A Method for Assessing Significant Changes in Serial ECG Comparison

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Abstract

Our method for the evaluation of serial ECG records is based on the assumption that major intra-individual quantitative changes of ECG measurements are associated with the development of - or recovery from - pathophysiologic changes. The criteria for significant changes were derived from standardized twelve lead resting ECGs of 860 men and women, who were participants of a population-based survey and a two year follow-up study of the KORA Project Augsburg.

The ECG changes derived from repeated records by this approach were significantly associated with the individuals' history of cardiac disease.

1. Introduction

The conventional computerized ECG interpretation is primarily focussed on the analysis of single ECG records based on predefined more or less complex criteria, indicating whether measurements (single or in combination) exceed thresholds limiting the 'normal' range. The application of this approach in repeated ECG records derived from the same individual has mainly two limitations: (1) It may result in a change of diagnostic classification even in the case of minor changes in the ECG, or (2) the diagnostic classification may be identical even in the case of major quantitative serial changes of the ECG if the measurements do not exceed the predefined thresholds. In contrast, our approach considers major individual changes of quantitative ECG measurements as significant rather than deviations from measurements characterizing normality.

2. Methods

2.1. Study population

Our study is based on the standard twelve lead ECGs of 10 sec duration recorded in the population-based KORA study [1]. Baseline data was gathered from the KORA S4 study which included men and women aged 25-74 years. Two years after the initial S4 study we reinvestigated a subsample in the KORA Magic Control study; thus from 860 individuals follow-up ECG data was available. The ECG examinations in both studies were performed according to a standard protocol, after ten minutes resting in supine position. We applied detailed procedures of quality control especially with respect to signal quality conditioning and electrode positioning. All examinations were performed using the same equipment for data collection and analysis. Characteristics of the study population are shown in Table 1.

Table 1. Characteristics of the study population

ECG record pairs (N)	860
Sex (m/f) (%)	53.4/46.6
Age at the baseline examination	
m±s (years)	63.3±10.2
range (years)	25-74
Information about cardiac disease and ECG records of good quality (n)	764
Prevalence of cardiac disease (%)	16.6%

2.2. Computerized ECG analysis

Computerized ECG analysis of the 12 lead resting ECGs was performed using the Hannover ECG System (HES-Version 3.22-12). In a comprehensive international validation study the HES System turned out to be one of the programs with the best diagnostic performance [2], also providing superior measurement precision [3]. The HES System analysis considers all ECG cycles within a 10 second record to compute a representative cycle for final measurement estimates. This procedure minimizes measurement imprecision due to possible noise effects on single ECG cycles. All 12 leads are considered

simultaneously. The final measurement estimates consist of 216 variables which quantitatively describe the ECG morphology.

2.3. Criteria for significant serial changes

Criteria defining significant changes of quantitative measurements were derived from the distributions of the individuals' measurement differences. We focussed, according to clinical expertise, on 96 (of 216) measurements consisting of global measurements (heart rate, QRS duration, QTc interval, QRS magnitude, QRS angle, T magnitude, T angle) and lead specific measurements (durations and amplitudes of the QRS complex, ST segment, T wave and R/S amplitude ratios). The quantitative changes were primarily characterized by absolute measurement differences. With respect to heart rate and R/S amplitude ratios, relative changes were used.

The individual absolute change Δx of the measurement x was determined as follows:

$$\Delta x = x(t_2) - x(t_1) \quad (1)$$

t_1: point in time at the baseline examination
t_2: point in time at the follow-up examination

The individual relative change Δy_{rel} of the measurement y was determined as follows:

$$\Delta y_{rel} = (y(t_2) - y(t_1))/\max(|y(t_1)|,|y(t_2)|) \quad (2)$$

Measurement changes exceeding predefined percentiles - e.g. 99% as upper limit and 1% as lower limit (P1/P99) of the distributions of measurement differences - were considered significant. With respect to each variable we differentiated between a significant positive (towards pathology) and a significant negative (towards normality) change. The results presented here focus on positive changes.

Adjustment for the prevalence of significant changes was performed (a) using different thresholds (P1/P99, P2.5/P97.5, P5/P95), and (b) using different minimal numbers of measurement differences (e.g. ≥1, ≥2, ≥5) exceeding the variable-specific thresholds of the individual's ECG analysis.

To enhance robustness of the measurement-specific threshold estimates, we defined minimal requirements with respect to amplitude differences, i.e. we only considered differences ≥100 µV. We also excluded ECG measurements derived from records with reduced signal quality (high frequency noise levels ≥30 µV or baseline sway ≥300 µV/sec in any of the twelve leads) because of a possibly increased risk of measurement variability according to measurement imprecision.

The results of the intra-individual comparison were compared with the disease status derived from a standardized interview performed at the baseline examination considering the history of cardiac medication use, of cardiac disease or of cardiac surgery. A proband was classified as having the disease if any of these items was positive.

3. Results

With respect to a single variable, the prevalence of significant serial changes is by definition determined by the thresholds of the upper and the lower limit. As an example, Figure 1 shows the distribution of the probands' differences of QRS duration, the lower and upper limits according to different percentiles; e.g. changes of ≥16 ms were classified as 'significantly increased' using the P99 criteria, of ≥8 ms using the P97.5 criteria, and of ≥4 ms using the P95 criteria.

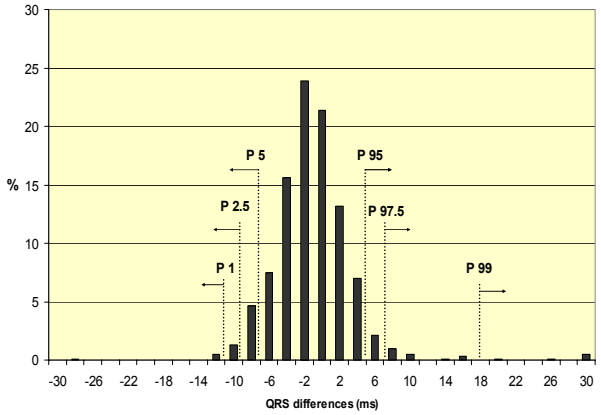

Figure 1. Distribution of differences of QRS duration and upper/lower limits defining ranges of significant deviations

The prevalence of significant changes on a multivariate scale considering 96 variables simultaneously is shown in Figure 2. The prevalence shows a wide range of variation depending on the thresholds (upper/lower limits) and the individuals' minimal number of measurement differences exceeding the thresholds. It ranges from 3.0% (≥5 measurements affected, P1/P99 thresholds) up to 69.5% (≥1 measurement affected, P5/P95 thresholds).

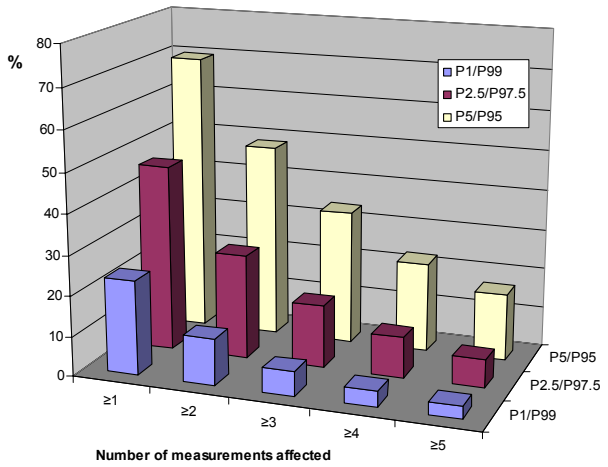

Figure 2. Prevalence of cases classified as 'significantly changed' by numbers of affected measurements and different thresholds (percentiles) for upper and lower limits.

The association between significant serial ECG changes and the independently derived information of cardiac disease is shown in Table 2. The cardiac disease status and ECG records of good quality was available from 764 probands. According to the P1/P99 criteria and n≥2 variables affected, the association was statistically significant (OR=2.76, p<0.01).

Table 2. Cardiac disease status from self-report vs. significant serial ECG changes (significant according the P1/P99 criteria and n≥2 variables affected (OR=2.76, p<0.01)

	Cardiac disease		
Serial ECG change	Positive	Negative	Total
Positive	25	52	77
Negative	102	585	687
Total	127	637	764

4. Discussion and conclusions

For several applications, e.g. monitoring of ischemia or monitoring of drug effects, serial analyses of repetitive ECG recordings have become a useful tool. These applications are focussed on the monitoring of specific ECG parameters (e.g. concerning the ST segment, QTc interval). In contrast, our approach considers a large amount of parameters simultaneously characterizing the ECG morphology for the quantitative ECG analysis on a multivariate scale to derive additional diagnostic information. Certainly, some general limitations according to physiologic factors (e.g. normal day to day variability), to technical factors (e.g. variation due to electrode position inconsistencies) [4] or to measurement imprecision according to noise exposure [5] have to be considered. However, in our approach these factors play a minor role, since our criteria are based on extreme deviations. Electrode position effects were minimized by our study protocol and a continuous quality monitoring. Nevertheless, our approach has some limitations: (1) The thresholds defining significant changes have primarily been defined from a statistical point of view. Further studies will be necessary to prospectively quantify each threshold. (2) To all variables considered the same diagnostic relevance has been attributed so far. (3) Due to our study design the criteria derived are based on population-based data of limited size. Refinement of the criteria can be derived from larger data bases, a prolonged follow-up interval providing more incident cases and also from clinically oriented populations with detailed description of cardiac events.

Despite these limitations, our approach showed significant associations with the probands' history of cardiac diseases. It obviously provides meaningful additional diagnostic information. In principle, these criteria can easily be implemented into current computerized ECG analysis systems if adequate algorithms providing precise measurements are available.

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