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Programmed Ventricular Stimulation in Coronary Artery Disease and Dilated Cardiomyopathy: Influence of the Underlying Heart Disease on the Results of Electrophysiologic Testing

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Summary: In order to evaluate the clinical and prognostic significance of programmed ventricular stimulation (PVS), 100 patients were investigated. Twenty-four of 51 patients with coronary artery disease and 22 out of 49 with dilated cardiomyopathy had clinical ventricular tachycardia (VT). The study protocol included 24-h Holter ECG, cardiac catheterization and angiography, and PVS employing 1 and 2 premature extrastimuli and incremental pacing. In patients with coronary artery disease, VT was induced in 67% with prior VT and in 18% without such episodes ($p<0.01$). In dilated cardiomyopathy, however, patients with and without clinical VT did not differ with regard to VT inducibility (18% vs. 15%, NS). The inducibility of monomorphic sustained VT—most frequently induced in VT patients—was significantly higher in patients with coronary artery disease ($p<0.05$). Polymorphic nonsustained VT (in both coronary artery disease and dilated cardiomyopathy) was only initiated in patients without clinical VT. In patients with coronary artery disease, left ventricular ejction fraction could be correlated to clinical arrhythmia ($p<0.001$), while induced VT could only be correlated to depressed left ventricular function in patients with left ventricular aneurysm. Neither clinical nor induced VT could be correlated to left ventricular ejection fraction in patients with dilated cardiomyopathy. During a mean follow-up of 21 months, 7 patients died from sudden cardiac death. Six of them had clinical VT, but in only 1 patient with coronary artery disease was VT initiated. There was no apparent difference in the antiarrhythmic therapy of the patients with sudden death with respect to the surviving population. In conclusion, the response to PVS with the stimulation protocol applied is different in patients with coronary artery disease and dilated cardiomyopathy. The prognostic significance of the results obtained from PVS remains uncertain.

Key words: programmed ventricular stimulation, coronary artery disease, dilated cardiomyopathy

Introduction

Several studies have established the clinical relevance of programmed ventricular stimulation (PVS) in patients with high-grade ventricular ectopy or recurrent ventricular tachycardia (VT).[1-5] Most of the patients investigated so far suffered from coronary artery disease. Despite the preponderance of this disease, however, the study populations were largely heterogeneous. Thus, there is still a degree of uncertainty as to whether or not different underlying heart diseases alter the results from electrophysiologic testing. The following study, therefore, was designed to evaluate the influence of coronary artery disease and of dilated cardiomyopathy on the results obtained from PVS in patients with and without clinical VT.

Patients and Methods

The study population consisted of 100 patients, 88 men and 12 women with a mean age of 55 ± 10 (range 23-72). The underlying heart diseases were coronary artery disease and dilated cardiomyopathy in patients with and without clinical VT. Patients with syncope of unknown origin and patients with drug-induced ventricular ectopy as well as patients with tachyarrhythmias due to acute myocardial infarction were excluded.

Fifty-one patients had coronary artery disease, 34 of them with prior myocardial infarction at least 3 months

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before entry into the study. Twenty-four patients had a history of sustained (21) or nonsustained (3) VT, documented either by standard ECG, by 24th Holter ECG or on the scope in the coronary care unit.

In 49 patients with dilated cardiomyopathy, the criteria for diagnosis were based on clinical, electrocardiographic, hemodynamic, and morphological findings according to Goodwin and Oakley.[6] All of them had at least two of the following criteria:

Symptoms and signs of congestive heart failure
Radiological evidence of cardiomegaly and cardiothoracic ratio >0.5
Electrocardiographic abnormalities in the form of left ventricular conduction delay (QRS complex >0.11 s), intraatrial conduction delay or left ventricular hypertrophy
Abnormal contraction or wall motion observed during cardiac catheterization and two-dimensional echocardiography
Morphological findings in cardiac biopsy

Patients with evidence of coronary artery disease were excluded. Twenty-two patients with dilated cardiomyopathy had a history of sustained (8) or nonsustained (14) VT.

The whole study population underwent diagnostic cardiac catheterization-at the beginning of the study with biplane left ventriculography and coronary cineangiography. Ejection fraction was determined by biplane left ventricular angiography according to the area-length method.

Electrophysiological Study

Electrophysiological investigations were employed for either clinical or research purposes after informed written consent was obtained. Antiarrhythmic treatment had been suspended at least 3 half-lives before the examinations. No patient was on amiodarone at that time. All patients were in an unsedated, postabsorptive state, serum electrolytes were normal and QT intervals were not prolonged.

A quadripolar catheter (1 cm interelectrode distance) was introduced into the femoral or cubital vein and advanced to the right ventricular apex, and a bipolar catheter was inserted into the high right atrium. Intracardiac electrograms from the proximal two poles of the ventricular catheter and from the right atrium were recorded simultaneously with the standard leads I, II, and III. The distal two poles of the quadripolar catheter were used for pacing. All signals were displayed on a multichannel oscilloscope and recorded with a paper speed of 50 mm/s at filter settings of 0.05–500 Hz (Mingograf 7, Siemens-Elema). PVS was performed with a programmable stimulator (Medtronic 5325). The stimuli were 1.8 ms in duration and twice the diastolic threshold (mean 1 mA).

The stimulation protocol was the same in all patients and included the introduction of single and double ventricular extrastimuli during sinus rhythm and at a driven basic cycle length of 600, 500, 428, 375, and 330 ms. After every 8 beats, 1 premature stimulus (S_2) was introduced late in diastole and then progressively shortened by 10 ms steps until ventricular refractoriness was reached. Thereafter, S_2 was set 30 ms outside the effective refractory period. A second extrastimulus (S_3) was added 340 ms after S_2 and scanned at 10 ms intervals up to the refractory period of the right ventricle. Finally, incremental pacing with 250/min for 6 s and 250–300/min for 12 s was performed.

The endpoint of testing was either the initiation of sustained VT or each extrastimulus brought to its refractory period. PVS was stopped if patients complained of symptoms such as angina or dyspnea.

Definitions

Repetitive ventricular response: Reproducible initiation of 2–4 consecutive nonpaced ventricular premature beats (VPBs). HV intervals were not measured and no attempt was made to distinguish between interventricular and bundle-branch re-entry.

Induced nonsustained VT: ≥ 5 VPBs with a rate of ≥ 100 beats/min, lasting <30 s and with no intervention required for termination.

Induced sustained VT: VPBs with a rate of ≥ 100 beats/min, lasting >30 s or requiring termination by PVS or cardioversion before that time because of hemodynamic deterioration.

VT patients: Patients with documented spontaneous sustained or nonsustained VT (≥ 3 consecutive VPBs) before or at the time of the electrophysiological study.

No-VT patients: Patients without such episodes.

Sudden cardiac death: Cardiac death within 1 hour after the onset of new symptoms.

Twenty-four-hour Holter ECG (Reynolds Pathfinder II) was carried out on all patients in the absence of antiarrhythmic treatment for up to 3 days before or after PVS. The maximal grade of ventricular ectopy was classified according to the proposal of Lown and Wolf.[7]

Follow-Up

During follow-up, all VT patients were treated with antiarrhythmic drugs. Furthermore, some patients with ventricular pairs or polymorphic VPBs (Lown IVa, III) underwent antiarrhythmic therapy, independent of the response to PVS. Therapy was begun empirically in all patients. Patients were seen in individual intervals in our outpatient clinic. If this was not possible, at the endpoint of the study their referring physicians were contacted or they were interviewed personally by telephone about the follow-up. In case patients were found dead at home, family physicians or relatives were asked about circumstances and symptoms prior to death. If possible, an autopsy was performed. The mean follow-up period was 21 ± 11 months (range 1 week to 39 months).

Statistical Methods

Data were expressed as mean ± standard deviation. To describe the disease-related incidence of repetitive ventricular response and VT in VT and no-VT patients as well as to describe differences of the characteristics of induced VT, the Chi-square analysis was employed. For the comparison of the left ventricular ejection fraction in VT and no-VT patients with coronary artery disease and dilated cardiomyopathy, the Wilcoxon U test for independent samples was used. Statistical significance was accepted at a level of $p=0.05$ using 2-tailed tests.

Results

Clinical Findings

The clinical and electrocardiographic data of patients with coronary artery disease are listed in Table I. Twenty-four had clinical VT which was sustained in 21 and nonsustained in 3. Twenty-seven patients had no clinical VT. Nine of them had ventricular pairs, 9 polymorphic and 9 no or a low incidence of monomorphic VPBs.

In patients with coronary artery disease, there was a significant difference in left ventricular performance between VT and no-VT patients. In VT patients, left ventricular ejection fraction was 42 ± 13% compared to 55 ± 16% in no-VT patients ($p<0.001$). Myocardial infarction had occurred almost as frequently in both groups (71% vs. 63%, NS). Six patients with left ventricular aneurysm had documented sustained VT and 2 were Lown I. The mean ejection fraction in patients with left ventricular aneurysm was 41 ± 9%.

The clinical and electrocardiographic data of patients with dilated cardiomyopathy are listed in Table II. Twenty-two had documented VT which was sustained in 8 and nonsustained in 14. Of 27 patients without such episodes, 13 had ventricular pairs, 4 polymorphic, and 10 no or a low incidence of monomorphic VPBs. Patients who had episodes of VT did not differ significantly from those without VT with regard to left ventricular ejection fraction (37 ± 13% vs. 42 ± 15%, NS). In 3 patients with an ejection fraction >60%, the diagnosis had been confirmed by morphological findings in cardiac biopsy.

PVS in Patients with Coronary Artery Disease

Stimulation protocol was complete in all but 2 patients. In Patient No. 46 and Patient No. 48 (both no-VT patients), the examination had to be stopped because of angina. In 1 of these patients, repetitive ventricular response with 3 consecutive VPBs and in the other a nonsustained VT had been induced.

In 16 VT patients (67%), VT with ≥5 consecutive VPBs was induced at PVS, in 6 (25%) 2–4 nonpaced VPBs, and in 2 (8%) no response. In no-VT patients, VT was induced in 5 (18%), 2–4 nonpaced VPBs in 15 (56%),

TABLE I Clinical and electrophysiological data of patients with coronary artery disease

Pt	Age & Sex	MI	LV Aneurysm	LVEF (%)	Clinical arrhythmia	Morphology of VT	Heart rate	Response to stimulation	Morphology of VT	Heart rate	Mode of stimulation	Time since PVS (m)	Anti-arrhythmic drugs	Death	Cause
1	60M	+	+	43	sVT	m	200	sVT	m	224	$S_1S_2S_3$	39	+	0	
2	66M	+	0	37	sVT	m	220	sVT	m	230	S_1S_2	15	+	0	
3	54F	+	+	25	sVT	m	240	sVT	m	210	$S_1S_2S_3$	6	+	+	CHF
4	52M	+	0	40	sVT	m	150	sVT	m	225	$S_1S_2S_3$	14	+	+	SCD
5	51M	+	+	48	sVT	—	—	sVT	m	270	$S_1S_2S_3$	38	+	0	
6	69M	+	0	24	sVT	m	130	sVT	m	136	$S_1S_2S_3$	22	+	+	CHF
7	70F	+	+	42	sVT	m	176	sVT	m	180	S_1S_2	0	+	+	CHF at CABG
8	59M	+	0	52	sVT	m	115	sVT	p	260	$S_1S_2S_3$	27	+	0	
9	53M	+	0	42	sVT	m	230	sVT	m	155	S_1S_2	17	+	0	
10	70M	0	0	45	sVT	m	175	sVT	m	240	$S_1S_2S_3$	13	+	0	
11	64M	+	+	42	sVT	m	150	sVT	m	200	S_1S_2	14	+	0	
12	52M	+	0	55	sVT	m	230	sVT	m	240	$S_1S_2S_3$	7	+	0	
13	65M	0	0	22	sVT	—	—	sVT	p	260	IP	8	+	0	
14	57F	+	+	45	sVT	—	—	sVT	m	240	IP	6	+	0	
15	52M	+	0	50	sVT	n	146	nsVT	n	250	IP	30	+	0	

Pt	Age & Sex	MI	LV Aneurysm	LVEF (%)	Clinical arrhythmia	Morphology of VT	Heart rate	Response to stimulation	Morphology of VT	Heart rate	Mode of stimulation	Time since PVS (m)	Anti-arrhythmic drugs	Death	Cause
16	64M	+	0	45	sVT	m	180	nsVT	m	250	$S_1S_2S_3$	24	+	0	
17	60F	0	0	65	sVT			3			$S_1S_2S_3$	0	+	+	CHF at CABG
18	64M	0	0	28	sVT			3			S_1S_2	12	+	+	SCD
19	67M	+	0	33	sVT			3			S_1S_2	24	+	0	
20	72M	0	0	65	sVT			2			S_1S_2	8	+	0	
21	56M	+	0	31	sVT			0				30	+	0	
22	49M	0	0	42	nsVT			4			S_1S_2	26	+	0	
23	55M	0	0	55	nsVT			2			S_1S_2	28	+	0	
24	66M	+	0	9	nsVT			0				0	+	+	SCD
25	52M	0	0	70	IVa			nsVT	p	180	$S_1S_2S_3$	36	+	0	
26	61M	+	0	60	IVa			4			$S_1S_2S_3$	14	0	0	
27	65M	+	0	55	IVa			4			$S_1S_2S_3$	9	+	+	SCD
28	70F	0	0	54	IVa			3			$S_1S_2S_3$	32	0	0	
29	69M	0	0	38	IVa			3			$S_1S_2S_3$	22	0	0	
30	55M	0	0	57	IVa			2			$S_1S_2S_3$	31	0	0	
31	42F	0	0	50	IVa			0				22	+	+	MI
32	66M	+	0	50	IVa			0				7	+	0	
33	52M	0	0	18	IVa			0				25	0	0	
34	54M	0	0	68	III			2			$S_1S_2S_3$	23	0	0	
35	65M	+	0	45	III			2			$S_1S_2S_3$	35	0	0	
36	56M	+	0	52	III			2			S_1S_2	28	+	0	
37	48M	+	0	45	III			2			$S_1S_2S_3$	30	0	0	
38	48M	0	0	66	III			2			$S_1S_2S_3$	28	0	0	
39	55M	+	0	72	III			0				35	0	0	
40	56M	+	0	67	III			0				30	0	0	
41	52M	+	0	41	III			0				35	0	0	
42	47M	+	0	61	III			0				31	0	0	
43	56M	+	+	53	I			sVT	m	190	$S_1S_2S_3$	25	0	0	
44	60M	+	+	30	I			sVT	m	160	S_1S_2	33	0	0	
45	65M	+	0	51	I			nsVT	m	240	S_1S_2	35	0	0	
46	69M	+	0	66	I			3			S_1S_2	28	0	0	
47	50M	+	0	19	I			2			S_1S_2	34	0	0	
48	63M	0	0	63	0			nsVT	p	130	S_1S_2	35	0	0	
49	59M	+	0	76	0			2			$S_1S_2S_3$	34	0	0	
50	52M	0	0	77	0			2			S_1S_2	34	0	0	
51	53M	+	0	70	0			2			S_1S_2	23	0	0	

Abbreviations: MI = myocardial infarction, LV aneurysm = left ventricular aneurysm, LVEF = left ventricular ejection fraction, VT = ventricular tachycardia, PVS = programmed ventricular stimulation, sVT = sustained ventricular tachycardia, nsVT = nonsustained ventricular tachycardia, m = monomorph, p = polymorph, S_1S_2 = single extrastimulus, $S_1S_2S_3$ = double extrastimuli, IP = incremental pacing, CHF = congestive heart failure, CABG = coronary artery bypass grafting, SCD = sudden cardiac death, + = positive or present, 0 = negative or absent, − = not available.

TABLE II Clinical and electrophysiological data of patients with dilated cardiomyopathy

Pt	Age & Sex	LVEF (%)	Clinical arrhythmia	Morphology of VT	Heart rate	Response to stimulation	Morphology of VT	Heart rate	Mode of stimulation	Time since PVS (m)	Anti-arrhythmic drugs	Death	Cause
1	67F	36	sVT	p	230	sVT	p	250	$S_1S_2S_3$	5	+	0	
2	58M	41	sVT	m	220	sVT	p	270	IP	22	+	0	
3	26M	50	sVT			4			S_1S_2	29	+	0	
4	51M	47	sVT			4			$S_1S_2S_3$	27	+	0	
5	23M	21	sVT			3			IP	19	+	0	
6	58M	17	sVT			0				25	+	0	
7	64M	39	sVT			0				23	+	0	
8	61M	35	sVT			0				15	+	+	SCD
9	49M	59	nsVT	m	128	sVT	m	110	S_1S_2	12	+	0	
10	42M	12	nsVT	m	180	nsVT	m	230	$S_1S_2S_3$	1	T	+	Immun.
11	45M	37	nsVT			4			IP	14	+	0	
12	50M	28	nsVT			4			S_1S_2	12	+	0	
13	48M	59	nsVT			4			S_1S_2	34	+	0	
14	42M	33	nsVT			3			$S_1S_2S_3$	3	+	0	
15	54F	32	nsVT			3			S_1S_2	1	+	+	SCD
16	51M	32	nsVT			2			IP	19	+	0	
17	58M	56	nsVT			2			$S_1S_2S_3$	14	+	0	
18	58M	40	nsVT			2			$S_1S_2S_3$	6	+	+	CHF
19	56M	30	nsVT			0				15	+	+	SCD
20	61F	35	nsVT			0				17	+	+	CHF
21	65F	40	nsVT			0				7	+	0	
22	36M	43	nsVT			0				22	+	0	
23	45M	15	IVa			nsVT	p	240	IP	5	0	0	
24	40M	51	IVa			nsVT	p	250	$S_1S_2S_3$	35	+	0	
25	56M	41	IVa			nsVT	p	260	$S_1S_2S_3$	3	+	0	
26	46M	15	IVa			3			$S_1S_2S_3$	6	+	0	
27	46M	35	IVa			3			$S_1S_2S_3$	15	+	0	
28	51M	49	IVa			2			S_1S_2	25	0	0	
29	49M	47	IVa			2			$S_1S_2S_3$	21	+	0	
30	47M	20	IVa			0				19	+	0	
31	45M	20	IVa			0				36	T	0	
32	56M	42	IVa			0				29	+	0	
33	34M	24	IVa			0				6	0	0	
34	32M	54	IVa			0				30	0	0	
35	32M	67	IVa			0				30	0	0	
36	42M	49	III			4			$S_1S_2S_3$	21	0	0	
37	43M	39	III			3			$S_1S_2S_3$	17	0	0	
38	53M	47	III			0				23	+	0	
39	58M	33	III			0				35	0	0	
40	48M	50	I			nsVT		195	S_1S_2	18	0	0	
41	49M	63	I			3			S_1S_2	35	0	0	
42	52M	39	I			0				34	0	0	
43	54M	49	I			0				20	0	0	
44	49F	40	I			0				26	0	0	
45	43M	49	I			0				5	0	0	
46	34M	65	0			4			$S_1S_2S_3$	22	0	0	
47	39F	44	0			2			S_1S_2	21	0	0	
48	36M	51	0			0				24	0	0	
49	52M	22	0			0				24	0	0	

Abbreviations: see Table I. T=cardiac transplant, Immun.=immunological complications.

TABLE III Clinical arrhythmias in relation to the response to programmed ventricular stimulation in patients with coronary artery disease and those with dilated cardiomyopathy

Clinical arrhythmia		Coronary artery disease					Dilated cardiomopathy				
		Φ RVR	2-4	nsVT	sVT	Σ	Φ RVR	2-4	nsVT	sVT	Σ
VT	Sustained	1	4	2	14	21	3	3	0	2	8
	Nonsustained	1	2	0	0	3	4	8	1	1	14
no-VT	Lown IVa	3	5	1	0	9	6	4	3	0	13
	III	4	5	0	0	9	2	2	0	0	4
	0-II	0	5	2	2	9	6	3	1	0	10
Total		9	21	5	16	51	21	20	5	3	49

Abbreviations: see Table I, RVR = repetitive ventricular response.

and no response in 7 (26%). Thus, the inducibility of VT was significantly higher in the VT group as compared to the no-VT group ($p<0.01$) (Table III) (Fig. 1).

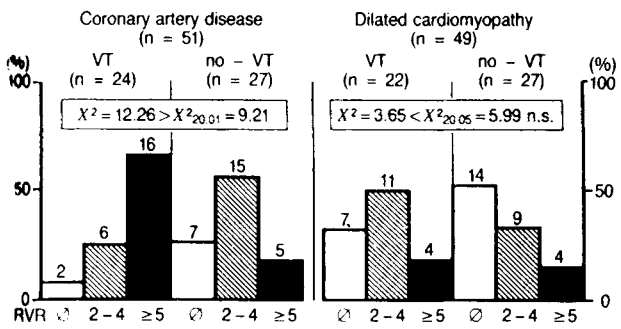

FIG. 1 Response to programmed ventricular stimulation in VT and no-VT patients with coronary artery disease and dilated cardiomyopathy. RVR = repetitive ventricular response.

Characteristics of Induced VT

Ventricular fibrillation was not induced primarily. Remarkable differences were found in VT and no-VT patients with regard to the characteristics of induced VT (Table IV). In VT patients, induced VT was sustained in 14 and nonsustained in 2, whereas in no-VT patients, induced VT was sustained in 2 and nonsustained in 3 ($p<0.05$). Monomorphic VT was induced in 14 out of 16 VT patients compared to 3 out of 5 no-VT patients. Thus, induced VT in patients with coronary artery disease was most frequently monomorphic and sustained (14 out of 21). Polymorphic nonsustained VT was only induced in no-VT patients ($p<0.05$). The ventricular rate during induced VT was ≥ 200 in 13 patients with clinical VT and <200 in 3 VT patients, whereas the heart rate was ≥ 200 in only 1 out of 5 patients without clinical VT ($p<0.05$).

In 13 patients, the heart rates of clinical and induced VT could be compared. In 6 of these patients, they were

TABLE IV Characteristics of induced VT in patients with coronary artery disease and those with dilated cardiomyopathy with and without clinical VT

Induced VT	Coronary artery disease			Dilated cardiomyopathy			Coronary artery disease	Dilated cardiomyopathy	p value
	VT	no-VT	p value	VT	no-VT	p value			
Sustained	14	2	<0.05	3	0	NS	16	3	NS
Nonsustained	2	3		1	4		5	3	
Monomorph	14	3	NS	2	1	NS	17	3	<0.05
Polymorph	2	2		2	3		4	5	
Monomorph sustained	12	2	NS [a]	1	0	NS[a]	14	1	<0.05[a]
Monomorph nonsustained	2	1		1	1		3	2	
Polymorph sustained	2	0		2	0		2	2	
Polymorph nonsustained	0	2	<0.05[b]	0	3	NS[b]	2	3	NS[b]
Heart rate ≥200	13	1	<0.05	3	3	NS	14	6	NS
<200	3	4		1	1		7	2	

[a] Monomorphic sustained VT compared to all other forms of induced VT.

[b] Polymorphic nonsustained VT compared to all other forms of induced VT (4-field Chi-square analysis).

almost identical, while in 6 patients the heart rate of clinical VT was lower, and in 1 patient higher than that of induced VT. The morphology of clinical and induced VT was identical in all but 1 patient whose ECGs were adequate enough to allow this criterium to be determined (Table I).

In VT patients, VT was induced in 4 patients with single, in 9 with double extrastimuli, and in 3 at incremental pacing. In no-VT patients, a single extrastimulus induced VT in 3 and double extrastimuli in 2 patients. None of them responded to incremental pacing with VT.

Patients with inducible VT at PVS did not differ significantly from those without inducible VT with regard to left ventricular ejection fraction ($45 \pm 11\%$ vs. $51 \pm 18\%$, NS).

Seventeen of 21 patients (81%) with inducible VT and 17 of 30 (57%) without inducible VT had prior myocardial infarction (NS). In all 8 patients with left ventricular aneurysm, monomorphic sustained VT was inducible.

PVS in Patients with Dilated Cardiomyopathy

Stimulation protocol was complete in all 49 patients with dilated cardiomyopathy. Only in 4 VT patients (18%) was VT induced at PVS, in 11 (50%) 2–4 nonpaced VPBs, and in 7 (32%) no response. In no-VT patients, VT was induced in 4 (15%), 2–4 nonpaced VPBs in 9 (33%), and no response in 14 (52%). Thus, no statistically significant difference could be assessed between VT and no-VT patients with regard to the inducibility of repetitive ventricular response and VT (Table III) (Fig. 1). Furthermore, in VT patients with dilated cardiomyopathy, the rate of inducibility was significantly lower than in VT patients with coronary artery disease ($p < 0.01$).

Characteristics of Induced VT

In patients with dilated cardiomyopathy, too, ventricular fibrillation was not induced primarily. In VT patients, induced VT was sustained in 3 out of 4 and nonsustained in all 4 patients without clinical VT (Table IV). In VT patients, the morphology of induced VT was monomorphic in 2 of 4 and in no-VT patients polymorphic in all but 1. Monomorphic sustained VT was induced significantly less often in patients with dilated cardiomyopathy than in patients with coronary artery disease (2 of 8 versus 14 of 21, $p < 0.05$). In both—patients with dilated cardiomyopathy and patients with coronary artery disease—polymorphic nonsustained VT was only induced in no-VT patients. The ventricular rate during induced VT was similar in VT and no-VT patients with dilated cardiomyopathy. In 3 of 4 patients in each group, maximal heart rate was ≥ 200.

The morphology of induced VT corresponded to that of clinical VT in 3 out of 4 patients whereas in 1 patient with clinical monomorphic VT, induced VT was polymorphic in configuration. The heart rates of clinical VT were almost similar to those of induced VT in 2 patients and lower in the other 2 (Table II).

The mode of stimulation for induced VT was the same for VT and no-VT patients. In both groups, VT was induced in 1 patient with single, in 2 with double extrastimuli, and in 1 at incremental pacing.

No statistically significant difference could be determined between VT and no-VT patients with regard to left ventricular ejection fraction ($38 \pm 17\%$ vs. $40 \pm 13\%$, NS).

Follow-Up

All patients were followed up over a period of 21 ± 11 months (range 1 week to 39 months). During this time, 15 patients died, 7 of them as a result of sudden cardiac death, 4 with coronary artery disease (8%), and 3 with dilated cardiomyopathy (6%). The cause of death in all patients who died is demonstrated in Tables I and II. Two patients with dilated cardiomyopathy underwent a cardiac transplant (Patient No. 10 and Patient No. 31, Table II). One of them died 1 month later due to immunological complications, the other is well.

VT Patients With Inducible VT

All 20 patients with inducible VT were discharged with antiarrhythmic drug therapy. Five patients died during the follow-up (4 coronary artery disease, 1 dilated cardiomyopathy), only 1 patient with coronary artery disease as a result of sudden cardiac death 14 months after PVS.

VT Patients Without Inducible VT

These 26 patients, too, were treated with antiarrhythmic drugs. Eight of them died, 2 of 3 with coronary artery disease and 3 of 5 with dilated cardiomyopathy as a result of sudden cardiac death 1 week to 15 months after entry into the study. In 3 of them, the response to PVS was negative and in 2, three nonpaced VPBs were inducible.

No-VT Patients With Inducible VT

Only 3 of these 9 patients were discharged with antiarrhythmic drug therapy, required because of ventricular pairs documented during 24-h Holter ECG at the time of the electrophysiological examination, 1 with coronary artery disease and 2 with dilated cardiomyopathy. During the follow-up period, no one died and in no patient was there an aggravation of documented arrhythmias requiring medical intervention.

No-VT Patients Without Inducible VT

Of the remaining 45 patients, 4 with coronary artery disease and 6 with dilated cardiomyopathy were treated

with antiarrhythmic drugs on the basis of their 24-h Holter ECG findings at the beginning of the study. Two patients with coronary artery disease died, 1 from sudden cardiac death. None of the surviving patients demonstrated ventricular arrhythmias which were unknown before and needed medication.

Sudden Cardiac Death

During the follow-up period, 7 patients died from sudden cardiac death 1 week to 15 months ($\bar{x}$=9 months) after PVS (Table V). Six patients had clinical VT and 1 had ventricular pairs necessitating medical treatment. There was no apparent difference in the antiarrhythmic therapy of the patients with sudden death respective to the surviving population. Left ventricular ejection fraction was <40% in all patients with dilated cardiomyopathy and in 3 of 4 with coronary artery disease. There was no difference in response to PVS between patients who survived and patients who died suddenly. VT was induced in only 1 patient with coronary artery disease, and in 3 of 7 sudden cardiac death victims the response to PVS was negative.

Discussion

In this study, we have reported our experience with PVS in a series of 51 consecutive patients with coronary artery disease and 49 with dilated cardiomyopathy who were part of a prospective electrophysiological study. Concerning the clinical arrhythmia, 24 patients with coronary artery disease and 22 with dilated cardiomyopathy had documented sustained or nonsustained VT. All patients were examined by means of cardiac catheterization, 24-h Holter ECG and PVS with a standardized stimulation protocol.

The aim of our study was to answer the following questions: What differences can be determined by PVS between patients with coronary artery disease and those with dilated cardiomyopathy with regard to (1) the inducibility of repetitive ventricular response and VT, (2) the characteristics of induced VT, (3) the relation between left ventricular dysfunction and the inducibility of VT, and (4) the relevance of electrophysiological results in predicting sudden cardiac death.

Incidence and Type of Repetitive Ventricular Response at PVS in Patients with Coronary Artery Disease and Dilated Cardiomyopathy

The inducibility of repetitive ventricular response with 2–4 consecutive VPBs was high in no-VT patients with coronary artery disease as well as in those with dilated cardiomyopathy (56% and 33%). This result underlines the lack of specificity of this type of response.[8]

It is an established fact that in patients with coronary artery disease PVS can reliably reproduce clinical VT.[1,2,9,10] However, VT can also be initiated in patients with coronary artery disease without such episodes, but at a significantly lower rate.[11,12]

In patients with dilated cardiomyopathy considered to be at a high risk because of clinical VT, the inducibility of VT is significantly lower. Meinertz *et al.*[13] previously reported his experience with 42 patients. Fifteen had a history of VT, but in none of them could VT be induced. Of the remaining 27 patients, 2 had inducible nonsustained VT and 1 inducible ventricular fibrillation. Naccarelli *et al.*[3] induced VT in 17 of 37 patients with different forms of cardiomyopathy, 30 of them with dilated cardiomyopathy. Buxton *et al.*[1] studied 18 patients with cardiomyopathy—16 with the dilated form—with a history of nonsustained VT and could induce VT in 6 of them. Wellens *et al.*[14] reported 3 patients with dilated cardiomyopathy, out of 50 with VT, in whom no VT was inducible. Only Poll *et al.*[15] could reproduce clinical VT in all patients with dilated cardiomyopathy, but with a more extensive stimulation protocol including 3rd and 4th extrastimuli and several stimulation sites.

In our study, the inducibility of VT in VT patients was only 18% and 15% in no-VT patients. Thus, the response

TABLE V Clinical and electrophysiological data of patients who died as a result of sudden cardiac death

Patient	Age & Sex	Heart disease	MI	LV aneurysm	LVEF (%)	Clinical arrhythmia	Response to stimulation	Morphology of VT	Heart rate	Mode of stimulation	Time since PVS
	52M	CAD	+	0	40	sVT	sVT	Monomorph	225	$S_1S_2S_3$	14 mos.
	64M	CAD	0	0	28	sVT	3			S_1S_2	12 mos.
	66M	CAD	+	0	9	nsVT	0				1 week
	65M	CAD	+	0	55	IVa	4			$S_1S_2S_3$	9 mos.
	61M	DCM			35	sVT	0				15 mos.
	54F	DCM			32	nsVT	3			S_1S_2	1 mo.
	56M	DCM			30	nsVT	0				15 mos.

Abbreviations: see Table I. CAD=coronary artery disease, DCM=dilated cardiomyopathy.

to PVS in patients with dilated cardiomyopathy as compared to those with coronary artery disease seems to be of different clinical significance. In these patients, a more aggressive stimulation protocol might be necessary to reproduce clinical VT.

Characteristics of Induced VT

Our results indicate that the induction of sustained VT is a specific response in VT patients with coronary artery disease as well as in those with dilated cardiomyopathy. The lack of statistical significance in patients with dilated cardiomyopathy might be due to the relatively small number of patients with inducible VT. Nevertheless, interpretation of the characteristics of induced VT in patients with dilated cardiomyopathy must be viewed with caution.

In both patients with coronary artery disease and dilated cardiomyopathy, the inducibility of a nonsustained VT has to be considered as less specific. This form was observed more frequently in no-VT patients. These data are similar to those reported by Brugada *et al.*[8] In patients with different cardiac diseases, he could initiate a nonsustained VT in 50% of a no-VT and in 20% of a prior VT group.

The clinical relevance of induced monomorphic and polymorphic VT is not clear. Clinically significant VT is either believed to be of monomorphic configuration,[8] or, as Torres *et al.*[16] suggested, the inducibility of a polymorphic arrhythmia might be an index of electrical instability in high-risk patients. In our study, induced VT in VT patients was most frequently of monomorphic configuration showing no significant difference between patients with coronary artery disease and those with dilated cardiomyopathy. The inducibility of monomorphic sustained VT, however, was significantly higher in patients with coronary artery disease. Polymorphic nonsustained VT was only observed in no-VT patients with no difference regarding the underlying heart disease.

The rate of induced VT represents another difference between patients with coronary artery disease and dilated cardiomyopathy. In VT patients with coronary artery disease, it was significantly higher than in those without such episodes. This is supported by the findings of Mann *et al.*[12] in a study population with a preponderance of patients with coronary artery disease. In patients with dilated cardiomyopathy, the rate of induced VT did not differ between both groups. Thus, some characteristics of induced VT seem to be different in patients with coronary artery disease as compared to those with dilated cardiomyopathy.

ECGs adequate enough to allow the determination of morphology and heart rate of clinical VT were not available for all patients, especially not always for those who had been referred with hemodynamically symptomatic VT to other hospitals. The morphology of clinical VT was monomorphic in 16 of 17 patients with available ECGs and corresponded to induced VT in 15 of them. Only 1 patient had polymorphic VT clinically that corresponded to induced VT. In 1 patient with coronary artery disease having monomorphic VT clinically, induced VT was polymorphic. Thus, the inducibility of sustained VT, especially monomorphic sustained VT seems to be of superior clinical value. The heart rate of clinical VT corresponded to that of induced VT in 7 patients, whereas in 9 patients it was lower and in only 1 patient higher than that of induced VT.

Implications of Left Ventricular Function

In patients with coronary artery disease, clinical arrhythmias can be correlated to impaired left ventricular function.[17-19] This is underlined by our finding that patients with coronary artery disease and clinical VT had a significantly reduced ejection fraction in comparison to no-VT patients. But as outlined in previous reports,[1,20] the inducibility of VT at PVS does not depend on left ventricular dysfunction. In addition, in this study, a history of myocardial infarction did not predispose patients to spontaneous or inducible VT.

On the other hand, the occurrence of left ventricular aneurysm and impaired left ventricular function could be related to VT. Six of 8 patients with left ventricular aneurysm had clinical sustained VT and in all 8 patients sustained VT was inducible. The mean ejection fraction of these patients was $41 \pm 9\%$. Marchlinski *et al.*[21] pointed out that the presence of left ventricular aneurysm or left ventricular dysfunction resulted in the greatest risk of sudden cardiac death.

In patients with dilated cardiomyopathy, the impairment of left ventricular function had no influence on the occurrence of spontaneous arrhythmias and on the inducibility of VT.[22,23]

Follow-Up

During a mean follow-up period of 21 ± 11 months, 4 patients with coronary artery disease (8%) and 3 with dilated cardiomyopathy (6%) died as a result of sudden cardiac death. These data correspond to those reported by Buxton *et al.*[24] with a 12% 3-year incidence of sudden cardiac death in patients with clinical nonsustained VT.

Clinical characteristics of patients who died from sudden cardiac death were spontaneous malignant arrhythmias (6 of 7 had prior VT, 1 patient had ventricular pairs) and depressed left ventricular function (6 of 7 with an ejection fraction $<40\%$).

The results of several studies suggest that PVS might be useful in defining patients at increased risk of sudden cardiac death.[25,26] Gomes *et al.*[27] reported a significant incidence of sudden cardiac death or clinical sustained VT in patients with inducible VT. Buxton *et al.*[24] pointed out the inducibility of sustained VT in patients with coronary artery disease as an independent risk factor for sudden cardiac death.

In this study, however, no higher incidence of sudden cardiac death was found in patients with inducible VT.

Only 1 patient out of the 7 cardiac death victims had inducible VT. These results correspond to those recently reported by Marchlinski *et al.*[21] and Veltri *et al.*[20]

Although these results suggest that PVS might not provide predictive accuracy with respect to prognosis, they have to be viewed with caution. The discrepancies between the studies might be due to different study populations and stimulation protocols or to the medical management.

Induced VT in no-VT patients does not seem to indicate poor prognosis, as none of these 9 patients died and none of them developed clinical arrhythmia during the follow-up, not being treated with antiarrhythmic drugs during the whole time. Induced VT in these patients was most frequently polymorphic and nonsustained, a finding which did not occur in any VT patient with inducible VT. Thus, it might be of no prognostic significance.[12,28,29]

Limitations of the Study

Study population: VT patients with coronary artery disease and dilated cardiomyopathy were not completely homogeneous regarding electrical instability, as patients with coronary artery disease more often had clinical sustained VT whereas patients with dilated cardiomyopathy more frequently showed the nonsustained form. In addition, the interpretation of the characteristics of induced VT in patients with dilated cardiomyopathy is limited due to the relatively small number of patients with inducible VT.

Stimulation protocol: The applied stimulation protocol included single and double extrastimuli during sinus rhythm and during defined paced cycle lengths as well as incremental pacing. The only stimulation site was the apex of the right ventricle. This is a moderate stimulation protocol. However, it has been demonstrated that it is a specific protocol for induction of VT in VT patients with coronary artery disease,[28] whereas patients with dilated cardiomyopathy might need a more extensive stimulation protocol. The use of more than two extrastimuli or other stimulation sites (right ventricular outflow tract, left ventricle) was not employed. This was due to the duration of the whole examination which was most frequently performed after diagnostic left ventricular coronary angiography.

Definition of induced VT: Induced VT was defined as ≥ 5 consecutive VPBs. This might be a debatable definition, for several authors defined VT as ≥ 3 consecutive VPBs, which explains in part higher rates of inducibility. But as pointed out before, it has been demonstrated that repetitive ventricular response consisting of 2–4 nonpaced VPBs seem to be an unspecific phenomenon during PVS with no relation to clinical arrhythmia.[8,30]

Conclusions

This study reveals that the inducibility of VT markedly depends on the underlying heart disease. Patients with dilated cardiomyopathy have a significantly lower induction rate of VT and no significant difference of VT inducibility between VT and no-VT patients. Furthermore, the inducibility of monomorphic sustained VT, most frequently induced in VT patients, is significantly higher in patients with coronary artery disease. In both patients with coronary artery disease and dilated cardiomyopathy, polymorphic nonsustained VT can only be induced in no-VT patients. Left ventricular function in terms of biplane left ventricular ejection fraction can only be correlated to clinical arrhythmias in patients with coronary artery disease. Neither in patients with coronary artery disease nor in those with dilated cardiomyopathy can left ventricular ejection fraction be correlated to the inducibility of VT. Finally, the response to PVS with the applied stimulation protocol does not allow a clear prediction of prognosis on the basis of a mean follow-up period of 21 months.

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