i.e. to the values that the patients should properly achieve. Before the stay, the average distance walked and its median were lower than they should have been.

In case of the **Borg score**, a statistically significant change was proved for the better after the spa stay. Thus, a rate of breathlessness demonstrable dropped in the patients after experiencing this therapeutic programme.

In case of the **SpO2** values no statistically significant change in the values measured before the physical fitness test was noticed after the spa stay. The values measured after the physical fitness test showed the same result, however, due to the *p*-value close to the significance level, we recommend to follow this variable further in further studies to make a clear decision.

A statistically significant change in **FVC** was confirmed after the spa stay. It means that after only 3 weeks, the maximum volume of air exhaled after maximum inspiration increased significantly. In the scope of the follow-up study, we recommend to measure and analyse this parameter also 3 months after leaving the spa to verify a long-term effect of the spa stay. **To obtain further results, we recommend recording not only the FVC parameter but also FEV1 during spirometry.**

For all variables, we calculated the percentage differences in the results before and after the treatment, i.e. By how many % the patients improved or worsened with individual parameters. The analysis shows that these changes do not depend on gender in any case, thus men and women improve/worsen equally.

In case of the analysis of the dependence of these changes on age, it turned out in the majority of cases, that it does not matter, i.e. all age groups improve/worsen equally after the stay. The only exception is SpO2 measured after the physical fitness test. In this case, there is a weak dependence on age, i particular, the SpO2 values improve more in younger people. **However, as this dependence is not strong, it would need to be further investigated in further studies to confirm or reject it unequivocally.**

Another variable, of which influence on the changes in the values of the measured parameter was analysed was the time between experiencing Covid-19 disease and the admission to the spa therapy. There was a weak dependence only in case of the 6MWT test results showing a possible negative correlation, i.e. the difference between the value before and after the spa stay decreases with increasing number of days since the disease. In other words, the probands, who arrived at the spa after a longer period of time after disease (after about 135 days) do not show as good results as those who arrived earlier. **This statement would need to be investigated in future studies, as there is not a large number of probands in our study population entering the spa after 135 days.** In case of other parameters measured, no evidence of an effect of the time between disease and the admission to the spa on post-stay results.

The last effect we analysed was the influence of comorbidities and their combination on changes in measured parameters before and after the spa stay. In all cases, the general hypothesis of a difference between the probands without comorbidity and the patients with any comorbidity was not confirmed. This could be caused by the fact that we had only 15 probands without any comorbidity in our research group. Due to this, we used for the detailed analysis so-called variance analysis (ANOVA) which was used to analyse the influence of individual comorbidities and their combination on the change in the values of the parameters measured, i.e. if the existence of any comorbidity significantly affected the treatment results. In the scope of this analysis, when evaluating the 6MWT test, obesity was found out statistically significant. **in the scope of the subsequent study, to confirm or reject the influence of obesity on FVC it would be suitable to monitor the dependency of the changes on these parameters in the patients' BMI.** In next cases, no statistically significant influence of some comorbidities was proved.

Based on the study we can state that the comprehensive spa rehabilitation treatment in Mariánské Lázně is an effective therapeutic procedure providing the improvement of physical, mental, social and work abilities of the patients. There is a significant positive influence on post-covid complications, namely pulmonary functions and drill of correct daily regimen, including breathing. Referring the patients to the spa treatment within 4 months from the beginning of disease appears as a very short time because the complications after experiencing COVID-19 disease persist for a year.

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