Dynamic Analysis of Multi Lead ECG Recordings for Detection and Categorization of Respiratory Events during Sleep

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Abstract

Our study compares three methods for extraction of respiratory information from single- and multi-lead ECG (QRS-area, Lead-pair loop-area/angle and vector-loop alignment). Polysomnograms and 8-channel Holter-ECGs were simultaneously registered in 90 patients. In 469 segments of 1-5 min duration (total duration: 1553 min), we assessed the similarity of ECG-derived signals with respiratory movements and air-flow by correlation analysis. Moreover, the accuracy for second-by-second detection of central apnea was determined by means of ROC-analysis. Our results show that multi-lead information can substantially improve the quality of ECG-derived respiration. Angle and area of the 2D-QRS-loop spanned by pairs of two leads provided the most consistent and robust estimates, especially in the presence of arrhythmia. Detection of central apnea from the median envelope of the lead-pair loop-angles was possible with 85% sensitivity and 89% specificity.

1. Introduction

Inspired by the CinC-Challenge 2000, detection of sleep apnea from the electrocardiogram has attracted considerable research interest in recent years [1]. However, mostly single-lead ECGs have been available or analyzed in this context. Moreover, only few studies address the problem of delineating single respiratory events or characterizing them with respect to obstructive or central origin.

Our study compares three methods for extraction of respiratory information from single- and multi-lead ECGs with respect to similarity of the estimated signals to measured respiratory movements and air flow. Moreover, their suitability for second-by-second detection of central apnea - i.e. absence of respiratory activity - is assessed by means of ROC-analysis, and the influence of arrhythmia on detection accuracy is studied. Finally, potential indicators of obstructed breathing are discussed.

2. Methods

In 90 patients referred to a sleeping lab for polysomnography (PSG), 8-channel Holter-ECGs (sampling rate 1 kHz, leads I, II, V1-V6) were simultaneously registered over night and mutually synchronized. From all patients, we selected a total of 469 segments of 1-5 min in duration containing a broad variety of normal and pathologic respiratory activity. Within these segments, the PSGs were annotated for occurrence of central apnea (CA) with 1s-accuracy. The total duration of the segments was 1553 min with 60 min labeled as central apnea. 58 of the 469 segments contained severe cardiac arrhythmia like atrial fibrillation or extensive ectopy.

For further analysis, we extracted respiratory flow and thoracic and abdominal movements (measured with two strain belts) from the PSGs and used these as gold standard against which the ECG-based respiratory estimates were compared by mutual cross-correlation.

We implemented three methods for extraction of respiratory activity from the ECG. All depend on the QRS-region and provide a set of respiratory estimates dependent on the number of available leads or lead pairs. Parameters derived from ectopic beats were replaced by interpolated values (except for arrhythmia absoluta during periods of atrial fibrillation).

The ECG-derived respiration (EDR) method [2] for single-lead ECGs tracks changes of the area under the QRS-complex. Here, it is calculated for each lead i ∈ {I, II, V1 - V6} and each heart cycle k in a window of 150 ms around QRS-trigger Θ_k of beat # k

$$QRSA_{lead\_i}(k) = \frac{1}{151}\sum_{n=-75}^{75}\left|ECG_{lead\_i}(n+\Theta_k)\right|$$

In a multi-lead variant, EDR makes use of lead pairs to estimate the mean cardiac electrical axis. The original article [2] employs the arctangent of the ratio of QRS areas in two leads. In our study, we use the loop

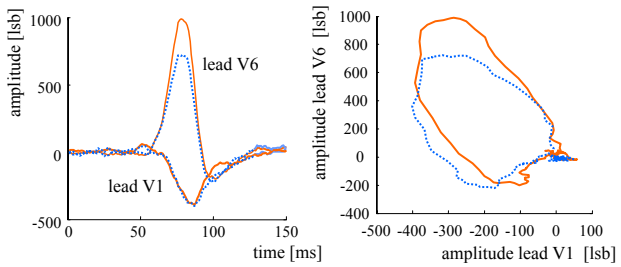

Figure 1. Loops of lead pair V1 and V6 for the QRS-complexes of two heart cycles (solid line and dotted line). Respiration introduces a shift of angular loop orientation as well as a change of the loop area.

spanned by pairs of two leads, which undergoes changes in angular orientation as well as in loop area during respiration (Figure 1). The loop angle of a lead pair (LPLAn) is estimated as the arctangent of the slope of a least-squares-fitted line to the loop. The respective area (LPLAr) is calculated employing Green's theorem. The procedure is performed for all possible lead-pairs resulting in (8x7)/2 = 26 respiratory estimates for LPLAn and LPLAr.

A third method, vector-loop alignment (VLA, [3]), is based on reconstruction of the orthogonal vector-cardiogram from the recorded eight leads using the inverse Dower matrix. A reference 3D-XYZ-loop is selected (in our case the median of X, Y, Z-lead), and the vector loops of each heart cycle are individually transformed to optimally align with the reference loop. Beat-to-beat variations of the respective alignment parameters – a scaling-factor alpha and three rotation angles phiX, phiY, phiZ – are known to be modulated by respiration and have been used for tracking of the respiratory frequency during stress test.

All irregularly-spaced respiratory estimates were interpolated using cubic splines, and then equidistantly re-sampled at 10 Hz. We correlated the estimates for each lead or each lead pair individually with the three measured respiratory waveforms. Prior to correlation, we high-pass filtered the signals using a Gaussian FIR-Filter with a width of 9.1s. This aimed at quantifying, to which extent the deflection of single breath cycles are mirrored in the respiratory estimates. Since during airway obstruction often paradoxical breathing is found (with out-of-phase movements between thorax and abdomen), we additionally extracted the envelope of the respiratory signals (Figure 2) and subjected the latter to cross-correlation. In both cases, we selected the modulus maximum of the normalized cross-correlation function within a delay window of ±1s to compensate for potential inaccuracy of synchronization between PSG and ECG.

For detection of CA, we down-sampled (1 Hz) the envelope of all respiratory estimates corresponding to the

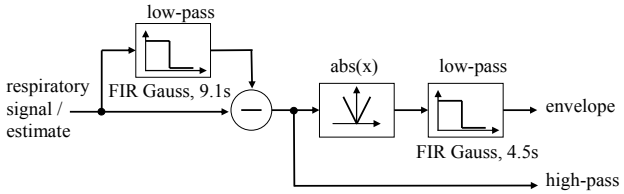

Figure 2. Derivation of the envelope of respiratory signals and estimates: after highpass-filtering (Gaussian FIR-Filter of with 9.1s, i.e. 91 coefficients) the signal is rectified and the modulus is again lowpass-filtered using a second Gaussian FIR-Filter of width 4.5s.

time-resolution of our CA-annotations. Then we calculated the median of envelopes of all leads (n=8) or all lead pairs (n=28) within each method, and used the second-by-second annotations to perform ROC-analysis. This yields one value of sensitivity, specificity and area under the ROC-curve (AUC) for each method. Additionally, the individual lead and lead-pair showing the highest correlation value with the measured respiratory signals were tested.

3. Results

Figure 3 shows exemplary time-courses for respiratory signals and their estimates during normal respiration as well as central (CA) and obstructive apnea (OA). All derived signals are clearly related to respiratory activity. During OA, respiratory efforts are obvious in the estimates and appear – except for the loop angle - more pronounced than in the recorded movements. During central apnea (CA) the variability is clearly reduced. Consequently, the occurrence of CA coincides with minima in the estimates' envelopes.

Figure 4 shows the results for the correlation of the estimates against measured respiratory waveforms. The bars in Figure 4 reflect the range of average correlation values for fixed leads or lead-pairs. The highest average correlation for both envelope and highpass-filtered signals, (up to 0.69) is obtained from the LPLAn-method (in leads I-V4) closely followed by LPLAr (0.67 leads I-V4), QRS-Area (0.67 for lead I). VLA exhibits the weakest overall agreement (<0.58). Generally, the highest correlation is found versus abdominal movements. In the envelopes, the lowest correlation is always found versus air-flow.

When the restriction to fixed leads or lead-pairs is abolished, the averaged maximal correlation values found within a record for any lead or lead-pair (dots in Figure 4) rise up to 0.86 for LPLAn. Here the lead-pair based methods apparently perform superior than QRS-area (0.81) or VLA (0.72).

Figure 5 summarizes the results for recognition of central sleep apnea from the different methods. When

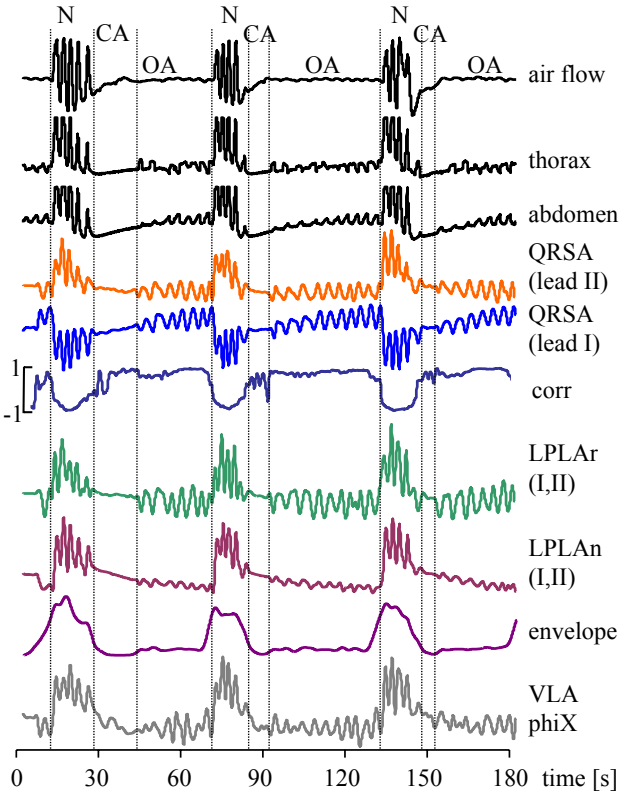

Figure 3. Exemplary time-courses of measured air-flow, thoracic/abdominal movements and ECG-based respiratory estimates as described in the methods. Additionally, the correlation of QRS-area in lead I and II, calculated instantaneously in a sliding window of 4.5s duration ('corr'), and the envelope of the loop-area between leads I and II is shown. Vertical lines indicate the transitions between different respiratory modes (N – normal respiration; CA – central apnea; OA – obstructive apnea).

severe arrhythmias are excluded, and the median of the envelope of all available leads or lead pairs is considered, loop angle (AUC=92.0), loop area (92.6) and QRS area (91.7) perform comparable with respect to AUC. The best positive predictive accuracy, however, is obtained from LPLAn owing to its higher specificity (89.3%) compared to QRS-area (86.3%) and LPLAr (85.9%) with still good sensitivity (84.9%). When arrhythmias are included, the performance of all methods decreases. However the decrease is less for the loop-based methods compared to QRS-area.

On the other hand, when only single leads or single lead pairs are considered, the QRS area in lead I outperforms the loop area and especially loop angle in lead-pair I-V4 as long as there is no strong arrhythmia. Consistent with the correlation results, the lowest detection rate for central apnea is obtained from the envelope of the VLA parameters.

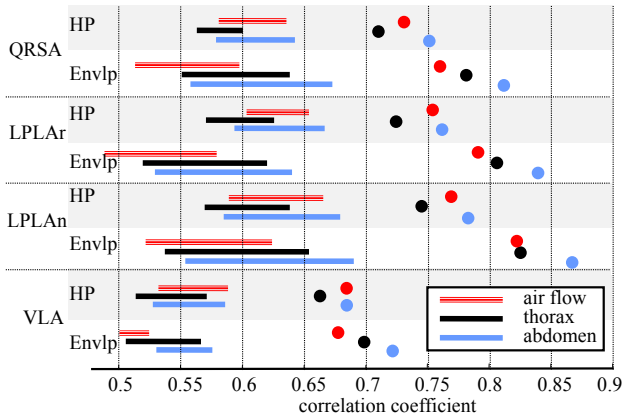

Figure 4. Range of average correlation for fixed lead/lead pair (bars) and average maximal correlation found within each record in any lead/lead pair (dots) for the methods considered in the study. Arrhythmic records (n=58) were excluded. Averaging is performed over remaining records (n=411). For each method, six bars and six dots are shown: three for the highpass-filtered signals (gray background) and three for the envelopes. Each triplet corresponds to correlation with air flow, thoracic and abdominal movements (see legend in lower right corner).

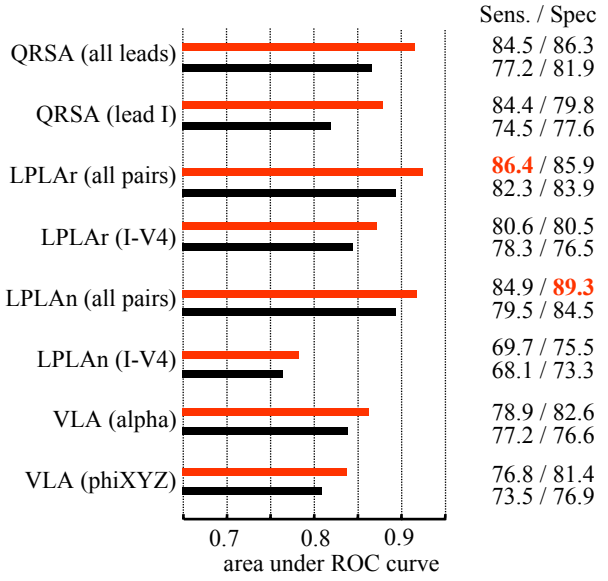

Figure 5: Recognition accuracy for central apnea from the envelope of the respiratory estimates. The length of the bars mirrors the area under the ROC-curve (AUC). Sensitivity and specificity are given as numbers. For each method, two bars are shown corresponding to exclusion (red) and inclusion (black) of records with arrhythmia. In brackets, the considered leads/lead pairs are given. When more than one lead/lead pair is indicated for a method, the median envelope has been used for ROC analysis.

Whereas in normal respiration thorax and abdomen move in-phase, this is often found to reverse during OA. This is known as 'paradoxical breathing'. We observed a manifestation of this phase-reversal phenomenon in the modulation of the ECG. Figure 3 shows the time-course of QRS-area for leads I and II as well as their correlation coefficient calculated instantaneously in a sliding window of 4.5s duration. It is obvious that during obstructed episodes the QRS-area of both leads varies in-phase whereas in normal respiration there is an out-of-phase relation in magnitude of the leads. This clearly separates normal from obstructive activity. We observed this phase-shift phenomenon in several recordings and also in loop- and VLA-parameters. However the lead-pairs were not stable across patients and owing to the lack of reliable annotations for obstructive events we were not able to address the problem statistically.

4. Discussion and conclusions

One question addressed by our study is whether there exist 'universally' superior leads or lead-pairs which are applicable for detection of respiratory activity in all patients. From both Figure 4 and Figure 5 we clearly have to answer in the negative. There is a considerable discrepancy (up to ~0.2) between average correlation values for fixed leads (≤0.69) on one hand, and maximal correlation values found within a record for any lead or lead-pair (≤0.87) on the other (Figure 4). This clearly calls for patient-specific selection of leads. The optimal choice is likely to depend on individual heart axis orientation and breathing pattern (abdominal vs. chest) but will presumably also change with body position during sleep. Additionally, variations of intra-thoracic pressure, and associated accumulation and displacement of air and blood might - especially during obstructive episodes - cause rather anisotropic variations of thoracic impedance. This may provide an explanation for the comparatively poor performance of the VLA method (Fig. 4). Although we did not refine the VLA-results by repeated iteration, and the method is reported to be more accurate at higher sampling rates (3-4 kHz), it seems likely that the inherent assumption of isotropic modulation – the same scaling factor alpha is applied to all three leads X, Y and Z - is violated in the face of OA. Similarly, it is not clear whether the application of the inverse Dower matrix is appropriate in this setting. Overall, the variation of the loop angle LPLAn consistently produced the highest correlation values with measured respiratory signals, and the level of accordance achievable for perfect individually optimized lead selection (0.87) is encouraging. In contrast to [2], we generally observed higher correlation of EDR-signals with abdominal movements in our sample suggesting a predominant effect of abdominal activity on respiratory modulation of the ECG.

The results of correlation analysis are largely reflected in detection accuracy of CA from the median envelopes of the ECG-derived respiratory signals, although the difference in AUC is smaller than suggested by the correlation results (Figure 5). Notably, the median envelope of QRS-area achieves almost the same AUC as the two loop-based methods when strong ectopy is excluded. However, consistent with the correlation results, the best detection accuracy is obtained from the loop angle LPLAn owing to the highest specificity (89.3%); the difference of ≥3% is quite substantial in relation to the prevalence of 3.9% for CA in our sample. When arrhythmias are included, it is remarkable that the decrease in performance is smaller for the methods based on lead-pairs compared to QRS-area (Figure 5). This better robustness against ectopy is in agreement with our visual notion that estimates from lead-pair loops mirror respiratory activity more distinct than those from QRS-area of the same leads. Figure 5 again clearly documents the beneficial effect of considering multiple ECG leads. When restricted to a single lead (lead I) or lead-pair (I, V4), the performance decreases considerably for all methods, especially for the loop angle LPLAn.

We conclude that multi-lead information can substantially improve the reliability of ECG-derived respiration, and that in this setting, angle and area of the 2D-QRS-loop spanned by lead-pairs provide the most consistent and robust estimates, especially in the presence of arrhythmia. The key problem to be solved is the selection of appropriate lead combinations. Detection of CA by simply applying a threshold to the median envelope of all possible lead-pairs already achieves encouraging results of 85% sensitivity and 89% specificity which very likely can be improved to practically sufficient accuracy by more sophisticated techniques for lead selection. Finally, we observed a phase-reversal phenomenon in the interaction of respiratory estimates derived from different leads that seems related to paradoxical breathing and appears promising with respect to identification of obstructed respiration. Again, lead selection is the major issue here.

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