

Incidence of Complex Ventricular Arrhythmias in Asymptomatic Patients with Recent Myocardial Infarction

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Summary: The incidence of ventricular extrasystoles (VES) was documented in 50 patients with recent uncomplicated myocardial infarction, with a 72-h two-channel ambulatory electrocardiogram. All patients were free of symptoms of arrhythmias; unstable angina pectoris and heart failure were absent. A total of 82% of the patients had VES: 23/50 patients had multiform or complex VES, 8/50 patients had ventricular tachycardia. VES were independent of heart rate and stable angina pectoris. Thus, frequent and complex VES are common in *asymptomatic* patients with *uncomplicated* recent myocardial infarction. Even in the absence of symptoms, ambulatory electrocardiography is useful. The prognostic significance of asymptomatic complex VES in these patients remains unsettled.

Key words: ventricular arrhythmias, ambulatory ECG, myocardial infarction

Introduction

Ambulatory electrocardiography is valuable for the detection of arrhythmias (Bertel *et al.*, 1979, Bethge *et al.*, 1983; Bigger *et al.*, 1977; Bjerregaard *et al.*, 1982; Brodsky *et al.*, 1977; Burkart, 1984; Coronary Drug Project Research Group, 1974; Harrison *et al.*, 1978; Hinkle *et al.*, 1974; Kennedy and Underhill, 1976; Lipski *et al.*, 1976; Manger Cats *et al.*, 1979; Michelson and Morganroth, 1980; Monti *et al.*, 1975; Morganroth *et al.*, 1978; Moss *et al.*, 1979; Ruberman *et al.*, 1977; Sculze *et al.*, 1975; Stein and Jungmann, 1979; Thavanaro *et al.*, 1980). Twenty-four hour ambulatory electrocardiograph is considered to be sufficient, but increasing the hours of recording is more effective (Kennedy *et al.*, 1978; Roberts *et al.*, 1982). Simple ventricular arrhythmias are common in individuals without detectable heart disease and, at times, complex ventricular arrhythmias may be observed (Bethge *et al.*, 1983; Bjerregaard *et al.*, 1982; Brodsky *et al.*, 1977; Hinkle *et al.*, 1974; Kennedy and Underhill, 1976). Several investigations have shown that in patients with recent myocardial infarction (MI) complex and frequent ventricular arrhythmias are common (Burkart, 1984; Coronary Drug Project Research Group, 1974; Manager Cats *et al.*, 1979; Moss *et al.*, 1979; Ruberman *et al.*, 1977; Sculze *et al.*, 1975; Stein and Jungmann, 1979; Thavanaro *et al.*, 1980). All these studies, however, were obtained in patients with recent MI who were suspected to be *at high risk for sudden cardiac death*, the majority of these patients being *symptomatic*. The authors considered complex ventricular arrhythmias in patients with recent MI a risk for sudden death, and suggested treatment of these arrhythmias (Burkart, 1984; Coronary Drug Project Research Group, 1974; Moss *et al.*, 1979; Ruberman *et al.*, 1977, Stein and Jungmann, 1979). However, most of our patients attending a

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rehabilitation program after MI are asymptomatic and the majority of these patients had an *uncomplicated* MI. Therefore, their clinical picture is different than the patients described above. Since ventricular arrhythmias are common in individuals without detectable disease (Bethge *et al.*, 1983; Bjerregaard *et al.*, 1982; Brodsky *et al.*, 1977; Hinkle *et al.*, 1974; Kennedy and Underhill, 1976), we thought that ventricular arrhythmias might be common in our patients with recent uncomplicated MI. Data in this subset of patients were unavailable, and we decided to assess the incidence of arrhythmias in patients with recent and uncomplicated MI, who were free of symptoms of cardiac arrhythmias, had a normal heart function, were free of unstable or variant angina pectoris, and were not taking drugs affecting myocardial vulnerability.

Patients and Methods

Patients

All patients had suffered a *first transmural* MI 10–16½ weeks (mean 12.3 weeks) prior to selection. According to published criteria (Birk Madsen, 1983) the MI had been *uncomplicated*. The MI was lateral in 30 cases, posterodiventricular in 13, and anterior in 7. Fifty consecutive patients (followed between 1981 and 1984) fulfilled these criteria and were selected for the study. The group consisted of 43 males and 7 females, aged 50–74 years (mean 57 years). Their body weight was within 10% of the ideal range (mean 72 kg, range 50–98 kg). Blood pressure was normal in 46 patients and only slightly elevated in 4 (no need for active therapy). All patients were free of acute or relevant concomitant diseases and were eligible for a normal cardiac rehabilitation program. Signs of heart failure were absent. All patients could perform a 10-min or longer exercise (sitting bicycle ergometry) against at least 100 W (females) and 125 W (males) without signs of heart failure, frequent cardiac arrhythmias, or severe angina pectoris. The mean systolic blood pressure \times heart rate peak product was 20,725 (SD \pm 238). Unstable or variant angina pectoris was absent, and effort angina pectoris was absent or mild and stable. The patients *did not* present *symptoms related to cardiac arrhythmias*.

Drugs

Eight patients were taking diuretics, four digoxin (anamnesic heart failure, at least 1 year prior to selection), three oral hypoglycemic agents (for mild diabetes). Sublingual nitroglycerin was used for angina pectoris (on need), but antianginal drugs were not used prophylactically.

Ambulatory Electrocardiography

From the 4th to the 6th day of observation a continuous 72-h dynamic electrocardiogram was obtained. The

patients were free to move within the hospital and the surrounding garden area. No rehabilitation was performed and stressful procedures were avoided during ambulatory electrocardiography. Dual-channel tape records were used, and both bipolar leads were checked in various body positions in order to avoid significant changes of the R/S relation. As previously reported (Bigger *et al.*, 1981; Cocco *et al.*, 1982, 1984; Pansini *et al.*, 1983; Smerlow *et al.*, 1983; Strozzi *et al.*, 1982) tape analysis was completed by integral continuous trend-transcription at 10 mm/s with a real-time constant of 1 min. Complex arrhythmias were validated by documentation with the built-in recorder at 25 mm/s, and verified by a cardiologist. Arbitrarily, ventricular extrasystoles (VES) were classified as <30 VES/h ≥ 30 VES/h, and complex VES (multiform or consecutive, bigeminy, R' on T). The hourly incidence and type of VES were calculated. The first 24-h registration was compared to the total 72-h registration. At least 94% of tapes were of sufficient quality to allow analysis. Patients were instructed and encouraged to keep full diaries of activities and symptoms, and mark symptoms on the tapes. All were able to do so properly. Tapes and diaries were checked and whenever necessary additional information was obtained by personal interview.

Results

24-Hour Ambulatory ECG

The mean heart rate was 88 beats/min, with a range of 38 (during sleep) and 146 (climbing stairs). Ten patients (20%) were arrhythmia-free. Eight patients (16%) had <30 VES/h; 32 (64%) had ≥ 30 VES/h: mean 4 episodes/24 h (range 2–24), mean number 49 (range 32–130 VES/h). Nineteen of 32 patients also had complex VES, 18 of 32 patients also had multiform VES. Six patients had paired VES: mean 37 episodes (range 1–90). Five patients had R' on T VES: mean 18 (range 3–32). Ventricular tachycardia (5–18 consecutive VES) was detected in 4 patients: mean 23 episodes (range 1–34). Complex arrhythmias varied greatly within and between patients. Data are shown in Table I.

72-Hour Ambulatory ECG

The mean heart rate was 86 beats/min, with an average of 38 (during sleep) and 152 (spontaneous sinus tachycardia). Four patients (8%) were arrhythmia-free. Three patients (6%) had <30 VES/h; 43 patients (84%) had ≥ 30 VES/h: mean 4 episodes/24 h (range 1–24), mean number 56 (range 30–192 VES/h); 23 patients had complex VES and 23 patients had multiform VES. Thirteen patients had paired VES: mean 28 episodes/24 h (range 1–102). Six patients had triple VES: mean 18 episodes/24 h (range 1–33). Ventricular tachycardia (5–23 consecutive VES) was detected in 8 patients: mean 16 epi-

TABLE I Ambulatory ECG data

	24-h ECG	72-h ECG
HR (beats/min)		
Mean (per 24 h)	88	86
Range	38-146	38-152
VES (patients)		
C-0	10 (20%)	4 (8%)
C-1	8 (16%)	3 (6%)
C-2	32 (64%)	43 (84%)
Type of VES		
Complex	19	23
Multiform	18	20
Paired	6	13
Mean (per 24 h)	37	28
Range	1-90	1-102
Triple	4	6
Mean (per 24 h)	19	18
Range	1-29	1-33
Ventricular tachycardia (4 or more consecutive)	4	8
Mean	23	16
Range	1-34	1-36

Abbreviations: HR, heart rate; VES, ventricular extrasystoles; C-0, no VES; C-1, <30 VES/h; C-2, \geq 30 VES/h.

sodes/24 h (range 1-36). Complex arrhythmias varied greatly within and between patients. However, there is a linear relationship between number and complexity of VES: the correlation coefficient between 80 VES/h and triple or more VES is .84 ($p < 0.005$).

Six patients were arrhythmia-free in the 24-h and 72-h dynamic ECG. In the other 44 patients some VES were detected with 72-h ECG. Data are shown in Table I.

Symptomatology

Only 12% of the VES were symptomatic. While the incidence of VES did not differ during sleep and wake, the VES during sleep were asymptomatic. About 65% of the symptoms were due to frequent VES (>60 VES/h). Only 5% of symptoms were without detectable electrocardiographic changes. Only two symptoms were reported as "important". The other symptoms were only reported because the patients were motivated to do so, and the symptoms were rated as "irrelevant" or "minor". Data are shown in Table II.

Fifteen patients reported 22 episodes of effort-induced angina pectoris. All episodes had corresponding repolarization changes on the ECG. Furthermore, 49 additional ST-T changes (myocardial ischemia) were detected on the dynamic ECG, but they were asymptomatic. Data are also shown in Table II.

TABLE II Ambulatory ECG and symptomatology (72-h dynamic ECG)

Ventricular extrasystoles
12% were symptomatic
88% were asymptomatic
5% of reported symptoms were without ECG changes
Symptomatic VES (12%)
35% were complex
65% were simplex but frequent (60 VES/h)
Myocardial ischemia
71 episodes of ST-T changes were detected
22 were symptomatic
49 were asymptomatic

Arrhythmias and Drugs

Fifteen of 50 patients were taking drugs. Some drugs may have influenced the VES. However, treated and untreated patients had similar arrhythmias. Diuretics and digoxin were not more frequent in patients with complex or frequent VES than in untreated patients. Furthermore, patients using sublingual nitroglycerin for stopping effort-induced angina pectoris had similar VES to patients who did not take the drug. It is therefore unlikely that treatment influenced the VES. Data are shown in Table III.

Discussion

Our results confirm the value of ambulatory ECG in detecting arrhythmias as a well-established fact (Bertel *et al.*, 1979; Bigger *et al.*, 1977; Burkart, 1984; Coronary Drug Project Research Group, 1974; Harrison *et al.*, 1978; Lipski *et al.*, 1976; Manger Cats *et al.*, 1979; Michelson and Morganroth, 1980; Monti *et al.*, 1975; Morganroth *et al.*, 1978; Moss *et al.*, 1979; Ruberman *et al.*, 1977; Sculze *et al.*, 1975; Stein and Jungmann, 1979; Thanavaro *et al.*, 1980). Our study confirms also the superiority of a dynamic registration longer than 24 h over the standard 24-h registration (Kennedy *et al.*, 1978; Roberts *et al.*, 1982). However, our results provide clinically relevant data unavailable in other studies. Indeed, other authors have demonstrated the high incidence of complex VES in symptomatic patients, or in patients at high risk for sudden death (Coronary Drug Project Research Group, 1974; Moss *et al.*, 1979; Ruberman *et al.*, 1977; Sculze *et al.*, 1975; Stein and Jungmann, 1979; Thanavaro *et al.*, 1980). Our results, however, were obtained in *asymptomatic* patients, with a recent *uncomplicated* first myocardial infarction, and *without* overt risks for sudden death. Our study provides evidence that frequent and complex VES are detectable in a large percentage of these patients, as

TABLE III Arrhythmias and drugs

Drugs	Total no. of patients	VES/h (patients)			Complex VES
		0	< 30	≥ 30	
Dr+Dg+Ni	3	1	0	2	1
Dr+Dg	1	0	1	0	0
Dr+Hy	1	0	1	0	0
Dr+Hy+Ni	2	0	1	1	1
Dr+Ni	1	1	0	0	0
Ni	9	1	4	4	3
Drugs alone					
Di	8	2	3	3	2
Dg	4	1	1	2	1
Hy	3	1	2	0	0
Ni	15	3	5	7	5

For the therapeutic schedule please see the text (Methods). The upper listing shows the combinations of drugs, the lower shows the single drugs. Fifteen out of 50 patients were taking some drugs, some patients more than one. Patients with ≥ 30 VES/h sometimes also had complex VES. It appears that the drugs did not induce any significant effect on the severity of VES: patients taking drugs did not present more frequent or severe VES than untreated patients.

Abbreviations: Dr = diuretics, Dg = digoxin, Hy = hypoglycemics, Ni = nitroglycerin.

in patients "at high risk" for sudden death. Clearly enough, a dynamic ECG must be obtained in all patients with a recent MI, without relying on symptoms.

One should also reflect about the prognostic significance of these asymptomatic arrhythmias. Should they be treated?

In *symptomatic* patients, it has been suggested that complex VES are a separate risk for sudden death and should be treated (Coronary Drug Project Research Group, 1974; Moss *et al.*, 1979; Ruberman *et al.*, 1977; Sculze *et al.*, 1975; Stein and Jungmann, 1979; Thanavaro *et al.*, 1980). Treatment should be possible without exaggerated problems (Burkart, 1984) and in treated patients mortality seems to be reduced (Bigger *et al.*, 1981; Smerlow *et al.*, 1983). However, we are not sure that results from symptomatic patients may be extrapolated to *asymptomatic* patients, even if the type of arrhythmia is similar. Patients should not be treated merely because of electrocardiographic changes. Large epidemiological studies in asymptomatic patients would be greatly welcome. Until they are available, the decision about treatment must be taken empirically in the individual patient, considering the age, presence of relevant diseases, risks of coronary artery disease, psychological profile, and so on. Because complex VES are common in asymptomatic patients with recent MI, treatment in all cases might become a problem (number of ambulatory ECGs, personnel involved, determination of plasma levels of antiarrhythmic drugs, monitoring of side effects, cost of the procedure, etc.).

In conclusion, our results show that complex VES are common in asymptomatic patients with a recent uncomplicated MI. These arrhythmias are similar to those described in symptomatic patients considered to be at high

risk for sudden cardiac death. However, while the type of complex VES is similar in symptomatic and asymptomatic patients, our limited experience does not allow a final decision about the need for treatment. The decision whether to treat or not in asymptomatic patients must, at least for now, be taken empirically.

References

- Bertel O, Braun S, Schmid P, Burkart F: Hohe Spontanvariabilität ventrikulärer Rhythmusstörungen limitiert Aussagekraft von Langzeit-Ekg-Untersuchungen. *Schweiz Med Wschr* 109, 1670 (1979)
- Bethge K-P, Bethge D, Meiners G, Lichtlen PR: Incidence and prognostic significance of ventricular arrhythmias in individuals without detectable heart disease. *Eur Heart J* 4, 338 (1983)
- Bigger JT, Wenger TL, Hessenbittel RH: Limitations of the Lown grading system for the study of human ventricular arrhythmias. *Am Heart J* 93, 727 (1977)
- Bigger JT, Welt FM, Rozinsky LM: Prevalence, characteristics and significance of ventricular tachycardia (three or more complexes) detected with ambulatory electrocardiographic recording in the late hospital phase of acute myocardial infarction. *Am J Cardiol* 48, 815 (1981)
- Birk Madsen E: Time of discharge for patients with acute myocardial infarction. *Cardiovasc Res* 4, 1301 (1983)
- Bjerregaard P: Premature beats in healthy subjects 40-79 years of age. *Eur Heart J* 3, 493 (1982)
- Brodsky M, Wu D, Denes P, Kanakis C, Rosen KM: Arrhythmias documented by 24 hour continuous electrocardiographic monitoring in 50 male medical students without apparent disease. *Am J Cardiol* 39, 390 (1977)

- Burkart F: Rhythmusstörungen nach Herzinfarkt. *Praxis* 73, 67 (1984)
- Cocco G, Braun S, Strozzi C, Leishman B, Chu D, Rochat N: Asymptomatic myocardial ischemia in patients with stable and typical angina pectoris. *Clin Cardiol* 2, 403 (1982)
- Cocco G, Strozzi C, Pansini R, Rochat N, Bulgarelli R, Padula A, Sfrisi C, Al Yassini K: Antiarrhythmic use of cibenzoline, a new class 1 antiarrhythmic agent with class 3 and 4 properties, in patients with recurrent ventricular tachycardia. *Eur Heart J* 5, 108 (1984)
- Coronary Drug Project Research Group: The prognostic importance of premature ventricular complexes in the late post-infarction period. Experience in the Coronary Drug Project. *Acta Cardiol* 18 (suppl.), 33 (1974)
- Harrison DC, Fitzgerald JW, Winkle RA: Contribution of ambulatory electrocardiographic monitoring to antiarrhythmic management. *Am J Cardiol* 41, 996 (1978)
- Hinkle LE, Carver ST, Argyros DC, Stevens M, Horvath J: The prognostic significance of ventricular premature contractions in healthy people and in people with coronary heart disease. *Acta Cardiol* 18 (suppl.), 5 (1974)
- Kennedy HL, Underhill SJ: Frequent or complex ventricular ectopy in apparently healthy subjects. *Am J Cardiol* 38, 141 (1976)
- Kennedy HL, Chandra V, Syther KL, Caralis DG: Effectiveness of increasing hours of continuous ambulatory electrocardiography in detecting maximal ventricular ectopy. *Am J Cardiol* 42, 925 (1978)
- Lipski J, Cohen L, Espinoza J, Motro M, Dack S, Donoso E: Value of Holter monitoring in assessing cardiac arrhythmias in symptomatic patients. *Am J Cardiol* 37, 102 (1976)
- Manger Cats V, Lie KI, Van Capelle FJL, Durre D: Limitations of 24 hour ambulatory electrocardiographic recording in predicting coronary events after myocardial infarction. *Am J Cardiol* 44, 1257 (1979)
- Michelson EL, Morganroth J: Spontaneous variability of complex ventricular arrhythmias detected by long-term electrocardiographic recording. *Circulation* 61, 690 (1980)
- Monti JM, Folle LE, Peluffo C, Artucio R, Ortiz A, Severini O, Dighiero J: The incidence of premature contractions in coronary patients during the sleep-awake cycle. *Cardiology* 60, 257 (1975)
- Morganroth J, Michelson EL, Horowitz LN, Josephson ME, Pearlman AS, Dunkman WB: Limitations of routine long-term electrocardiographic monitoring to assess ventricular ectopic frequency. *Circulation* 58, 408 (1978)
- Moss AJ, Davis HT, DeCamilla J, Bayer LW: Ventricular ectopic beats and their relationship to sudden death and nonsudden cardiac death after myocardial infarction. *Circulation* 60, 998 (1979)
- Pansini R, Strozzi C, Cocco G, Chu D, Sfrisi C, Bulgarelli R, Padula A: Alterazioni pseudoischemiche durante lo sforzo agonistico strenuo in campioni sani allenati. *G Clin Fisiopat Cardiovasc* 1 (suppl. 1), 33, (1983)
- Roberts WC, Mason DT, Engle MA, Cohn LH: (Eds.) *Cardiology 1982*, (1982) 161
- Ruberman W, Weinblatt E, Goldberg JD, Franck WS, Shapiro S: Ventricular premature beats and mortality after myocardial infarction. *N Engl J Med* 297, 750 (1977)
- Sculze RA, Rouleau J, Rigo P, Bowers S, Strauss HW, Pitt B: Ventricular arrhythmias in the late hospital phase of acute myocardial infarction. *Circulation* 52, 1006 (1975)
- Smerlow TD, Winkle RA, Mason JW: Determinants of survival in patients with ventricular tachyarrhythmias. *N Engl J Med* 308, 1436 (1983)
- Stein P, Jungmann H: Spontanschwankungen von Rhythmusstörungen bei Infarkt-rehabilitanden. *Herz Kreisl* 11, 346 (1979)
- Strozzi C, Cocco G, Pansini R, Bulgarelli R, Padula A, Sfrisi C, Rochat N: Scelta delle derivazioni nel monitoraggio con elettrocardiografia dinamica allo scopo di studiare le variazioni del segmento S-T. *Atti I Conv. Naz. ECG Dinamica*, 154 (1982)
- Thanavaro S, Kleiger RE, Hieb BR, Krone RJ, deMello VR, Oliver GC: Effect of electrocardiographic duration on ventricular dysrhythmia detection after myocardial infarction. *Circulation* 62, 262 (1980)