# Significance of QRS Duration Changes in the Evaluation of ST-Segment Depression Presenting Exclusively During the Postexercise Recovery Period

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**Background:** The aim of this study was to evaluate the contribution of QRS prolongation in the diagnosis of coronary artery disease (CAD) in patients with exercise-induced ST-segment depression exclusively during the recovery period.

**Methods:** The study population consisted of 107 patients (90 males and 17 females) aged 39–70 (mean 59 ± 7) years who underwent a treadmill exercise test using Bruce protocol and presented ST-segment depression limited to the recovery period. Angiographic data were available for all studied patients.

**Results:** Among studied patients, 74 (69%) were found to have hemodynamically significant CAD, while the remaining 33 (31%) had normal coronary arteries. Concomitant QRS prolongation was revealed in 61 (82%) of the patients with angiographically documented CAD, while in 13 (18%) patients QRS duration remained unchanged. On the contrary, only 4 (12%) of the 33 patients with normal coronary arteries showed prolonged QRS duration during ST depression, while in the remaining 29 (88%) QRS duration remained unchanged.

**Conclusions:** The evaluation of the concomitant QRS duration changes may discriminate patients with truly ischemia-induced ST-segment depression limited to the recovery period.

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QRS prolongation; ST-segment depression; recovery period; coronary artery disease

## INTRODUCTION

Although ST-segment depression remains the "gold standard" for the detection of myocardial ischemia during exercise testing (ET), the persistent effort of clinical investigators to discover accessory indicators, markers or scores in order to improve its diagnostic accuracy points out the limited diagnostic power of this index. Moreover, concerning ST-segment depression limited to the recovery period, its diagnostic value has not yet been completely clarified. Although it is supported to have similar diagnostic ability to ST-segment changes during the active phase of ET, there are only a limited number of studies investigating its clinical significance.[1–6] On the other hand, exercise-induced QRS prolongation has been considered as a reliable electrocardiographic (ECG) index that improves accuracy of concomitant ST-segment depression during the active phase of ET, as the QRS duration increases in the presence of exercise-induced ischemia and shortens or remains unchanged in its absence.[7–10]

The aim of this study was to assess the diagnostic value of ST-segment depression induced exclusively during the recovery period with the concomitant evaluation of the QRS duration changes.

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# METHODS

## Study Population

Among 2236 patients who underwent treadmill ET using Bruce protocol from 1999 to 2002 in our laboratory, we selected those who developed ST-segment depression limited to the recovery period and who underwent coronary angiography within 1 month of the test. All the selected patients had performed ET for angina-like symptoms evaluation and none of them had known coronary artery disease (CAD). Patients with significant CAD were considered and those who had a stenosis ≥70 in diameter in at least one major coronary artery were angiographically documented.

We excluded patients with impaired left ventricular function or cardiomyopathy, ECG evidences of left ventricular hypertrophy, known valvular or congenital heart disease, left or right bundle brunch block, preexcitation syndromes, pacing rhythm,or atrial fibrillation in resting ECG.

The study population finally consisted of 107 patients (90 males, 17 females) aged 39–70 (mean 59 ± 7) years. A full medical history for all subjects was obtained and a complete physical examination was performed. All medications were discontinued for at least five half-lives before testing performance.

The study was approved by our hospital's Ethics Committee and written informed consent was obtained from all participants.

## Exercise Testing

All patients performed exercise on a Quinton 5000 treadmill system (Quinton Instruments, Seattle, WA, USA), according to the multistage Bruce protocol, after a supine rest ECG was obtained. Blood pressure was measured every minute during exercise with sphygmomanometer. Exercise was terminated because of severe angina, fatigue, dyspnea, or severe arrhythmias. In the absence of symptoms, the test was terminated at the occurrence of a 3-mm ST-segment depression or a 2-mm ST-segment elevation, a decrease in systolic blood pressure ≥20 mmHg, severe arrhythmias, or an inability to exercise in addition because of fatigue.

An ischemic ST-segment response was defined as horizontal or downsloping ST-segment depression of ≥1 mm below the baseline, taken 60 ms after the J-point, upsloping ST-segment depression of ≥1.5 mm, taken 80 ms after J-point, or ST-segment elevation of 1 mm or more.

In each patient, the duration of QRS complex in leads aVF and $V_5$ was measured at a paper speed of 50 mm/s, before exercise (in both standing and supine positions), at the peak of exercise, and at the point of maximal ST-segment depression during the recovery period. The duration of the QRS complex was measured from the beginning of the Q wave until the cut-point between the isoelectric line and the perpendicular line starting from the end of the S wave (J-point). In case of Q wave absence, the measurement was done from the beginning of the R wave. If there was an obscurity of the S wave ending, the patient was not included in the study. QRS complex duration was measured in five beats each time in leads aVF and $V_5$. We used the mean values to calculate the change of QRS duration between the resting ECG in standing position and of that obtained at the peak of exercise and we compared it with the respective change of QRS duration between resting ECG in supine position and of that obtained at the time of maximal ST-segment depression during the recovery period.

ECG measurements were performed with a magnifying lens, by two of the investigators, who were unaware of the angiographic results. The intraobserver variability was 0.07 ± 0.05 mm for ST-segment changes and 0.21 ± 0.97 ms for QRS duration changes, respectively. Interobserver variability was 0.08 ± 0.05 mm for ST-segment changes and 0.14 ± 1.2 ms for QRS duration changes, respectively.

## Coronary Arteriography and Left Ventriculography

All patients underwent left ventriculography in the 30° right anterior oblique projection, at 40 frames/s. The area-length method was used for the calculation of the left ventricular ejection fraction. All patients underwent selective coronary arteriography, using the percutaneous (Judkins) technique. The left coronary artery was visualized in the 60° left anterior oblique, in the 30° right anterior oblique and in the left lateral, with 30° cranial angulation positions. The right coronary artery was visualized in the 60° left anterior oblique and the 30° right anterior oblique positions.

Significant coronary stenosis was considered a more than 70% diameter narrowing of the lumen of the left anterior descending, the left circumflex and the right coronary artery, or a diameter narrowing of at least 50% of the left main coronary artery. The

interpretation was performed by two investigators, who were unaware of ET results.

### Statistical Analysis

Values are expressed as mean ± SD. Chi-square test for categorical variables and *t*-test for continuous variables were used to compare the baseline characteristics of the groups of interest and the differences of the exercise parameters in the subgroups of the study population (patients with CAD and individuals with normal coronary arteries). All tests were considered to be significant at a 0.05 level of statistical significance. Statistical analyses were performed with SPSS statistical software (release 8.0).

## RESULTS

Demographic characteristics and also catheterization data of the studied patients are presented in Table 1. Out of 107 patients who presented ST-segment depression limited to recovery and underwent coronary angiography, 74 (69%) had significant coronary artery stenosis, while 33 of them (31%) had no significant artery stenosis or had normal coronary arteries. Among patients with CAD, 34 (46%) had one-vessel disease, 25 (34%) had two-vessel disease, and the rest 15 (20%) had three-vessel disease.

According to demographic and catheterization data (also presented in Table 1.), among dominant risk factors for atherosclerosis, patients with CAD presented only a higher prevalence of hyperlipidaemia, while they also revealed a lower average left ventricular ejection fraction, in comparison to subjects with normal coronary arteries.

Exercise parameters of the studied patients are described in Table 2. According to our findings, subjects without CAD achieved a significantly better exercise performance than patients with CAD, with greater exercise duration and higher maximal heart rate. In addition, there was no significant difference in the magnitude of the ST-segment depression between patients with and without CAD, pointing out that the severity of ST-segment depression limited to the recovery period could not be used as an index of presence of CAD.

The mean QRS duration at maximal ST-segment depression for the total 107 patients was found to be prolonged for 14.4 ± 15 ms from the baseline QRS duration. The duration of QRS at maximum ST-segment depression was found to be increased by more than 14.4 ms in 72 (97%) of the 74 patients with CAD and in only 1 (3%) of the 33 patients without CAD.

Among the 74 patients with angiographically documented CAD, simultaneous appearance of QRS prolongation and ST-segment depression during the recovery period was revealed in 61 (82%), while in the remaining 13 (18%) patients QRS duration shortened or remained unchanged. On the contrary, only 4 (12%) of the 33 patients with normal coronary arteries showed prolonged QRS duration during ST-segment depression, while in the remaining 29 (88%) QRS duration was shortor remained unchanged. Patients with CAD developed

**Table 1.** Demographic Characteristics and Catheterization Data of the Studied Patients

| | Patients with CAD (n = 74) | Patients without CAD (n = 33) | P-Values |
|---|---|---|---|
| Male/female | 64/10 | 26/4 | NS |
| Age (years) | 61 ± 4 | 57 ± 6 | NS |
| Arterial hypertension | 10 (14%) | 6 (18%) | NS |
| Hypercholesterolemia | 52 (70%) | 10 (30%) | <0.01 |
| Diabetes mellitus | 6 (8%) | 2 (6%) | NS |
| Smokers | 43 (58%) | 18 (55%) | NS |
| Number of diseased coronary arteries | | | |
| 1 | 34 (46%) | – | |
| 2 | 25 (34%) | – | |
| 3 | 15 (20%) | – | |
| EF (%) | 48 ± 6 | 54 ± 4 | <0.05 |

CAD = coronary artery disease; EF = ejection fraction. Values express mean ± 1SD.

**Table 2.** Exercise Parameters of the Studied Patients

| | Patients with CAD (n = 74) | Patients Without CAD (n = 33) | P-Values |
|---|---|---|---|
| Duration of exercise (seconds) | 486 ± 42 | 635 ± 51 | <0.05 |
| Maximal heart rate (bpm) | 149 ± 18 | 162 ± 16 | <0.05 |
| Maximal systolic BP (mmHg) | 186 ± 16 | 180 ± 14 | NS |
| Maximal ST-segment depression (mm) | 1.8 ± 0.8 | 1.7 ± 0.6 | NS |
| Baseline QRS duration (ms) | 102 ± 10 | 99 ± 12 | NS |
| QRS duration changes at peak exercise (ms) | 2 ± 8 | −3.3 ± 10 | NS |
| QRS duration changes at maximal ST-segment depression during the recovery period (ms) | 22.6 ± 6 | −4.2 ± 10 | <0.05 |

CAD = coronary artery disease; bpm = beats per minute; BP = blood pressure. Values express mean ± 1SD.

a slight prolongation of mean QRS duration at the peak of ET (2 ± 8 ms), but at the point of maximal ST-segment depression in the recovery period QRS was measured significantly prolonged (22.6 ± 6 ms). The extent of QRS prolongation in patients with CAD was correlated to the number of the diseased coronary arteries, as it is shown in Table 3. On the other hand, patients without CAD revealed a mild decrease of mean QRS duration both at the peak of ET and at the point of maximal ST-segment depression in the recovery period QRS (−3.3 ± 10 ms and −4.2 ± 10 ms, respectively).

According to our results, the sensitivity of concomitant QRS prolongation to discriminate true positive ST-segment depression limited to the recovery period was found 82%, while the specificity was found 88%.

## DISCUSSION

This is the first study to support that QRS duration measurement could be used as a reliable accessory ECG indicator in the evaluation of ST-segment depression limited to the recovery period of the treadmill ET. Using coronary angiography to confirm hemodynamic significant CAD, we found that in the group of patients with ST-segment depression exclusively during the recovery period and CAD, statistically significant QRS prolongation was detected, while in the absence of CAD the QRS duration did not change significantly.

**Table 3.** Correlation of the Extent of QRS Prolongation to the Number of Diseased Coronary Arteries

| Number of Diseased Coronary Arteries | QRS Duration Changes in the Recovery Period (ms) |
|---|---|
| One—VD (n = 34) | 18.8 ± 2.9 |
| Two—VD (n = 25) | 24.4 ± 6.1 |
| Three—VD (n = 15) | 28.5 ± 6 |

VD = Vessel disease. Values express mean ± 1SD.

The clinical meaning of ST-segment depression limited to the recovery period, as well as its pathophysiologic mechanism, remains unclear. Evaluating its diagnostic value, almost all the previous studies have suggested that it is comparable to that of ST-segment depression during the active phase of ET, using as a criterion either angiographic[1,3,6] or scintigraphic.[2,5] In addition, investigators have also described a similar prognostic power of these two different patterns of abnormal ET.[4,6] However, evaluation of ST-segment changes during the recovery phase of ET in clinical practice has not been currently established.

In most of the referred studies, although ST-segment depression exclusively during the recovery period was found of similar diagnostic value with "classic" active-phase ST-segment depression, there was a tendency toward lower sensitivity of the former pattern of ET changes. Among patients with ST-segment depression exclusively during the recovery period who underwent SPECT study, Soto and colleagues[5] found reversible scintigraphic defects in 72% of these patients with ST changes during exercise and in 65% of these with ST changes limited to the recovery period. In addition, among patients with ST-segment depression during the active and recovery phase of ET who underwent coronary angiography, significant CAD was detected in 85% and 78% by Lanza et al.[6] and in 87% and 84% by Lachtermann et al.,[3] respectively. However, none of the previous studies has ever tested any

methods to improve the accuracy of ST-segment depression exclusively during the recovery period, as has been widely in the past with "classic" exercise-induced ST-segment changes, with the use of a variety of additional criteria.

The value of QRS prolongation to assess exercise-induced myocardial ischemia has been previously supported by several studies.[7–10] It has been suggested that the QRS duration increases in the presence of exercise-induced myocardial ischemia and shortens or remains unchanged in its absence. Nevertheless, QRS prolongation has already been supported to decrease false-positive ET results in female population,[11,12] in patients who have undergone percutaneous transluminal coronary angioplasty (PTCA)[13] and in patients during the postmyocardial infarction period.[14]

According to previous reports, exercise-induced ST-segment depression attributed to true myocardial ischemia during the active phase of ET should be followed by QRS prolongation at the peak of ET, while QRS duration in patients with false-positive should remain unchanged or even shorten. In our study, in the group of patients with ST-segment limited to recovery period that was found to have normal coronary arteries, mean QRS duration was found slightly decreased (in comparison to baseline measurements) both at the peak of exercise ($-3.3 \pm 10$ ms) and at the point of maximal ST depression in the recovery period ($-4.2 \pm 10$ ms). On the other hand, in the group of patients with ST-segment depression limited to the recovery period and documented CAD, QRS duration had already, although nonsignificantly, increased at the peak of exercise, before ST-segment changes reveal ($2 \pm 8$ ms). However, a significant QRS prolongation was detected at the point of maximal ST-segment depression in the recovery phase ($22.6 \pm 6$ ms).

In the previous studies, QRS duration was measured at the peak of ET, independent of the point of ST-segment depression onset. In the current study, QRS duration was measured at two different points during ET. Although QRS duration measurement at the peak of ET did not show any significant difference between the group of patients with and without CAD, there was a slight tendency for QRS prolongation in the former group, while QRS duration slightly decreased in the latter group. We hypothesized that this could be a sign that ischemia-induced QRS prolongation may precede ST-segment depression. It seems technically difficult to successfully measure a continuous QRS duration during ET. However, in case ischemia-induced QRS prolongation really precedes ST-segment depression, this could be a significant improvement in the diagnosis of exercise-induced myocardial ischemia in a number of patients with false-negative ET, due to the inability to achieve adequate work.

## LIMITATIONS

The main limitation of this study is that it is a retrospective analysis of ECG findings within a selected population of patients who had ST-segment depression only during the recovery period. Study patients were also selected for coronary angiography thereafter. Therefore, the diagnostic yield of ST-segment depression during the recovery period in the current population is not known. Accordingly, it cannot be established from the present study results whether QRS prolongation accompanying ST-segment depression during the recovery period increases the sensitivity and specificity of the latter ECG finding for the diagnosis of significant CAD. Finally, although the change of QRS duration was significantly associated with the presence of CAD, this study was underpowered to examine if this association is independent of the possible effects of other confounding factors, which differ between the groups of the study population.

In conclusion, we could state that when exercise-induced ST-segment depression limited to the recovery period occurs in patients with significant CAD, it is usually accompanied by QRS prolongation; when it occurs in patients without significant CAD, QRS duration is not increased in most of them. Additional studies are needed to establish whether this finding increases the diagnostic yield of postexercise ST-segment depression.

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