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Validation of digital Holter ST segment analysis

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To date, there are no reports on the reliability of ST segment measurements provided by real-time Holter systems using a standard electrocardiogram in identical leads as reference. Therefore we compared the fully automatically analysed ST segment values of a newly developed 24-hour Holter-monitoring device with those of a reference electrocardiogram at rest and during exercise. Patients' signals were simultaneously recorded from identical leads in both electrocardiogram devices. For real-time analysis the electrocardiogram was digitized into 128 points per second and the trigger signal of the QRS-complex was used to define the points to be measured on the isoelectric line and the ST segment. Seventy patients with sinus rhythm, no bundle branch-block and no frequent arrhythmias were enrolled. At rest, the mean values for the ST segments agreed very well (1.8 ± 0.7 mm for the reference electrocardiogram and 1.6 ± 0.7 mm for the Holter electrocardiogram). The correlation coefficient for linear regression analysis was 0.94. During exercise, the corresponding mean values were identical (1.7 ± 1.1 mm each). The correlation coefficient for the results obtained during exercise was also highly significant ($r = 0.95$). Our data indicate that with the real-time Holter monitoring system tested, ST segment measurements can be reliably obtained on a digital, fully automatic basis.

Introduction

The clinical importance of ST segment Holter monitoring for the detection of silent myocardial ischaemia during daily life and for the assessment of the extent of symptomatic episodes has become increasingly evident [1–14]. Whereas amplitude-modulated Holter systems have undergone substantial criticism [15–17], frequency-modulated tape-recorder/replay units are usually regarded as reliable for the detection of ST segment changes [16–20].

As the assessment of the ischaemic status during daily life requires several recordings in each individual patient, the use of these systems is rather time consuming. Therefore, Holter-monitoring systems with computerized real-time analysis of the ST segment are very promising. However, in a recently published state-of-the-art review of 11 real-time systems, this category of instruments was criticized because of the 'unproved ability of the available algorithms to analyse ST segments' [21].

We have validated a newly developed 24-hour Holter-monitoring device by comparing the fully automatic, real-time analysed ST segments to those of a simultaneously recorded reference electrocardiogram at rest and during exercise in identical leads.

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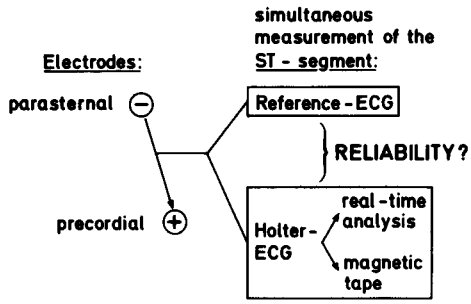

Figure 1. Schematic representation of the study set-up. Electrodes for the bipolar leads were attached proximally (negative) to the parasternal space and distally (positive) at precordial locations as described in the text. Patients' signals were simultaneously traced from identical bipolar leads. The ECG from the standard strip-chart recorder was used as a reference. The real-time Holter monitoring was performed with a system which represents a link between real-time analysis and the traditional tape recording. The magnetic tape serves for storage of the real-time analysed data and for retrospective full disclosure.

Patients and methods

In order to obtain a true reference-based comparison, patients' signals were simultaneously traced from identical bipolar leads in the frontal plane (figure 1). A standard strip-chart recorder (Cardiovit 3, Schiller, Switzerland; frequency range 0.05–85 Hz at −3 dB) was used for registration of the electrocardiogram taken as the reference. After the skin was abraded, standard silver–silver chloride electrodes were attached proximally to the second right and left parasternal intercostal space and distally at precordial locations as described below. The electrodes were connected with a coaxial cable to the inputs of the reference and the Holter electrocardiogram systems.

The real-time system used (Oxford Medilog 4000) represents a link between real-time analysis and the traditional tape recording: the four tracks on the tape (speed, 1 mm s^{-1}) are used for 24 hours continuous (amplitude-modulated) recording of two leads, the storage of the results of the arrhythmia real-time analysis (performed in both channels) and the results of the ST segment measurements (analysed in channel 1 only). The fourth track is used for the time and event markers. QRST complexes arising from premature beats or ventricular tachycardia are automatically excluded from ST segment analysis. The results of the ST segment analysis are given as the difference between the isoelectric line and the ST segment in millimeters. As the real-time analysis is performed immediately after the signals enter the Holter device, the problems which may arise from mechanical and electronic limitations of the magnetic heads in amplitude- and frequency-modulated tape-recordings are circumvented. The minicomputer used for real-time analysis has a 32 kB memory capacity, with 16 kB each available for the program and the electrocardiogram analysis. The frequency response of the digital part of the system is characterized by the range 0.07–70 Hz (at ±3 dB) [21]. The electrocardiogram signal is digitized into 128 points per second. The isoelectric line is measured at 56, 64 and 72 ms before and the ST segment at 96, 104 and 112 ms after the fiducial point. An averaging algorithm is then applied to both measurements using weighting factors of 1:2:1. After beat to beat analysis of each single ST segment, mean values are calculated for 30s intervals leading to a final effective temporal resolution of half a minute. The reference electrocardiograms were visually analysed by different observers who

were unaware of the result obtained from the fully automatic Holter device. These strip charts were recorded with a speed of 50 mm s^{-1} and a calibration of 1 mm = 0.1 mV. The exact time of registration as indicated by the Holter clock was noted on the strips to guarantee the synchronization of the corresponding ST segment evaluations. The reference electrocardiograms were uniformly analysed 60 ms before (isoelectric line) and 100 ms after (ST segment) the peak of the R-wave. Five consecutive beats were evaluated and averaged.

Seventy patients with sinus rhythm, no bundle branch-block and no frequent arrythmias were enrolled. As it was not the intent of this study to investigate silent myocardial ischaemia, the different underlying heart diseases have no meaning for the results and therefore are not listed. In 30 patients (with or without permanent ST segment abnormalities) the reference and Holter electrocardiograms were recorded simultaneously at rest in identical leads. For the two leads per patient registered, usually the V_2 and then the V_5 location were chosen as the distal electrode location. Two consecutive simultaneous registrations were obtained for 10 min each. Therefore 60 pairs of numbers were obtained in these 30 patients. Seventeen times the ST segment had a horizontal, 31 times an ascending and 12 times a descending shape. In 40 patients (with and without exercise-inducible ST segment depression) the reference and Holter electrocardiograms were recorded during ergometry and compared at peak exercise. During exercise, only one lead (distal electrode in V_5) served as simultaneous input for the Holter and reference electrocardiogram. In 15 patients the exercise-induced ST segment depression had a descending, in seven a horizontal and in 18 an ascending configuration. Exercise tests were performed on an electronically braked bicycle ergometer, which is self-adjusting and provides constant work-loads, in a semi-supine position (30° inclination). Exercise was started with 50 or 80 W and, if possible, increased automatically by a programmable computer (ELP 500; Bosch) by 30 W every 3 min.

For statistical interpretation a linear regression analysis was performed. Statistical analysis was performed by the two-tailed Wilcoxon's test for matched pairs with a probability (p) at the $p < 0.05$ level considered for significance. All mean values are given as the arithmetic mean ± one standard deviation. Further, the sensitivity and specificity with regard to the differentiation between abnormal and normal ST segments was calculated. An abnormal reference or Holter ST segment (depression or elevation) was defined as a value of $\geq \pm 1$ mm.

Results

At rest

The mean values of all 60 measurements agreed very well with 1.8 ± 0.7 mm for the reference electrocardiogram and 1.6 ± 0.7 mm for the Holter electrocardiogram. In 14 measurements the ST segment was classified as ST depression according to the reference electrocardiogram. These measurements revealed mean values of 2.7 ± 1.2 mm for the reference electrocardiogram and 2.9 ± 1.2 mm for the Holter electrocardiogram. The 24 measurements classified as ST elevation also showed a good agreement with 1.8 ± 0.7 mm for the reference and 1.6 ± 0.7 mm for the Holter electrocardiogram. Twenty two times the reference electrocardiogram revealed ST segment values within ± 1 mm. Here, the mean values for the reference

electrocardiogram were 0.2 ± 0.3 mm and those of the Holter electrocardiogram 0.4 ± 0.3 mm. No statistical difference was found between the results obtained using the Holter device and those obtained by the reference electrocardiogram.

The correlation coefficient for linear regression analysis was highly significant with $r = 0.94$ (figure 2). As the absolute differences between each pair of measurements was ≤ 1 mm, the y-intercept was very small (+0.2 mm) with an inclination of the regression line of almost one (figure 2).

The calculated over-all sensitivity for the detection of an abnormal resting ST segment was 87% (33/38). For ST segment depression alone the sensitivity was 100% (14/14) and for ST segment elevation 79% (19/24). The specificity to prove a normal ST segment was 95% (21/22).

During exercise

The mean values of all 40 measurements were identical with 1.7 ± 1.1 mm for the reference electrocardiogram and 1.7± 1.1 mm for the Holter electrocardiogram. In 29 patients an ST segment depression, as indicated by the reference electrocardiogram, could be provoked during ergometry. These measurements revealed mean values of 2.1 ± 1.1 mm for the reference electrocardiogram and 2.1 ± 1.1 mm for the Holter electrocardiogram. In the 11 patients without exercise-induced ST segment depression, the mean values for the reference electrocardiogram were 0.6 ± 0.3 mm and those of the Holter electrocardiogram 0.7 ± 0.3 mm. There was no statistical difference between the results of the Holter device and those obtained by the reference electrocardiogram.

The correlation coefficient for linear regression analysis was highly significant with $r = 0.95$ (figure 3). As during exercise the absolute difference between each pair of measurements was always <1 mm, the y-intercept was negligible (+0.07 mm) with an inclination of the regression line of almost one (figure 3).

The sensitivity for the detection of an exercise-induced ST segment depression was 90% (26/29). The corresponding specificity was 91% (10/11).

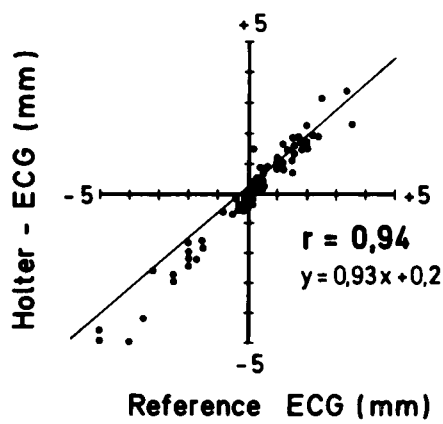

Figure 2. Results obtained at rest. *Each point represents an individual measurement of the simultaneously recorded reference electrocardiogram (abscissa) and the Holter electrocardiogram (ordinate). ST segment elevations are plotted in the upper right, ST segment depressions in the lower left quadrant. The correlation coefficient for linear regression analysis was highly significant (r = 0.94). As the absolute differences between each pair of measurement were ≤ 1 mm, the y-intercept was very small (+0.2 mm) with an inclination of almost one for the regression line.*

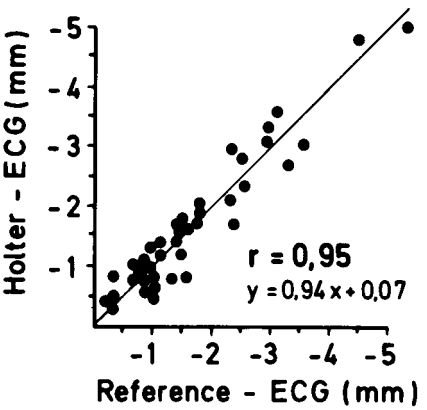

Figure 3. Results obtained during exercise. *Each point represents an individual measurement of the simultaneously recorded reference electrocardiogram (abscissa) and the Holter electrocardiogram (ordinate). The correlation coefficient for linear regressison analysis was highly significant (r = 0.95). As the absolute differences between each pair of measurement were always < 1 mm, the y-intercept was negligible (+0.07 mm) with an inclination of almost one for the regression line.*

Discussion

Our data show that the digital Holter system tested in this study allows a reliable, fully automatic measurement of the ST segment.

For this validation we chose a clinical approach rather than the measurement of technical specifications such as frequency response or phase characteristics. The American Heart Association's (AHA) standard suggests a frequency response within the range 0.05–100 Hz at ±3 dB cut-off points for faithfully recording and reproducing ST segment abnormalities [22 and 23]. In 1982, Bragg-Remschel *et al.* surprisingly found that none of the instruments (recorders plus replay units) met this AHA standard and the distortions detected were considerable [17]. On the other hand, Lambert *et al.* have shown that the frequencies below 2 Hz do not significantly affect the accurate reproduction of ST segments [24]. Further, considerable phase distortions (60–150°) were detected in a great number of systems causing tremendous errors in ST segment reproductions, even in the presence of an ideal amplitude response [17 and 25]. In order to estimate the net effect of amplitude and phase distortions, a simulated electrocardiogram signal with pre-set ST segment depressions was tested for its accurate reproduction. However, no relationship existed between ST segment depressions and the amplitude – phase characteristics [17]. Therefore, the clinical relevance of even carefully assessed laboratory tests remains questionable and even refining the requirements for technical specifications might not be of additional practical benefit.

To overcome this complexity we decided to use a clinical approach and considered the best method for validation the direct comparison of the Holter findings to a simultaneously recorded reference electrocardiogram. It is important to note that this approach uses electrocardiogram signals originating from patients and not from simulators. Although ST segments generated by machines may look virtually identical to patients' ST segments, they might contain strikingly different frequencies [17].

A clinical approach has been performed by only a few workers reporting identical sensitivities and specificities for both ST segment Holter recording and a standard 12-lead system in detecting coronary artery disease by exercise-induced ST segment changes [26 and 27]. However, no data have been published with regard to the

agreement of the absolute values for the ST segments and in identical leads. This is important, as the frontal plane used by Holter monitors (so-called 'modified' V-leads) is perpendicular to the precordial V-leads of a standard electrocardiogram. In our study, both electrocardiogram systems received their input from identical leads and the absolute differences between the Holter and the reference electrocardiogram were usually less than 1 mm. Our study was designed to investigate the reliability of ST segment measurements with real-time analysis. Therefore, the high degree of correlation between the reference and Holter electrocardiogram only refers to the measurement of ST segments *per se*. The issue of possible false positive ST segment shifts, of course, still remains [19,28–30].

The system tested in this study is restricted to the analysis of the ST segment in one channel only. Simultaneous analysis of at least two leads is desirable, as the sensitivity in detecting myocardial ischaemia may be enhanced by at least 10% due to a better recognition of anterior and inferior wall-related changes [26 and 31]. Further, all presently available Holter systems are limited to the registration in bipolar leads. As unipolar leads have demonstrated their superiority in the standard exercise electrocardiogram to detect ischaemic ST segment shifts [32], further developments are necessary.

The software tested in this study did not characterize the shape of the ST segment deviations. Therefore, no statements could be made regarding the possible distortions of the ST segment configuration [17]. As it is known from the exercise electrocardiogram that ascending ST segment deviations have to undergo more strict criteria to be classified as pathologic [28 and 33], the characterization of the ST slope should be added to an Holter report.

The reference point for the determination of the ST segment used by the Holter system was the trigger signal caused by the QRS complex. Indeed, it is unusual to measure the ST segment 100 ms after the R-wave and not, as it is uniformly accepted for the exercise electrocardiogram, 80 ms after the J-point [28 and 34]. Therefore, the visual analysis of Holter recordings usually follows the J+80 rule [7 and 26]. Although there is equipment which measures the ST segment 60 or 80 ms after the J-point [10, 20 and 27], the question remains as to whether a fully automatic system is capable of defining the J-point in every patient. Further, the J+80 rule may lead to diagnostic problems in situations with accelerated heart rate. As until now there has been no generally accepted proposal for a heart rate correction of the J+80 method and as it is the primary goal to detect changes of the ST segment, the use of R+100 may be justified.

Practical implications

The real-time Holter equipment evaluated in this study proved its reliability for the digital ST segment measurements. As this fully automatic system saves time, it is basically suited for a widespread use. Nevertheless, due to the unique combination of real-time analysis with the traditional recording principle, it enables the retrospective examination of each single beat for plausibility.

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