Accuracy of Digital Holter Monitoring of Extent and Duration of Ischemic Episodes Compared to Analog Recording

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Analog amplitude-modulated Holter devices are in widespread use for arrhythmia detection, but their reliability remains questioned for ST-segment analysis. In contrast, recently developed digital Holter devices immediately digitize and analyze the electrocardiogram (ECG) on-line and may therefore be more reliable for ST-segment analysis. To test this hypothesis, the results of digital, on-line, 2-channel ST-segment analysis were directly compared to those of analog amplitude-modulated recordings in identical leads (CM_5 and CM_3), using a stripchart recorder meeting the American Heart Association specifications as the standard. Thirty-five patients (25 with coronary artery disease and 10 control subjects) underwent graded treadmill exercise testing. The reference ECG mean value for ST-segment depression in CM_5 was -1.4 ± 1.2 mm and in CM_3 -0.5 ± 1.2 mm. For digital analysis, the mean values and correlation coefficients for CM_5 were -1.5 ± 1.1 mm ($r = 0.97$) and for CM_3 -0.8 ± 1.3 mm ($r = 0.93$). For analog recording, the results for CM_5 were -2.1 ± 1.7 mm ($r = 0.88$) and for CM_3 -1.3 ± 1.9 mm ($r = 0.85$). The mean duration of ST-segment depression with the reference ECG was 7.1 ± 4.1 minutes. Digital Holter showed a significantly better agreement (7.4 ± 4.4 min, $r = 0.97$) than analog Holter (9.6 ± 5.6 min, $r = 0.84$). Because analog amplitude-modulated Holter recordings overestimated the degree and duration of ischemic episodes, digital, on-line and full disclosure devices should be preferred to assess myocardial ischemia.

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With the recognition that episodes of myocardial ischemia are frequently asymptomatic, the use of Holter monitoring[1] to assess the "total ischemic burden" of patients with coronary artery disease has become increasingly important.[2] ST-segment Holter monitoring is clinically useful in patients with angina pectoris to assess the efficacy of antiischemic therapy during daily activities and for prognostication.[3–7] Analog amplitude-modulated Holter devices are in widespread use for arrhythmia detection, but their reliability remains questioned for ST-segment analysis.[8–12] Analog amplitude-modulated devices are inherently limited by signal distortion due to their need for recording on and replaying from magnetic tape. In contrast, recently developed digital Holter devices immediately digitize and analyze the electrocardiogram (ECG) with microprocessors and may therefore be more reliable for ST-segment analysis. The recently published American College of Cardiology/American Heart Association Task Force on Ambulatory Electrocardiography report attributes to digital Holters "primary advantages due to elimination of mechanical parts and improvement of signal to noise ratio."[13] However, digital Holters have been criticized because of the "unproved ability of the available algorithms to analyze ST-segments."[14] To test the hypothesis that digital Holter recording is more reliable than analog amplitude-modulated recording, we compared the results of digital, on-line, 2-channel (CM_5 and CM_3) ST-segment analysis directly to those of analog amplitude-modulated recordings in identical leads, using a stripchart recorder that meets the American Heart Association specifications as the standard.

METHODS

Thirty-five patients were enrolled. Twenty-five had coronary artery disease with known exercise-induced ST-segment depression and 10 had no evidence of coronary artery disease and a normal treadmill test result. Further inclusion criteria were sinus rhythm, no resting ST-segment depression or conduction disturbances and no digitalis therapy. A symptom-limited graded treadmill exercise test was performed using the standard Bruce protocol (Burdick T500 treadmill/ExTol 700 stress system).

After skin abrasion, silver/silver chloride electrodes were attached in CM_5 and CM_3 locations. For the reference ECG, an ESAOTE Biomedica 3-channel stripchart recorder with a frequency response of 0.05 to 100 Hz at −3 dB, meeting the US (AAMI EC11) and Eu-

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TABLE I Sensitivity and Specificity for Detection of ST-Segment Depression by Digital and Analog Holter Recordings in Leads CM_5 and CM_3

	CM_5	CM_3	$CM_5 + CM_3$
Pts with ST-segment depression on the reference electrocardiogram (n)	24	15	25
Sensitivity (%)			
Digital Holter	23/24 (96)	15/15 (100)	25/25 (100)
Analog Holter	24/24 (100)	15/15 (100)	25/25 (100)
Pts without ST-segment depression on the reference electrocardiogram (n)	10	10	10
Specificity %			
Digital Holter	9/10 (90)	9/10 (90)	9/10 (90)
Analog Holter	6/10 (60)	7/10 (70)	6/10 (60)

ropean (IEC62D, C06) standards, was chosen. It was attached together with the Holter recorder using split leads to CM_5 and CM_3, so that identical leads were simultaneously seen by both devices. A high fidelity external signal was used for calibration of the reference ECG and the Holter ECG (1 mm = 0.1 mV).

We used the Oxford Medilog-4500 with MR 45 recorders (Oxford Medical Ltd.) because it represents an innovative link between digital on-line analysis and analog AM recording in 1 device.

The on-line component has a frequency response of 0.06 to 70 Hz at −3 dB. There are 32,000 bytes of memory for digitizing the ECG, with a sample rate of 128 Hz. The isoelectric line is automatically measured at 56, 64 and 72 ms before the R wave ("fiducial point"), the ST segment at 96, 104 and 112 ms after the R wave. An averaging algorithm is then applied to both measurements with weighting factors of 1:2:1. Both channels are simultaneously analyzed. The software excludes arrhythmias as well as noisy beats from ST-segment measurements. Digital numbers were directly obtained from the automatic printout.

The analog component is a traditional amplitude-modulated recording/replay unit with a frequency response of 0.08 to 60 Hz at −3 dB. To compare the analog tracings to the digital ST-segment measurements, the isoelectric line was determined 60 ms before the peak of the R wave and the ST-segment at 100 ms after the R wave. ST-segment measurements were averaged by taking 5 consecutive heart beats at peak exercise.

The magnetic tape records the information for both the analog and the digital components. Two of the 4 tracks are used for continuous analog 2-channel registration of the ECG, enabling retrospective analysis of each single heart beat. A third track stores the on-line continuous digital ST-segment analysis. The fourth track records the time markers.

The stripcharts were recorded at 25 mm/s. The reference ECG was synchronized to the Holter device and ST-segments were determined at peak exercise. The reference and analog ST-segment measurements were made in identical fashion, and independently by 2 observers. In case of disagreement, consensus was achieved.

An abnormal episode was defined as ≥1 mm of ST-segment depression for at least 1 minute. The sensitivity and specificity of the Holter to detect or exclude ST-segment depression was based on the reference ECG. The duration of an ischemic episode was determined in the lead with the greater ST depression.

Statistical analysis: The results are expressed as mean ± 1 standard deviation. Linear regression analysis was performed and characterized by the estimated

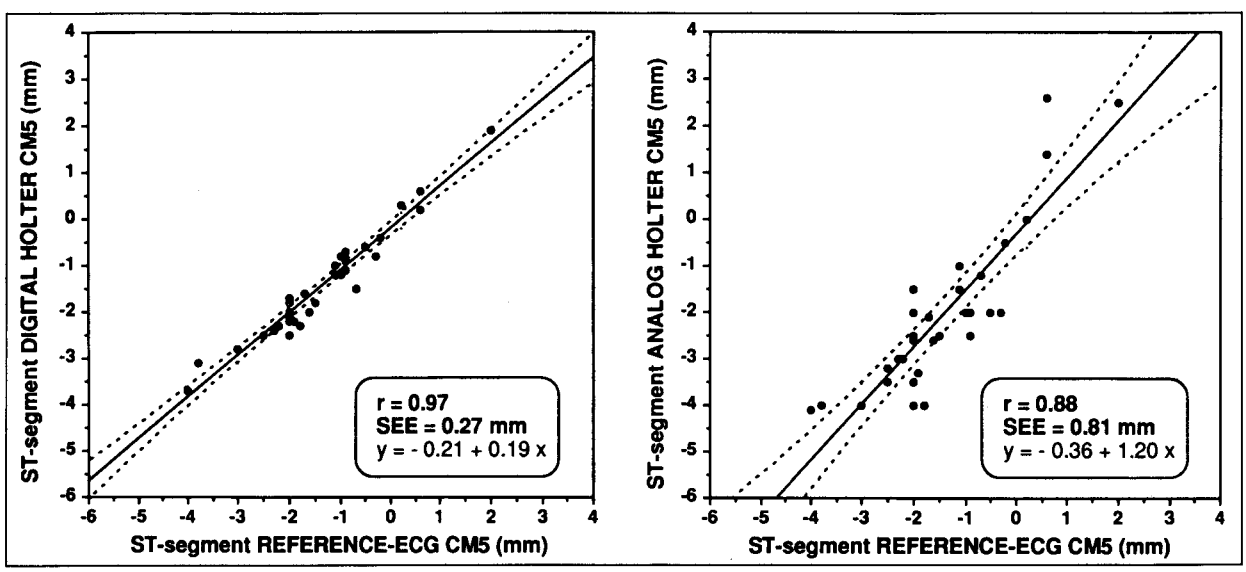

FIGURE 1. Correlation coefficients (r), standard error of the estimates (SEE) and estimated equations for linear regression analysis between ST-segment measurements by the reference ECG versus digital Holter (*left*) and analog Holter (*right*) in lead CM_5. The *solid line* represents the regression line, and the *dashed line* the upper and lower 95% confidence limits. The digital analysis correlated significantly better with the reference ECG than the analog recording.

equations, correlation coefficients and standard error of the estimates. The significance of the linear regression analysis was tested with the usual F statistic, and *t* tests for the equality of the slope to unity and the intercept to 0 (the line of identity) were performed. The Fisher test for homogeneity of correlation coefficients was used to compare the regression analysis of the analog and digital recordings. The chi-square test was used to compare sensitivity and specificity. A p value <0.05 was considered to be significant.

RESULTS

Reference electrocardiogram: According to the inclusion criteria, all 25 patients with coronary artery disease had an abnormal exercise-induced ST-segment depression in CM_5 or CM_3 of the reference ECG. Lead CM_5 alone revealed an abnormal ST-segment depression in 24 of 25, and lead CM_3 in 15 of 25 patients. The combination of both leads resulted in an abnormal ST-segment depression in all 25 patients (Table I). As also required by the inclusion criteria, neither lead CM_5 nor lead CM_3 of the reference ECG showed an abnormal ST-segment depression in the 10 control patients (Table I).

The mean value for all ST-segment measurements in CM_5 was -1.4 ± 1.2 mm and in CM_3 -0.5 ± 1.2 mm. The mean duration of transient episodes of ST-segment depression was 7.1 ± 4.1 minutes.

Digital Holter: Using the reference ECG as standard for ST-segment depression, digital Holter resulted in a sensitivity of 96% (23 of 24) for CM_5 and of 100% (15 of 15) for CM_3 (Table I). The combination of lead CM_5 and CM_3 showed a sensitivity of 100% (25 of 25). The specificity for CM_5 as well as for CM_3 was 90% (9 of 10) with a combined (CM_5 and CM_3) specificity of 90% (9 of 10, Table I).

The mean value for all ST-segment measurements in CM_5 was -1.5 ± 1.1 mm and in CM_3 -0.8 ± 1.3 mm. There was no significant difference between the mean values of the digital Holter and the reference electrocardiogram in CM_5 or CM_3.

The correlation coefficient between the digital measurements and the reference ECG was $r = 0.97$ with a standard error of the estimate of 0.27 mm for CM_5 (Figure 1) and $r = 0.93$ with a standard error of the estimate of 0.47 mm for CM_3 (Figure 2). For both regression lines, the inclination and the intercepts with the y axis were not significantly different from the line of identity (Figures 1 and 2).

The mean duration of the episodes of transient episodes of ST-segment depression was 7.4 ± 4.4 minutes, which was not significantly different from the reference ECG. The correlation coefficient between the duration of transient ST-segment depression as determined with digital Holter and that from the reference ECG was 0.97 with a standard error of the estimate of 1.1 min (Figure 3).

Analog Holter: Based on the ST-segment depression on the reference ECG, analog Holter resulted in a sensitivity of 100% for CM_5 (24 of 24) as well as for CM_3 (15 of 15, Table I). The specificity for CM_5 was 60% (6 of 10) and for CM_3 70% (7 of 10). The combination of CM_5 and CM_3 revealed a specificity of 60% (6 of 10, Table I).

The mean value for all ST-segment measurements in CM_5 was -2.1 ± 1.7 mm and in CM_3 -1.3 ± 1.9 mm. The mean values for CM_5 as well as those for CM_3 were significantly different from the corresponding values on the reference ECG.

The correlation coefficient between the analog measurements and the reference ECG was 0.88 with a standard error of the estimate of 0.81 mm for CM_5 (Figure

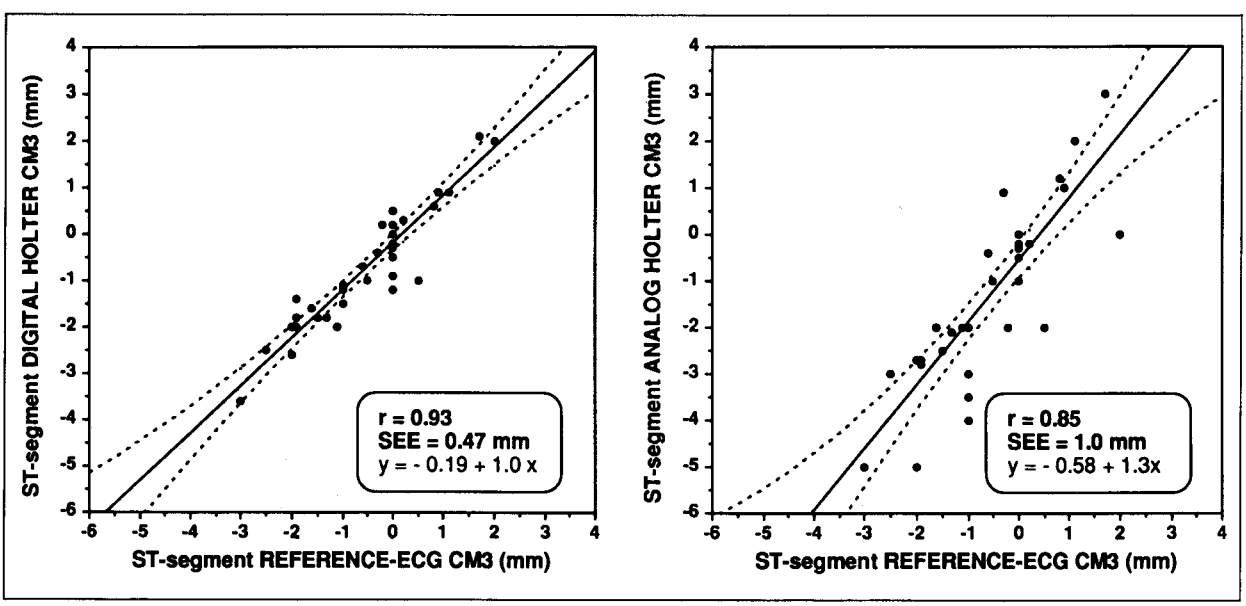

FIGURE 2. Comparison between ST-segment measurements by the reference ECG versus digital Holter (*left*) and analog Holter (*right*) in lead CM_3. This lead also showed a significantly better correlation between digital analysis and the reference ECG than the analog recording. Symbols and abbreviations as in Figure 1.

1) and 0.85 with a standard error of the estimate of 1.0 mm for CM_3 (Figure 2). For both regression lines, the inclination and the intercepts with the y axis were not significantly different from the line of identity (Figures 1 and 2).

The mean duration of the episodes of transient episodes of ST-segment depression was 9.6 ± 5.6 minutes and significantly longer than the duration determined from the reference ECG. The correlation coefficient of the duration of ST-segment depression with analog Holter compared to reference ECG was 0.84 with a standard error of the estimate of 3.1 minutes (Figure 3).

The comparison of the sensitivity and specificity of the analog and digital recordings showed a significantly higher specificity for the digital technology (Table I). Also the regression analysis revealed significant differences for the amount of ST segment in CM_5 (Figure 1), CM_3 (Figure 2) and duration of ischemia (Figure 3).

DISCUSSION

As our results show, digital Holter monitoring is more reliable for the assessment of extent and duration of transient myocardial ischemia than analog amplitude-modulated recording. Analog amplitude-modulated systems, which represent the vast majority of the Holters used for arrhythmia detection, have been substantially criticized regarding their reliability to detect ST-segment changes.[8-11] Our results, of course, apply only to the system tested, but even recently developed amplitude-modulated systems with newer technology have shown limited value for ST-segment analysis.[12]

Laboratory tests: Characteristically, several laboratory parameters, such as frequency response and phase shift, have been used to describe the electric properties of Holter devices.

An inadequate frequency response distorts the ECG by inconsistent degrees of amplification of its different frequency components.[9,15,16] In 1975, the American Heart Association recommended a standard frequency response of 0.05 to 100 Hz at −3 dB for faithful recording with bedside electrocardiographs.[17] However, in 1982, Bragg-Remschel et al[11] tested equipment from 8 Holter manufacturers and noted that none of the recorder plus replay units met the American Heart Association standard.

An inadequate phase response may delay low frequencies of the QRS complex and make them appear in the ST segment, causing artifactual changes resembling those seen in ischemic heart disease. Initially, the American Heart Association recommendations did not mention the phase response.[17] In the subsequent years, considerable phase distortions (60 to 150°) have been detected in a number of systems.[11] Consequently, the American Heart Association added the standard of a linear phase response from 0.05 Hz to 60 Hz.[18] Using digital analysis, phase distortions should not be expected.[14,19,20]

There is a complex interaction between amplitude and phase response. This became more evident from a study by Lambert et al,[21] showing that the American Heart Association's minimum frequency response criteria do not apply when using a high fidelity instrument with a flat frequency response and no measurable phase shifts. Therefore, the "ideal" electrocardiograph should have a flat amplitude (i.e., all components equally amplified) and a linear phase response (i.e., all components equally delayed) between 0.5 Hz and 60 Hz.[12]

In contrast to analog amplitude-modulated units, analog frequency modulated units are accepted for faithful reproduction of ST-segment shifts.[11,22] Because

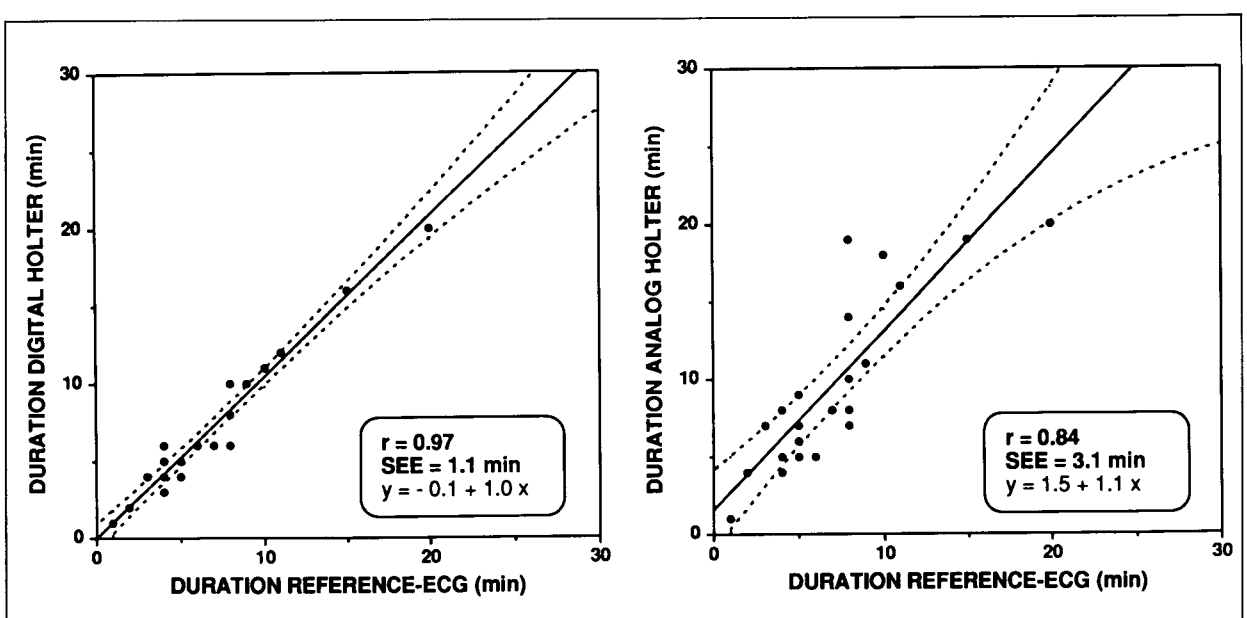

FIGURE 3. Duration of exercise-induced ST-segment depression as determined by digital analysis (*left*) and analog recording (*right*) compared with the reference ECG. The digital analysis correlated significantly better with the reference ECG than the analog recording. Symbols and abbreviations as in Figure 1.

these frequency-modulated devices, however, are rarely used clinically, we preferred to compare digital recording to the overwhelmingly used amplitude-modulated technology. In addition, because it has been suggested that the accurate assessment of the ischemic status of patients requires a total recording of 72 hours,[23] the reading of so many tapes would be time consuming and subject to interobserver variability. For frequency-modulated tapes, a retrospectively computerized reading has been developed, but is not generally available.[22]

Since "the exact effect of amplitude and phase distortion is difficult to predict," electronically simulated ECGs have been used to validate ST-segment Holter monitoring.[11] These synthesized signals, however, may contain different frequencies compared to real, patient-generated signals.[21] Therefore, electronic laboratory studies alone are not sufficient to predict the accuracy of ST-segment measurements, especially in a noisy patient environment such as during exercise.

Patient evaluation: We used the clinical approach, recording real, patient-generated signals. To reference the Holter results to an electrocardiograph meeting the American Heart Association standards, we chose the treadmill test as the model to induce transient myocardial ischemia. It is important to emphasize that we registered the Holter and reference ECGs from identical leads, which is essential for validation purposes.[24,25] Others have used patient-generated signals, however, registering from different leads for recording of Holter and reference ECG, which makes a direct comparison difficult.[20,26]

The high sensitivity and specificity found in this study should not be confused with those reported for Holter monitoring to detect coronary artery disease.[19] Our data were related to the detection of ST-segment changes compared to identical leads on the reference ECG (Table I). Of course, with Holter monitoring, the issue of false-positive ST-segment shifts remains. Therefore, ST-segment changes in patients without known coronary artery disease must be interpreted with caution.

For ambulatory monitoring, only bipolar leads are available. Chaitman et al[27] have shown that the bipolar, frontal lead CM_5 is more sensitive, but less specific than the unipolar, horizontal V_5. There is no doubt that the sensitivity of a single lead to detect myocardial ischemia can be increased by the addition of multiple leads. Accordingly, compared to CM_5 alone, the addition of CC_5 increased the sensitivity by 9 to 17%[27-29] and the addition of CM_3 by 7%.[26] The combined use of CM_5 and CM_3 had the same sensitivity and specificity for the detection of coronary artery disease as the standard 12 leads.[26] The addition of a third bipolar lead may additionally increase the diagnostic information.[30]

Clinical impact: The digital Holter system tested in this study accurately detects extent and duration of transient ST-segment changes. Digital Holter devices are reliable and their on-line, fully automatic measurement of ST-segment shifts make them suitable for widespread and repeated applications.[19,20] Because analog amplitude-modulated recordings appear to overestimate the degree and duration of ischemic episodes, digital, on-line and full disclosure devices should be preferred to assess myocardial ischemia with Holter monitoring.

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