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Original Article

Sleep apnea diagnosis using an ECG Holter device including a nasal pressure (NP) recording: Validation of visual and automatic analysis of nasal pressure versus full polysomnography

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ABSTRACT

Background: New simplified techniques for diagnosing sleep apnea should be specially tailored for easy use in cardiologic practice.
Objectives: e dedicated one of the channels of a Holter Electrocardiogram (ECG) device (SpiderView™ ELA Medical, France) to nasal pressure (NP) recordings. We also developed an automatic analysis of NP signal providing an apnea–hypopnea index (AHI) for physicians without the know-how in sleep medicine.
Methods: Thirty-four unselected patients referred for symptoms suggesting sleep apnea underwent a polysomnography (PSG) with simultaneous NP and Holter ECG recordings. An expert blinded to PSG results visually scored the Holter plus NP recordings. The results of the AHI obtained in PSG (AHI-PSG) were compared, respectively, to the AHI-NP obtained by visual analysis and automatic analysis (AHI-NP Auto) of Holter ECG nasal pressure.
Results: In 10 randomly selected subjects (development set), the best cut-off on Holter ECG for diagnosing sleep apnea patients as defined by AHI > 20/h in PSG was determined at 35 events/h by a receiver operator curve (ROC) analysis. Prospective testing of this threshold was then performed in 19 subjects (test set). For visually scored recordings of Holter ECG plus NP, we obtained a negative predictive value (NPV) of 80% and a positive predictive value (PPV) of 100% for sleep apnea. The area under the ROC curve was 0.97. For the automatic analysis, the NPV was 86% and the PPV value 100%. The area under the ROC curve was 0.85.
Conclusions: NP recording using a Holter system is an efficient and easy-to-use tool for screening for sleep-disordered breathing in routine cardiology practice.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) corresponds to recurrent episodes of partial or complete pharyngeal collapse occurring during sleep (hypopneas or apneas). It is a growing health concern affecting up to 5% of middle-aged men and women in the general population [1]. It is a critical issue for cardiologists as OSAS is independently associated with hypertension, arrhythmias and coronary heart disease occurrence [2]. Subjects with obstructive sleep apnea (OSA) have a peak in sudden death from cardiac causes during the sleeping hours [3] and exhibit an increased prevalence of fatal and non-fatal cardiovascular events [4]. Continuous positive airway pressure (CPAP), the first line therapy for obstructive sleep apnea syndrome (OSAS), has been demonstrated as effective for reducing fatal and non-fatal cardiovascular events in overall OSAS patients [4] and for improving cardiac function in OSAS patients presenting with cardiac failure [5].

Thus, OSAS is highly prevalent and associated with demonstrated cardiovascular morbidity and mortality. As CPAP, the reference treatment of OSA, is effective and widely available, diagnostic capabilities have to be developed. Sleep apnea diagnosis is primarily based on the expensive, labor intensive and time-consuming PSG, requiring access to expert centers with sleep physicians and technicians. This contributes worldwide to unacceptable waiting time for treatment initiation (from 2 to 60 months) [6]. Simplified alternative diagnosis procedures are therefore strongly encouraged [7]. Limited number channel

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recordings using, as a single signal or in combination, SaO_2 (nocturnal oximetry) [8] and/or NP measurements have been proposed [9]. NP allows us to accurately identify flow amplitude reductions and to separate central versus obstructive events. The "flow-limited aspect" of the inspiratory part of the flow curve is specific of increases in upper airway resistance and allows identifying obstructive versus central events. A recent study has demonstrated that NP associated with SaO2 provides the potential for reliable diagnosis and exclusion of OSAS [10].

Among these simplified techniques for diagnosing sleep apnea, some should be specially designed for and tailored to clinical cardiologic practice. Holter ECG recording is one of the most frequent investigations required in cardiologic routine [11]. Thus we decided to dedicate one of the channels of a classical Holter ECG device (SpiderView™ ELA Medical, France) to NP recording. As cardiologists are not familiar with NP signal, we also developed a specific automatic analysis of this signal providing a count of the respiratory events, expressed per hour of recording (AHI) for the non-expert physicians.

The aim of our study was thus to assess the capability of this ECG Holter device including NP for sleep apnea syndrome recognition. The validation of visual and automatic analysis of NP was done against PSG.

2. Methods

Patients referred to the Grenoble University Hospital sleep laboratory with symptoms suggesting OSAS were consecutively included. All patients underwent a full PSG and, simultaneously, ECG/nasal pressure Holter monitoring. Using a T-deviation system, the airflow NP cannula was the same for both systems.

This protocol was reviewed and approved by the institutional review board of the Grenoble University Hospital. None of the participants received compensation for their participation in the study and all of them gave written consent.

2.1. Polysomnography analysis

PSG included airflow measurements using both nasal cannula and thermistors. Respiratory efforts were assessed using thoracic and abdominal movements and pulse transit time. Sleep stages were scored according to Rechtschaffen and Kales' criteria [12]. Micro-arousals were recognized following the AASM rules [13]. Apnea episodes were defined as airflow amplitude less than 10% of baseline and lasting more than 10 s. Hypopneas required a more than 50% airflow amplitude decrease or a 30–50% airflow reduction associated with a micro-arousal or a 3% oxygen desaturation [13]. Apneas and hypopneas were classified as obstructive based on the presence of or an increase in respiratory efforts. The inspiratory flow limitation pattern associated with obstructive events corresponded to a "plateau" aspect of the inspiratory flow curve ending by a micro-arousal or returning to a rounded aspect of the flow curve.

AHI was defined as the mean number of detected events per hour of recording – not per hour of sleep as defined in PSG, because the Holter ECG and the NP recording device do not give information about total sleep time. On PSG abnormal respiratory events were scored only when the electroencephalogram (EEG) showed sleep.

2.2. Holter recording (Fig. 1)

We used the ELA MEDICAL Holter recorder system: Spiderview™. We recorded three channels of ECG and one channel of NP (sampling rate 1000 Hz) during the night concomitantly to PSG.

2.3. Visual analysis of nasal pressure signal

The Holter recordings were read with Synescope™ and were exported in the ISHNE format to SynelabSAS (ELA Medical software). This software can read ECG signals and also NP signal. The user easily visualizes all the patient recordings and can change amplitude of each signal independently.

The Holter recordings were scored by a sleep expert blinded to polysomnographic results. While viewing only the airflow signal and ECG, respiratory events were identified. Apneas were scored when the airflow signal amplitude was less than 10% of baseline during at least 10 s. Apneas were scored as obstructive when inspiratory flow limitation was identified on the respiratory cycles preceding apnea occurrence. Hypopneas were identified in one of the following situations:

- When the airflow amplitude on NP recording was less than 50% of baseline during at least 10 s.
- When there was a discernable reduction in NP amplitude ended by an autonomic associated micro-arousal (significant acceleration of the heart rate (i.e., +20 bpm) [14] visible on the ECG) or ended by the occurrence of a big breath on NP recording with a sudden resolution of the flow limitation shape.

Then AHI was calculated for each recording as the number of apneas and hypopneas per hour of recording in NP.

2.4. Automatic analysis of nasal pressure

The same Holter recordings were analyzed with SynelabSAS providing an algorithm automatically detecting respiratory events. Square root of the NP signal was used for analysis. A calculation of period, inspiratory surface and maximal amplitude of the respiratory cycles was then initiated. An apnea was defined by NP signal amplitude reduction of at least 80% compared to the five previous valid cycles with at least 10 s duration. A NP reduction of at least 50% compared to the five previous valid cycles lasting at least 10 s defined hypopneas. A maximal duration for events was accepted until 120 s. This allowed us to discard artefact events explained by loss of NP signal. Analysis of heart rate swings and recognition of inspiratory flow limitation were not implemented in the version of the software. Then, automatic analysis did not allow separating central and obstructive events.

Then AHI was calculated for each recording as the number of apneas and hypopneas per hour of recording (AHI-NP Auto).

2.5. Statistical analysis

Statistical analysis was performed to evaluate the ability of the NP signal included in the ECG Holter and the ability of the derived automatic analysis to identify abnormal respiratory events during sleep. The diagnosis of OSAS for both methods was compared to the gold standard PSG. The subject was considered as having the disease when exhibiting an AHI on PSG equal or above 20/h of recording.

The relationship between PSG and Holter ECG results was investigated by correlation analysis (Spearman test). Bland and Altman plot [15] was used to compare the measurement techniques. In this graphical method the differences between the two compared techniques were plotted against their averages. Bias and variability in the index were evaluated by calculating the mean difference together with its 95% confidence interval.

2.6. Development set

Ten subjects were randomly selected to determine the best cut points for AHI-NP and AHI-NPAuto. A ROC was constructed for