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A New Semiautomated Algorithm to Quantify Holter-Detected Myocardial Ischemia: Preliminary Experience in the Trimetazidine European Multicenter Trial (TEMS)

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Summary. Holter-detected myocardial ischemia, either painful or painless, is an important issue in the functional and prognostic evaluation of coronary patients. This paper describes one of the first attempts to reliably quantify the duration and severity of the ischemic ST-segment changes over a given period of time; the algorithm described here provides physicians with a global index of ischemia that is the total ischemic area, namely, the integral of ST-segment depression or elevation over time (expressed in mm × min). The diagnostic and prognostic power of this new index remains to be established and to be compared with the actually used simple measurements, i.e., the number and duration of ischemic events.

Key Words. myocardial ischemia, ischemic area, Holter, ST segment

Although painful and silent ischemia may be important markers of the severity and prognosis of patients with documented coronary artery disease (CAD), 24–48 hours of Holter monitoring of ST-segment shifts has yet to prove its real place in the diagnosis of CAD. This should be based on history (complaints), risk factor evaluation, and modern (i.e., computer-assisted) symptom-limited maximal exercise testing combined, whenever clinically useful, with stress perfusion scintigraphy and late imaging [1–6].

On the other hand, Holter monitoring has a specific place in the evaluation of the total ischemic burden, which is the addition of both the painful and silent (painless) episodes of myocardial ischemia [7–12]. Classical techniques rely on the analysis of the number of ischemic episodes and their total duration, and allow the identification of a circadian variation in myocardial ischemia. The latter is strongly reminiscent of the circadian variation of other major markers of CAD, i.e., angina pectoris, myocardial infarction, and ischemic sudden death [12,13].

A major limitation of all available Holter moni-

toring systems is their lack of quantitative and reproducible data. Another parameter still lacking in the literature available today is a global, duration- and severity-adjusted index of myocardial ischemia. In order to improve the presently available methodology, we have designed and tested a semi-automated algorithm that allows the detection of all ischemic episodes and their quantification in a global ischemic score. It provides the integral of ischemic ST-segment depression over time during a given period of time. The Holter system was tested with an identical signal recorded on a previously designed and described system for the analysis of the exercise-induced ST-segment shifts [6,15,16].

Methods

Holter monitoring
We use A.M. Avionics recorders for 24-hour Holter monitoring and the Avionics Trendsetter 11-9000A for further analysis.

During the trend operation of the Holter reader, two analog signals, one for ST-segment level (ST) (0.06 or 0.08 seconds after the J point) and another for heart rate (HR), are digitized and stored on the floppy disc of a homemade microprocessor system. The acquisition rate is 120 conversion by second. As we store only the average of five successive acquisitions and as the playback of the tape is 240 times faster than the recording time, the real-time equivalent sampling rate becomes one sample every 10 seconds. Thus, for a 24-hour tape, 8640 points for the ST segment and 8640

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points for the heart rate (HR) are kept on the floppy disc. The resolution of the conversion is equal to 0.1 mm for the ST and 1 unit for HR. After this acquisition is performed, the system could be disconnected from the reader for further processing.

The technician can then access the data curves (ST and HR) on a graphic screen. The curves displayed on the screen represent 1 hour of the trend, giving an important enlargement as compared with the usual paper trend given by the Holter reader. The use of a mouse on such an enlarged display is very useful for the technician, who can easily make any corrections on the curves and mark the exact beginning and end of the ST depression (or elevation) events.

A short ECG trace can be obtained from the Holter reader for all suspected ST events given by the trend, enabling the technician to classify or discard each ST event, e.g., in case of noise.

The system can report four different categories of ST events:

1. Symptomatic ST depression   (ST −)
2. Symptomatic ST elevation   (ST +)
3. Silent ST depression   (SST −)
4. Silent ST elevation   (SST +)

Finally the system computes some parameters, such as the total duration for each event, the area of depression, i.e., the integral of the ST segment (mm × min), the beginning HR and the mean HR of each event, and the HR corresponding to the maximal depression. The system is very flexible. On the one hand, it allows the technician to discard all the noisy periods while, on the other hand, it permits the use of any desirable cut-off points in the ST segment (i.e., 1, 2, or 3 or . . . mm of ST depression or elevation). The measurements and the results of the computation are printed.

Exercise testing

In order to test the accuracy of the whole Holter system, calibration signals and two leads (X and Y of the Frank system) were simultaneously recorded during a maximal bicycle exercise test through the same electrode system on a Holter tape and on our computerized system for the analysis and interpretation of the exertional ECG [6,15,16]; this was done in 20 coronary patients, yielding 47 simultaneous measurements for comparison.

Patients

The Holter system described above was used in 35 patients who have been included in the TEMS

(Trimetazidine European Multicenter Study) and completed the protocol. Briefly, the TEMS is a double-blind, randomized comparison of the antiischemic effects of propranolol and trimetazidine; at days −15 and 0, the patients underwent both a symptom-limited test of maximally tolerated exercise and 24-hour ambulatory Holter monitoring. These tests are repeated 30 and 40 days after inclusion (n = 30), with an option to continue the study for 180 days (n = 5). At the present state of the study, 145 Holter tapes are available in the data bank, and their results have been analyzed blindly.

Results

Figure 1 represents the analog display of the output of the Holter system (ST segment 80 ms after the J point and heart rate) and shows one ischemic episode occurring at 12 hours 48 minutes, with a duration of 36 minutes and 20 seconds. The digitized output corresponding to these episodes are shown in Figure 2, where the time base has been widened on the horizontal axis, which corresponds to only 1 hour. By analyzing the actual ECG recording in real time (on the Holter system screen), the technician can smooth the curve and discard any noisy records by using a mouse (+). The methods of calculating the ischemic ST segment area are depicted in Figure 3, which indicates that several definitions of ischemic ST-segment depression can be used.

The comparison between exercise-induced Holter and our computerized ECG system is depicted in Figures 4 and 5; the relationship between the two measurements is excellent (r = 0.968) with, however, a systematic difference of 0.25 mm, which is more marked on the Holter system than on the computerized ECG system.

Preliminary Holter data from the TEMS

Among the 145 Holter tapes available, 103 showed ischemia (that is 71%, which is a high score due to the selection of ischemic patients). Among the 209 ischemic episodes, 134 (64%) were silent; the circadian distribution of these silent and painful episodes is depicted in Figure 6.

Discussion

The algorithm described in this paper is one of the first to attempt to really quantify the electrocardiographic signs of myocardial ischemia during a given period of time. Counting only the number and duration of the
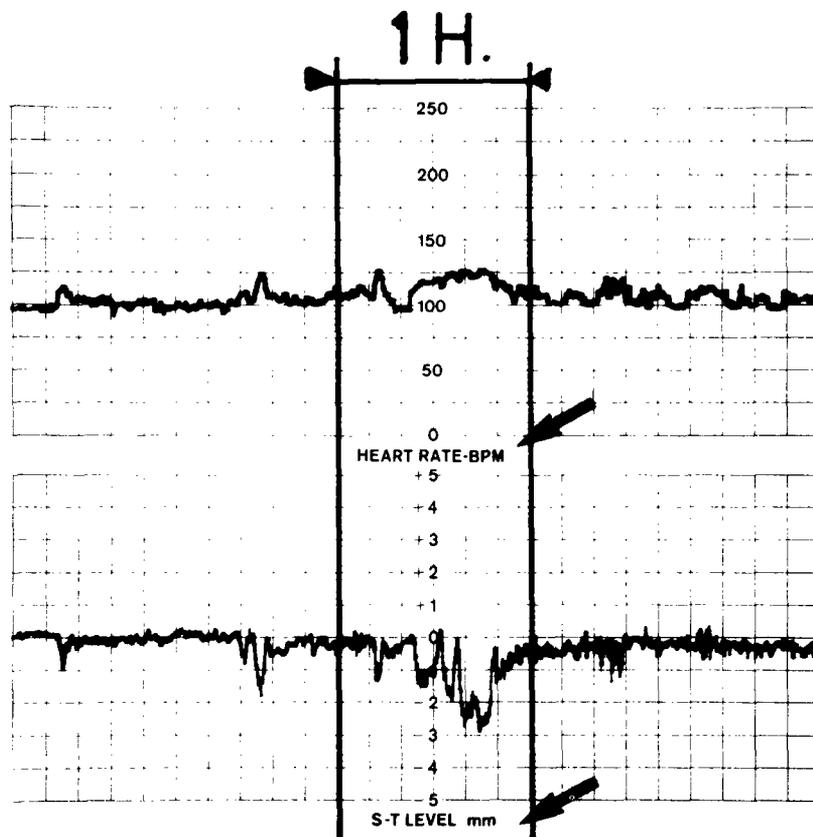
Fig. 1. Analog reports from the Holter data (heart rate, upper channel and ST segment, lower channel). In this example, the patient exhibits an ST-segment depression starting at 12 hours 48 min and lasting for 36 minutes 20 sec.
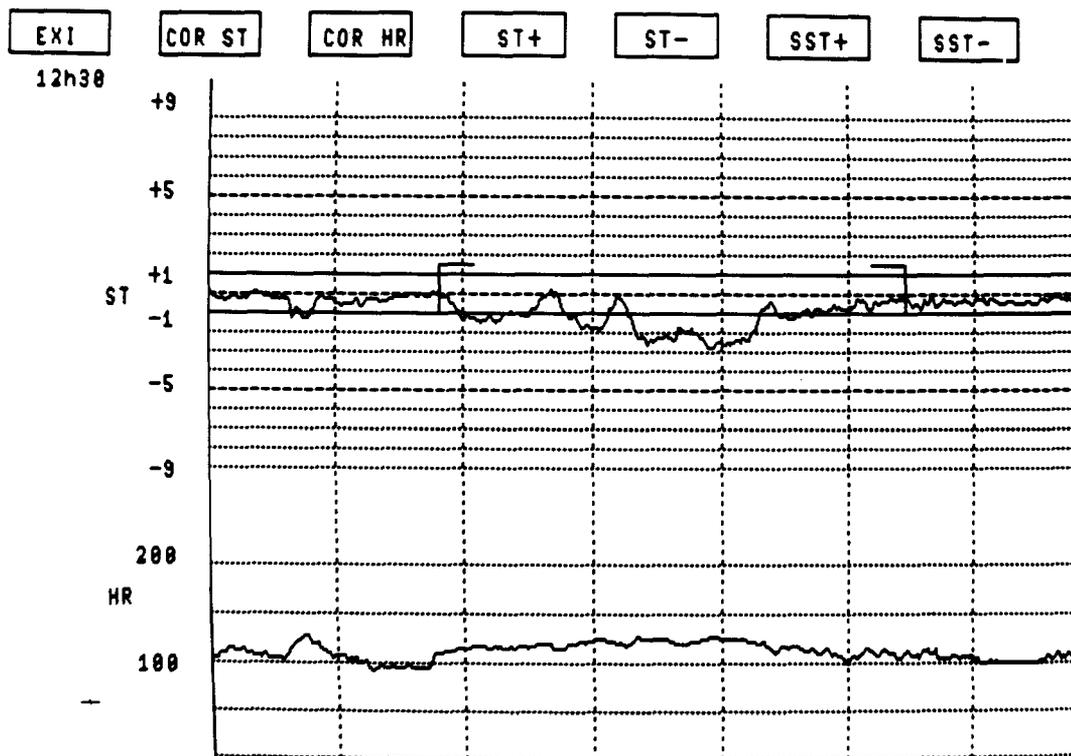

Fig. 2. Picture of the screen of the computerized system, which allows to analyze the HR (lower channel) and ST-segment signals (upper channel) during one hour; the time scale is thus considerably increased when compared to the usual Holter report. The technician is able to identify by markers the start (⌐) and the end (⌐) of the ST segment abnormalities and to eventually smooth the curve; when the tracing is too noisy, it can be disregarded. This digital screen output corresponds to the ischemic episodes depicted in Figure 1.
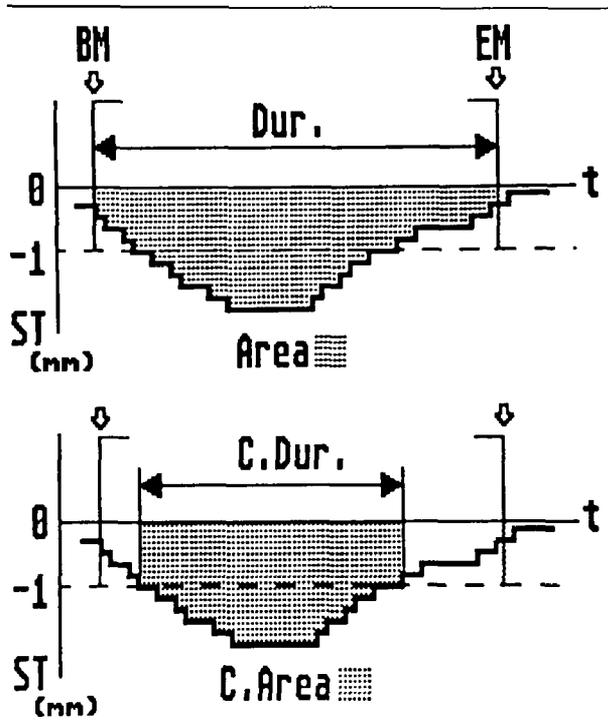
Fig. 3. Schematic representation of the analysis of the digitized Holter ST segment data. BM and EM = the beginning and the end of the ST-segment shift from the 0 voltage baseline; dur. = the duration of the ischemic episode; the area is the product of the duration and of the depth of the ischemic shift, expressed in mm.min; C.Dur. and C.Area = the duration of area of the ischemic ST depression once the ST segment has crossed (C) the −0.1 mV border (the latter being considered by many to be the real ischemic episode).
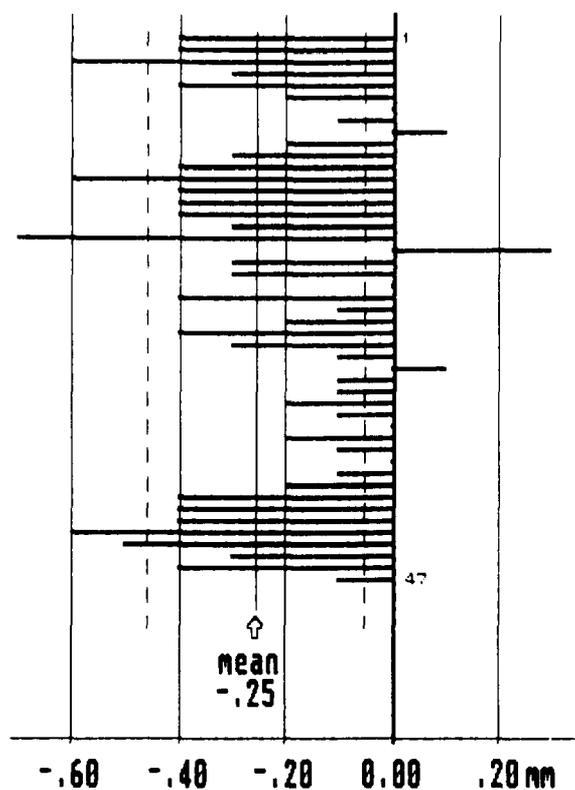

Fig. 5. This illustrates, point by point, the difference between the two systems compared in Figure 4.
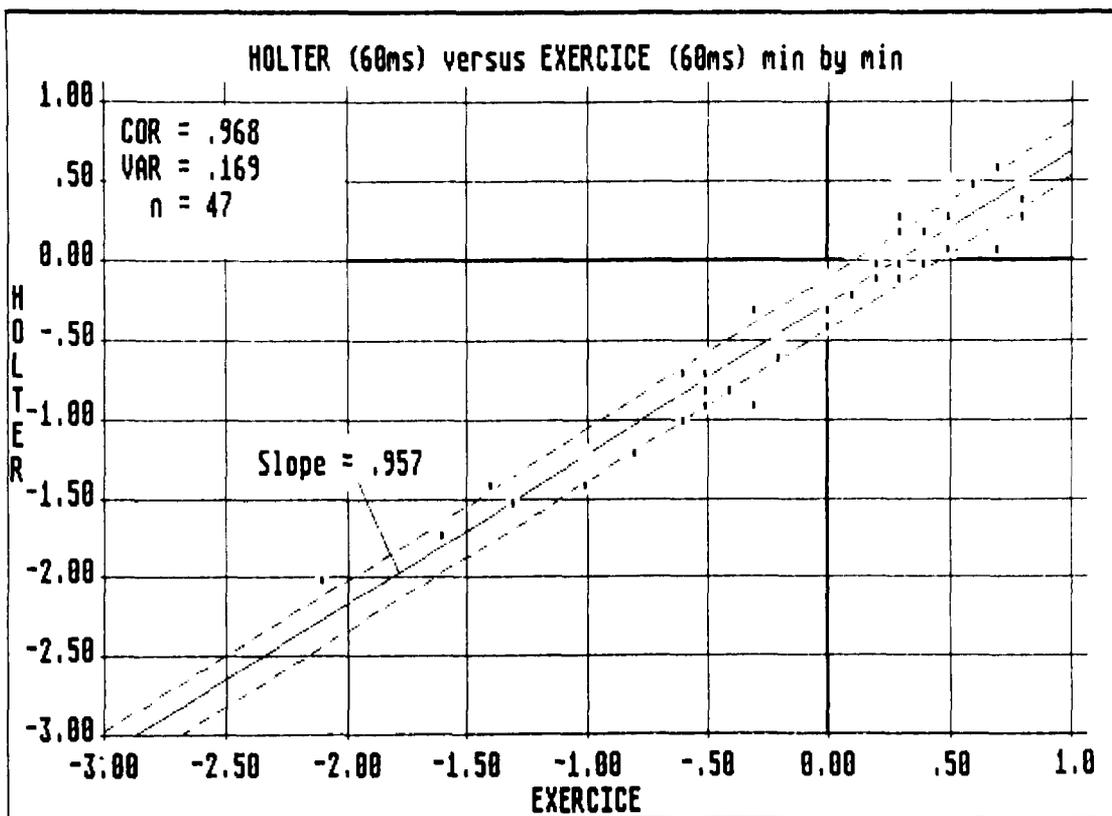

Fig. 4. Relationship between the amount of ST-segment depression (60 ms, after J. Point) measured simultaneously and through a strictly identical lead system by the Holter Avionics system and our exercise ECG system. The correlation is excellent, although there is a systematic difference.
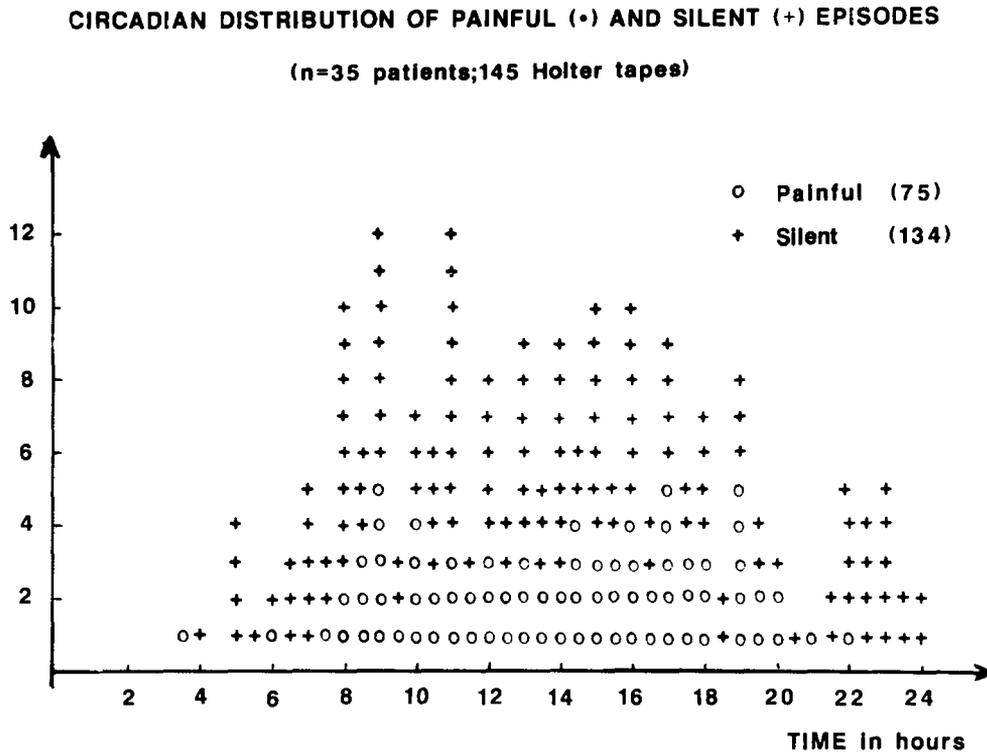
CIRCADIAN DISTRIBUTION OF PAINFUL (•) AND SILENT (+) EPISODES

(n=35 patients;145 Holter tapes)

o **Painful** (75)
+ **Silent**   (134)

Fig. 6. The figure illustrates the circadian variation of the ischemic episodes (painful = 0; painless = +) within 24-hour Holter monitoring records (n = 145) from TEMS. It documents the greater frequency of painless episodes and the previously described circadian distribution.

ischemic transient events seems to overlook the degree and duration of the ST-segment shifts. Our new index of ischemic area over time, however, needs further documentation, and its diagnostic and prognostic interest remains to be demonstrated [17,18].

The systematic difference in the severity of the ST-segment depression measured 0.08 seconds after the J point noted between the Avionics Holter data and our computerized exercise data remains largely unexplained. It is probably due to a systematic error in the detection of the J point, which is determined on a single lead, and probably sooner, with the Holter system, while it is determined with a three-lead, spatial velocity curve in our computerized system for the analysis of the exercise ECG [15,16]. As the difference is systematic and reproducible, it should not interfere with the usefulness of the new algorithm in clinical research.

Interestingly, the preliminary data collected in the TEMS study confirm the importance of silent ischemia, which is, as recently documented, more frequent than painful ischemia [13,14]. Also, the circadian variation of ischemia, painful or silent, was confirmed by our preliminary results.

Acknowledgments

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