ST Segment Depression Criteria and the Prevalence of Silent Cardiac Ischemia in Hypertensives

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Abstract—The reported prevalence of silent cardiac ischemia as assessed by ambulatory electrocardiographic recording varies widely. The influence of the stringency of the analysis criteria has never been reported. We performed 24-hour, 12-lead ambulatory electrocardiographic recording in patients with hypertension but without proven coronary artery disease. The recordings were analyzed according to strict ST segment depression criteria adapted from the American College of Cardiology/American Heart Association guidelines and according to basic ST segment depression criteria adapted from studies with only concise descriptions of ambulatory electrocardiographic recording analysis. Also, we performed 24-hour ambulatory blood pressure monitoring. More than 4400 hours of ambulatory electrocardiographic recording and ambulatory blood pressure monitoring in 194 patients with hypertension were analyzed. Medication was withdrawn in 45% of the patients. The average systolic blood pressure during the day was 152±13 (mean±SD); diastolic blood pressure was 94±17 mm Hg. According to the basic ST segment depression criteria, we found a prevalence of silent ischemia of 11.3%, and with the strict criteria the prevalence was 5.2%. The patients who were considered positive according to the basic criteria but not according to the strict criteria (false-positive) in the majority of cases (58%) had depression of an elevated baseline ST segment. We found a lower prevalence of silent cardiac ischemia as assessed by ambulatory electrocardiographic recording than generally reported. The stringency of applied analysis criteria appear to play an important role in this outcome. (Hypertension. 2003;41:476-481.)

Key Words: hypertension, essential ■ electrocardiography ■ ischemia ■ blood pressure monitoring, ambulatory

Patients with symptomatic cardiac ischemia often have silent ischemia as well.1,2 Studies on this topic may seek to induce ischemia during physiological or pharmacological exercise testing. However, documentation of silent ischemia in daily life depends on methods that allow continuous ambulatory monitoring of cardiac ischemia. ST segment analysis on ambulatory electrocardiographic (ECG) monitoring is frequently applied for this purpose. In different groups of patients, cardiac ischemia on ambulatory ECG recording (symptomatic or silent) has been shown to correlate with an adverse prognosis.3–6 Hypertensive patients without proven coronary artery disease (CAD) may also exhibit cardiac ischemia,7 and the presence of silent ischemia may be a link to the high prevalence of adverse cardiac events in this patient group.6,8 The reported prevalence of cardiac ischemia as assessed by ambulatory electrocardiographic recording ranges from 11% to 57%, of which almost all episodes are silent.6,8–18 This large variation in prevalence can partly be attributed to the heterogeneity of the populations studied. For example, some studies included only elderly subjects8,14,17 and some studies investigated patients with complaints,9,10,13,18 Obviously, the stringency of applied ambulatory ECG recording criteria in the definition of ischemia is important as well. However, the description of applied criteria is often concise and allows a broad interpretation. The influence of different sets of criteria on the prevalence has never been investigated. We sought to verify the prevalence of cardiac ischemia as determined by 12-lead ambulatory ECG recording in a large outpatient population with essential hypertension, with 2 sets of criteria: so-called stringent criteria, adapted from the American College of Cardiology/American Heart Association guidelines,19 and less strict criteria that only take into consideration the relative change in the ST segment level as assessed by Holter software.11–13

Methods
In our center, an academic referral hospital, we recruited patients with hypertension from the hypertension clinic or general internal medicine outpatient clinic. Exclusion criteria were known CAD; secondary hypertension; arrhythmias such as atrial fibrillation; left bundle branch block (LBBB); digoxin use; clinical heart failure <6 months before inclusion; and age <30 years. Medication was withdrawn 7 days before the screening investigation if possible. The study was approved by the institutional review board, and all patients provided written informed consent.

Ambulatory ECG Recording
A Mortara H12 recorder (Mortara Instruments, Bilthoven, the Netherlands) was used for ambulatory ECG recording. This is a...
12-lead, digital Holter recorder, allowing 24-hour recording of a normal surface ECG with full disclosure possibilities. Electrodes (Red dot, 3M) were attached to the skin after meticulous preparation with a mild abrasive and a razor if needed. Electrodes were placed by following the standard 12-lead configuration, with modified aVL, aVR, and aVF attached to, respectively, the left shoulder, the right shoulder, and the left lower costal margin. Data were sampled at 180 Hz and stored on a flash card and were transferred to a computer for further analysis. Ambulatory ECG recording analysis was done with dedicated software (H-Scribe version 3.4, Mortara Instruments). The trend for ST segments was observed for ST segment depressions, and all possible episodes were visually verified by the investigator. Both reference and measurement points for ST segment level determination were averages of 4 samples, that is, equivalent with a duration of 22 ms. The reference point was automatically taken in the PQ segment; the measurement point was 60 ms beyond the J-point.

Significant ST depression was defined in 2 ways: (1) basic definition: depression of the ST segment level >0.1 mV compared with the baseline ST level for at least 1 minute, separated from another episode by at least 1 minute. Baseline ST level was defined as the predominant ST level throughout the registration; (2) strict definition: at least 0.1 mV horizontal or downsloping ST segment depression compared with the baseline ST level for at least 1 minute, separated from another episode by at least 1 minute. Additional criteria for the strict definition were changes in the ST segment caused by changes in body position (as shown by sudden ST segment changes accompanied by muscle artifacts) were excluded; in case of ST depression >0.05 mV but <0.1 mV on the resting ECG, 0.2 mV additional ST depression was required to be classified as significant ST depression; in case of resting ST elevation >0.1 mV but <0.2 mV, 0.1 mV relative ST depression was not sufficient to be defined as significant ST depression; instead, the recording was analyzed as if the baseline ST level was isoelectric; recordings with resting ST levels >0.2 mV ST segment depression or elevation were excluded from analysis.

When an ambulatory ECG recording was considered positive, the absence of complaints was verified with the patient as soon as possible after the recording.

Ambulatory Blood Pressure Monitoring
Ambulatory blood pressure monitoring (ABPM) was performed with a Spacelabs recorder type 90207. The recorder performed a measurement every 15 minutes from 7 AM to 11 PM and every 30 minutes from 11 PM to 7 AM. For every patient, the day-night dip in diastolic blood pressure (DBP) and systolic blood pressure (SBP) was calculated, expressed in percentage change from the daytime SBP and DBP. Nondipping was defined as a dip <10% in SBP or DBP. In case of large differences between the defined nighttime (11 PM to 7 AM) and the sleeping time in a subject, the nighttime was adjusted accordingly to calculate the dip.

Both recorders were carried around the waist, allowing full mobility. Patients were encouraged to follow a normal daily pattern and not to refrain from their usual physical activities. Subjects were asked to note the following events in a diary: walking, eating, sleeping, other physical or sedentary activities, and complaints.

Statistics
Categorical data were compared by use of the Fisher exact test; means from continuous data were compared by use of the unpaired Student t test.

Results
One hundred ninety-four patients were screened. In total, 4400 hours of successful ABPM and ambulatory ECG recording were obtained (mean per patient, 23 hours; range, 8 to 25 hours). In 45% of the patients, antihypertensive medication was withdrawn 2 to 7 days before the screening (in 50 patients for 7 days; in 2 patients for 3 days; in 3 patients for 2 days; and in 1 patient for 1 day). In 3 patients, the medication was resumed after 2 (1 patient) and 3 (2 patients) days because of complaints accompanying elevated blood pressure. There were no adverse events. The characteristics of the subjects are summarized in Table 1.

Ambulatory ECG Recording
Evaluation of the ambulatory ECG recordings with the basic definition of significant ST depression yielded 22 positive recordings, suggesting a prevalence of 11.3% of myocardial ischemia in our population of hypertensive patients. However, when we evaluated the recordings according to the strict definition of significant ST segment depression, we found 10 positive recordings, a prevalence of 5.2%. This means that noncritical analysis of ambulatory ECG recordings may lead to doubling of the prevalence of silent ischemia. When the patients with a positive recording according to the strict criteria only are considered as “true-positives” (n=10) and are compared with the so-called false-positives (the patients with a positive recording according to the basic criteria; n=12), there were no differences in cardiovascular risk factors, blood pressure level, or use of medication, but there was a higher proportion of men in the false-positive group (83% versus 40% P=0.04; see Table 1).

A description of the individual recordings that were labeled as positive according to the basic definition is given in Table 2. The most frequent cause of labeling these recordings as positive was an ECG with an elevated ST segment that was shaped normally (upsloping) at rest but that became relatively depressed (>0.1 mV) during a higher heart rate (n=7). However, the absolute ST segment level never became lower than −0.1 mV, as was required in adhering to the strict criteria. An example is given in Figure 1. Other reasons were right bundle branch block (RBBB) in conjunction with either baseline elevation or T-wave alterations, upsloping ST depression, and ST segment change caused by body position change. All together, in 10 recordings, the ST segment level was not horizontal or downsloping during the ST segment depression. An example of a “true-positive” ischemic event is shown in Figure 2.

Two patients with ST depression, both in the strict criteria group, had dyspnea during the ST segment depression that was only reported after we asked confirmation of the absence of complaints in the diary.

Ambulatory Blood Pressure Monitoring
The average ambulatory SBP in all patients during the day time (7 AM to 11 PM) was 152±13 (mean±SD), the DBP was 94±17 mm Hg, and heart rate was 77±9 bpm. During the night, SBP was 137±12 and DBP was 82±10 mm Hg. Fifty patients (25%) were nondippers. There was no difference in the blood pressure level between the false-positive recordings and the true-positive recordings (see Table 1).

Discussion
In a large population of patients with primary hypertension without known CAD, we investigated the prevalence of silent ischemic episodes in daily life. This may be of importance, since the high prevalences previously reported may shed light on the link between the presence of hypertension and the
occurrence of ischemic heart disease in later life. Furthermore, the applied criteria in the definition of significant ST depression differ between various studies, and we thought that this should have a large influence on the reported prevalence and accuracy.

We found that the prevalence was considerably lower than previously reported in the literature. The use of 2 sets of criteria allowed us to analyze possible reasons for overestimation of ischemic episodes. Nonspecific ST depression consisted of upsloping ST depression, pseudonon-
malization (ie, lowering of an elevated resting ST level during a higher heart rate), ST segment changes caused by changes in body position, changes in T-wave amplitude, rate-dependent or (in)complete RBBB, or combinations of these elements. In all of these cases, relative ST level change was at least 1 mm, leading to the possible misdiagnosis of significant ST depression.

The first step in Holter (ST-) analysis is software based, which is objective but nondiscriminate. Only visual correction of recognized episodes may lead to a meaningful conclusion. This last step is subjective and may be misleading even when apparently clear-cut criteria are used. In our study, the inclusion of false-positive ambulatory ECG recordings led to a more than doubled prevalence of silent ischemia in hypertensive patients. The prevalence corrected for these episodes (5.2%) is considerably lower than reported in the literature. Several factors may be responsible for this variation in prevalence, such as severity and duration of hypertension, presence of other cardiovascular risk factors, subject age, and cessation of medication. We assessed the severity of hypertension by using ABPM, which gives an accurate representation of the blood pressure level during the day, and found more or less similar blood pressure levels as other studies did. The low prevalence was present despite the use of 12-lead Holter recording, which has been shown to increase the detection of ischemic episodes. Medication was not withdrawn in less than half of the patients in our study. This may have affected the prevalence, but it is not likely that the difference in prevalence according to the different analysis criteria, which is our main finding, would be changed with a higher proportion of patients in whom medication would have been withdrawn. Furthermore, in the true-positive and false-positive groups, patients with continued medication and patients with withdrawn medication were labeled positive, in a similar percentage.

One would assume that all studies apply the same criteria in defining significant ST segment depression, but the description of these criteria is often concise and includes large variations. For example, for ST segment analysis, some studies include modified lead V1, a lead with a low R-wave amplitude and therefore not recommended for ST-level detection. Furthermore, studies differ in the exclusion of recordings due to either "rest" or "(marked) baseline ECG changes suggestive of myocardial ischemia at rest," which allows a broad interpretation, and studies may differ in the exclusion of (rate dependent) bundle branch block or only LBBB. Finally, not all studies explicitly define only horizontal or downsloping ST segment depression as meaningful or mention the exclusion of recordings with ST segment changes caused by body position changes.

We did not perform echocardiography to assess left ventricular mass. In our study, the presence of resting ECG changes that may be the result of left ventricular hyper-

Figure 1. Example of false-positive ischemic event. Note that the baseline ST level is elevated, with additional upsloping ST depression >1 mm during activity, which was labeled as positive by Holter software. Seven of 12 patients had this type of false-positiveness.

Figure 2. Example of true-positive ambulatory ECG recording. At rest there is a normal ST segment (upper panel), but during an increase in heart rate (lower panel) >1 mm horizontal ST depression ensues.
trophy was especially important. It is not known to what extent the presence of echocardiographic hypertrophy without baseline ECG changes affects the interpretation of ST segment changes. ECGs with baseline ECG changes that accompany ventricular hypertrophy appear to be prone to false labeling as positive, since 8 of 12 ECGs in the false-positive group and only 1 of 10 in the true-positive group showed these kinds of baseline changes.

A criticism of our study could be that we did not substantiate the ECG findings with another method of ischemia detection. However, a gold standard is not available for the verification of cardiac ischemia in this particular patient group. Some studies use quantitative coronary angiography as gold standard and consider cardiac ischemia in the absence of CAD documented by angiography as false-positive. Nevertheless, coronary angiography has its limitations to assess the functional significance of intermediate lesions, suggesting that angiography cannot be used as a gold standard without any reserve. Furthermore, it may very well be that ST depression that does not concur with angiographic findings or with other diagnostic modalities represents ST depression caused by microvascular abnormalities. By following that line of reasoning, the reported low sensitivity of ECG investigations may be ready for revision by newer techniques that can measure flow at the tissue level (MRI, positron emission tomography).

It would be interesting to assess the outcome of the 2 patient groups to see whether a difference in prognosis is present. Moreover, it would be especially interesting to investigate whether patients in the false-positive group have a worsened prognosis compared with hypertensive patients without ambulatory ECG changes, but it is too soon to perform such an analysis and it would probably require a larger study group.

We conclude that the prevalence of silent cardiac ischemia in hypertensive patients may not be as high as previously reported in literature. The stringency of applied criteria seems to have an important influence on this prevalence. This finding may have important implications for population-based studies investigating silent ischemia in hypertensive and other patient groups.

**Perspectives**

In summary, the prevalence of silent cardiac ischemia in hypertensive patients as assessed by ambulatory ECG monitoring was highly dependent on the criteria used for ST segment analysis. Furthermore, even with the application of strict criteria, adapted from those advised by the American Heart Association/American College of Cardiology, the prevalence of silent ischemia was remarkably low in our hypertensive population. This may have important implications for population-based, interventional studies performed in this patient group.

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**References**


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