Detection of transient myocardial ischemia by computer analysis of standard and signal-averaged high-frequency electrocardiograms in patients undergoing percutaneous transluminal coronary angioplasty

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ABSTRACT Electrocardiographic manifestations of transient myocardial ischemia were studied, in 11 patients undergoing angioplasty (PTCA) of a left anterior descending coronary artery stenosis, by the visual inspection of the standard surface electrocardiogram (S-ECG) and the intracoronary ECG (IC-ECG) as well as computer-assisted analysis of the S-ECG. Cross-correlation analysis (CCA) performed by computer was used to compare beat-to-beat variability in ST-T morphology of the S-ECG during different stages of PTCA. CCA was also applied to the signal-averaged high-frequency QRS (SA-HFQ). All patients developed angina during balloon inflation, accompanied by transient marked ST-T changes in IC-ECG in 10 of 11 patients (90%). Visual inspection of S-ECG revealed transient ST-T changes in only 6 of 11 (54%). In contrast, CCA of the S-ECG revealed transient ST-T changes in 9 of 11 (82%). Analysis of SA-HFQ revealed that balloon inflation was associated with a marked reduction in the calculated root-mean-square (RMS) voltage for such signals (2.31 ± 1.04 μV) as compared with RMS values before (3.27 ± 1.12 μV, p < .05) PTCA or after conclusion of PTCA (3.79 ± 1.39 μV, p < .01). Balloon inflation was also accompanied by changes in waveform morphology of the SA-HFQ, including the development of new or more prominent time zones of reduced amplitude in 10 of 11 individuals (90%). Such zones may represent slow conduction in regions of the heart rendered ischemic during PTCA. CCA of the S-ECG and of SA-HFQ appears to detect evidence of transient ischemia with greater sensitivity than simple visual inspection of S-ECG, and may therefore prove to be of use in the evaluation of patients with chest pain of uncertain origin.


THE SURFACE ELECTROCARDIOGRAM (ECG) is relied upon heavily in the diagnosis of ischemic heart disease but may not always reflect ischemia in all regions of the heart. Insensitivity of the standard surface ECG stems, in part, from the observation that the magnitude of potentials recorded from leads on the body surface varies inversely with the distance between such leads and the heart itself. 1, 2 Potentials recorded from the body surface may also be influenced by the lead field of the recording lead relative to the local potential source such as a region of ischemia. Profound abnormalities of depolarization or repolarization caused by ischemia may, as a consequence, be reflected by relatively minor changes in the surface ECG or may not be apparent at all during casual inspection. Recent studies have focused attention on new techniques that may enhance the diagnostic information present on the ECG. Signal-averaging to improve signal-to-noise ratios is one such technique. Another is to record ECGs with an extended bandwidth of up to 1000 Hz, yielding what have variously been referred to as "high frequency," "high fidelity," or "wideband" ECGs. Studies of high-fidelity ECGs, both with and without signal aver-
aging, have revealed abnormalities in and immediately after the QRS complexes in some patients with hypertrophy, prior infarction, or ventricular aneurysms that are not apparent from inspection of the standard ECG and that are usually absent in individuals with normal hearts.3-8 However, such techniques have not yet been used in patients to examine the effects of transient ischemia on the ECG. The present study was designed to test the ability of computer-assisted analysis of standard as well as high-frequency ECGs to detect effects of transient ischemia in patients undergoing percutaneous transluminal coronary angioplasty (PTCA).

Methods

Eleven patients with disabling angina undergoing PTCA of a critical stenosis in the left anterior descending coronary artery (LAD) were selected as subjects for this study after giving written informed consent in accordance with guidelines established by the Human Subjects Committee of the hospital. All patients underwent PTCA by a femoral approach according to previously described standard techniques that are routine for our laboratory.9

Recording protocol. In each patient surface electrocardiographic leads I, aVL, and V₅ were continuously monitored and recorded during PTCA by means of a photographic multichannel oscillographic recorder (Electronics for Medicine VR-16, Pleasantville, NY) at paper speeds of 10, 25, and 50 mm/sec. Band-pass filters of the ECG amplifiers were set of 0.01 to 100 Hz for leads I and aVL. V₅ was recorded as a high-fidelity signal with the use of band-pass filters between 0.01 to 500 Hz. In addition to three surface electrocardiographic leads, a local unipolar intracoronary ECG from myocardium distal to the LAD stenosis being dilated was also continuously monitored and recorded according to our previously described method.10 In brief, the intracoronary unipolar ECG was obtained by positioning a standard PTCA guidewire and balloon catheter across the target stenosis and then connecting the proximal end of the guidewire as it exited from the balloon catheter to a precordial lead of a standard surface electrocardiographic cable by means of a sterile double alligator connector. With the use of Wilson's Central Terminal for the indifferent electrode, the intracoronary ECG was filtered between 0.01 and 500 Hz and recorded simultaneously with the three surface electrocardiographic leads being monitored. In addition to real-time paper recordings, the surface and intracoronary ECGs were also stored on tape (TEAC R-71 FM recorder, frequency response DC-1250 Hz, TRITEK, Burlington, MA) for later playback and analysis. Before advancement of the guidewire and balloon catheter across the target LAD stenosis, the three surface electrocardiographic leads were recorded for a control period of 2 min. These leads and the intracoronary ECG were then recorded continuously immediately after the guidewire and balloon catheter had been positioned across the stenosis and during all subsequent balloon inflations and deflations. Throughout the procedure all patients were questioned repeatedly about the presence or absence of chest pain; these responses were recorded along with the surface and intracoronary ECGs. Ten minutes after completion of the dilatation and withdrawal of both the guidewire and balloon catheter from the LAD another recording of the surface electrocardiographic leads was obtained for 10 min.

Beat-to-beat variability of the ECG. With the use of a computer algorithm based on a previously described normalized cross-correlation scheme,11 ECGs recorded during PTCA were examined for transient morphologic changes associated with balloon inflation and deflation. This method was applied to surface leads I, aVL, and V₅ to detect abnormalities in the ST segment and T wave and to the high-fidelity signal recorded from V₅ to detect abnormalities in the high-frequency components of the QRS complex (see below). For each lead a single electrocardiographic waveform recorded during the initial 2 min control period before advancement of the guidewire or balloon catheter across the stenosis was chosen as a reference template. Electrocardiographic waveforms recorded during subsequent phases of the PTCA were then compared with this reference template to determine whether transient abnormalities appeared during subsequent phases of the procedure. For analysis of beat-to-beat variability in the ST segment and T wave, the ST segment and T wave of the single template waveform was used as a reference for the cross-correlation procedure. Similarly, beat-to-beat variability of high-frequency QRS complexes was assessed by use of the single high-frequency QRS complex of the template waveform as a reference for cross-correlation analysis. Before cross-correlation, baselines were removed. A decrease in the cross-correlation coefficient of 10% during balloon inflation accompanied by a stable baseline before balloon inflation was arbitrarily defined as evidence of a significant change in waveform morphology.

In addition to computer analysis, surface ECGs recorded during PTCA were subsequently also analyzed visually for transient changes in waveform morphology resulting from balloon inflation and deflation. Visual analysis was performed independently by two investigators. In most instances there was agreement between the two individuals about whether changes in waveform morphology had occurred. In the few instances when one investigator noted a change in waveform morphology and the other did not, the analysis of the investigator who noted a change took precedence.

Signal-averaging of the high-frequency ECG. During playback of tape-recorded high-fidelity ECGs from lead V₅ the analog data were passed through a low-pass 6 pole Butterworth filter with a high-frequency cutoff at 360 Hz and then digitized by a 12-bit analog-to-digital converter with a sampling rate of 1024 Hz. The digitized data from surface lead V₅ were divided into three time segments. The first segment consisted of records obtained during the initial control recording period before advancement of the guidewire or balloon catheter across the target stenosis. The second and third time segments were, respectively, records obtained during the last 30 sec of initial balloon inflation and during the 10 min recording period after the conclusion of the procedure. Electrocardiographic waveforms in each time segment were averaged together to reduce the relative contribution of noise, with the use of a previously described cross-correlation scheme to align electrocardiographic waveforms during the averaging process.11 Processing of the digitized data was done off-line with a Masscomp MC-500 laboratory computer. Before signal averaging each of the digitized electrocardiographic waveforms was passed through a nonrecursive digital filter with a low-frequency cutoff at 30 Hz and a high-frequency cutoff at 250 Hz, as previously described.12 Filtering of the signals took place in the frequency (Fourier) domain by using a fast-Fourier transform algorithm. During signal averaging of nonfiltered waveforms, the point of maximum correlation for each filtered waveform as compared with a reference filtered waveform in the same time segment was taken as its fiducial point for averaging the nonfiltered waveforms. Averaged original waveforms from each time segment were then bandpass filtered between 150 and 250 Hz and were used to compute the root-mean-square (RMS) voltage of the filtered QRS complex as well as the envelope of the filtered QRS complex.
**RMS determination.** The RMS value of the averaged high-frequency QRS complex was defined as

\[
\text{RMS} = \left[ \frac{1}{n} \sum_{j=1}^{n} f(t_j)^2 \right]^{1/2}
\]

where \( t_j \) = jth sample point; \( f(t_j) \) = electrocardiographic amplitude at the jth sample point. RMS values were computed from the averaged high-frequency QRS complex in each time segment, and a computer algorithm was used to define the time of onset and termination of the QRS complex. The computer accomplished this by measuring RMS noise level in the TP segment and then searching between the PR interval and the ST segment for a signal with RMS amplitude greater than three times the RMS of the noise.

**High-frequency QRS complex envelope determination.** Averaged and filtered high-frequency QRS complexes obtained by the methods described above were sampled by computer at intervals of 1/1024 sec and then analyzed to determine the boundaries or envelopes of the waveforms. The upper and lower boundaries of the envelope were defined as the line segments connecting local maxima and minima, respectively. A local maximum, \( V_{\text{max}} \), was determined to be located at sample point \( t_i \) if and only if the amplitude of the high-frequency ECG, \( V(t_i) \), at this point exceeded by the amplitude of the three sample points preceding and following \( t_i \):

\[ [V(t_i-3), V(t_i-2), V(t_i-1)] < V(t_i) > [V(t_i+1), V(t_i+2), V(t_i+3)] \]

Similarly, a local minimum, \( V_{\text{min}} \), was determined to be located at sample point \( t_i \) if and only if the amplitude of the high-frequency ECG, \( V(t_i) \), at this point was lower than the amplitude of three sample points preceding and following \( t_i \):

\[ [V(t_i-3), V(t_i-2), V(t_i-1)] > V(t_i) < [V(t_i+1), V(t_i+2), V(t_i+3)] \]

A reduced amplitude zone within the envelope of the averaging high-frequency QRS complex was considered to be present if at least two local maxima of the upper envelope or two local minima of the lower envelope were found. In such cases an RAZ was defined to be the region lying between two neighboring maxima or minima. As has been described previously, \( 13 \) zones of reduced amplitude are usually not present in the signal-averaged high-frequency QRS complex of normal individuals. Figure 1 is a representative example of the signal-averaged nonfiltered QRS complex of lead \( V_5 \) (top trace) from a normal individual without coronary artery disease. The middle and bottom traces in this figure are, respectively, the signal-averaged high-frequency QRS and the computer-generated delineation of the envelope of the averaged high-frequency QRS. As can be seen, no zone of reduced amplitude is apparent within the envelope of this signal (bottom trace, figure 1).

**Statistical methods.** RMS values computed for each of the three time segments during PTCA were compared with one

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**FIGURE 1.** Signal-averaged nonfiltered QRS of surface lead \( V_5 \) (top), the signal-averaged high-frequency (150 to 250 Hz) QRS (middle), and the computer-generated delineation of the envelope of the signal-averaged high-frequency QRS (bottom) from a normal subject with no coronary artery disease. Note smooth contour of the envelope and absence of a zone of reduced amplitude.
ABBOUD et al.

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Coronary stenoses</th>
<th>Baseline ECG</th>
<th>Prior MI</th>
<th>Angina during PTCA</th>
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<td>WNL</td>
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</tr>
<tr>
<td>4</td>
<td>49</td>
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<td>5</td>
<td>71</td>
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<td>LAD,LCX</td>
<td>Q waves V1,V2</td>
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<td>6</td>
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<td>9</td>
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<td>M</td>
<td>LAD,RCA</td>
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<td>11</td>
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<td>M</td>
<td>LAD</td>
<td>ST-TW-A</td>
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LCX = left circumflex artery; RCA = right coronary artery; WNL = within normal limits; ST-TW-A = nonspecific ST segment and T wave abnormalities; LVH = left ventricular hypertrophy; MI = myocardial infarction.

another by a t test. Values were expressed as the mean ± SD with statistical significance defined as p<.05.

Results

The clinical characteristics of the 11 patients studied are summarized in table 1. All patients were men with ages ranging between 42 and 71 years. The mean age for the group was 54 years. Seven patients had significant stenosis only of the LAD, whereas four patients had disease involving the circumflex or right coronary arteries as well as the LAD. In this latter group the LAD stenosis was the most critical lesion and was the first lesion targeted for PTCA. Baseline 12-lead ECGs before PTCA were interpreted as within normal limits in four patients. Q waves suggestive of infarction were present in only one individual, although prior infarction had been documented by typical enzyme elevation in two patients. The remaining patients had nonspecific ST segment or T wave abnormalities on the resting ECG.

Visual inspection of the ECG during PTCA. A typical pattern of response of the surface and intracoronary ECGs to balloon inflation in the LAD, recorded during PTCA in subject 5 (table 1), is illustrated in figure 2. After advancement of the balloon catheter and guidewire across the stenosis but before balloon inflation only nonspecific ST segment and T wave abnormalities were apparent from visual inspection of the surface ECG (first two complexes, figure 2, A). At this time, ST segment elevation in the intracoronary ECG was absent (figure 2, A). Within seconds of balloon inflation (arrow figure 2, A), marked ST segment elevation in the intracoronary ECG appeared, accompanied by angina, even though the surface ECG revealed very little change. After 30 sec of balloon inflation ST segment elevation of 1.75 mV was easily detectable on the intracoronary ECG, but was still only barely detectable on the surface ECG (figure 1, B). After balloon deflation ST segment elevation on the intracoronary ECG disappeared promptly, along with resolution of angina.

Among the 11 patients studied, 10 individuals (90%) developed transient marked ST segment and T wave abnormalities that were obvious by visual inspection of the intracoronary ECG during balloon inflation (table 2). In contrast, visually apparent ST segment and T wave abnormalities in one or more of the surface leads during balloon inflation were found in only six patients (54%). When both the intracoronary and surface ECG developed ST segment abnormalities during balloon inflation, the changes appeared earlier and were always of greater magnitude on the intracoronary ECG. Only a single patient was encountered in whom the intracoronary ECG remained unchanged during balloon inflation, even though ST segment elevation on the surface ECG appeared, accompanied by angina (table 2). In all 11 subjects visual analysis of QRS complexes in the surface leads failed to disclose any transient changes in response to balloon inflation or deflation.

Beat-to-beat variability of ECG. Computer-assisted cross-correlation of ST segments and T waves on the surface ECG revealed evidence of transient morphologic changes in these waveforms during PTCA. An example of such an analysis is illustrated in figure 3. These records were derived from analysis of the ST segment and T waves in lead V5 from patient 5, the individual depicted in figure 1 in whom visual inspection of the surface ECG failed to reveal any ST segment or T wave abnormalities during balloon inflation, even though transient marked ST segment elevation developed on the intracoronary ECG. The morphology of
FIGURE 2. Surface leads I, aVL, and V₅ along with the intracoronary ECG (IC-ECG) during PTCA of an LAD. A, Arrow denotes balloon inflation, which is followed by marked ST segment elevation in the IC-ECG with little change in the surface leads. B Records obtained after 30 sec of balloon inflation. Time lines = 1.0 sec; calibrations at left = 1.0 mV for I, aVL, and V₅, 2.0 mV for IC-ECG.

TABLE 2
Intracoronary and surface electrocardiographic changes during PTCA

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>ST-T changes in IC-ECG</th>
<th>ST-T changes in S-ECG by visual inspection</th>
<th>ST-T changes in S-ECG by cross-correlation</th>
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<tbody>
<tr>
<td>1</td>
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<td>+</td>
<td>+</td>
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<tr>
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</tr>
<tr>
<td>11</td>
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</table>

IC-ECG = intracoronary ECG; S-ECG = surface ECG; ST-T = ST segment and T wave.

Each ST segment or T wave after balloon inflation was compared by cross-correlation with the morphology of the ST segment and T wave of a single reference template waveform recorded before balloon inflation. As shown in figure 3, 35 beats after balloon inflation the cross-correlation coefficient fell from an initial value of 0.93 to a nadir of 0.83, indicating the appearance of a change in the ST segment and T wave morphology as compared with baseline. The cross-correlation coefficient then returned to its control value within 20 beats after balloon deflation.

The results of cross-correlation analysis of the ST segment and T waves on the surface ECG for each of the 11 patients studied are listed in table 2. Nine of the 11 patients (82%) demonstrated ST segment and T wave abnormalities during PTCA by cross-correlation analysis, where only six individuals (54%) developed transient ST segment and T wave abnormalities that were apparent by visual inspection of the surface ECG.
alone (table 2). No individuals were encountered in whom cross-correlation analysis failed to detect transient abnormalities that were apparent by visual inspection.

An example of computer-assisted cross-correlation analysis of the ST segments and T waves of standard surface lead V5 together with the high-frequency (150 to 250 Hz) nonaveraged QRS complex from surface lead V5 during PTCA is illustrated in figure 4. Nonaveraged high-frequency QRS complexes are characterized by very low signal-to-noise ratios. Because of this problem, acceptable cross-correlation curves for analysis of beat-to-beat variability in QRS morphology could be generated in only three patients. Figure 4 depicts the curve derived for one of these patients (subject 10, table 1). In the top panel of figure 4, a change in morphology of the ST segment and T waves of standard surface lead V5 became apparent 50 beats after balloon inflation, manifested by a precipitous decline in the cross-correlation coefficient from its initial value of .99 nadir of .91. The cross-correlation coefficient for the ST segments and T waves then returned to its control value within 20 beats after balloon deflation (figure 4, top). Cross-correlation analysis of the nonaveraged high-frequency QRS complex during PTCA in the same patient is shown in figure 4, bottom. Because of the low signal-to-noise ratio for this waveform, note that the initial cross-correlation coefficient of complexes recorded before balloon inflation derived by comparison with a reference pre-PTCA complex was lower than the coefficient derived during analysis of ST segments and T waves of the standard surface ECG (.74 before balloon inflation, figure 4, bottom, vs .99 before balloon inflation, figure 4, top). Within several beats after balloon inflation cross-correlation analysis of the high-frequency QRS complex revealed a prompt decline in the correlation coefficient to a nadir of .38, indicative of a morphologic change in this waveform in response to balloon inflation (figure 4, bottom). After balloon deflation, the correlation coefficient returned to its control value within 20 beats (figure 4, bottom). Thus, in spite of a lower initial cross-correlation coefficient, beat-to-beat analysis of the high-frequency QRS complex revealed a change in

FIGURE 3. Computer-generated cross-correlation analysis of ST segment and T wave morphology of the surface ECG during PTCA in the same patient whose records are illustrated in figure 1. See text for discussion.
morphology more quickly than similar analysis of the ST segment and T waves of the standard surface ECG.

**Signal-averaged high-frequency QRS analysis.** Analysis of the signal-averaged high-frequency QRS and of the envelopes of these signals recorded during the control period, before advancement of the balloon catheter across the target stenosis, disclosed two distinctly different morphologic patterns. The most common pattern, occurring in nine of the 11 patients, is depicted in figure 5, left. The upper trace in this panel is the

![Heart Beat Graph]

**FIGURE 4.** Computer-generated cross-correlation analysis of ST segment and T wave morphology of the standard surface ECG (top) and of the nonaveraged high-frequency QRS complexes in lead V3 (bottom) during PTCA in patient 10. Balloon inflation was followed by a fall in the cross-correlation coefficient for the ST segments and T waves after 50 beats (top). Cross-correlation coefficient for the high-frequency nonaveraged QRS complexes fell more quickly after inflation (bottom). Note prompt return of cross-correlation coefficients for both variables after balloon deflation.
averaged nonfiltered ECG lead of V₃ recorded before PTCA. The middle and bottom traces in this panel show, respectively, the averaged high-frequency ECG waveform obtained after filtering and the delineation of the envelope of this signal. The envelope of the averaged high-frequency QRS clearly reveals a zone of reduced amplitude in the midportion of the signal (RAZ and arrow, figure 5, bottom left), a feature that is usually not present in averaged high-frequency QRS complexes of normal individuals (figure 1, bottom trace). A less frequent morphologic pattern found before PTCA, occurring in only three individuals, is shown in figure 5, right. Inspection of the envelope of the averaged high-frequency QRS in this patient revealed no zone of reduced amplitude (note absence of RAZ in figure 5, bottom right). When present, these zones of reduced amplitude were not the product of artifact introduced by the averaging process, since they were also apparent in nonaveraged single waveforms, albeit less clearly because of the poorer signal-to-noise ratio.

During the course of PTCA, striking changes were noted in the signal-averaged high-frequency QRS and in the calculated envelopes of these waveforms. A typical example of such changes is illustrated in figure 6, obtained from subject 11. During the control recording period in this patient, the calculated RMS value for signal-averaged high-frequency QRS was 3.97 and analysis of the envelope of the signal revealed the presence of a zone of reduced amplitude (RAZ, figure 6, left). The middle panel shows records obtained during the second time segment, after 30 sec of balloon inflation in the LAD. Balloon inflation was associated with a reduction in the voltage of the high-frequency QRS (RMS = 2.60, figure 6, middle) and broadening of the zone of reduced amplitude in the envelope of the signal (RAZ, figure 6, middle). Records obtained during the third time segment, after balloon deflation and withdrawal of the balloon catheter from the LAD, are shown in figure 6, right. At this stage of the procedure the RMS value of the high-frequency QRS had increased to 5.13 and the zone of the reduced amplitude in the envelope of the signal was less obvious (figure 6, right). A slightly different sequence of events was observed during PTCA in subject 10 and is illustrated in figure 7. Before PTCA, the envelope of the signal-averaged high-frequency QRS in this patient did not disclose a zone of reduced amplitude (figure 7, left, lower panel). Balloon inflation was associated with a decline in the RMS value of the signal (3.54 to 2.60,
FIGURE 6. Signal-averaged high-frequency QRS (top) and envelope of the averaged high-frequency QRS (bottom) recorded during three different stages of angioplasty in patient 11. RMS = root mean square voltage (\(\mu V\)) of the signal; RAZ = reduced amplitude zone. See text for discussion.

The results of analysis of the signal-averaged high-frequency QRS in each of the 11 patients studied are listed in table 3. In six individuals (patients 1, 2, 5, 7, 8, and 11, table 3), zones of reduced amplitude were present before PTCA, after 30 sec of balloon inflation, and also at the conclusion of the procedure. In two individuals (patients 3 and 9, table 2) zones of reduced amplitude that were present initially were no longer apparent after PTCA. Two subjects (patients 6 and 10, table 3) developed a reduced amplitude zone only during balloon inflation and one subject (patient 4, table 3) had no evidence of such a zone at any time. In all 11 patients studied, balloon inflation was uniformly associated with a decrease in voltage of the high-frequency QRS, followed by a subsequent increase in voltage after conclusion of PTCA in all but one individual (table 3). It is of interest to note that the single patient studied who had evidence of left ventricular hypertrophy on the standard surface ECG also had the largest calculated RMS value of the high-frequency QRS (patient 9, tables 1 and 3). For the entire group, the mean value for RMS was 3.27 ± 1.12 \(\mu V\) before PTCA as compared with 2.31 ± 1.04 \(\mu V\) during balloon inflation (p<.05). The mean value for RMS after conclusion of PTCA was 3.79 ± 1.39 \(\mu V\), a difference compared with the pre-PTCA value that was not significant, but that was significantly higher than the mean value during balloon inflation (p<.01).

Discussion
Clinicians have long know that the standard surface ECG is not always reliable in the diagnosis of myocardial ischemia. The present study confirms this clinical observation, since visual inspection of the surface ECG revealed ST segment and T wave abnormalities...
sugges­tive of ischemia in only 54% of the pa­tients un­der­go­ing PTCA of the LAD, ev­en though every pa­tient com­plained of an­gi­na during bal­loon in­fla­tion and 90% of the pa­tients had ev­i­dence of ischemia on the in­tra­coro­nary ECG. As sug­gested in pre­vi­ous stud­ies, in­sen­sitivity of the sur­face ECG for de­tect­ing tran­si­ent myocar­dial ischemia stems in part from the fact that the re­corded mag­ni­tude of po­ten­tials gen­er­ated by the heart falls precip­i­tously with in­creas­ing dis­tance be­tween the re­cording elec­trode and the heart; leads on the body sur­face may sim­ply be too dis­tant to de­velop vis­i­bly ob­vi­ous changes to is­chemia in a lo­cal­ized area of myocar­di­um.¹ ²

Pre­vi­ous stud­ies in dogs have dem­on­strat­ed that com­puter-assisted an­a­lysis of the ECG dur­ing such in­ter­ven­tions as hy­po­thermia or cor­o­nary ar­tery liga­tion can dis­close beat-to-beat var­i­a­tions in the mor­phol­ogy of the T wave that are not ap­par­ent from vi­sual in­spec­tion of the ECG.¹⁵ This tech­nique has not, how­ever, been stud­ied in pa­tients to as­sess its clin­i­cal util­ity. In the pre­sent study com­puter-assisted cross­cor­re­la­tion an­a­lysis of the sur­face ECG in pa­tients with tran­si­ent ischemia dur­ing PTCA re­vealed beat-to-beat changes in ST seg­ment and T wave mor­phol­ogy in re­sponse to bal­loon in­fla­tion that of­ten were not ap­par­ent from vi­sual in­spec­tion alone. Sim­i­lar changes were

FIGURE 7. Sig­nal-averaged high-fre­quency QRS (top) and en­velope of the aver­aged high-fre­quency QRS (bottom) re­corded dur­ing three dif­fer­ent stages of an­gi­oplasty in pa­tient 10. RMS = root mean square vol­tage (µV) of the signal; RAZ = re­duced am­pu­larity zone. See text for dis­cus­sion.
also apparent in the morphology of nonaveraged high-frequency QRS complexes, even though QRS abnormalities were usually not visually obvious. In the present study, cross-correlation analysis of beat-to-beat ST segment and T wave variability was not as sensitive an indicator of transient ischemia as the unipolar intracoronary ECG. However, the technique does appear to be a noninvasive means of detecting transient abnormalities on the ECG with greater sensitivity than by simple visual inspection alone. Cross-correlation analysis of ST segments, T waves, and high-frequency QRS complexes in patients with intermittent chest pain due to causes other than ischemia have not yet been done. However, noncardiac causes of chest pain may not cause the same changes in waveform morphology as were encountered in the present study. If such proves to be the case, computer-assisted electrocardiographic analysis may prove useful as a noninvasive diagnostic method in patients with chest pain of uncertain cause.

The electrocardiographic signal contains energy over a wide range of frequencies, although most conventional recording systems filter out all energy above 100 Hz. The resulting conventional "low frequency" ECG reflects primarily global patterns of depolarization and repolarization in the heart. Recent studies have focused on energies of higher frequency (150 to 250 Hz) contained with the ECG. Because these higher frequency ECGs are generally smaller in amplitude than the conventional ECG (microvolts vs millivolts), signal-averaging techniques have been used to improve signal-to-noise ratios. In this manner the high-frequency ECG has been used to derive information on relatively localized events in the heart, such as His bundle depolarization or delayed local ventricular depolarization in patients with prior infarction, from the body surface.

In the present study signal-averaging of the high-frequency (150 to 250 Hz) QRS was performed in patients undergoing PTCA by use of a computerized cross-correlation method. As described previously, this method ensures accurate waveform alignment during the averaging process, and has been used successfully to record His bundle activity and late potentials within the ST segment from the body surface. The effect of myocardial infarction on high-frequency QRS potentials has been studied previously.4, 5, 8 Although prior infarction increases the number of high-frequency components in the QRS, presumably due to fragmentation of the depolarization wavefront in scarred tissue, the overall voltage of the high-frequency components in the QRS is actually reduced by infarction.8 This attenuation of voltage has been attributed to a decrease in overall electromotive force as well as slowing of conduction in and around the region of infarction.8 The effect of transient ischemia rather than infarction on the high-frequency QRS has not previously been examined. Using balloon inflation in the LAD in patients undergoing PTCA as a model, we found in the present study that transient ischemia uniformly resulted in attenuation of the high-frequency component in the QRS, manifested by a decrease in calculated RMS values for each individual as well as for the overall group of 11 patients. When coronary blood flow was reestablished after balloon deflation, RMS values for the high-frequency QRS complexes returned to their preischemic levels. Acute ischemia in myocardial cells leads to a decline in maximum diastolic potential and in the maximum upstroke velocity of phase 0 of the action potential, accompanied by slowing of conduction velocity.18 Since reduction of conduction velocity in ventricular myocardium would be expected to shift high-frequency activity in the QRS to lower frequencies, slow conduction in the anterior wall may explain the transient decreases in RMS values that were observed during balloon inflation in the present study.

An interesting finding in the present study was the presence of zones of reduced amplitude in the high-frequency QRS of many of the patients during various stages of PTCA. Unlike late low-amplitude potentials in the terminal portion of the QRS or early part of the ST segment, which have been described in patients with prior infarction and which have been related to the occurrence of ventricular arrhythmias,19 the reduced amplitude zones observed in the present study were generally located in the midportion of the high-frequency QRS. Theoretically, zones of reduced amplitude in the midportion of the high-frequency QRS may become manifest or more prominent in either of two

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**Table 3**

<table>
<thead>
<tr>
<th>Presence of RAZ</th>
<th>RMS (µV) QRS complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject No.</td>
<td>Before</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
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<tr>
<td>6</td>
<td>-</td>
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<tr>
<td>7</td>
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<td>+</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>+</td>
</tr>
</tbody>
</table>

RAZ = reduced amplitude zone.
ways. As shown in figure 6, the zone of reduced amplitude may become apparent when voltage in the midportion of the signal becomes attenuated. Alternatively, as suggested by figure 7, zones of reduced amplitude may also become apparent if voltage in the initial portion of the signal increases. The origin and significance of these zones is unknown at present. Similar reduced amplitude zones were recently reported in patients with coronary artery disease and normal conventional ECGs but usually were not found in individuals without coronary artery disease. 13

It is of interest to note that, in the present study, many of the patients who had reduced amplitude zones before PTCA developed widening of the zone during balloon inflation. These zones then became narrower after PTCA was completed and, in two individuals, actually disappeared altogether. In two other patients a zone of reduced amplitude was present only during balloon inflation. It is conceivable that reduced amplitude zones in some patients may reflect localized regions of ischemic-induced slow conduction. If such were the case, one would expect these zones to become more evident during interruption of coronary blood and to diminish or disappear after relief of obstruction to flow. On the other hand, it should be noted that many of the patients in the present study still had zones of reduced amplitude at the conclusion of an apparently successful PTCA procedure. Thus, in some patients, persistence of reduced amplitude zones after PTCA may reflect the presence of nonrevascularized viable myocardium in the distribution of other nondilated diseased vessels or, alternatively, regions of prior infarction rather than ischemia. These hypotheses require further study.

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Circulation. 1987;76:585-596
doi: 10.1161/01.CIR.76.3.585

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