Summary

Introduction

Sleep-related breathing disorders are widespread in general population. The estimated prevalence may vary from 22% of men to 17% of women. Obstructive sleep apnea syndrome (OSAS), which is responsible for more than 90% of sleep-related breathing disorders, is a disease caused by episodes of airways repeatedly collapsing (causing hypopnea and apnea) at the level of the pharynx and larynx, while the respiratory muscles continue to work.

There are tools which we can use to diagnose OSAS – the so called gold standard - polysomnography, and simpler in use, though still not widely available – polygraphy. There are also other methods – for example standardized questionnaires that are used in the screening process of sleep-related breathing disorders.

The risk assessment of sleep-related breathing disorders, performed as an additions analysis during routine Holter ECG monitoring, may be clinically relevant in early diagnosis, and thus in more effective treatment of sleep-related breathing disorders, which are an independent risk factor, e.g. cardiovascular diseases (inadequate control of the treatment of arterial hypertension) or social problems including, among many, persistent daytime sleepiness, especially when operating a vehicle.

Aims

The following aims were established:

1. The assessment of the sensitivity and specificity of the analysis of sleep-related breathing disorders using a 24h Holter ECG system in comparison to the reference method - polygraphy.

2. The assessment of factors influencing the probability of analyzing sleep-related breathing disorders, clinical usefulness and factors influencing reliability of the method (as a screening tool).
3. The assessment of the frequency with which a 24h Holter ECG analysis indicated the possibility of significant sleep-related breathing disorders in consecutive patients diagnosed with cardiovascular diseases, taking into account factors that may limit analysis as well as those affecting the reliability of the results.

Material and methods

To achieve the set aims, the study was carried out in two stages, with the separation of two different research groups - **study population A** and **study population B**. In total, 422 patients were enrolled in this prospective study.

Study **population A** consisted of 206 patients for whom polygraphy registration was performed simultaneously during Holter EKG registration. Similarly for the AHI index - the apnea and hypopnea index (polygraphy), the so called estimated AHI - eAHI were evaluated at the same time.

Study **population B** included 216 patients, treated or diagnosed for cardiovascular diseases. Considering the factors limiting the assessment of eAHI (data from population A), the study was designed to assess the potential scale of the prevalence of sleep-related breathing disorders among cardiac patients. Additionally, the patients were screened for sleep-related breathing disorders through the use of the Berlin Questionnaire.

Results

Population A

The study group consisted of 206 patients. 58% of patients (n = 120) were male, 42% were female (n = 86). The age range for the study group ranged from 18 to 86 years (M = 54 years, SD = 15.8), and the BMI value from 18.3 to 46.5 (M = 28.3, SD = 4.6). The mean AHI in the study group was 16.6 (SD = 15.9), and the mean eAHI was 21.7 (SD = 17.0). In the study group, 10% of patients (n = 20) suffered for permanent atrial fibrillation.

In the study group 30% of patients had mild, 23% moderate, and 18% severe sleep-related breathing disorders. 30% of patients did not have any sleep-related breathing disorders (AHI <5). In order to assess sleep-related breathing disorders by using 24h Holter ECG, it was assumed that the main aim was to detect moderate and severe breathing disorders - AHI> 15.

Two results should be noted:

- the mean AHI and eAHI scores in the study group are different: the mean AHI in the study group was 16.6 +/- 15.9, and the mean eAHI was 21.7 +/- 17 (p <0.0001),

- correlation analysis shows a moderate, on the border of high correlation, relationship between the AHI index and eAHI (r = 0.52; p <0.001).

Results above indicate that the two methods can not be used as equal. Particularly noticeable was the high percentage of false positive results - 26%, while only 8% were false negative (sensitivity 81%, specificity 55%). Due to higher mean values of eAHI in relation to AHI, the threshold value of eAHI> 20 was additionally considered (instead of the classic cut-off point of AHI> 15 in polygraphy). Thanks to that, the rate of false positive results was reduced to 19%, and false negative was 12% (sensitivity 70%, specificity 67%).

The factors influencing the occurrence of false positive results were analyzed, taking into account eAHI> 20. By using one-way analysis of variance it was proven that age of the patients (the younger the patient, the higher the risk of a false positive result - OR = 0.98 (95% CI 0.06-0.99), p = 0.040); body mass index - BMI (the lower the index, the higher the risk of a false positive result - OR = 0.89 (95% CI 0.82-0.97), p = 0.013) and the total number of arrhythmias per day in 24h Holter ECG were significant. Each 1000 extrasystoles increased 1.1-fold risk of qualifying for the false-positive group (OR = 1.1 (95% CI 1.07-1.18), p = 0.0001). In the multivariate analysis, the BMI (OR = 0.90 (95% CI 0.82-0.98), p = 0.028) and the total number of arrhythmias in 24h Holter ECG were significant (OR = 1.12 (95% CI 1.06-1 , 18), p = 0.0001).

Due to the significant adverse effect of arrhythmia on the eAHI results, in the next stage of the analysis, patients with the number of additional beats above five thousand / day were excluded from the analysis - 45 patients. In multivariate analysis, the number of arrhythmias still remained a risk factor for a false positive result (OR = 2.26 (95% CI 1.5-3.3), p = 0.0001). Using the eAHI limit above 20 and excluding patients with the number of arrhythmias over five thousand / day, the sensitivity level was achieved around 70%, the specificity significantly improved to 77%. Overall analysis with the use of 24h Holter ECG allowed in such patients, an effective exclusion of sleep-related breathing disorders in 77%, and confirmed in 70%. However, caution is advised in the interpretation of studies in patients with coexisting arrhythmias above one thousand / day.

Population B

216 patients were included in the study. 51% of patients (n = 110) were male, 49% were women (n = 106). The age range for the study group ranged from 19 to 90 years (M = 58 years, SD = 16.2), BMI value from 17.5 to 38.3 (M = 26.5, SD = 8.6), and the neck circumference range from 30 up to 50 cm (M = 38.5 cm, SD = 3.9).

Sixteen patients, due to the high percentage of stimulation from the previously implanted device (in 15 patients the stimulation rate above 98%, in 1 patient 36% - mainly nocturnal stimulation), were excluded from the analysis due to the inability to assess eAHI for technical reasons (result eAHI = -1.0).

Among remaining 200 patient 50% of the respondents (n = 100), have been previously diagnosed for arterial hypertension. In 89% of patients (n = 178) the basic rhythm was sinus rhythm and 22 patients (11%) had permanent atrial fibrillation.

Out of 200 patients, in 20 patients the total number of arrhythmias exceeded five thousand per day, which excluded them from the analysis of the potentially having sleep-related breathing disorders. In total, 180 patients were assessed in this stage of study, for eAHI.

29% of patients (n = 52) scored eAHI > 15, which may indicate sleep-related breathing disorders in moderate or advanced stage. In the case of eAHI> 20, clinically significant sleep-related breathing disorders may be suspected in every fourth patient in the study group (n = 44).

In addition, the relationship between eAHI with other clinical data was assessed and the results can be summarized as follows:

1. Estimated AHI, obtained from the Holter EKG analysis, is a tool which, to a significant extent like the AHI index (from polygraphy), correlates with similar risk factors for obstructive sleep apnea: advanced age, male gender, obesity, increased neck circumference.

2. There was a significant correlation between symptomatic patients (objectification of symptoms using the Berlin Questionnaire) and the severity of eAHI. The link between high risk of sleep-related breathing disorders assessed by using the Berlin Questionnaire (score higher than or equal to 2 points) and the severity of eAHI (M = 18.3; SD = 16) compared to patients with low risk of sleep-related breathing disorders in the Berlin Questionnaire - the result lower than 2 points - (M = 12.3; SD = 12.3), t (111) = -2.72; p = 0.008, Cohen's d = -0.52. The results indicate a moderate relationship.

3. A relationship has been shown between the presence of hypertension and the severity of eAHI (M = 18.1; SD = 15.9), compared to patients without hypertension (M = 10.6; SD = 10.5), t (171) = -3.96; p <0.001, Cohen's d = -0.62. The results indicate a moderate relationship.

4. In the study group, the severity of ventricular arrhythmias is associated with the severity of the estimated AHI index.

Conclusions:

1. The sensitivity and specificity of the analysis of sleep-related breathing disorders using the 24h Holter ECG analysis system is relatively high, indicating the possibility of using this method, especially to exclude the presence of sleep-related breathing disorders. The use of the eAHI > 20 as an indicator of significant sleep-related breathing disorders slightly improves the results of the analysis.

2. The presence of cardiac arrhythmias is a factor that significantly disturbs the reliability of the assessment of respiratory disorders using the 24h Holter ECG. The specificity of the results is significantly improved when the analysis is not performed in patients with a total number of arrhythmias greater than five thousand / day.

3. Taking into account the factors limiting the possibility of performing a reliable analysis of sleep-related breathing disorders using the 24h Holter ECG, it should be estimated that it will be possible in approximately 83% of patients taking a routine Holter monitoring. Under these conditions, significant sleep-related breathing disorders should be suspected in 24% of the respondents.