Repeatability of Sleep Apnea Detection in 48-Hour Holter ECG Monitoring

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Background: There is a significant relationship between obstructive sleep apnea (OSA) and cardiovascular diseases. Reliability of new methods evaluating apnea in Holter ECG monitoring is still the matter of investigators' studies.

Methods: In 48-hour Holter ECG monitoring recordings of 63 patients, we assessed repeatability, comparing the results from both sleep periods.

Results: We found good repeatability in evaluation of apnea-hypopnea index value. There was moderate agreement in three categories, that is, normal or borderline or apneic assignment. Assignment to "healthy" (normal and borderline) or apneic subgroup during consecutive sleep periods showed high repeatability.

Conclusions: Holter ECG monitoring is a repetitive method of preliminary diagnosis in patients evaluated for sleep apnea syndrome.

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Incidents of breathing disturbance during the night rest, with short-lasting but repeated significant reductions or cessations of airflow are called sleep apnea. There are three types of sleep apnea: central (when the respiration effort is weakened in neurological diseases, rare), obstructive (when flabby tissue of the pharynx collapses and forms obstruction, the respiration effort is enforced in order to restore the airflow), and mixed.

Apnea-hypopnea index (AHI), representing number of incidents per hour of sleep, is used to measure apnea. Usually $AHI \geq 15$ is considered as the marker of apneic sleep. Obstructive sleep apnea (OSA) concerns few percent of general population, but its prevalence rises with age, it is more common in diabetic, obese, cardiological patients, and in men.

There is a significant relationship between OSA and cardiovascular diseases:¹ coronary artery disease, myocardial infarction, heart failure, stroke, diabetes. OSA is one of the possible causes of secondary arterial hypertension, which may clinically present as resistant hypertension with nondipper profile and ESC guidelines recommend testing for

apnea in such cases.² Unfortunately, apnea is underdiagnosed because of the cost and scarcity of polysomnography—the "gold standard" examination. Recently, new methods of apnea assessment were designed. During apnea event and arousal, autonomic nervous system is stimulated and this causes modulation of heart rhythm. Thus, it is possible to extract data regarding apnea probability from ECG Holter monitoring. The index used in alternative diagnostic methods is called estimated AHI (est.AHI) in order to distinguish it from AHI obtained during polysomnography.

Reliability of new methods evaluating apnea in Holter ECG monitoring (HECGM) is still the matter of investigators' studies. We focused on one of the commercial programs, that is used in our clinic—Pathfinder with Lifescreen Apnea (Del Mar Reynolds). Lifescreen Apnea is useful for obstructive and mixed sleep apnea detection.

METHODS

Lifescreen Apnea calculates probability of apnea on the basis of RR intervals (time

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Figure 1. An example of a chart obtained from apneic patient. Probability of apnea is calculated for consecutive time intervals. On the x-axis is time, on the y-axis apnea probability. Darker bars mark apnea probability exceeding 50%, bright bars mark apnea probability below 50%. Above—estimated Apnea-hypopnea index for the whole sleep period (here—27.3).

measurements between the R waves of consecutive heartbeats) changes and ECG-derived respiration technique (EDR). As mentioned before, stimulation of nervous system leads to heart rhythm modulation and changes in RR intervals. Moreover, with chest respiration-related movements, when positions of electrodes move relative to the heart and impedance varies, the ECG signal amplitude changes. The program extracts this slow modulation signal, called EDR. The detailed description of the method was given by de Chazal et al.³ The probability of apnea sleep is calculated for consecutive one-minute intervals and then for longer intervals. Finally, the result is displayed on the graph (Fig. 1), where red bars on the chart mark probability greater than 50% and the est.AHI is calculated for the whole sleep period.

Est.AHI ≤ 5 is normal, result of est.AHI > 5 but ≤ 15 was considered as borderline and est.AHI > 15 as apnea.

We used 48-hour HECGM recordings of 63 patients. The patients had various indications for the examination so the group was clinically differentiated. We had surveys regarding sleep periods dur-

ing the examination from some of the patients. Otherwise, we observed heart rhythm trend and well-distinguished period of slower rhythm was considered the sleep period (Fig. 2).

We assessed three aspects of repeatability of sleep apnea detection in 48-hour Holter ECG monitoring:

- A) Raw est.AHI value.
- B) The repeatability of classifying the patient to three categories as having 1) normal sleep, 2) borderline sleep or 3) apnea sleep.
- C) The repeatability in defining "health" (category 1 and 2) versus apnea (category 3).

RESULTS

A) Mean AHI from first night was 18.6 ± 15 , from the second night— 16 ± 14 (Table 1). Linear Pearson's correlation coefficient between two outcomes was $r = 0.81$, $P < 0.001$. In order to assess repeatability, we used Altman-Bland method (Fig. 3). In this method, the differences between consecutive measurements are supposed not to exceed an

Figure 2. A well-distinguished decrease of heart rate on the trend chart during sleep period.

interval defined by value of the mean difference $\pm$ 2 standard deviations. The repeatability is good if 95% results are in mean $\pm$ 2SD interval—we obtained 96.83%.

B) Est.AHI categories from both nights were dependent variables (Spearman’s rank correlation coefficient $R = 0.79$, $P < 0.0001$). Chi-square test showed dependency of variables for the category assignment during consecutive sleep periods with $P < 0.0001$. Agreement between two measurements may be assessed using kappa (κ) Cohen’s coefficient. Kappa value 1 means full agreement, while kappa zero means agreement equal to random. In our group, coefficient κ was 0.514 that indicates moderate agreement in category assignment. In 43 (68%) cases the assignment was alike during both nights. In the rest of group, shifts limited to one category were observed. Specifically, 9 patients shifted from category 3 to 2, 7 patients shifted from category 2 to 1, 3 patients from category 2 were assigned to category 3 during the second night and one patient changed category from 1 to 2. (Table 2).

C) Assignment to “healthy” or apneic subgroup during consecutive sleep periods were dependent variables (McNemara test). The results from both nights are presented in Table 3. Repeatability of

health or apnea recognition was assessed using Cohen’s kappa coefficient. The value of kappa was $\kappa = 0.62$, which confirms the results were alike (high repeatability). In 51 cases (81%) the assignments were identical, 3 patients shifted from “healthy” subgroup to apneic, 9 patients shifted from apneic to “healthy” subgroup.

DISCUSSION

Polysomnography in an attended sleep laboratory has established the “gold standard” for apnea detection and for assorting treatment with evaluated sleep disturbances. The good repeatability of sleep apnea detection in polysomnography allows one night examination.⁴ However, even one night polysomnography is quite rarely applied in everyday clinical practice, because of its cost and scarcity. Many different simplified, ambulatory systems were therefore proposed in order to ease the presumptive diagnosis of apnea. Their usefulness is being compared with attended polysomnography,^{5,6} including the assessment of repeatability of the outcomes.

Ninety-nine selected participants of The Sleep Heart Health Study underwent two nights of unattended nonlaboratory polysomnography. All

Table 1. Results of Estimated Apnea-Hypopnea Index (Est.AHI) from Both Sleep Periods

	Mean	–95%CI	+95%CI	SD	Min	Max	Median
Est.AHI 1st night	18.59	14.70	22.49	15.45	0.60	63.90	14.50
Est.AHI 2nd night	16.03	12.39	19.68	14.47	0.00	59.80	11.20

Figure 3. Altman-Bland method. Over 95% of differences between two consecutive measurements are within interval defined by value of the mean difference ± 2 standard deviations.

studies were performed in participants' homes (in 3 cases—in motel room). However, the recording montage was complicated and included electroencephalogram, electrooculograms, electromyogram, thoracic and abdominal movement, oxymetry, ECG, body position, ambient light sensor. The interval between consecutive examinations was up to 4 months. The authors observed a high level of agreement between two examinations performed several months apart.⁷

Oldenburg et al.⁸ conducted in-hospital cardiorespiratory polygraphy in 50 patients with congestive heart failure. Nasal air flow, chest and abdominal effort, pulse oxymetry, and body position were recorded. The authors found high reproducibility of cardiorespiratory polygraphy recordings, especially in patients with clinically relevant sleep disordered breathing (AHI > 15).

There were also attempts of using, for example, a portable device with oxymetry, heart rate detection on the basis of single-lead ECG, microphone and body position detector.⁹ Nevertheless, these methods seem still too complicated to become a widely

used tool in everyday practice.¹⁰ We believe that methods based on Holter ECG monitoring have the potential to balance simplicity, reliability, accessibility and cost effectiveness.

A reasonable measurement error may and is accepted not only in novel HECGM-based methods, but also in polysomnography. The "gold standard" also has some repeatability limitations. The problem of possible differences in the quality of sleep during consecutive sleep periods has been discussed from early studies in this matter. Mosko et al. reported that in some individuals clinical decisions based on one night would be very different depending on which of the three nights of examination they considered.¹¹ Ahmadi et al.¹² compared sleep apnea diagnosis based on single night versus two nights of polysomnography. From a total number of 193 patients, in 21% the difference in AHI was above 5. Moreover, 48% patients had significantly higher AHI in the first night examination, while 41%—in the second night examination. Using cutoff value of AHI > 15, apnea would be overlooked in 20% patients when assessed on the

Table 2. Categories from Both Sleep Periods

1st Night Category	2nd Night Category			Total
	1	2	3	
1	13	1	0	14
2	7	8	3	18
3	0	9	22	31
Total	20	18	25	63

Table 3. Health or Apnea Recognition from Both Sleep Periods

1st Night	2nd Night		Total
	"Healthy"	Apneic	
"Healthy"	29	3	32
Apneic	9	22	31
Total	38	25	63

basis of single night examination. The authors estimate that 13% patients may benefit from repeated polysomnography.

In spite of these limitations, the new methods are being compared with the "gold standard" when their accuracy in diagnosing apnea is assessed. And so, Ożegowski et al.¹³ conducted simultaneous polysomnography and HECGM in 74 patients, enrolled to the study using Epworth Sleepness Scale and "Poznań" Scale, regarding sleep disturbances and day-time sleepiness. These authors also used Lifescreen Apnea to evaluate apnea in HECGM. Polysomnography results were assessed using three categories of AHI like presented for est.AHI in our Methods section. The authors obtained 68% (50 patients) agreement in category assignment between HECGM method and polysomnography. Excluding patients assigned to the borderline category from analysis, HECGM method had the sensitivity of 91.2% and specificity 85.7% in comparison to polysomnographic apnea detection. When these patients were counted as apneic, sensitivity was 71.7% and specificity 89.3%. When these patients were counted as healthy—91.2% and 87.5%, respectively. The authors found a cutoff value of est.AHI > 17, which gave the best reliability of apnea detection in HECGM method. These data and our outcomes prove that Pathfinder with Lifescreen Apnea (Del Mar Reynolds) is a reliable tool, providing good agreement with polysomnography and good repeatability of obtained results. As mentioned before, there are other commercial programs offering apnea assessment, but our experience in using them is limited.

CONCLUSIONS

Holter ECG monitoring is a repetitive method of preliminary diagnosis in patients evaluated for sleep apnea syndrome. Twenty-four hour Holter ECG monitoring is a relatively cheap and widely available examination, thus it may contribute to reduction of undetected and untreated apnea cases.

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