TABLE IV Predictors of Revascularization in the Year Following Hospital Discharge

Variable	Odds Ratio	95% Confidence Interval
Coronary surgery	0.08	0.04–0.15
Age (per decade)	0.84	0.77–0.90
Coronary angiography	1.50	1.22–1.84
Angina pectoris	1.36	1.18–1.57
Congestive heart failure (history)	0.60	0.42–0.86
Nonwhite race	0.60	0.42–0.86
Thrombolytic therapy	1.30	1.06–1.60
Systemic hypertension (history)	1.19	1.01–1.40

able, and were in part related to failed social support systems, as well as noncompliance with respect to medications or diet and inadequate follow-up.[7] Another study of older patients with congestive heart failure indicated that a nurse-directed multidisciplinary intervention reduced hospital readmission for heart failure by half.[8] These findings indicate that increased professional support is needed in patients with extensive cardiac histories and poor quality of life. Finally, cardiac rehabilitation programs may also reduce the need for further hospitalization.[9]

In this study, coronary angiography or coronary artery bypass surgery performed during the index hospitalization were associated with lower likelihood of rehospitalization. The situation with respect to revascularization in the year following the index hospitalization was different in that bypass surgery was asso-ciated with a lower likelihood of revascularization, but the use of coronary angiography and/or thrombolytic therapy increased the likelihood of revascularization procedures. Thus, coronary bypass surgery was associated with lower likelihood of rehospitalization and revascularization.

In conclusion, in Seattle area hospitals, rehospitalization of patients surviving AMI was frequent, particularly for women and those with extensive cardiac histories.

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Dynamic Analysis of Heart Rate May Predict Subsequent Ventricular Tachycardia After Myocardial Infarction

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Twenty-four-hour electrocardiographic recordings provide information on the vulnerability of patients with heart disease to life-threatening arrhythmias.[1–4] Assessment of ventricular ectopic beats and episodes of nonsustained ventricular tachycardia (VT) have been used to predict the risk of future life-threatening arrhythmias. More recent investigations have shown that analysis of heart rate (HR) variability can also predict the risk of arrhythmic events after an acute myocardial infarction (MI).[5,6] However, traditional indexes of HR variability based on mean and variance[1,2] may lack the ability to detect subtle but important changes in interbeat HR behavior.[7] The purpose of this study was to test the hypothesis that dynamic analysis of RR intervals can reveal abnormalities in HR behavior in patients with vulnerability to VT that are not detected by traditional measures of HR variability. We compared fractal correlation properties and approximate entropy with conventional measures of HR variability in 3 age-matched groups: patients with a prior Q-wave MI with vulnerability to VT, patients with a prior Q-wave MI without vulnerability to VT, and a control group of healthy subjects.

TABLE I Characteristics of the Postinfarction Patient Groups

	VT-MI Group	Non VT-MI Group
Clinical data		
Age (yr)	62 ± 14	60 ± 6
Men/women	39/6	39/6
NYHA class 2	19 (42%)	17 (38%)
NYHA class 3	26 (58%)	28 (62%)
Time since prior MI (mo)	33 (range 2–118)	40 (range 2–132)
Location of prior MI		
Anterior	21 (47%)	19 (42%)
Inferior	11 (24%)	13 (29%)
Anterior + inferior	13 (29%)	13 (29%)
Angiographic data		
1-vessel disease	9 (20%)	6 (13%)
2-vessel disease	17 (38%)	12 (27%)
3-vessel disease	19 (42%)	27 (60%)
LV ejection fraction (%)	44 ± 11	45 ± 8
Cardiac medication		
Digitalis	20 (44%)	13 (29%)
Diuretic	22 (49%)	19 (42%)
β blocker	32 (71%)	26 (58%)
Calcium antagonist	13 (29%)	8 (18%)
ACE inhibitor	9 (20%)	9 (20%)
Nitrate	35 (78%)	39 (87%)

Values expressed as mean ± SD unless otherwise indicated. ACE = angiotensin-converting enzyme; LV = left ventricular; MI = myocardial infarction; NYHA = New York Heart Association Classification.

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We retrospectively analyzed 24-hour HR data from 90 patients with a history of chronic Q-wave MI and 45 healthy subjects. The VT subgroup consisted of 45 consecutive patients who had a documented cardiac arrest or spontaneous sustained VT and in whom sustained monomorphic VT was inducible by programmed electrical stimulation. Patients in whom ventricular fibrillation or nonsustained VT was inducible and with recent MI (<1 month), atrial fibrillation, or diabetes mellitus were excluded. Antiarrhythmic treatment had been withdrawn at least 4 half-lives before electrophysiologic testing. Studies were performed 2 to 10 days after the occurrence of VT. The post-MI control group consisted of 45 patients with a history of prior Q-wave MI (>1 month since infarction) but without any history of VT events. Patients with inducible nonsustained (>5 consecutive beats) or sustained VT, diabetes mellitus, or atrial fibrillation were excluded. All control patients also had an arrhythmia-free survival during a follow-up of 2 years. The groups were matched with respect to age, sex, and left ventricular ejection fraction. The characteristics of the patient groups are listed in Table I. Forty-five age-matched healthy subjects (59 ± 9 years) without clinical, echocardiographic, or exercise electrocardiographic evidence of heart disease and without hypertension or diabetes mellitus served as normal controls (39 men, 6 women).

Electrophysiologic testing included incremental ventricular pacing and programmed ventricular stimulation. The stimulation protocol has previously been described in detail.[8] VT was defined as sustained when its duration was >30 seconds. Left heart catheterization was performed by the Judkins technique, and stenoses >50% were considered significant.

Electrocardiographic data from 24-hour recordings were sampled digitally and transferred to a microcomputer for analysis.[9] RR intervals were edited manually and non-sinus beats were deleted. The sinus origin of the RR intervals was confirmed by printing out the questionable portions of electrocardiograms with visual confirmation. In the final analysis 24-hour measurements were divided into segments of 8,000 RR intervals, and only segments with >80% sinus beats were included. The mean length of all RR intervals and standard deviation of all RR intervals were computed as time domain measures. The power spectra were quantified by measuring the area in 2 frequency bands: 0.04 to 0.15 Hz (low frequency) and 0.15 to 0.40 Hz (high frequency).[9] For quantitative 2-dimensional vector analysis, the SD of continuous long-term RR intervals (SD 2) and instantaneous beat-to-beat variability of RR intervals (SD 1) were analyzed (see Figure 1).[7] From 24-hour recordings, approximate entropy, a measure that quantifies the regularity of time series data, was calculated.[10,11] To quantify fractal correlation properties of HR, the detrended fluctuation analysis technique, which is a modified root-mean-square analysis of a random walk, was used. The method has been validated for physiologic time series and quantifies the presence or absence of fractal correlation properties.[12,13] In this study, HR correlation properties were defined separately for short-term ($\leq$11 beats, α_1) and for long-term (>11 beats, α_2) correlations of RR interval data (short- and long-term scaling exponents).[12] The details of this methods have previously been described.[12,13] Analysis of variance followed by Bonferroni's post hoc multiple range tests were used to compare the differences between the groups. Spearman's correlation coefficient was used to estimate the correlations between the measures of HR variability. A p value <0.05 was considered significant. When analyzing the sensitivity, specificity, and predictive accuracy of the different measures, the 95% percentile of the values obtained for healthy subjects was defined as the normal range for each measure.

There were no differences between the patient groups in clinical characteristics (Table I). Neither frequency of ventricular premature depolarizations nor the occurrence of nonsustained VT differed significantly between the arrhythmia and post-MI control groups. Mean SD of all RR intervals did not differ between patient groups. Low-frequency spectral power was significantly lower in the VT group than in post-MI patients (p <0.01), but high-frequency spectral power did not differ between the study groups (Table II). However, the shape of the high-frequency spectral band was different in the VT group to the extent that the high-frequency band was flatter with more power distributed in the very high frequency area (Figure 1). The short-term scaling exponent (α_1) was significantly smaller in the VT group (0.85 ± 0.25) than in the post-MI control group (1.06 ± 0.13, p <0.001) or
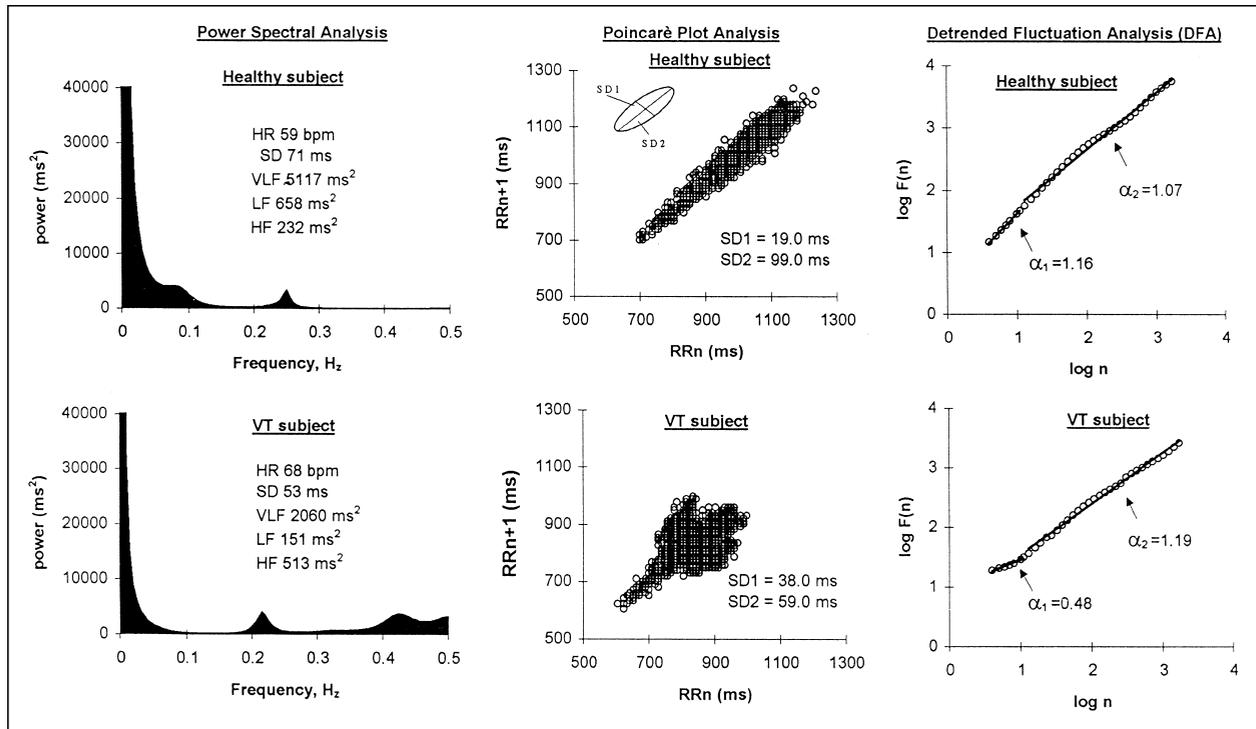
FIGURE 1. Examples of power spectra, Poincarè plot, and detrended fluctuation analysis (DFA) data from a healthy subject and a patient with ventricular tachycardia (VT). The healthy subject typically shows a relatively discrete, smooth, high-frequency component and comet-shape Poincarè plot correlating an α_1 value ~1.0. In contrast, the patient with history of ventricular tachycardia shows a widened high-frequency spectral band, complex Poincarè plot, and an α_1 ~0.5. α_1 = short-term scaling exponent; SD = standard deviation of each measurement segment; VLF = very low frequency component; LF = low-frequency power component; HF = high-frequency power component; HR = heart rate; SD1 = standard deviation of instantaneous beat-to-beat variability; SD2 = standard deviation of long-term continuous RR interval variability.

TABLE II Data from 24-Hour Electrocardiographic Recordings

	Healthy Subjects	Non VT-MI Group	VT-MI Group
Mean RR interval (ms)	888 ± 117	944 ± 146§	953 ± 168#
SDNN (ms)	150 ± 40	106 ± 30¶	90 ± 35††
VPD class 1/2/3	45/0/0	31/7/7¶	28/7/10††
NSVT	0	8¶	13††
HF power (ln)	5.4 ± 0.9	5.2 ± 0.9	5.2 ± 1.3
LF power (ln)	6.3 ± 0.9	5.9 ± 1.0	5.3 ± 1.2†,††
α_1	1.09 ± 0.13	1.06 ± 0.13	0.85 ± 0.25‡,††
α_2	1.05 ± 0.06	1.03 ± 0.07	1.07 ± 0.09
SD1	21 ± 7	20 ± 10	23 ± 17
SD2	125 ± 38	104 ± 36‖	85 ± 35*,††
ApEn	1.03 ± 0.14	1.17 ± 0.22‖	1.20 ± 0.28**

*p <0.05; †p <0.01; ‡p <0.001, significance levels for differences between VT-MI and non–VT-MI group. §p <0.05; ‖p <0.01; ¶p <0.001, significance levels for differences between non–VT-MI group and healthy subjects. #p <0.05; **p <0.01; ††p <0.001, significance levels for differences between VT-MI group and healthy subjects.

Values are expressed as mean ± SD.

α_1 = short-term scaling exponent; α_2 = long-term scaling exponent; ApEn = approximate entropy; HF = high-frequency power component of heart rate variability; LF = low-frequency power component of heart rate variability; VPD = ventricular premature depolarization (class 1 = <10 VPDs/hour, class 2 = from 10 to 30 VPDs/hour, class 3 = >30 VPDs/hour; NSVT = nonsustained ventricular tachycardia; SDNN = standard deviation of all RR intervals; Mean RR = average of lengths of RR intervals; ln = logarithm to the natural base of the absolute value.

The SD long-term continuous RR interval variability was smaller in the VT group than in the post-MI control group (p <0.05). Detailed examination of ambulatory electrocardiographic recordings revealed that the abnormally low short-term scaling exponent appeared to correlate with periods of abrupt changes in sinus cycle lengths, sometimes associated with alternating types of HR behavior in sinus intervals without a change in P-wave morphology or evidence of significant sinus pauses (Figure 2). The short-term scaling exponent had only weak correlations with all single measures of HR variability (r <0.6 for all). The short-term scaling exponent had a high specificity (93%) and the best overall accuracy (73%) compared with other measures in detecting vulnerability to VT. In stepwise multiple regression analysis, the short-term scaling exponent was also the strongest independent predictor of vulnerability to VT.

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The new finding of this study is that the short-term fractal correlation properties of RR interval dynamics

in healthy controls (1.09 ± 0.13, p <0.001). The long-term scaling exponent (α_2) did not differ between study groups. Approximate entropy was significantly lower in healthy subjects than in post-MI patients (p <0.001), but did not differ between the arrhythmia and control groups.

FIGURE 2. Tachogram of a short RR interval time series *(top)* and corresponding portion of the Holter recording *(bottom)* from one of the patients with ventricular tachyarrhythmia with an α_1 value ~0.5. There were subtle changes in sinus cycle lengths (RR intervals given in milliseconds above the electrocardiographic [ECG] tracings) associated with alternating cycle lengths (*a*, upper 2-lead recording) followed by a smoother apparent respiratory modulation of sinus cycle lengths with smaller amplitude of changes between the successive cycles (*b*, lower 2-lead recording). The P-wave morphology and PR interval did not differ noticeably during the episodes of abrupt changes in interbeat cycle lengths. Note also the tachogram beats from 40 to 60 where abrupt temporal changes in RR intervals reduces the short-term exponent value.
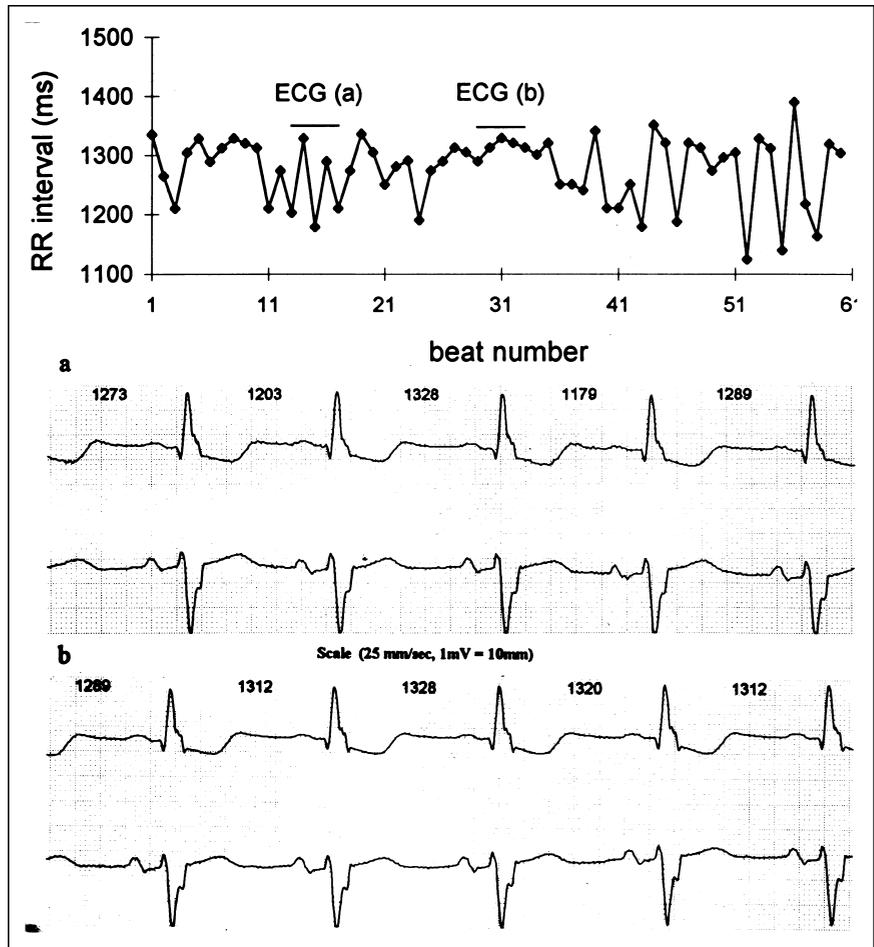
are altered in post-MI patients with vulnerability to VT. The short-term scaling exponent (α_1) quantifies correlation properties of time series. Analysis of short-term scaling subtends mainly fluctuations in the high-frequency, and also partly in the low-frequency, region of the frequency signal spectrum. An exponent value of 0.5 occurs when short-term fluctuation is completely random. Values <0.5 correspond to time series in which large and short RR intervals are more likely to alternate.[12] This type of RR interval behavior was only observed in subjects (6 patients) with vulnerability to VT (Figure 2). Consistent with this observation, our previous study showed the presence of alternating HR behavior before the spontaneous onset of VT,[7] and the present study extends these observations by offering a method to detect not only alternating behavior, but also the aperiodic abrupt temporal changes in RR intervals (Figure 2, tachogram of beats 40 to 60). Approximate entropy was higher in patient groups than in healthy controls, indicating more irregular interbeat dynamics of HR after MI despite reduced total variance. However, approximate entropy was not able to differentiate the patients groups. Consistent with a previous study, the low-frequency spectral component, but not the high-frequency component of HR variability, was smaller in the VT patients than in post-MI controls,[6] but it did not perform as well as

the short-term scaling exponent in differentiating patients with and without VT.

Short-term RR interval behavior in patients with a propensity for VT was not strongly related to any other single measure of HR variability or HR, suggesting that reduction in short-term correlation properties of RR interval dynamics may not be determined by the same physiologic mechanisms as other specific components of HR variability. Instantaneous changes in RR intervals are most likely to be vagally mediated, because vagal effects on the sinus node occur faster than sympathetically mediated effects. A potential explanation for the abnormal short-term correlation properties could be altered autonomic interaction.[14] High norepinephrine levels may result in altered beat-to-beat RR interval dynamics, possibly via accentuated sympathovagal interaction.[15,16] Alternatively, the altered short-term correlation properties could be due to nonautonomic factors related to disturbed sinus node conduction or automaticity. In either case, the reduced value of the short-term scaling exponent in patients susceptible to VT implies the loss of fractal stability of HR dynamics.[13,17] Future studies are needed to establish the pathophysiologic basis for altered beat-to-beat behavior of HR dynamics and to determine its utility in predicting life-threatening arrhythmic events in prospective follow-up studies.

In conclusion, this study shows that short-term fractal correlation properties of RR intervals are altered in post-MI patients with vulnerability to VT and that measurement of a short-term fractal scaling exponent gives complementary information on abnormal HR behavior in patients with vulnerability to VT.

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The Magnitude of Inotropic Reserve Is Unrelated to Basal Systolic Function or Wall Thickness in Patients With Chronic Ischemic Left Ventricular Dysfunction

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Coronary stenoses may induce chronic myocardial dysfunction as a consequence of either replacement of the normal myocardium by scar tissue following the occurrence of myocardial infarction(s) or through processes that lead to reversible dysfunction in the setting of viable myocardium.[1–4] The mechanisms responsible for systolic dysfunction at rest may also modulate the ability of the myocyte to respond to inotropic stimulation. For example, critical reductions in coronary blood flow may not support the increasing myocardial oxygen demands that necessarily follow an enhancement in contractility and lead to the induction of ischemia even with minimal inotropic stimulation.[5] Thus, a relation may exist between the processes leading to systolic dysfunction at rest and the preservation of contractile reserve in response to inotropic stimulation.

In patients with chronic coronary artery disease and impaired left ventricular systolic function, both myocardial contraction at rest[6] and the contractile response to dobutamine[7–9] have been shown to indicate myocardial viability. However, whether coronary stenoses affect myocardial contraction at rest and during inotropic stimulation to a similar extent within the same region of the dysfunctional myocardium is not known. The purpose of the present study, therefore, was to investigate, in a quantitative fashion, the relation between basal contractile function and the inotropic response to dobutamine in coronary artery disease patients with chronic left ventricular dysfunction.

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The study included 44 patients (40 men and 4 women; aged 60 ± 10 years) with coronary artery disease (≥70% stenosis of ≥1 coronary artery) and depressed left ventricular function (ejection fraction at rest <45% [mean 33 ± 9%]). Previous revascularization had been performed in 16 patients and a myocardial infarction recorded in 23 (none in the preceding 3 months). Antianginal medications were discontinued ≥48 hours before the study, which was approved by the National Heart, Lung and Blood Institute Investigational Review Board. Each patient gave informed written consent.

Transesophageal echocardiograms were performed