

Influence of coronary artery bypass grafting on ventricular late potentials as a predictive factor for ventricular arrhythmias during short- and long-term follow-up

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KEY WORDS: Ventricular late potentials, signal-averaged electrocardiogram, coronary artery bypass grafting, ventricular arrhythmias, coronary heart disease.

Ventricular late potentials have been identified as a prognostic factor in the prediction of ventricular arrhythmias in patients after myocardial infarction. In this prospective study the possible impact of late potentials on the prediction of ventricular arrhythmias in the short- and long-term follow-up after coronary artery bypass grafting was evaluated. In 188 patients (165 men, 23 women, age 57 ± 8 years) with chronic coronary heart disease 48 (26%) had late potentials before bypass grafting; after the procedure this was reduced to 39 (21%) (ns). In 16 (33%) of the 48 patients with late potentials before bypass grafting, late potentials were no longer present in the short-term follow-up (9 ± 6 days). Conversely, seven (5%) of the 140 patients without late potentials before bypass grafting had late potentials in the short-term follow-up after grafting. Nine (19%) of the 48 patients with late potentials before bypass grafting had ventricular arrhythmias in the peri-operative phase, which had to be treated with antiarrhythmic agents. In contrast, only three (2%) of the 140 patients without late potentials before bypass grafting had to be treated for ventricular arrhythmias ($P < 0.001$). In the long-term follow-up of 29 ± 3 months, there were no events in the group of 149 patients without late potentials after grafting. In the 39 patients with late potentials after grafting, there were two (5%) events (two patients with arrhythmic syncope).

Conclusions: (1) Patients with late potentials before bypass grafting have a markedly higher risk of developing serious ventricular arrhythmias in the peri-operative period than patients without late potentials. (2) Patients without late potentials have a very low risk of developing serious ventricular arrhythmias in the peri-operative period. (3) During long-term follow-up there was only a low probability of developing symptomatic ventricular arrhythmias in patients with or without late potentials.

Introduction

Ventricular late potentials are high-frequency, low-amplitude signals in the terminal portion of the QRS complex, which can be detected on the surface electrocardiogram (ECG) by computer signal-averaging and band-pass filtering techniques^[1-3]. Late potentials are generally thought to represent delayed and inhomogeneous conduction in regions with normal myocardium and patchy scar tissue, which is considered to be the electrophysiological substrate of reentrant ventricular tachycardia^[4-6]. In recent years late potentials have been identified as a strong and independent prognostic factor in the prediction of spontaneous and inducible ventricular tachycardia and sudden death in patients with coronary heart disease after myocardial infarction^[1-3,7-15]. In several studies^[16-20] a correlation between patency of infarct-related arteries and the prevalence of late potentials was found. Early reperfusion by thrombolytic therapy seems to reduce the prevalence of late

potentials^[18-20], the incidence of inducible ventricular tachycardia^[21,22] and mortality independent from left ventricular ejection fraction^[23,24]. There are hardly any reports on the effect of aortocoronary bypass grafting on the occurrence of ventricular arrhythmia in relation to the signal-averaged ECG^[25,26].

The aim of the present study was to predict the occurrence of ventricular arrhythmias by ventricular late potentials in the short- and long-term follow-up after coronary artery bypass grafting.

Methods

STUDY PATIENTS

The study group consisted of 188 consecutive patients (165 men, 23 women, mean age 57 ± 8 years) admitted for coronary artery bypass grafting. The extent of coronary heart disease was determined by counting the number of major vessels (left main, anterior descending, circumflex and right coronary artery) with a diameter stenosis $>70\%$. Left ventricular ejection fraction was determined by ventriculography in all patients, and the diagnosis of a previous myocardial infarction was based

Revision submitted 23 August 1994, and accepted 5 September 1994.

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on a history of documented infarction with enzyme increase or significant Q waves in the resting ECG. A peri-operative myocardial infarction was diagnosed if there were either new pathological Q waves on the ECG or an at least two-fold increase of creatinine phosphokinase, with a significant myocardial fraction of more than 10%. Patients with a history of syncope or sustained ventricular tachycardia before bypass surgery were not included.

ECG SIGNAL-AVERAGING

Signal-averaged ECGs were registered on admission and at discharge (9 ± 6 days later). Patients with bundle branch block, atrial fibrillation, pre-excitation, pacemaker rhythm and patients with a history of myocardial infarction 3 months prior to coronary bypass grafting were excluded from analysis.

RECORDINGS

The signal-averaged ECGs were performed with a marquette MAC 15 HiRes ECG recorder. The ECG was recorded during sinus rhythm using standard bipolar orthogonal X, Y and Z leads. Signals were amplified, averaged (250 complexes) and filtered with a 40–250 Hz filter. To avoid the problems with filtering often seen with bidirectionally multi-pole time domain filters, the system used a Fourier transform filtering technique. For analysis, the filtered leads were combined into a vector magnitude plot. A computer algorithm determined the duration of the filtered QRS complex, the duration of low amplitude signals $<40 \mu\text{V}$ and the root mean square voltage in the terminal 40 ms of the QRS complex. Late potentials were defined as present if two of following three criteria were fulfilled: (1) filtered QRS duration >120 ms; (2) duration of low amplitude signals ($<40 \mu\text{V}$) >38 ms; (3) root mean square voltage in the terminal 40 ms of the QRS complex $<25 \mu\text{V}$. The end-point and onset of the filtered QRS complex were verified visually. We mainly followed the standards of the ACC policy statements^[15,27].

SHORT-TERM FOLLOW-UP

After coronary bypass grafting patients were permanently monitored in the intensive care unit by a Hewlett Packard system (Orion arrhythmia detection and analysis system). The patients' charts were reviewed for the occurrence of ventricular arrhythmias in the monitored period and thereafter, when clinically indicated, by means of 24-h ECG recordings. Ventricular arrhythmias were judged as serious and all were treated with an antiarrhythmic therapy when haemodynamically relevant (if there were more than 8–10 premature ventricular beats per min, R on T and ventricular tachycardia). The cardiac surgeons who assigned the antiarrhythmic therapy were not aware of the results of the signal-averaged ECG.

Table 1 Clinical data before coronary artery bypass grafting

	Late potentials		P value
	negative (n=140)	positive (n=48)	
Age (years)	57 ± 9	57 ± 8	ns
Men	124 (89%)	41 (82%)	ns
Data before CABG.			
Prior MI	71 (51%)	30 (62%)	0.05
EF $<50\%$	17 (12%)	10 (20%)	ns
Narrowed arteries (n)	2.5 ± 0.6	2.7 ± 0.6	ns
CABG grafts (n)	3.6 ± 1.2	3.9 ± 1.2	ns

CAB=coronary artery bypass, CABG=coronary artery bypass grafting; EF=ejection fraction; MI=myocardial infarction.

LONG-TERM FOLLOW-UP

All patients were seen for an outpatient examination with exercise testing 3 months after coronary bypass surgery. Thereafter, follow-up data were acquired by means of telephone communication with the referring physicians, who all followed the patients regularly. No physician was aware of the results of the signal-averaged ECG. End-points were syncope or sudden cardiac death.

STATISTICAL ANALYSIS

Values were expressed as mean \pm standard deviation. Chi-square analysis was used for the comparison of proportions from two independent groups. Student's paired and unpaired t-test was used to compare variables with normal distribution. Statistical significance was set at the 0.05 level.

Results

CLINICAL FINDINGS

Of the 188 patients 101 (54%) had a history or ECG signs of a previous myocardial infarction, whereas 87 (46%) had none. Twenty-one (11%) were in NYHA class I, 153 (81%) in class II or III and 14 (8%) in class IV. Fourteen (7%) had single-vessel, 54 (29%) two-vessel and 120 (64%) three-vessel disease. Twenty-seven (14%) had a left ventricular ejection fraction $<50\%$. Ninety-seven patients (52%) had one or more occluded vessels whereas 91 (48%) had only stenosis. Except for myocardial infarction, clinical data were comparable for patients with and without late potentials (Table 1).

SIGNAL-AVERAGED ECG AND LATE POTENTIALS

Before coronary artery bypass grafting there were 48 (26%) patients with late potentials, whereas after coronary artery bypass grafting 39 (21%) patients had late potentials (ns), but the mean pre- and postoperative parameters of the signal-averaged ECG of the entire study population did not show any significant difference: filtered QRS duration 110 ± 11 ms and 110 ± 15 ms,

Table 2 Pre- and postoperative findings of late potentials and signal-averaged ECG in 188 patients

SAECG	Late potentials before and after CABG											
	Before negative	After negative	p	Before negative	After positive	p	Before positive	After positive	p	Before positive	After negative	p
	(n=133)			(n=7)			(n=32)			(n=16)		
QRS (ms)	106 ± 8	106 ± 13	ns	110 ± 7	122 ± 7	0.02	123 ± 16	124 ± 17	ns	118 ± 10	112 ± 8	0.02
RMS (µV)	47 ± 46	50 ± 25	ns	39 ± 19	17 ± 4	0.05	14 ± 5	14 ± 7	ns	15 ± 5	36 ± 15	0.001
Duration of LAS (ms)	32 ± 31	29 ± 13	ns	32 ± 3	52 ± 6	0.001	50 ± 14	53 ± 15	ns	45 ± 7	28 ± 9	0.001

CABG=coronary artery bypass grafting, LAS=low amplitude signals, RMS=root mean square voltage, SAECG=signal averaged ECG.

Table 3 Individual parameters of the signal-averaged ECG before and after CABG in 16 patients whose pre-operative late potentials became negative postoperatively

Patient number	QRS (ms)		RSM (µV)		LAS (ms)	
	Before	After	Before	After	Before	After
1	119	112	16	38	43	30
2	102	104	17	21	44	37
3	122	117	18	23	49	49
4	119	102	12	67	45	34
5	121	115	19	23	37	31
6	123	114	13	45	42	33
7	115	110	8	23	49	36
8	135	127	13	31	41	24
9	122	124	23	25	42	27
10	111	101	18	68	40	32
11	118	103	18	42	44	17
12	109	115	17	32	44	29
13	108	115	15	25	42	19
14	125	115	15	43	39	22
15	134	110	4	35	69	12
16	102	104	14	37	44	21
Mean ± SD	118 ± 10	112 ± 8	15 ± 5	36 ± 15	45 ± 7	28 ± 9
P	0.02		0.001		0.001	

CABG=coronary artery bypass grafting, LAS=low amplitude signals, RMS=root mean square voltage.

respectively, (ns); duration of low amplitude signals 36 ± 29 ms and 33 ± 15 ms, respectively, (ns); and root mean square voltage 39 ± 43 µV and 43 ± 26 µV, respectively, (ns). In 16 (33%) of the 48 patients with late potentials before coronary artery bypass grafting, late potentials were no longer present in the short-term follow-up (9 ± 6 days), which was accompanied by a significant change of all three criteria of the signal-averaged ECG in these 16 patients (Tables 2 and 3). On the other hand, seven (5%) of the 140 patients without late potentials before coronary artery bypass grafting had late potentials in the short-term follow-up after coronary artery bypass grafting, which was again reflected by a significant change in the signal-averaged ECG (Tables 2 and 4). Two (29%) of these seven patients had a documented peri-operative myocardial infarction, whereas of the remaining five (71%) patients two had three-vessel disease, a pre-operative history of inferior myocardial infarction and one occluded vessel,

one patient had three-vessel disease and one occluded vessel, and two patients had three-vessel disease without occluded arteries and no history of myocardial infarction.

PERI-OPERATIVE MORTALITY

Five patients died in the peri-operative period, which is a mortality of 2.6%. They were excluded from analysis. Only one of these patients had late potentials. He died of low output syndrome. Two of the remaining four patients died of sepsis and two of low output syndrome.

VENTRICULAR ARRHYTHMIA IN THE PERI-OPERATIVE PERIOD (TABLE 5)

Nine (19%) of the 48 patients with late potentials before bypass surgery had haemodynamically relevant

Table 4 Individual parameters of the signal-averaged ECG before and after CABG in seven patients with newly acquired late potentials postoperatively

Patient number	QRS (ms)		RMS (μ V)		LAS (ms)	
	Before	After	Before	After	Before	After
1	107	120	41	19	30	49
2	107	119	25	10	27	47
3	109	112	22	18	36	43
4	112	119	40	17	32	58
5	120	125	21	21	32	55
6	98	125	63	13	32	59
7	114	133	64	20	33	52
Mean \pm SD	110 \pm 7	122 \pm 7	39 \pm 19	17 \pm 4	32 \pm 3	52 \pm 6
P	0.02		0.05		0.001	

CABG=coronary artery bypass grafting, LAS=low amplitude signals, RMS=root mean square voltage.

ventricular arrhythmias in the peri-operative phase, such as frequent premature ventricular beats associated with non-sustained ventricular tachycardias in eight patients and persistent ventricular bigeminus in one patient, which had to be treated with intravenous antiarrhythmic agents (lidocaine or amiodarone). Six of these patients had a history of inferior or posterior myocardial infarction. Another two late potential-positive patients with non-sustained ventricular tachycardias were shown to have a peri-operative myocardial infarction. In contrast, only three (2%) of the 140 patients without late potentials before revascularization had to be treated for non-sustained ventricular tachycardia ($P < 0.001$). One of them had a history of inferior myocardial infarction. A fourth late potential-negative patient showed non-sustained ventricular tachycardia during peri-operative myocardial infarction. There was no difference between the arrhythmias in patients with and without peri-operative myocardial infarction.

EVENTS AT LONG-TERM FOLLOW-UP (TABLE 5)

The mean follow-up was 29 ± 3 months. One patient left the district and could not be followed. No patient died during this period. There were no serious ventricular arrhythmias during exercise testing. In patients who remained late potential-negative there were no events after coronary revascularization. In two (5%) patients, who remained late potential-positive and who had already been treated peri-operatively with intra-

venous lidocaine because of ventricular arrhythmia, arrhythmic events reoccurred within 6 months of bypass surgery. Four months after coronary revascularization the first patient suffered several cardiac syncope and on Holter recordings several episodes of dizziness correlated with ventricular tachycardias. He objected to antiarrhythmic therapy and his follow-up showed non-sustained asymptomatic ventricular tachycardias. The second patient had a cardiac syncope 5 months after bypass surgery. He was monitored in the intensive care unit and intravenous lidocaine was administered, again because of ventricular tachycardias. He remained event-free on amiodarone. Both patients had a history of pre-operative inferior and posterior myocardial infarction and an occluded right coronary artery. There were too few patients with arrhythmic events in the long-term follow-up to allow meaningful statistical comparison.

Discussion

PREVIOUS STUDIES

Based on prospective studies, 14–29% of post-infarction patients with late potentials will experience sustained ventricular tachycardias within the first year^[9,28] and 4–40% will die suddenly^[9,28]. Gomes *et al.*^[29] showed that the signal-averaged ECG was the most powerful of different variables to predict ventricular tachycardia and sudden death after myocardial infarction.

Early successful reperfusion with thrombolytic therapy or coronary angioplasty of an infarct-related artery in acute myocardial infarction was associated with a reduction in late potentials, ventricular arrhythmias and mortality^[19–22,30–32]. The limited data on the effect of late successful reperfusion on the signal-averaged ECG with coronary angioplasty or coronary revascularization has shown that approximately two-thirds of the patients remained late potential-positive and the other third lost their positivity^[25,26,33]. The effect of coronary revascularization on ventricular

Table 5 Pre-operative findings of signal-averaged ECG and arrhythmic events peri-operative and during long-term follow-up in 188 patients

Late potentials pre-operative	Number	Arrhythmic events	
		Peri-operative	Follow-up
Negative	140	3	0
Positive	48	9	2

arrhythmias has remained controversial. Some reports have described no effect^[34-36], while others revealed a beneficial effect^[37,38]. Manolis *et al.*^[39] evidenced less inducible ventricular tachycardias after coronary revascularization. Rasmussen *et al.*^[40] showed a favourable follow-up of patients with coronary bypass surgery in exercise-induced ventricular tachycardia. Positive observations on the effect of bypass surgery to reduce sudden death have been made by several investigators^[41-44].

PRE-OPERATIVE FINDINGS

Using the previous described definition 26% of our patients with chronic coronary heart disease had late potentials before coronary bypass grafting. The prevalence corresponds well with the data found in the other studies^[1-3,7-15], especially when we consider the differences in study population and the diverging definitions of an abnormal signal-averaged ECG.

SHORT-TERM EFFECT OF CORONARY ARTERY BYPASS GRAFTING ON LATE POTENTIALS AND VENTRICULAR ARRHYTHMIAS

In the present study, late potentials disappeared after coronary artery bypass grafting in 33% of the patients with late potentials before surgery, which is comparable to 18%–36% in the available data^[25,26,33]. Previous studies showed that early patency of the infarct-related artery is the main independent predictor of late potentials^[16-20,45], but the exact mechanism of late reperfusion of occluded arteries on the signal-averaged ECG remains unclear. Late potentials originate from a zone of electrically abnormal ventricular myocardium in an area of previous myocardial infarction and are related to the degree of slow conduction^[1-6,9,46-48]. There is some evidence that even late reperfusion improves the function of viable myocardium that is present within the infarct zone^[49,50], which might influence the substrate for ventricular reentry. In seven (5%) patients without late potentials before coronary artery bypass grafting, late potentials were evident for the first time. In two of these patients a new myocardial infarction was documented, which may explain the appearance of new late potentials. The remaining five patients showed advanced coronary artery disease; a myocardial infarction might have occurred unnoticed.

There was a strikingly higher percentage of peri-operative ventricular arrhythmias (19%) in patients with late potentials than in patients without late potentials (2%), while the long-term follow-up showed a low occurrence of symptomatic ventricular arrhythmias. This suggests that the increase in peri-operative ventricular arrhythmias is probably associated with temporary changes in the arrhythmogenic milieu which may trigger the arrhythmogenic substrate. The initiation of ventricular arrhythmias by triggering events is favoured by the bypass operation through additional factors, such as increased sympathetic nerve activity, acute withdrawal

of beta-blockers, myocardial ischaemia, hypoxemia, acidosis, electrolyte dysbalance and hypothermia.

LONG-TERM FOLLOW-UP AFTER CORONARY ARTERY BYPASS GRAFTING

In the current study there was a low complication rate due to ventricular arrhythmia after bypass surgery for the whole population (1%) and the few events only occurred in patients with positive late potentials. In two patients with positive late potentials after aortocoronary bypass grafting, there was a documented arrhythmic event within the first half year of follow-up. Both patients had a syncope during follow-up and episodes of dizziness correlated to ventricular tachycardias on Holter-recordings as well as a history of pre-operative non-anterior myocardial infarction with an occluded right coronary artery. Their follow-up had been event-free for more than 2 years. Kuchar *et al.*^[51] and Gang *et al.*^[52] revealed that in patients with syncope the signal-averaged ECG is a sensitive and specific non-invasive screening test for detecting serious ventricular arrhythmias, especially in patients with coronary heart disease.

Results of multivariate analysis in patients with myocardial infarction have indicated that risk stratification based on late potentials is independent of more traditional determinants of risk that include left ventricular ejection fraction or the presence and complexity of ventricular ectopy^[10-14]. However, the influence of coronary artery bypass grafting on the risk of ventricular arrhythmias, based on late potentials, has not been subject to intensive investigation. Only Borbola *et al.*^[25] and Lacroix *et al.*^[26] followed patients with signal-averaged ECG recorded before and after coronary artery bypass grafting. They found that after coronary revascularization late potential-positive patients did not show a higher complication rate due to ventricular arrhythmias than late potential-negative patients.

LIMITATIONS OF THE STUDY

(1) A possible limitation of the study is the varied medication used before and after coronary bypass grafting. Before revascularization almost all patients were on beta-blockers, calcium channel blockers, nitrates and platelet inhibitors, whereas after bypass grafting most patients had only platelet inhibitors. From earlier studies we know that heart rate alone, which was significantly higher after revascularization, does not affect the parameters of signal-averaged ECG^[53-55]. Preliminary data on the effect of beta-blockers showed no significant change to the parameters of signal-averaged ECG^[56]. (2) Patients who were included in this study probably have a lower risk profile because none had known severe ventricular arrhythmias before coronary bypass surgery.

CLINICAL IMPLICATIONS

Peri-operative ventricular arrhythmias appear particularly in patients with positive late potentials. These

patients should be monitored more intensely in the peri-operative period to avoid unfavourable additional factors which might trigger the arrhythmogenic substrate. During long-term follow-up there was only a low probability of developing symptomatic ventricular arrhythmias in patients with or without late potentials.

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