Effect of Myocardial Infarction on High-frequency QRS Potentials

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SUMMARY Studies have shown that the number of high-frequency QRS notches increases after myocardial infarction (MI). To assess overall high-frequency (> 80 Hz) potentials more quantitatively, we adapted a microprocessor system capable of averaging 256 QRS complexes to reduce noise. The QRS was digitally filtered and the root-mean-square (RMS) voltage of the residual (80–300 Hz) signal computed. High-frequency RMS values were significantly (p < 0.01) greater in leads II, III and aV in normal subjects (n = 12) than in patients with inferior infarction (n = 12). Similarly, high-frequency RMS values were higher (p < 0.01) in leads V, and V in normal subjects (n = 14) than in patients with prior anterior MI (n = 14). A reduction in high-frequency RMS values with inferior infarction was independently confirmed using Fourier analysis of the QRS in lead II.

QRS notching in these subjects was also quantified by computing the number of baseline crossings of the first derivative (dV/dt). As predicted, notching was significantly greater (p < 0.05) both with inferior MI (lead II) and anterior MI (lead V). However, contrary to classic theory, the number of notches correlated negatively with direct measurements of high-frequency RMS voltage in lead II (r = −0.63) and lead V (r = −0.49). Positive correlations were obtained between high-frequency potentials and two new indexes that measure the amplitude of QRS dV/dt — peak-to-peak amplitude of dV/dt and RMS dV/dt. Using these indexes, absolute separation of inferior MI patients and normal subjects was obtained.

We conclude that MI increases low-amplitude QRS notching but diminishes total high-frequency voltage, probably because of an overall decrease in electromotive potentials and slowing of ventricular conduction.

ALTHOUGH the net contribution of high frequencies (> 80 Hz) to the QRS complex is less than 3%, some investigators have suggested that these low-amplitude, high-frequency potentials might be helpful in diagnosis. Previous studies, however, have been limited by the technical difficulty of quantitating the magnitude of high-frequency potentials accurately. In most reports, high-frequency "components" were estimated by counting the number of notches and slurs on QRS complexes recorded at high gain with wide band-pass filters (high-fidelity electrocardiography). Using this technique, Langner et al., Flowers et al., and others reported an increase in high-frequency QRS components in patients with prior myocardial infarction (MI) and also with ventricular hypertrophy. Analysis of the first derivative of the QRS confirmed an increase in notching in patients with ischemic heart disease.

According to classic theory, high-frequency QRS components after MI are increased due to fragmentation of the depolarization wave front by fibrous tissue. However, MI leads to a regional loss of electrical potentials, sometimes reflected by diminished QRS voltage or abnormal Q waves; slowing of conduction velocity due to ischemia or infarction may also attenuate high-frequency potentials. Therefore, one might predict a decrease in overall high-frequency QRS voltage after MI.

Data from our laboratory suggested that infarction may decrease high-frequency QRS potentials as evidenced by diminished peak amplitude of a filtered (80–300 Hz) QRS signal. To test this hypothesis quantitatively, we developed three techniques for measuring high-frequency QRS potentials. First, a commercially available microprocessor ECG system (Marquette Electronics) equipped with a signal-averaging program to reduce noise and a high-frequency band-pass filter was adapted. The analog high-frequency output of this system was digitized to compute its root-mean-square (RMS) value, a direct index of high-frequency voltage. Second, high-frequency potentials were quantitated by performing Fourier analysis on the unfiltered, signal-averaged QRS complexes. Third, we used the first derivative of the ECG. However, in contrast to other investigators, who only evaluated QRS notches with the derivative, we also measured the amplitude of the QRS derivative.

Methods and Patients

The Marquette MAC-1 electrocardiograph is a portable microcomputer system designed for ECG signal averaging and for recording low-amplitude, high-frequency potentials. This system records standard leads I and II (or any two bipolar leads) directly.

*QRS notches were defined as changes in slope that interrupted the monotonic ascent or descent of the QRS. Slurs were defined as changes in QRS slope that did not interrupt the monotonic QRS wave form.

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Supported in part by the Veterans Administration Cardiovascular Research Award at San Diego Veterans Administration Medical Center and the SCOR on Ischemic Heart Disease and NIH grant HL-17682 from the NHLBI.

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Received May 21, 1980; revision accepted November 6, 1980.

Circulation 64, No. 1, 1981.
The other extremity leads are derived as follows: III = II − I; aVF = (I − II)/2; aVR = (I + II)/2 and aVL = (II − I)/2.

The input leads are digitized using a 12-bit analog/digital converter at 2000 samples/sec. These samples are stored in a circular buffer allowing 1.024 seconds of ECG data. Enhancement of signal-to-noise ratio is accomplished by summation (signal averaging) of 256 QRS cycles. QRS timing for this signal-averaging algorithm is based on the initial 20 msec of QRS depolarization. A template of this interval is developed during the initial sampling period. Subsequent complexes are then shifted with respect to this template to minimize the sum of absolute differences. If this minimal sum of absolute differences is less than 6 μV, the beat is accepted. The signal-averaged QRS output is passed through a digital 80–300 Hz three-pole Butterworth filter for selective recording of higher frequencies. The 80–300-Hz bandpass was chosen because the high-frequency QRS notches recorded in other studies were estimated to be in this frequency range.

Excessive variability ("jitter") in the trigger point for the averaging algorithm could attenuate higher frequency signals. Validation studies have shown ≤1 sample (0.5 msec) variability in sampling, which should not affect frequencies ≤300 Hz.

The signal-averaged output is presented at two gains (fig. 1). The unfiltered (0–300 Hz) signal is recorded at low gain (10 or 20 mm/mV). The filtered high-frequency (80–300 Hz) signal is recorded at high gain (200 or 400 mm/mV). Effective paper speed for these recordings is 100 mm/sec.

**Direct Measurement of RMS Values From Filtered QRS**

The analog high-frequency (80–300 Hz) wave form was digitized by passing it in parallel with the MAC-1 writer to a Tektronix 4051 computer at a sampling rate of 4000 samples/sec. The signal was reconstructed in analog form and QRS onset (0 time) was determined by visual inspection of the original high-frequency signal along with a simultaneously recorded 0–300-Hz QRS complex. An isoelectric baseline was constructed and the RMS value of the digitized high-frequency signal was computed for various QRS intervals. The RMS value of a signal is computed as:

\[
\left[ \frac{1}{n} \sum_{j=1}^{n} f_j^2 \right]^{1/2}
\]

where \( t_j = j^{th} \) sample point, \( f(t_j) = ECG \) amplitude at \( j^{th} \) sample point, and \( t_k = \) beginning of QRS.

were measured using this technique in leads II, III and aVF in 12 normal male subjects (mean age 30 years, range 20–35 years) and 12 male patients (mean age 59 years, range 38–81 years) with prior (older than 1 week) transmural inferior MI. One patient also had pathologic anterior Q waves. RMS measurements in these two groups were made over the following QRS intervals in leads II, III and aVF: 0–30 msec, 0–60 msec, and 30–60 msec. In lead II, RMS values were also computed for the 0–90-msec interval.

In a separate study, high-frequency RMS measurements (over a 0–80-msec QRS interval) were made in leads V_2 and V_6 in 14 normal male subjects (mean age 44 years, range 20–72 years) and 14 patients (mean age 57 years, range 40–91 years) with prior transmural anterior wall infarction. Two of the anterior infarct patients also had pathologic inferior lead Q waves.

Subjects with ECG, echocardiographic or angiographic evidence of left ventricular hypertrophy and patients with left bundle branch block were excluded.

**Fourier Analysis**

The RMS value of the high-frequency QRS in lead II was independently measured using a fast Fourier transform (FFT). The Fourier transform of \( f(t) \) is defined as:

\[
C_0 + C_1 \cos (\omega t + \phi_1) + C_2 \cos (2\omega t + \phi_2) + C_3 \cos (3\omega t + \phi_3) + \ldots
\]

where \( C_j \) is the amplitude of the \( j^{th} \) harmonic; \( \phi_j \) is the corresponding phase shift of the \( j^{th} \) harmonic; \( \omega \) is the fundamental frequency in radians/sec. Using the coefficients in the FFT, the RMS value for any frequency "window" (\( n^{th} \) to \( m^{th} \) harmonic) can then be calculated as:

\[
\left( \sum_{j=n}^{m} C_j^2 \right)^{1/2}
\]
The FFT was performed using the Tektronix 4051 computer at a sampling rate of 4000 samples/sec. A 512-point FFT was obtained yielding a 128-msec window (512 samples/4000 samples/sec = 128 msec). Because the fundamental frequency equals the reciprocal of the sample window, this 128-msec time window corresponded to a fundamental frequency of 7.81 Hz or 49.07 radians/sec. The 128-msec interval was chosen so that the origin and end point of the sampling window would be at approximately the same voltage, eliminating major step-discontinuities that might artificially introduce high-frequency potentials. Using the unfiltered, signal-averaged QRS complexes, RMS values were then computed over the 85.9-304.7-Hz frequency band in lead II for the 12 inferior infarct patients and 12 controls.

First Derivative Studies

Using the Tektronix 4051 computer, the first derivative (dV/dt) of the QRS complex was obtained (fig. 2). The derivative was computed with a five-point Lagrange polynomial, using the second and fourth sample points on either side of the point at which dV/dt was taken. Three variables of the first derivative were measured: the number of times the derivative crossed the isoelectric baseline, its peak-to-peak amplitude (peak-to-peak dV/dt), and the RMS of the derivative (RMS dV/dt). The number of baseline crossings was used as an index of the number of QRS notches because each QRS notch should result in two baseline crossings. The peak-to-peak amplitude was measured from the maximal positive to the maximal negative deflection of the first derivative. The RMS of the derivative was computed by the formula given earlier. These measurements were made over the 0-90-msec QRS interval in lead II for the inferior infarct group and control subjects to allow direct comparison with high-frequency RMS measurements made over the same QRS interval. For the anterior infarct group and controls, these measurements were made in lead V5 over the entire QRS interval, which varied from subject to subject. In other studies, the number of QRS notches was also reported for the entire QRS interval. The QRS interval in these cases was determined by visual determination of QRS onset and offset with the complex displayed at high gain with an expanded time scale on the Tektronix 4051 cathode ray tube.

Statistical Methods

Statistical comparisons for the high-frequency data in leads II, III, aVF comparing different QRS intervals were made using repeated measures analysis of variance. Unpaired t tests were used for other comparisons. Correlation coefficients were calculated using a least-squares fit. Mean values are expressed as the mean ± SD. Statistical significance is defined as p < 0.05.

Results

RMS Measurements on Filtered (80-300 Hz) Signals

Inferior Infarction

There was no significant difference in resting heart rate immediately before signal averaging between normal subjects (76.5 ± 14.4 beats/min) and infarct patients (75.4 ± 20.8 beats/min). The RMS values for the 0-30-, 0-60- and 30-60-msec QRS intervals in leads II, III and aVF for both groups are presented in table 1; data on the 0-90-msec QRS interval in lead II are shown in table 2. For each QRS interval, the patients with inferior infarcts had significantly lower RMS values than control subjects (p < 0.01). In lead II, all normal subjects had RMS values ≥ 12.6 μV for the 0-90-msec QRS interval, while nine of 12 MI patients (75%) had lower values.

Figure 1 compares the high-frequency QRS signals from a representative normal subject and a patient with inferior infarction. The unfiltered (0-300 Hz) QRS complexes are of about equal amplitude, yet the high-frequency signal from the patient with infarction shows markedly reduced amplitude.

Anterior Infarction

There was no significant difference in resting heart rate immediately before signal averaging between normal subjects (77.0 ± 9.9 beats/min) and anterior infarct patients (74.8 ± 12.9 beats/min). High-frequency RMS values in leads V5 and V6 are shown in tables 3 and 4. For the 0-80-msec QRS interval, RMS values in lead V5 were significantly greater (p < 0.01) in normal subjects (29.5 ± 10.5 vs 19.7 ± 5.0 μV). Similarly, for lead V6, the RMS values were significantly higher in normal subjects than in infarct patients (26.3 ± 9.2 vs 15.5 ± 6.1 μV, p < 0.001).
FFT Analysis of High-frequency RMS: Lead II

Table 2 shows the RMS values derived by FFT analysis of the unfiltered, signal-averaged QRS complex in lead II in the 12 normal controls and 12 inferior infarct patients. For the 85.9–304.7-Hz spectrum, the RMS values in the normal group (18.2 ± 5.0 μV) were significantly greater (p < 0.01) than those in the infarct group (11.4 ± 3.8 μV). The RMS values in lead II for the 85.9–304.7-Hz band derived by FFT over a 128-msec window were then compared with the RMS values obtained in these same subjects by direct analysis of the 80–300-Hz filtered wave form over a 0–90-msec interval (table 2, columns 1 and 5). These independently measured high-frequency RMS determinations correlated well (r = 0.81, p < 0.001).

First Derivative Studies

Inferior Infarction (Lead II)

Data on the first derivative of the QRS in lead II are shown in table 2. As predicted from several reports, the number of baseline crossings, an index of QRS notching, was significantly higher in the infarct patients than in the normal subjects (124 ± 39 vs 73 ± 25 crossings/90 msec; p < 0.01). However, both peak-to-peak dV/dt and RMS dV/dt were greater in the control group (p < 0.001). Further, there was a nega-
TABLE 2. **Lead II QRS**

<table>
<thead>
<tr>
<th>Normal subjects (n = 12)</th>
<th>RMS 80-300 Hz (μV)</th>
<th>Baseline X/90 msec</th>
<th>Peak dV/dt (mV/sec)</th>
<th>RMS dV/dt (mV/sec)</th>
<th>Fourier RMS 85.9-304.7 Hz (μV)</th>
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<td>112</td>
<td>208</td>
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**Mean ± SD** 17.4 ± 3.4 73 ± 25 205 ± 47 38 ± 8 18.2 ± 5.0

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<tr>
<th>Inferior MI (n = 12)</th>
<th>RMS 80-300 Hz (μV)</th>
<th>Baseline X/90 msec</th>
<th>Peak dV/dt (mV/sec)</th>
<th>RMS dV/dt (mV/sec)</th>
<th>Fourier RMS 85.9-304.7 Hz (μV)</th>
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</table>

**Mean ± SD** 9.1 ± 4.0 124 ± 39 130 ± 28 20 ± 6 11.4 ± 3.8

RMS values in column 1 were obtained over 0–90-msec QRS interval. RMS values derived by Fourier analysis (column 5) were obtained over 128-msec time window.

Abbreviations: baseline X = baseline crossings of first derivative; RMS = root mean square; peak dV/dt = peak-to-peak amplitude of first derivative; NA = data not available.

Positive correlation ($r = -0.63$, $p < 0.01$) between baseline crossings/90 msec and the RMS voltage of the high-frequency QRS for the same interval. However, both the peak-to-peak dV/dt and the RMS dV/dt were positively correlated with the direct measurements of high-frequency voltage ($r = 0.67$, $p < 0.001$; and $r = 0.81$, $p < 0.001$, respectively). The criterion of peak-to-peak dV/dt > 158 mV/sec or RMS dV/dt > 29 mV/sec in lead II provided absolute separation of normal subjects and patients with inferior infarction.

Figure 2 shows representative examples of the first derivative of the QRS in a normal subject and in a patient with inferior infarction, illustrating the disparity between the number of baseline crossings and peak amplitude of the derivative.
TABLE 3.  Lead V₂ High-frequency (80–300 Hz) Root-mean-square Values

<table>
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<th>No.</th>
<th>Normal Subjects (µV)</th>
<th>Anterior MI (µV)</th>
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<td>14</td>
<td>23.7</td>
<td>15.0</td>
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</table>

Mean ± SD 29.5 ± 10.5 19.7 ± 5.0

*p < 0.01

Root-mean-square values were determined for the 0–80-msec interval.
Abbreviation: MI = myocardial infarction.

Anterior Infarction (Lead V₆)

Data on the first derivative of the QRS in lead V₆ in anterior infarct patients are presented in table 4. As in lead II, the number of baseline crossings (measured for the entire QRS interval) was significantly (p < 0.05) greater in infarct patients than in normal controls (94 ± 57 vs 54 ± 30), but the peak-to-peak dV/dt and the RMS dV/dt were greater in normal subjects (p < 0.001). The number of baseline crossings was again negatively correlated with direct measurements of high-frequency (80–300 Hz) voltage (r = −0.49, p < 0.01). Strong positive correlations were noted between directly measured high-frequency RMS voltage and peak-to-peak dV/dt (r = 0.87, p < 0.001) and between RMS voltage and RMS dV/dt (r = 0.92, p < 0.001).

Discussion

Signal averaging is a well-established technique for improvement of signal-to-noise ratio in electrocardiography. The level of noise will be reduced by a factor of 1/√N, where N is the number of averaged complexes. In the present study, where 256 QRS complexes were averaged, the noise level should have been reduced to 6% of its original value. Noise reduction is crucial to accurate quantitation of high-frequency QRS voltage, which may be lower than 5 µV. Signal-averaging techniques have been used for body surface recordings of the His bundle electrogram and of ventricular electrical activity during the ST segment, but have not been used to quantitate high-frequency QRS potentials. In this study, QRS onset, which affords a stable time reference, was used as the fiducial point for signal averaging.
Using this signal-averaging technique, we found that high-frequency (> 80 Hz) QRS potentials are reduced by MI. These observations were made by three indexes: RMS value of a digitally filtered (80–300 Hz) QRS signal, FFT analysis of high-frequency QRS content, and amplitude of the first derivative of the QRS.

At the same time, our computer analysis confirmed the reports of previous investigations that MI increases QRS notching.* The number of baseline crossings of the first derivative was increased in patients with prior inferior MI (lead II) and anterior MI (lead V4). The first derivative was initially used by Langner and colleagues6, 7 to estimate QRS notching. Langner and Geselowitz further suggested that these low-amplitude QRS notches and slurs were a reflection of overall high-frequency potentials.8 Subsequent investigators6–18 referred to QRS notches only as high-frequency "components" and did not attempt to estimate high-frequency "content." Our data are of particular interest because they indicate that QRS notching actually correlates negatively with directly measured high-frequency voltage and also with the amplitude of the first derivative.

This apparently paradoxical negative correlation between QRS notching and total high-frequency content has several explanations. First, not all QRS notches have the same content of high-frequency voltage. In other studies, equal weighting was accorded to all notches and slurs, only the number of low-amplitude notches and slurs was analyzed, and the high-frequency potentials required to generate the primary QRS wave form were not assessed. In particular, the high-frequency potentials constituting the peak of the R wave or nadir of the S wave were omitted in early studies of low-amplitude QRS notches.6–7 However, the peak amplitude of the high-frequency signal corresponds in timing to the peak voltage of the R or S waves ("macronotches") (fig. 1). The contribution of these high-amplitude R- or S-wave peaks to overall high-frequency content should be expected to outweigh the RMS value of low amplitude "micronotches" on the ascending and descending limbs of these waves.

The number of apparent notches and slurs is also a function of the slope of the intrinsic QRS. Sapochnikov and Weinman7 pointed out that a change in QRS "sign" (i.e., a notch) might appear only as a slur on a QRS with steeper slope. Our data show that QRS slope as measured both by peak-to-peak dV/dt and RMS dV/dt are reduced with infarction. Therefore, one might predict that QRS notching should be more prevalent in patients with ischemic disease, but that QRS slurring might be more common on normal QRS complexes with steeper slope. Reynolds et al.11 reported increased QRS notching in patients with myocardial disease, but increased QRS slurring in normal subjects.

Finally, notches tend to interrupt the rapid ascent and descent of the QRS and may reflect abnormal ventricular activation.16 Such slowing or asynchrony of conduction should also attenuate high frequencies, which give the QRS complex its rapidly rising slope and sharp contours. We have shown how the slope of the QRS can be quantitatively measured using the amplitude of the first derivative, an index of the maximum rate of change of QRS slope. Very good correlations were obtained between the RMS of the derivative and direct measurements of high-frequency voltage in leads II (r = 0.81) and V4 (r = 0.92). As noted, the first derivative was introduced by Langner and colleagues to assess QRS notches. However, the amplitude of the derivative was not quantitated in their studies.6, 7 Our data suggest that the amplitude of the first derivative is an excellent index of total high-frequency voltage, while the number of notches is actually a negative correlate of total high-frequency potentials.

Langner and Geselowitz6 tried to assess the magnitude of high-frequency QRS potentials more quantitatively. They used a high-frequency filter capable of passing up to 1000 Hz in combination with a low-pass filter to selectively exclude lower frequency QRS potentials. The ratio of the total amplitude of the filtered signal to the total amplitude of the original QRS was used as an index of high-frequency potentials. Using this index, considerable overlap was observed between high-frequency voltage in normal subjects and patients with infarction; therefore, statistical comparisons were not performed. The authors suggested that measurement of RMS values would have provided the optimal index of high-frequency "energy," and concluded that further studies would be required to determine whether the quantitative estimate of high-frequency energy would add significant diagnostic information or merely confirm information obtainable by simple inspection of the high-fidelity ECG made with an expanded time scale. Our data show that QRS notching recorded by high-fidelity ECGs is not an index of overall high-frequency voltage ("energy") and that other techniques are required to make quantitative high-frequency measurements.

In another early study, Franke et al.6 measured high-frequency activity by power-spectrum analysis of the ECG. Their data suggested an increase in high-frequency potentials with acute, but not with chronic, infarction. However, their technique provided only an indirect estimate of high-frequency potentials and did not use signal-averaging to reduce noise. Shick and Powers48 reported increased high-frequency potentials measured by Fourier analysis in association with increased QRS notching in rabbits with acute myocardial contusion. However, their data were based on small sample size (n = 7) and they averaged only eight to 12 QRS complexes, which might not have provided adequate noise reduction. Finally, acute

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*We recorded considerably more notches in both normal and abnormal ECGs than were recorded in studies based on visual counts or analog filtering. This apparent increase in QRS "micronotches" in our study may, in part, reflect enhanced sensitivity of digital filtering techniques. Some of these notches may represent unfiltered noise riding on the QRS, or even minor levels of noise introduced by redigitizing the QRS signal. However, the ratio of notches per lead between infarct patients and controls was comparable to that in other reports.6, 14
myocardial contusion is not pathologically comparable to chronic MI.

Previous investigators have suggested that MI produces an increase in high-frequency "components" due to disruption and fragmentation of the wave of activation by fibrotic tissue. According to classic theory, therefore, infarction would have increased high-frequency QRS amplitude. Our data, however, show the opposite effect. From a pathophysiologic viewpoint, MI may attenuate higher QRS frequencies by at least two mechanisms. First, myocardial necrosis leads to a general decrease in electromotive potentials. The loss of myocardial "generator units" would be expected to diminish both low and high QRS frequencies. The loss of lower frequencies is reflected by the common appearance of low-voltage QRS complexes with ischemic disease. Second, slowing of ventricular activation owing to infarction may also attenuate higher frequencies, reflected on the surface ECG by less sharply inscribed QRS wave forms with reduced dV/dt.

Our results suggest that quantitative high-frequency electrocardiography may have practical applications as well as theoretical interest. In this study, dV/dt indexes provided absolute separation between normal subjects and patients with inferior MI, including one patient in whom pathologic Q waves were no longer apparent. Therefore, quantitative high-frequency electrocardiography may assist in the common clinical dilemma of deciding whether nondiagnostic inferior Q waves reflect a normal variant or prior infarction.

In leads V4 and V6, high-frequency voltage criteria did not absolutely discriminate normal subjects from infarct patients. Further studies are needed to determine whether distal limb leads (I and aVL) provide better separation of normal and anterior infarct groups than the proximal chest leads.

The effect of ventricular hypertrophy on high-frequency potentials also needs to be quantitatively reassessed. For example, it is possible that by augmenting overall electromotive forces, hypertrophy may mask the loss of high-frequency potentials caused by MI. The current study attempted to exclude patients with known left ventricular hypertrophy. However, echocardiographic and angiographic data were not available in all cases and it is possible that some of the overlap in high-frequency RMS values between normals and infarct patients was caused by ventricular hypertrophy. Additional data are also required to assess serial changes in high-frequency voltage after MI. Finally, quantitative high-frequency electrocardiography may prove useful in diagnosing myocardial disease in the presence of left bundle branch block or preexcitation patterns that may mask or mimic infarction.

Acknowledgment

The authors thank John Ross, Jr., M.D., and Ralph Shabetai, M.D., for their helpful reviews, Elizabeth Gilpin, M.S., for statistical advice, Gary O'Hara for technical help, and Sue Connolly for secretarial assistance. The authors express particular appreciation to David Mortara, Ph.D., of Marquette Electronics, who designed the MAC-1 electrocardiograph and made numerous helpful suggestions.

References

Use of Postmenopausal Hormones and Risk of Myocardial Infarction

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SUMMARY Information was collected by mail survey about myocardial infarction (MI), use of female hormones after menopause, and coronary risk factors from 121,964 registered nurses ages 30–55 years. One hundred twenty-three women with a known type of prior menopause reported hospitalization for MI. Overall, use of female hormones by these women was very similar to that of control women matched for age and type of menopause. Compared with nonusers, the relative risk (RR) for women who had ever taken female hormones was 0.9 (95% confidence limits 0.6–1.2), and for current users the RR was 0.7 (0.5–1.1). For women with bilateral oophorectomy, the RR for current users was 0.4 (0.2–0.8). These data imply that, at present, a decision to prescribe postmenopausal hormones should be based primarily on weighing possible benefits from the relief of menopausal symptoms against known or suspected risks of other diseases, particularly uterine cancer in women with an intact uterus.

ORAL CONTRACEPTIVE users have a substantially increased risk of myocardial infarction (MI)\(^1\) over nonusers. However, conflicting results have been reported about the role of noncontraceptive estrogens. In two case-control studies of older postmenopausal women, use of female hormones was not associated with hospitalization for MI\(^2\),\(^3\) while in a case-control study of women 39–45 years of age, current users appeared to have a rate of hospitalization for MI seven times that of nonusers\(^4\),\(^5\) This retrospective study evaluates the association between postmenopausal hormone use and reported hospitalization for MI among registered U.S. nurses.

**Methods**

**Subjects**

Married female nurses ages 30–55 years (in 1976) and residing in 11 of the larger U.S. states were identified from the American Nurses' Association 1972 membership file. In 1976, questionnaires were mailed to them requesting information on various health-related items, including whether they had been hospitalized for MI, their menopausal status, and their use of female hormones other than oral contraceptives. Dates of diagnosis and of menopause were requested, as well as information on duration of hormone use. Of the 172,413 women who presumably received questionnaires, 121,964 (71%) completed and returned them.

Among the respondents were 318 women who reported hospitalizations for MI, of whom 156 were premenopausal on the date of their hospitalization, 37 were perimenopausal (i.e., were hospitalized in the year their menopause occurred and could not be classified with certainty as to menopausal status at MI), and two did not specify a type of menopause. The remaining 123 women were hospitalized after their reported date of menopause and also indicated the type of menopause. Of these, 25 reported natural menopause, 50 reported hysterectomy with retention of at least one ovary, and 48 had bilateral oophorectomy.

For each case, 20 control women without a history of MI were selected randomly from respondents having the same year of birth as the index case and the same type of menopause before the date of hospitalization of the case.

The information reported included duration of female hormone use after menopause, but not dates of use. For cases, female hormone use was defined as
Effect of myocardial infarction on high-frequency QRS potentials.
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Circulation. 1981;64:34-42
doi: 10.1161/01.CIR.64.1.34

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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