Effects of Increased Heart Rate and Sympathetic Tone on Intraventricular Electrogram Morphology

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Electrogram pattern recognition by way of morphologic analysis has been proposed as a technique that may improve discrimination of ventricular tachycardia from sinus rhythm by antitachycardia devices. The potential impact that increases in heart rate and sympathetic tone could have on such techniques, however, has not been previously determined. A comparative study was undertaken to quantify possible changes in ventricular electrogram morphology using correlation waveform, area of difference, and amplitude analyses in 6 patients during atrial overdrive pacing at cycle lengths of 600 and 400 ms (group A), in 13 patients during infusions of physiologic doses of epinephrine (group B), and in 20 patients undergoing infusions of isoproterenol (group C). Four patients were in both groups A and B. A bipolar intraventricular template of cardiac depolarization during sinus rhythm at rest was compared with depolarization during subsequent passages of sinus rhythm at rest and subsequently increased heart rate.

In 36 of 39 patients, waveform configuration as assessed by correlation waveform analysis remained relatively stable during atrial overdrive pacing, epinephrine infusion, and isoproterenol infusion when compared with sinus rhythm at rest. The correlation value did not fall below 0.950 in any patient. Area of difference values for the same 36 patients changed by an average of 6 and 37% during atrial overdrive pacing at cycle lengths of 600 and 400 ms intervals, respectively, by 3% during epinephrine infusion,

and by 17% during isoproterenol infusion. In these same patients, there was an average change in electrogram amplitude of −1% during atrial overdrive pacing at 600 ms, 26% during pacing at 400 ms, −1% during epinephrine infusion, and 12% during isoproterenol infusion.

Little or no correlation was found between relative changes of amplitude and changes of correlation coefficient during any intervention. However, changes in amplitude and changes in area of difference exhibited weak to moderate correlation during infusion of epinephrine and isoproterenol. Despite some amplitude variation, overall waveform morphology remains relatively constant during increases in heart rate with or without concurrent changes in sympathetic tone. These findings suggest that heart rate increases are unlikely to confound time-domain detection schemes used in antitachycardia devices.
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A variety of methods for analyzing intracardiac electrograms have been proposed for arrhythmia detection by antitachycardia devices. Such methods include rate onset and stability,[1] multichannel timing analysis,[2-4] gradient pattern detection,[5,6] analysis of arrhythmia frequency spectra,[7-9] area of difference,[10,11] and correlation waveform analysis.[12-17] However, with the exception of preliminary investigations by Paul[18] and Rosenheck[19] and their co-workers in humans, and Tomaselli et al[20] in dogs, most studies to date have been performed on electrocardiographic signals recorded from patients in a resting state. Whether the results of waveform analysis techniques designed to recognize abnormal ventricular activation might be affected by increases in heart rate alone or by accelerations in heart rate due to changes in sympathetic tone has not been determined with certainty. This study examined the effects on intraventricular electrogram morphology caused by (1) increases in heart rate alone during atrial overdrive pacing, and (2) changes in heart rate and sympathetic tone due to intravenous infusions of either a β or a combined α and β agonist.

METHODS

Patient group: Thirty-five patients were entered into this study after giving informed consent and were categorized into 3 groups. Group A included 6 patients (3 women aged 40 ± 16 years and 3 men aged 49 ± 18 years) studied during atrial overdrive pacing rates of 100 beats/min (600 ms intervals) and 150 beats/min (400 ms intervals). Group B consisted of 13 patients (4 from group A and 9 additional) (5 women aged 44 ± 13 years and 8 men aged 50 ± 14 years) undergoing epinephrine infusion. Group C was composed of 20 patients (9 women aged 58 ± 16 years and 11 men aged 51 ± 16 years) studied during infusion of isoproterenol. No patient was receiving antiarrhythmic drugs at the time of the electrophysiologic study. Nineteen patients had no prior evidence of heart disease, 13 had coronary artery disease, 1 had a previous myocardial infarction, 1 had mitral valve prolapse and 1 had myotonic dystrophy.

Electrophysiology study: Patient data were acquired from bipolar electrode catheters with 1 cm interelectrode spacing during elective cardiac electrophysiologic studies as described previously.[14] In the resting state, a 12-lead electrocardiogram was recorded during sinus rhythm for baseline measurement purposes. The patient was then either stimulated with atrial overdrive pacing at a cycle length of 600 ms followed by pacing at intervals of 400 ms (group A), treated with a physiologic dose[21] of an α and β agonist, epinephrine (50 ng/kg/min) (group B), or given a clinical infusion[22] of a pure β agonist, isoproterenol (2 μg/min) (group C).

Electrocardiograms from 2 or 3 surface leads (from I, II, III and V_1), a high right atrial lead, and a right ventricular apical lead were amplified through either a Siemens Mingograf-7 (Siemens-Elema, Solna, Sweden) or a Honeywell Electronics-for-Medicine (Electronics-for-Medicine, Pleasantville, New York) data amplifier. Each channel was recorded with wide-band filter settings of 0.5 to 500 Hz (Siemens Mingograf-7) or 1 to 500 Hz (Honeywell Electronics-for-Medicine), and outputs were connected to a Hewlett-Packard 3968A FM tape recorder (Hewlett-Packard, San Diego, California). Signals were recorded on magnetic tape at a speed of 3¾ inches/s with an effective bandwidth of 0 to 1,250 Hz. All recordings were obtained while patients were lying supine.

Intraventricular electrogram analysis: Intraventricular electrograms were digitized at a sampling rate of 1,000 Hz using a personal computer. Two separate passages of sinus rhythm before clinical intervention were digitized; the first was used for template generation and the second for baseline analysis. Additional data were digitized from each pacing passage for group A patients, from a passage during epinephrine infusion for group B patients, and from a passage during isoprotere-

nol infusion for group C patients. The length of each digitized passage varied from 10 to 30 seconds.

The average cycle length of the control sinus rhythm passage and the passage during clinically accelerated heart rate was determined for each patient. The average decrease in absolute cycle length for each group was evaluated by a 2-tailed, paired Student's t test, and a p value was derived to represent the overall significance of the decrease.

To perform electrogram analysis and quantitate the similarity or dissimilarity between ventricular depolarizations, an appropriate window of electrogram depolarization for analysis was chosen for each patient. The window was selected from a typical depolarization of the first sinus rhythm passage and, in order to exclude acute injury current during repolarization, included ventricular depolarization only by beginning at the first deviation from baseline and ending at the first evidence of repolarization. The initial window size was imposed on all subsequent analysis for the same patient.

A representative, signal-averaged template of the patient's normal sinus rhythm was compared individually with each ventricular depolarization of the second baseline passage of sinus rhythm using correlation waveform, area of difference, and amplitude analyses. Accurate alignment of the ventricular depolarization under analysis was effected by a sliding window method[14] to compensate for misaligned trigger points. The template was then compared in a similar manner with every depolarization of the accelerated heart rate passage.

Correlation waveform analysis: The correlation co efficient[12–17] is a metric between ± 1 which represents the morphologic similarity between 2 waveforms. It is a statistically based measure that is independent of amplitude and baseline variations and measures only relative shape differences between the template and the waveform being examined. This technique was used to compare the template depolarization with each depolarization from the control passage of sinus rhythm based on a previously published formula[16] and correlation coefficients were averaged to yield a mean ± standard deviation (CWA:SR). The average ± standard deviation of correlation coefficients for each passage during subsequent intervention (CWA:INT) was also computed. Because correlation values of sinus rhythm were consistently high and approached 1, we defined the percent change of correlation coefficient from the control sinus rhythm passage to the passage during intervention (Δ:CWA) according to the following formula:

$$\Delta\text{:CWA} = \left(\frac{\text{CWA:INT} - \text{CWA:SR}}{\text{CWA:SR}}\right) \times 100\%.$$

Area of difference analysis: Area of difference[10,11] directly measures the absolute amplitude difference be-

TABLE I Results of Morphologic Analysis of Atrial Overdrive Pacing at 600 ms Intervals

Pt. No.	CWA:SR	CWA:600	AOD:SR (%)	AOD:600 (%)	AMP:SR (%)	AMP:600 (%)	Δ:CWA (%)	Δ:AOD (%)	Δ:AMP (%)
1	0.996 ± 0.003	0.995 ± 0.003	7 ± 3	34 ± 1	1 ± 2	8 ± 11	−0.1	+27	+7
6	0.994 ± 0.001	0.993 ± 0.001	16 ± 5	5 ± 1	−9 ± 6	5 ± 11	−0.1	−11	+14
8	0.998 ± 0.001	0.994 ± 0.003	6 ± 2	11 ± 3	1 ± 2	−6 ± 19	−0.1	+5	−7
10	0.997 ± 0.001	0.996 ± 0.002	8 ± 3	18 ± 8	1 ± 4	−12 ± 2	−0.1	+10	−13
34	0.988 ± 0.007	0.989 ± 0.013	12 ± 3	15 ± 4	1 ± 9	5 ± 6	+0.1	+3	+4
35	0.994 ± 0.001	0.988 ± 0.004	13 ± 2	17 ± 5	2 ± 14	−6 ± 13	−0.6	+4	−8

AMP:SR = average amplitude during sinus rhythm; AMP:600 = average amplitude during atrial overdrive pacing at cycle length of 600 ms; AOD:SR = average area of difference during sinus rhythm; AOD:600 = average area of difference during pacing at 600 ms; CWA:SR = average correlation coefficient during sinus rhythm; CWA:600 = average correlation coefficient during pacing at 600 ms; Δ:AMP = change in peak-to-peak amplitude; Δ:AOD = change in area of difference; Δ:CWA = change in correlation coefficient.

TABLE II Results of Morphologic Analysis of Atrial Overdrive Pacing at 400 ms Intervals

Pt. No.	CWA:SR	CWA:400	AOD:SR (%)	AOD:400 (%)	AMP:SR (%)	AMP:400 (%)	Δ:CWA (%)	Δ:AOD (%)	Δ:AMP (%)
1	0.996 ± 0.003	0.979 ± 0.004	7 ± 3	53 ± 2	1 ± 2	8 ± 2	−1.7	+46	+7
6	0.994 ± 0.001	0.995 ± 0.001	16 ± 5	30 ± 4	−9 ± 6	41 ± 10	+0.1	+14	+50
8	0.998 ± 0.001	0.987 ± 0.005	6 ± 2	20 ± 8	1 ± 2	7 ± 5	−1.1	+14	+6
10	0.997 ± 0.001	0.988 ± 0.002	8 ± 3	78 ± 13	1 ± 4	19 ± 16	−0.9	+70	+18
34	0.988 ± 0.007	0.952 ± 0.007	12 ± 3	73 ± 14	1 ± 9	50 ± 15	−3.6	+61	+49
35	0.994 ± 0.001	0.981 ± 0.006	13 ± 2	28 ± 9	2 ± 14	29 ± 18	−1.3	+15	+27

AMP:400 = average amplitude during atrial overdrive pacing at cycle length of 400 ms; AOD:400 = average area of difference during pacing at 400 ms; CWA:400 = average correlation coefficient during pacing at 400 ms; other abbreviations as in Table I.

tween associated sample points of the template and the waveform under analysis and is dependent on fluctuations in amplitude and baseline. To eliminate the effects of direct-current offset, a variation on this formulation that normalizes the absolute area of difference by the total area of the template has been derived.[16] With use of this format, the area of difference was computed between the template depolarization and each depolarization of both the control passage of sinus rhythm and that during subsequent intervention, and these values were averaged to yield a mean ± standard deviation for each passage (AOD:SR and AOD:INT). The percent change of the area of difference from the control passage of sinus rhythm to the passage during intervention (Δ:AOD) was calculated as follows:

$$\Delta{:}AOD = AOD{:}INT - AOD{:}SR$$

Amplitude analysis: The difference in peak-to-peak electrogram amplitude due to intervention was also analyzed for each patient. The absolute peak-to-peak amplitude of the template depolarization (PP_{tmp}) and each depolarization of the baseline sinus rhythm passage (PP_{dep}) was determined, and a normalized value representing the difference of amplitude between these depolarizations (AMP_{dep}) was calculated as follows:

$$AMP_{dep} = \frac{PP_{dep} - PP_{tmp}}{PP_{tmp}} \times 100\%.$$

The normalized difference of amplitude values for all depolarizations of the baseline sinus rhythm passage were averaged to yield a mean ± standard deviation for

the passage (AMP:SR). The average ± standard deviation of the difference of amplitude during subsequent intervention (AMP:INT) was computed similarly. Finally, the percent change of normalized difference of amplitude from the control passage of sinus rhythm to the passage during intervention (Δ:AMP) was calculated as follows:

$$\Delta{:}AMP = AMP{:}INT - AMP{:}SR$$

Scatter diagrams: Scatter diagrams of (1) the change of amplitude versus the change of correlation coefficient, and (2) the change of amplitude versus the change of area of difference were plotted for each intervention. When a linear probabilistic model was deemed appropriate (i.e., when the points tended to cluster about a straight line and when ≥10 data points were available), linear regression analysis[23] was used to obtain an equation of the estimated regression line. In each case, the change in amplitude was chosen to be the independent variable, and a best fit line to the data and the corresponding sample correlation coefficient, r, were determined.

RESULTS

Data from correlation waveform, area of difference and amplitude analyses during atrial overdrive pacing, infusions of epinephrine, and infusions of isoproterenol are summarized in Tables I to IV and are illustrated for 3 patients in Figures 1 to 3. The width of the depolarization analysis window for the 35 patients of this study ranged from 29 to 100 ms (mean 51.2 ± 14.8).

Cycle length: The sinus rhythm cycle length for group A patients was 765 ± 99 ms. Atrial overdrive pacing at 600 ms intervals decreased the cycle length by 161 ms (p <0.02) and pacing at 400 ms intervals decreased the cycle length by 363 ms (p <0.0005). Epinephrine infusion decreased the mean sinus rhythm cycle length of 773 ± 138 ms for group B patients by 88 ms (p <0.005), and isoproterenol infusion decreased

TABLE III Results of Morphologic Analysis of Epinephrine Infusion

Pt. No.	CWA:SR	CWA:EPI	AOD:SR (%)	AOD:EPI (%)	AMP:SR (%)	AMP:EPI (%)	Δ:CWA (%)	Δ:AOD (%)	Δ:AMP (%)
1	0.996 ± 0.003	0.996 ± 0.003	7 ± 3	14 ± 2	1 ± 2	8 ± 8	0.0	+7	+7
2	0.999 ± 0.001	0.998 ± 0.001	11 ± 3	11 ± 3	1 ± 13	−3 ± 10	−0.1	0	−4
3	0.992 ± 0.005	0.983 ± 0.006	13 ± 3	16 ± 2	−1 ± 7	−8 ± 9	−0.9	+3	−7
4	0.994 ± 0.005	0.983 ± 0.007	12 ± 5	15 ± 2	2 ± 9	1 ± 3	−1.1	+3	−1
5	0.996 ± 0.001	0.980 ± 0.003	9 ± 2	17 ± 2	−1 ± 3	1 ± 8	−1.6	+8	+2
6	0.994 ± 0.001	0.990 ± 0.002	16 ± 5	13 ± 2	−9 ± 6	−5 ± 5	−0.4	−3	+4
7	0.993 ± 0.002	0.989 ± 0.001	11 ± 2	16 ± 2	6 ± 6	6 ± 36	−0.4	+5	0
8	0.998 ± 0.002	0.993 ± 0.004	6 ± 2	12 ± 3	1 ± 2	5 ± 4	−0.5	+6	+4
9	0.982 ± 0.012	0.982 ± 0.009	44 ± 25	21 ± 7	18 ± 29	2 ± 23	0.0	−23	−16
10	0.997 ± 0.001	0.997 ± 0.001	8 ± 3	15 ± 6	1 ± 4	7 ± 6	0.0	+7	+6
11	0.996 ± 0.002	0.975 ± 0.009	18 ± 6	26 ± 5	5 ± 14	−8 ± 14	−2.1	+8	−13
12	0.994 ± 0.003	0.982 ± 0.008	12 ± 2	29 ± 9	3 ± 3	12 ± 13	−1.2	+17	+9
13*	0.982 ± 0.011	0.890 ± 0.018	17 ± 6	39 ± 5	−8 ± 4	−11 ± 19	−9.4	+23	−3

*This patient had a paradoxical change of correlation coefficient and is not included in the statistical analyses.
AMP:EPI = average amplitude during epinephrine infusion; AOD:EPI = average area of difference during epinephrine infusion; CWA:EPI = average correlation coefficient during epinephrine infusion; other abbreviations as in Table I.

TABLE IV Results of Morphologic Analysis of Isoproterenol Infusion

Pt. No.	CWA:SR	CWA:ISO	AOD:SR (%)	AOD:ISO (%)	AMP:SR (%)	AMP:ISO (%)	Δ:CWA (%)	Δ:AOD (%)	Δ:AMP (%)
14	0.995 ± 0.003	0.967 ± 0.030	19 ± 8	34 ± 11	−33 ± 10	−24 ± 15	−2.8	+15	+9
15	0.997 ± 0.002	0.994 ± 0.005	7 ± 2	12 ± 2	1 ± 4	−2 ± 6	−0.3	+5	−3
16	0.996 ± 0.022	0.973 ± 0.015	10 ± 4	54 ± 31	−1 ± 5	8 ± 23	−2.3	+44	+9
17	0.996 ± 0.002	0.997 ± 0.001	19 ± 5	23 ± 5	13 ± 15	25 ± 16	+0.1	+4	+12
18	0.996 ± 0.002	0.991 ± 0.002	15 ± 5	53 ± 13	2 ± 10	23 ± 13	−0.5	+38	+21
19	0.996 ± 0.003	0.995 ± 0.003	10 ± 4	14 ± 3	−2 ± 3	8 ± 4	−0.1	+4	+10
20	0.995 ± 0.003	0.975 ± 0.002	11 ± 2	43 ± 1	−4 ± 2	−4 ± 6	−2.0	+32	0
21	0.996 ± 0.002	0.997 ± 0.001	11 ± 5	11 ± 5	−9 ± 7	3 ± 11	+0.1	0	+12
22	0.967 ± 0.012	0.953 ± 0.007	39 ± 17	62 ± 17	29 ± 26	48 ± 14	−1.5	+23	+19
23	0.998 ± 0.002	0.981 ± 0.016	6 ± 2	26 ± 8	0 ± 3	17 ± 10	−1.7	+20	+17
24	0.997 ± 0.002	0.997 ± 0.001	5 ± 2	22 ± 4	0 ± 4	10 ± 6	0.0	+17	+10
25	0.997 ± 0.002	0.996 ± 0.002	15 ± 5	12 ± 5	−1 ± 6	−6 ± 6	−0.1	−3	−5
26	0.996 ± 0.001	0.996 ± 0.002	15 ± 7	48 ± 13	−3 ± 14	53 ± 15	0.0	+33	+56
27	0.990 ± 0.003	0.962 ± 0.009	24 ± 8	57 ± 2	−10 ± 11	−1 ± 7	−2.8	+33	+9
28	0.996 ± 0.002	0.993 ± 0.002	13 ± 5	14 ± 4	0 ± 8	4 ± 3	−0.3	+1	+4
29	0.996 ± 0.004	0.996 ± 0.002	10 ± 5	12 ± 2	−2 ± 12	26 ± 11	0.0	+2	+28
30	0.990 ± 0.005	0.961 ± 0.039	18 ± 3	50 ± 20	−10 ± 23	−6 ± 8	−3.0	+32	+4
31	0.995 ± 0.002	0.994 ± 0.002	10 ± 5	15 ± 5	−1 ± 5	4 ± 4	−0.1	+5	+5
32*	0.968 ± 0.012	0.759 ± 0.003	24 ± 5	63 ± 9	7 ± 5	130 ± 8	−21.6	+39	+123
33*	0.992 ± 0.004	0.786 ± 0.009	19 ± 9	261 ± 8	−1 ± 9	12 ± 7	−20.8	+242	+13

*These patients had paradoxical changes in correlation coefficients and were not included in the statistical analyses.
AMP:ISO = average amplitude during isoproterenol infusion; AOD:ISO = average area of difference during isoproterenol infusion; CWA:ISO = average correlation coefficient during isoproterenol infusion; other abbreviations as in Table I.
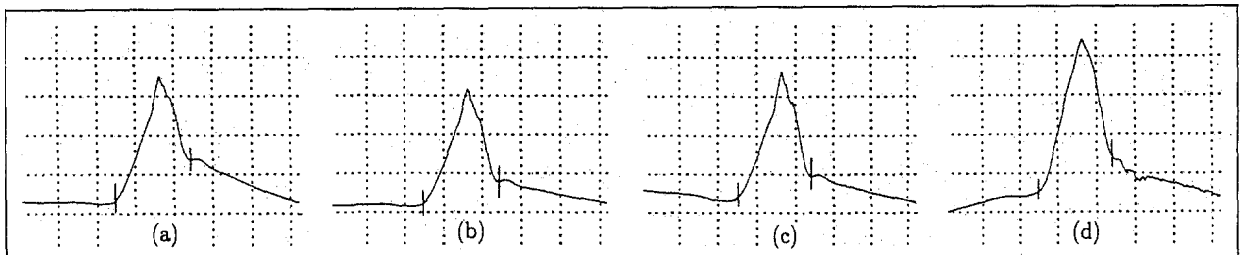
FIGURE 1. Electrograms from patient 6 during atrial overdrive pacing at rates of 600 and 400 ms. A signal-averaged intraventricular depolarization is shown from a passage during (a) sinus rhythm for template construction, (b) a subsequent control passage of sinus rhythm, (c) pacing at 600 ms, and (d) pacing at 400 ms. The figures are plotted at a paper speed of 200 mm/s with a gain of 100 mV/mm. The 51 ms analysis window of electrogram depolarization is marked by *vertical bars* on the original 180 ms window. Although the change in correlation coefficient was small during pacing at both 600 and 400 ms (−0.1 and +0.1%), larger changes in area of difference (−11 and +14%) and amplitude (+14 and +50%) occurred.

the sinus rhythm cycle length of 797 ± 151 ms for group C patients by 231 ms (p <0.0001). With the exception of 1 patient (no. 13), no consistent relationship could be found between the change in cycle length due to any intervention and the change of correlation coefficient, area of difference, or amplitude of the electrogram.

Correlation waveform analysis: For 6 of 6 group A patients (100%), the change in correlation coefficient during pacing at 600 ms intervals ranged from −0.6 to +0.1% and averaged −0.2%. During pacing at a cycle length of 400 ms, the change in correlation coefficient ranged from −3.6 to +0.1% and averaged −1.4%.

The change in correlation coefficient for 12 of 13 patients (92%) during epinephrine infusion (group B) ranged from −2.1 to 0% and averaged −0.7%. A large, unexplained change of correlation coefficient (9.4%) was seen in 1 patient (no. 13).

The change in correlation coefficient for 18 of 20 patients (90%) during isoproterenol infusion (group C) ranged from −2.8 to +0.1% and averaged −1.0%. Two group C patients (nos. 32 and 33) had a paradoxical change of correlation coefficient of −20.8 and −21.6%.

Area of difference analysis: For patients in group A, the change of area of difference during atrial overdrive pacing at a cycle length of 600 ms ranged from −11 to +27% and averaged +6%. Pacing at a cycle

length of 400 ms produced a change in area of difference that ranged from +14 to +70% and averaged +37%.

For the 12 of 13 group B patients with stable correlation coefficients during epinephrine infusion, the change in area of difference ranged from −23 to +17% and averaged +3%.

For the 18 of 20 group C patients with stable correlation coefficients during isoproterenol infusion, the change in area of difference ranged from −3 to +44% and averaged +17%.

Amplitude analysis: The change in amplitude for group A patients during atrial overdrive pacing at a cycle length of 600 ms ranged from −13 to +14% and averaged −1%. The change in amplitude during pacing at a cycle length of 400 ms ranged from +6 to +50% and averaged +26%.

For the 12 patients from group B with stable correlation coefficients during epinephrine infusion, the change in amplitude ranged from −16 to +9% and averaged −1%.

For the 18 group C patients with stable correlation coefficients during isoproterenol infusion, the change in amplitude ranged from −5 to +56% and averaged +12%.

Scatter diagrams: Figures 4 and 5 illustrate the scatter plots of change of amplitude versus change of correlation coefficient and change of amplitude versus
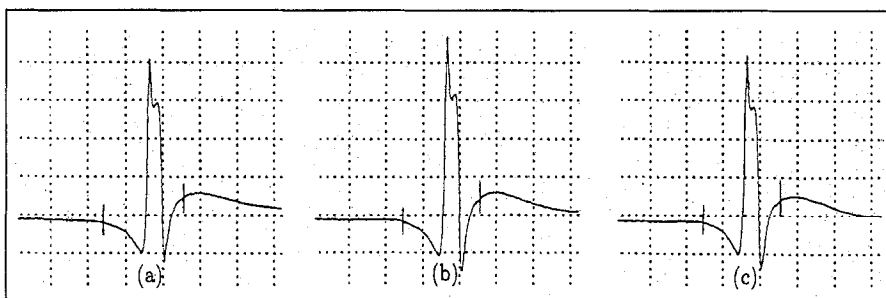
FIGURE 2. Electrograms from patient 9 during infusion of epinephrine. A signal-averaged intraventricular depolarization is shown from (a) passage of sinus rhythm for template construction, (b) a subsequent control passage of sinus rhythm, and (c) passage during epinephrine infusion. The figures are plotted at a paper speed of 200 mm/s with a gain of 50 mV/mm. The 53 ms analysis window of electrogram depolarization is marked on the original 180 ms window. This patient had no change in correlation coefficient. However, changes in area of difference (−23%) and amplitude (−16%) during epinephrine infusion occurred.
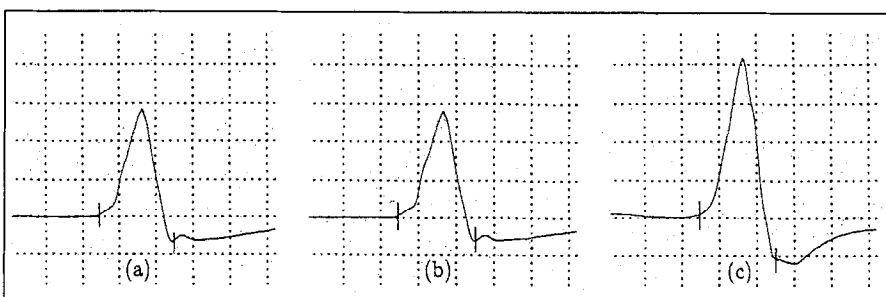

FIGURE 3. Electrograms from patient 26 during isoproterenol infusion. A signal-averaged intraventricular depolarization is shown from (a) passage of sinus rhythm for template construction, (b) a subsequent control passage of sinus rhythm, and (c) the passage during isoproterenol infusion. The figures are plotted at a paper speed of 200 mm/s with a gain of 75 mV/mm. The 52 ms analysis window of electrogram depolarization is marked on the original 180 ms window. Although no change of correlation coefficient occurred, a large change in area of difference (+33) and amplitude (+56%) during isoproterenol infusion occurred.

change of area of difference for the 36 patients with stable correlation coefficients during each intervention. Patients with paradoxical changes in correlation coefficient (nos. 13, 32 and 33) were not included in the analysis. For both figures, the data points for pacing at intervals of 600 and 400 ms are not clustered and are too few for linear regression to be appropriate. However, a tighter clustering of data is evident during infusions of epinephrine and isoproterenol, and results of linear regression analysis are included in these diagrams. Whereas changes in amplitude and correlation coefficient were only weakly correlated during both infusion of epinephrine (r = 0.187) and isoproterenol (r = 0.217), the change in amplitude and the change in area of difference were moderately correlated during

infusion of epinephrine (r = 0.649) and weakly correlated during infusion of isoproterenol (r = 0.292).

DISCUSSION

Correlation waveform analysis remains stable during interventional increases in heart rate, whereas the area of difference is less stable and exhibits moderate fluctuations associated with amplitude changes (Figures 1 to 3). Overall waveform morphology remains relatively constant (despite some amplitude variation) during increases in heart rate with or without concurrent changes in sympathetic tone. Therefore, it may be anticipated that a sophisticated scheme of pattern recognition, using a template-based system of arrhythmia identification and regular updating of the sinus rhythm
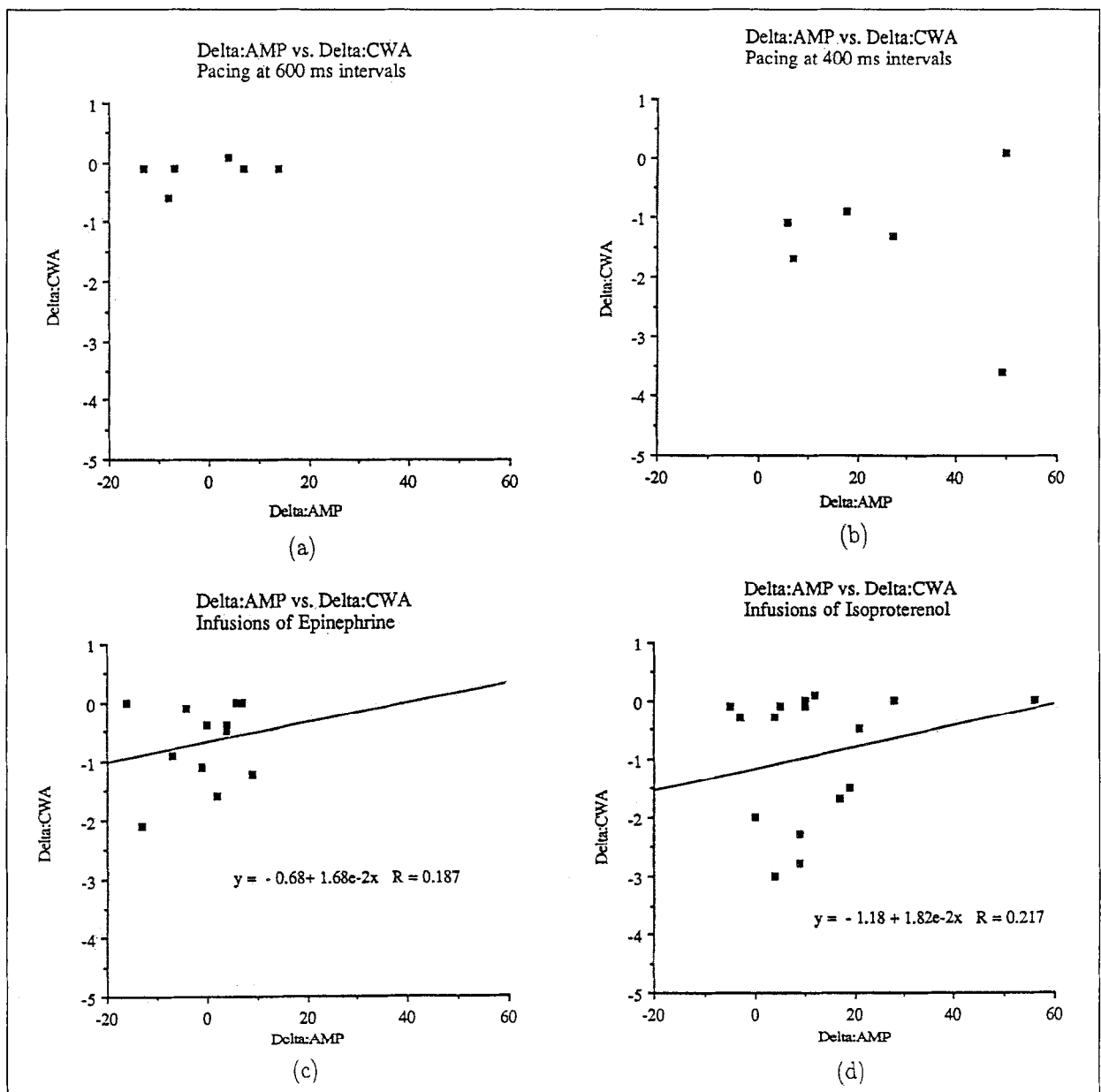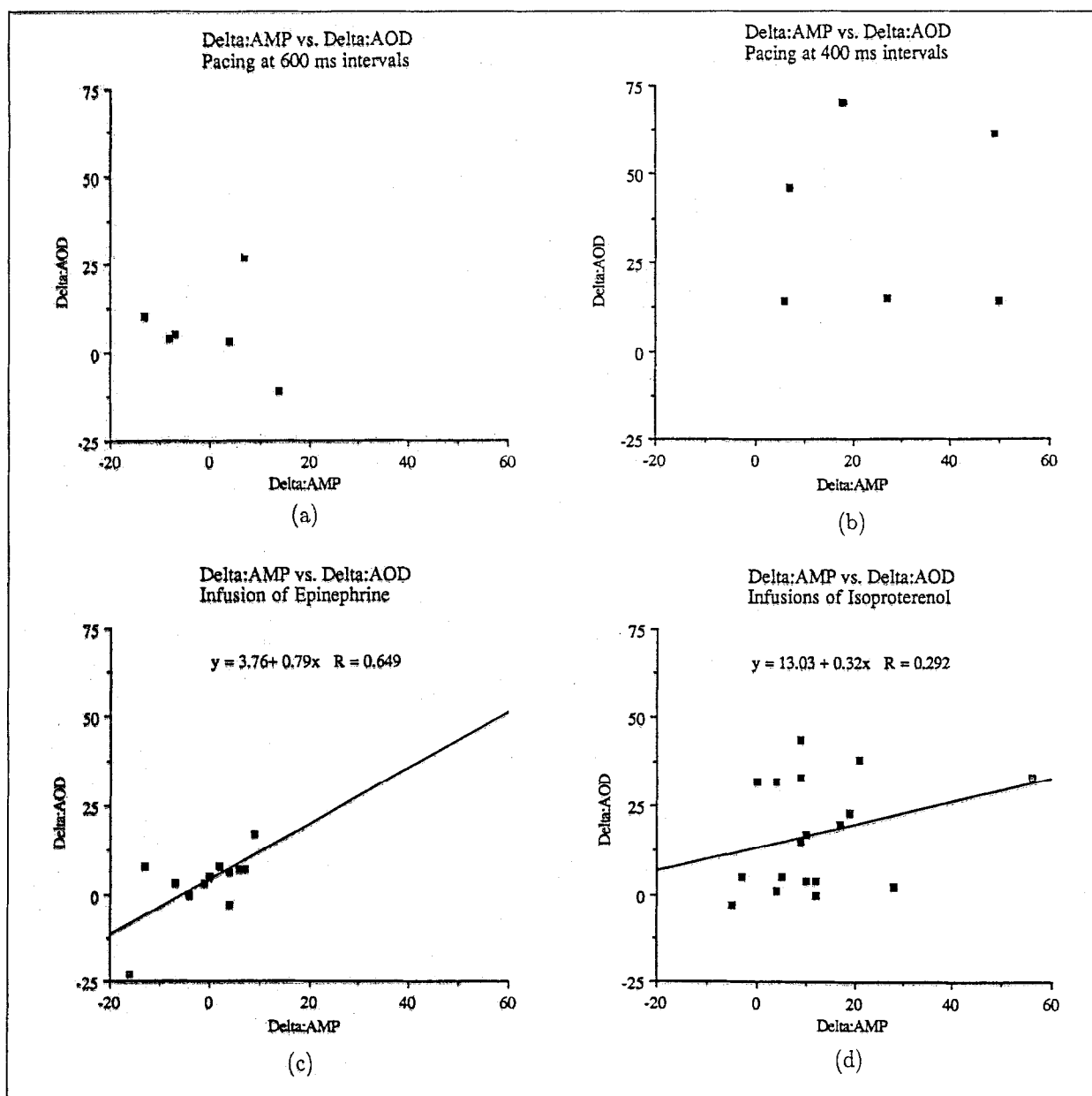

FIGURE 4. Scatter diagrams of the change in amplitude (Delta:AMP) versus the change of correlation coefficient (Delta:CWA) during (a) atrial overdrive pacing at a cycle length of 600 ms, (b) pacing at a cycle length of 400 ms, (c) epinephrine infusion, and (d) isoproterenol infusion. Panels (c) and (d) include linear regression analysis.

template, should not be confounded by increases in heart rate during sinus rhythm.

Results of 3 patients undergoing pharmacologic intervention, 1 during epinephrine (no 13) and 2 during isoproterenol (nos. 32 and 33) administration, were widely divergent from most patients evaluated in this study. The morphologic changes noted in these patients, as assessed by the 12-lead electrocardiogram, were not due to paroxysmal development of an intraventricular conduction delay (such as bundle branch block) during drug infusions. Because passive intracardiac electrode leads were used, and because baseline sinus rhythm passages after excretion of exogenously administered drugs were not reconfirmed for stability of electrode location, catheter movement cannot be ex-

cluded as a potential cause of the observed changes. For these reasons, we purposely excluded these 3 patients from our statistical analysis and conclusions because of the ambiguity they posed.

Correlation waveform analysis: Although this study indicated that correlation waveform analysis remains stable in the presence of accelerated heart rate, other investigators have shown contradictory results. Paul et al[18] demonstrated large changes in electrogram morphology using correlation waveform analysis in a small number of patients during changes in body position. As in the current study, Paul also used a passive electrode catheter, and although data were obtained immediately after exercise, electrograms were not recorded after complete recovery to confirm whether a close correla-

FIGURE 5. Scatter diagrams of the change in amplitude (Delta:AMP) versus the change in area of difference (Delta:AOD) during (a) atrial overdrive pacing at a cycle length of 600 ms, (b) pacing at a cycle length of 400 ms, (c) epinephrine infusion, and (d) isoproterenol infusion. Panels (c) and (d) include linear regression analysis.

tion with the original sinus rhythm template remained. Therefore, as with the 3 patients in the current study, catheter migration cannot be excluded as a cause for their observed results.

Area of difference analysis: In the present study moderate fluctuations in area of difference that occurred with interventional increases in heart rate were noted. They may not necessarily prove troublesome to template-matching schemes, because the range of area of difference values obtained during accelerated heart rate passages is similar to that previously reported for sinus rhythm at rest.[10,15] The findings of this study therefore suggest that accelerated heart rate may not confound the ability of this technique of analysis to differentiate ventricular tachycardia from sinus rhythm.

Amplitude analysis: Although changes in amplitude due to increased heart rate have been demonstrated in previous studies,[19,24,25] controversy exists concerning the value of electrogram amplitude in detecting diverse dysrhythmias.[10,11,26-28] The present study measured peak-to-peak amplitude changes on raw, unfiltered data. The observed effects of atrial overdrive pacing at fast cycle lengths and of isoproterenol administration on electrogram amplitude in the present study are compatible with those of Rosenheck et al.[19] However, they reported amplitude increases during atrial overdrive pacing at 400 ms intervals and during β agonism caused by isoproterenol administration as seen on a high-pass filtered version of the signal. As a result, their study consisted of analysis of the derivative of the intracardiac signal, rather than the signal itself.

Studies to date concerning time-domain analysis of intracardiac electrograms have been hampered by experimental limitations such as passive electrode leads, lack of confirmation of electrode migration, and use of artificial intervention to simulate physiologic changes in heart rate. Despite these limitations, the importances of the present study are twofold: (1) Amplitude changes, as seen in the presence of accelerated heart rate, are not necessarily accompanied by significant changes in electrogram morphology as assessed by correlation waveform or area of difference analyses. (2) Electrogram morphologic analysis for the discrimination of ventricular tachycardia from sinus rhythm should remain robust in the face of physiologically accelerated heart rate.

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