Significance of perfusion of the infarct related coronary artery for susceptibility to ventricular tachyarrhythmias in patients with previous myocardial infarction

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Abstract

***Objective*—To study the significance of perfusion of the infarct related coronary artery for susceptibility to ventricular tachyarrhythmias in patients with a remote myocardial infarction.**

***Setting*—Tertiary referral cardiac centre.**

***Methods*—Angiographic filling of the infarct related artery was assessed in a consecutive series of 85 patients with different susceptibilities to ventricular tachyarrhythmias after previous (> 3 months) Q wave myocardial infarction: 30 patients had a history of cardiac arrest (n = 16) or sustained ventricular tachycardia (n = 14), and sustained ventricular tachyarrhythmia was inducible in these by programmed electrical stimulation (arrhythmia group); 47 patients had no clinical arrhythmic events and no inducible ventricular tachyarrhythmias during programmed ventricular stimulation (control group). Eight patients without a history of any arrhythmic events were inducible into ventricular tachycardia.**

***Results*—The patients in the arrhythmia group were older (63 (SD 8) years) than the control patients (59 (6) years, $P < 0.05$), and had larger left ventricular volumes in cineangiography ($P < 0.01$), but ejection fraction, severity of left ventricular wall motion abnormalities, previous thrombolytic therapy, and time from previous infarction did not differ between the groups. Patients with susceptibility to ventricular tachyarrhythmias more often had a totally occluded infarct related artery on angiography (77%) than patients without arrhythmia susceptibility (21%) ($P < 0.001$), and complete collateral filling of the infarct artery in cases without complete anterograde filling was less common in the arrhythmia group than in the control group ($P < 0.001$). Patients without a history of malignant arrhythmia but with inducible ventricular tachyarrhythmia also had no or poor perfusion of the infarct artery more often than the patients without inducible arrhythmia ($P < 0.001$). Logistic multiple regression showed that no or poor anterograde or collateral filling of the infarct related artery was the most powerful predictor of susceptibility to ventricular tachyarrhythmias ($P < 0.001$). Left ventricular size and function were not independently related to arrhythmic susceptibility.**

***Conclusions*—No or poor angiographic filling of the infarct related artery is closely associated with susceptibility to ventricular tachyarrhythmias late after acute myocardial infarction, suggesting that perfusion of the infarct artery will modify favourably the electrophysiological substrate of the infarct scar independently of the myocardial salvage achieved by early reperfusion.**

(*Heart* 1996;75:17–22)

Keywords: arrhythmia; reperfusion; angiography; myocardial infarction

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Accepted for publication 17 July 1995

Ventricular tachyarrhythmia is the most common mechanism of arrhythmic death in survivors of acute myocardial infarction,[1] since a chronic infarct scar can create a substrate for reentrant tachyarrhythmias,[2] which can be triggered by various functional factors.[3 4]

Thrombolytic trials in acute myocardial infarction have suggested that an open infarct related artery can stabilise the arrhythmic substrate,[5–9] and recent research has suggested that the incidence of sudden cardiac death is lower in patients with an open infarct related artery than in those with an occluded infarct artery.[10–13] Thrombolytic treatment is associated with smaller infarct and ventricular size, which are important determinants of susceptibility to ventricular tachyarrhythmias,[2] and it has therefore been uncertain whether the electrical substrate is specifically modified by an open infarct related artery or whether reduced arrhythmic susceptibility is merely a result of salvage of the ischaemic myocardium caused by early thrombolysis. The present investigation was designed to test the hypothesis that an open artery stabilises the arrhythmic substrate in the presence of an old infarct scar, by comparing angiographic filling of the infarct related coronary artery in patients with different susceptibilities to ventricular tachyarrhythmias after previous myocardial infarction.

Methods

PATIENTS

The subjects were 85 patients with a history of previous Q wave myocardial infarction (> 3 months after acute infarction). The ventricular tachyarrhythmia group consisted

of 30 consecutive patients (26 men, four women) examined between January 1991 and December 1993 who had experienced documented cardiac arrest (n = 16) or sustained ventricular tachycardia (n = 14) and in whom sustained ventricular tachyarrhythmia was inducible by programmed electrical stimulation.

Fifty five patients without a history of any ventricular tachyarrhythmic event were selected from among a consecutive series of patients with a previous Q wave myocardial infarction (at least three months earlier) referred for angiographic examination on account of angina pectoris (n = 37) or for prognostic evaluation (n = 18). Patients with unstable angina pectoris were excluded from this consecutive patient group. After informed consent, all these patients were examined by programmed electrical stimulation. Forty seven of them had no inducible non-sustained or sustained ventricular tachycardia during the electrophysiological testing (control group), and eight had inducible non-sustained (n = 3) or sustained ventricular tachycardia (n = 5). The clinical data on the patients are summarised in table 1. All of them gave their informed consent to the examinations, and the protocol was approved by the ethics committee.

ELECTROPHYSIOLOGICAL AND ANGIOGRAPHIC EXAMINATIONS

The electrophysiological testing included programmed ventricular stimulation using up to three extrastimuli and two basic drive cycle lengths (600 and 400 ms) from the right ventricular apex and outflow tract. Ventricular tachycardia was defined as sustained when its duration was > 30 s or if defibrillation was required for its termination, and as non-sustained if it lasted more than five beats but < 30 s. Left heart catheterisation was performed by the Judkins technique. Left ventricular cineangiograms were recorded in the 45° right anterior oblique projection.

Table 1 Clinical data. Values are means (SD) or n (%)

	VT+ group (n = 30)	*VT− group (n = 47)*	*VT± group (n = 8)*
Age (years)	63 (7)*	59 (7)	60 (4)
Sex (females/males)	4/26	2/45	4/4
History of CHF	4 (13%)	6 (13%)	2 (25%)
Presence of AP	23 (77%)	44 (94%)	8 (100%)
Functional class			
1–2	16 (53%)	21 (45%)	2 (25%)
3–4	14 (47%)	26 (55%)	6 (75%)
Previous MI			
anterior	13 (43%)	21 (45%)	4 (50%)
inferior	13 (43%)	20 (43%)	3 (38%)
anterior+inferior	4 (14%)	6 (12%)	1 (12%)
Time from previous MI (months)	40 (41)	36 (40)	27 (26)
Previous thrombolytic treatment	10 (33%)	16 (34%)	3 (38%)
Number of Q waves in 12-lead ECG	2·4 (2·0)	2·2 (1·3)	2·5 (0·8)
Cardiac medication			
digitalis	11 (37%)	19 (40%)	0
diuretic	10 (33%)	20 (43%)	3 (38%)
β blocker	15 (50%)	35 (74%)	7 (87%)
ACE inhibitor	3 (10%)	8 (17%)	0

VT, ventricular tachyarrhythmia; CHF, congestive heart failure; AP, angina pectoris; MI, myocardial infarction; ECG, electrocardiogram; ACE, angiotensin converting enzyme.
*P < 0·05 between VT+ and VT− groups.

ANGIOGRAPHIC ANALYSES

Left ventricular volumes and ejection fractions were calculated by the biplane area-length method. Coronary artery disease in arteries other than the infarct related artery was defined as > 50% narrowing of the luminal diameter of the proximal or middle portion of a major epicardial vessel or its major branches.

An infarct related artery was defined as a major artery supplying the area with most severe angiographic wall motion abnormality associated with corresponding Q waves in the electrocardiogram. The anterograde flow in the infarct related artery was graded in accordance with the criteria described by the Thrombolysis in Myocardial Infarction investigators.[14] Each patient was classified as having either (1) no anterograde perfusion of the infarct related artery, (2) minimal anterograde perfusion, (3) partial perfusion, or (4) complete anterograde perfusion. The extent of perfusion of the infarct related artery by collateral vessels in angiography was scored as follows[15]: (1) no collateral vessels seen; (2) some filling of the collateral channels of side branches; (3) well formed collateral vessels partially reaching the epicardial segment with delayed filling of the infarct related artery; and (4) abundant collateral vessels seen filled the infarct artery rapidly and completely. The overall angiographic filling of the infarct related artery was defined as (1) no or poor filling, if there was no or minimal anterograde perfusion (grades 1 or 2) without collateral filling of the infarct artery (grades 1 or 2); (2) partial filling, if there was partial anterograde perfusion (grade 3) associated with collateral grades 1–3, or minimal anterograde perfusion associated with collateral grade 3; and (3) complete filling if there was either complete anterograde or complete collateral filling of the infarct related artery (grade 4).

The left ventricle was divided into five segments in the biplane ventricular angiograms, and each segment was coded for wall motion as normal (1 point), hypokinetic (2 points), akinetic (3 points), or dyskinetic (4 points).[16] The sum of the points for each segment was used as a scoring system for left ventricular contractility as follows: 5 or 6 points, normal or mild contraction abnormality; 7–9 points, moderate contraction abnormality; 10 or > 10 points, severe contraction abnormality.

The coronary angiograms and left ventricular cineangiograms were reviewed by three experienced observers who did not know the arrhythmia data on the patients. In cases with discrepancy in interpreting the angiographic grade of infarct related artery filling, collateral filling, or wall motion abnormality, the angiograms were reviewed by a fourth observer and the final result was defined when there was agreement between at least three observers.

STATISTICS

The data are reported as means (SD). The data for the groups were compared using the χ^2 test or Fisher's exact test for categorical variables, and by analysis of variance followed

by Student's *t* test or the Mann Whitney U test, as appropriate, for continuous variables. Forward stepwise logistic multiple regression analysis was used to define the independent significance of the various parameters for predicting susceptibility to ventricular tachyarrhythmia (SPSS for Windows, release 6·0, 1994). The standard definitions for sensitivity, specificity and predictive accuracy of angiographic filling of the infarct related artery for predicting the inducibility of ventricular tachyarrhythmia were used. A P value < 0·05 was considered significant in all the analyses.

Results

The clinical data summarised in table 1 show the patients with susceptibility to ventricular tachyarrhythmias (arrhythmia group) to be somewhat older than those without arrhythmic susceptibility (control group). No other group differences were observed in the clinical variables. The number of Q waves in the electrocardiogram, time since myocardial infarction, and the proportion of patients treated with thrombolytic therapy were similar between the groups.

ELECTROPHYSIOLOGICAL DATA

Sustained ventricular tachycardias were inducible with two extrastimuli in 13 patients and with three extrastimuli in 17 patients of the arrhythmia group. Two tachycardias were induced from the right ventricular outflow tract and 28 from the right ventricular apex. In eight patients without clinical history of ventricular tachyarrhythmias, two ventricular tachycardias became inducible with two extrastimuli and six with three extrastimuli from the right ventricular apex. Two of the sustained tachycardias degenerated into ventricular fibrillation and required defibrillation for termination, and three sustained ventricular tachycardias were terminated by rapid ventricular pacing. No complications occurred during the electrophysiological testing.

Table 2 Angiographic data. Values are means (SD) or n (%)

	VT+ group (n= 30)	*VT− group (n = 47)*	*VT± group (n = 8)*
Ejection fraction (%)	41±12	46±10	45±8
LVEDVI (ml/m²)	104±28‡	84±27	107±30
LVESVI (ml/m²)	63±25‡	46±20	58±13
motion score			
mild abnormality	6 (20%)	20 (43%)	3 (37%)
moderate abnormality	18 (60%)	18 (38%)	1 (13%)
severe abnormality	6 (20%)	9 (19%)	4 (50%)
Infarct related artery			
LAD	17 (57%)	21 (45%)	4 (50%)
LCX	5 (17%)	5 (10%)	1 (12%)
RCA	8 (26%)	21 (45%)	3 (38%)
Severity of CAD			
1-vessel disease	6 (20%)	3 (6%)	1 (12%)
2-vessel disease	14 (47%)	18 (38%)	3 (38%)
3-vessel disease	10 (33%)	26 (55%)	4 (50%)
Anterograde filling of IRA			
no filling	23 (77%)†	10 (21%)	6 (75%)
minimal filling	4 (13%)	12 (26%)	1 (12·5%)
partial filling	3 (10%)	9 (19%)	1 (12·5%)
complete filling	0	16 (34%))	0
Collateral filling of IRA			
no filling	8 (27%)	14 (35%)	0
minimal filling	6 (20%)	1 (2%)	1 (12·5%)
partial filling	11 (37%)	15 (32%)	6 (75%)
complete filling	5 (17%)*	17 (36%)	1 (12·5%)
Filling of IRA			
poor filling	22 (73%)†	3 (6%)	6 (75%)
partial filling	3 (10%)	11 (24%)	1 (12·5%)
complete filling	5 (17%)†	33 (70%)	1 (12·5%)

VT, ventricular tachyarrhythmia; LVEDVI, left ventricular end diastolic volume; LVESVI, left ventricular end systolic volume; LAD, left anterior descending coronary artery; LCX, left circumflex artery; RCA, right coronary artery; CAD, coronary artery disease; IRA, infarct related coronary artery.
†P < 0·001 between VT+ and VT− group; *P < 0·05 between VT+ group and VT− group; P < 0·001 between VT+ group and VT− group; ‡P < 0·05 between VT+ group and VT− group.

ANGIOGRAPHIC DATA

Left ventricular end systolic and end diastolic volumes were greater in the arrhythmia group than in the control group (P < 0·01 for both). The mean ejection fraction was also lower in the arrhythmia group, but the difference did not reach statistical significance, partly because of type II statistical error caused by the relatively small sample size. The severity of wall motion abnormalities did not differ significantly between the groups (table 2).

The patients with susceptibility to ventricular tachyarrhythmias more often had an angiographic finding of grade 1 anterograde filling of the infarct related artery (no filling) than the control group (table 2), and complete collateral filling was found less often in the arrhythmia group than in the control group, especially in patients without complete anterograde filling (6% of the patients in the arrhythmia group *v* 55% in the control group, P < 0·001). Only five out of the 30 patients with susceptibility to ventricular tachyarrhythmia (17%) had complete anterograde or retrograde filling of the infarct related artery, whereas 33 out of the 47 patients without arrhythmic susceptibility (70%) had complete infarct artery perfusion (P < 0·001 between the groups). On the other hand, only three out of the 47 patients in the control group (6%) had no or poor infarct artery perfusion compared to 22 out of the 30 patients in the arrhythmia group (73%).

Patients with inducible ventricular tachyarrhythmia but without any history of arrhythmia had greater left ventricular volumes than those in the control group and more often had an angiographic finding of no or poor perfusion of the infarct related artery (table 2).

PREDICTION OF SUSCEPTIBILITY TO VENTRICULAR TACHYARRHYTHMIA FROM PERFUSION OF THE INFARCT RELATED ARTERY

Perfusion of the infarct related artery was the most powerful predictor of susceptibility to ventricular tachyarrhythmia in multiple regression analysis (table 3). Age was also independently associated with the arrhythmic susceptibility, but left ventricular volumes or function had no independent association with it.

Grade 1 perfusion (no or poor perfusion) of the infarct artery had a sensitivity of 73%, a specificity of 95%, and a predictive value of 90% with respect to inducibility of ventricular tachyarrhythmia during programmed electrical stimulation. In the whole population, the patients with grade 1 perfusion of infarct artery had higher left ventricular end diastolic and end systolic volumes (P < 0·05 for both) than those with partial or complete perfusion (grades 2 and 3), but the ejection fraction and left ventricular wall motion score were not associated with perfusion of infarct related

Table 3 Forward multiple logistic regression analysis of susceptibility to ventricular tachyarrhythmias after previous myocardial infarction

	Coefficient	*Significance*
Variables in the equation		
Angiographic filling of IRA	−2·02	P < 0·0001
Age	0·13	P < 0·05
Variables not in the equation	Score:	
Ejection fraction	2·72	P = 0·10
LVESVI	3·75	P = 0·06
LVEDVI	2·48	P = 0·11
Wall motion score	0·14	P = 0·7

IRA, infarct related coronary artery; LVESVI, left ventricular end systolic volume; LVEDVI, left ventricular end diastolic volume.

artery. The proportion of patients treated with thrombolytic therapy did not differ between the patients with grade 1 perfusion and those with grade 2 or 3 perfusion.

Discussion

These results show that poor angiographic filling of the infarct related artery is closely associated with susceptibility to life threatening arrhythmias, independent of the location and size of the previous myocardial infarction. Earlier research has also shown that patency of the infarct related artery may have favourable electrophysiological consequences soon after acute infarction.[5-9] Sager *et al* documented a significant decrease in the incidence of inducible ventricular tachycardia and sudden cardiac death in a small series of patients with a patent vessel despite a similar degree of left ventricular dysfunction.[17] Reduced inducibility of ventricular tachycardia in patients with thrombolytic reperfusion of the infarct artery has also been noted by Kerschott *et al*[8] and Bourke *et al*,[9] but their data did not distinguish between reperfusion and left ventricular dysfunction with respect to arrhythmic susceptibility. An absence of late potentials has also been observed in signal averaged electrocardiograms of patients in whom thrombolysis has successfully restored the patency of the infarct artery.[5-7]

Previous investigations into the relationship of arrhythmic susceptibility to patency of infarct related artery were performed in the early postinfarction phase in patients randomised to either thrombolytic treatment or placebo.[5-9] These studies have not discriminated whether the risk of arrhythmia is dependent on the degree of myocardial salvage achieved by early thrombolysis or whether an open infarct related artery has contributed independently to electrical stability. Another problem of interpreting the results of previous studies is that the susceptibility to ventricular tachyarrhythmias is different during the time course after acute myocardial infarction, and there is some lack of specificity in electrophysiological testing and signal averaged electrocardiograms performed early after acute myocardial infarction relative to those performed later.[18-20] The present data confirm the previous findings and indicate that the infarct artery perfusion is a significant determinant of susceptibility to ventricular tachyarrhythmias in patients with a remote myocardial infarction, independent of the degree of left ventricular dysfunction.

An interesting finding was that not only the patency of the infarct related artery but also its collateral filling was related to arrhythmic propensity, suggesting that both anterograde perfusion and development of a collateral circulation can modify the electrophysiological substrate of the infarct scar independent of the myocardial salvage achieved by thrombolysis. Only one third of the patients had received thrombolytic therapy and there were no differences in the proportion of patients with and without previous thrombolytic treatment between the groups with different susceptibility to ventricular tachyarrhythmias. However, more than half of the patients had angiographic evidence of a patent infarct related artery. It is known that spontaneous reperfusion occurs in about 50% of the patients after acute myocardial infarction,[21] and the development of a collateral flow to the infarct area is common[22]; both these factors seem to be important in preventing the susceptibility to life threatening arrhythmias.

Many clinical, non-invasive and invasive variables have been used to predict the inducibility of ventricular tachyarrhythmias and the spontaneous occurrence of life threatening arrhythmias.[23-27] History of arrhythmias, functional class, signal averaged electrocardiogram, various Holter parameters, baroreflex sensitivity, ejection fraction, and left ventricular wall motion abnormalities have been shown to predict the risk of future arrhythmias, but none of these variables used alone has shown a high specificity in predicting the susceptibility to ventricular tachyarrhythmias.[23-27] The present findings show that an angiographic pattern of no or poor filling of the infarct related artery had a high specificity for predicting inducibility in this patient population. If these data can be confirmed in a larger, unselected patient population with remote myocardial infarction, angiographic findings could perhaps be used for more precise risk stratification among patients in terms of susceptibility to arrhythmias.

POSSIBLE BENEFICIAL EFFECT OF INFARCT ARTERY PERFUSION ON ELECTRICAL STABILITY OF THE INFARCT SCAR

The border zone between the edge of the infarct and the normal myocardium that results from healing of the infarct has been proposed as a critical determinant of reentrant ventricular arrhythmias.[1 28] Inhomogeneous electrical activation and slow conduction have been identified in these border zones,[29] and it is possible that both early and late perfusion of the infarct related artery may modify the electrophysiological properties of the peri-infarct areas by providing the ischaemic cells in the border zone with oxygen and nutrients.

An occluded infarct related artery after myocardial infarction has been shown to result in dilatation and remodelling of the left ventricle,[30-32] and increased ventricular volume has been shown to increase the inducibility of ven-

tricular arrhythmias in animal models, a phenomenon which has been attributed to inhomogeneity in refractoriness produced by ventricular dilatation.[33] Clinical observations also point to an increased risk of sudden cardiac death in postinfarction patients with dilated ventricles.[34] Poor perfusion of the infarct related artery was similarly associated here with larger ventricular volumes and somewhat lower ejection fraction, suggesting that ventricular dilatation may partly explain why poor infarct artery perfusion increases the risk of ventricular tachyarrhythmias. In addition to preventing left ventricular dilatation, late perfusion of infarct artery can affect the shape and stiffness of the infarct, diastolic filling, and remodelling, all of which may modify the electrophysiological properties of the infarcted ventricles.[10]

LIMITATIONS

The patient population examined here was not a consecutive series of all survivors of myocardial infarction but was selected from among patients with Q wave infarction referred for invasive examinations on account of a history of arrhythmic events or angina pectoris, or for prognostic evaluation. The data cannot therefore be directly applied to all patients with a remote myocardial infarction. However, a subgroup without a history of arrhythmic events but with inducible ventricular tachycardia also differed in terms of perfusion of the infarct related artery from those without inducible ventricular tachyarrhythmia, suggesting that perfusion of the infarct area is specifically associated with risk of arrhythmias even in patients who have not experienced a clinical event of life threatening arrhythmia. In order to generalise the present findings, a larger consecutive series of patients with previous myocardial infarction might be needed, but the ethical justification for performing moderately aggressive electrophysiological testing on patients without clinical indications for programmed electrical stimulation limits a larger study of this type.[35]

The low incidence of thrombolytic or angiotensin converting enzyme treatment at the time of acute myocardial infarction in the present patient population may have some relevance for the results of this study. It is possible that the present method of treatment after acute myocardial infarction reduces the proportion of the patients with occluded infarct related artery and dilatation of left ventricles, and thereby reduces the susceptibility to ventricular tachyarrhythmias. However, many patients still present with the total occlusion of the infarct related artery, and the present findings support the concept that these patients have increased risk for ventricular tachyarrhythmias.

IMPLICATIONS

There is evidence that late perfusion of the infarct related artery reduces mortality,[10-13] perhaps because of a reduction in the occurrence of sudden cardiac death,[17] which is the predominant mechanism involved in cardiac mortality after myocardial infarction.[1] The present results support the theory that an open infarct related coronary artery reduces the risk of life threatening arrhythmias even late after acute infarction. Surgical revascularisation reduces the inducibility of ventricular tachyarrhythmias in only a proportion of patients,[36] however; it may therefore be desirable for reperfusion of the infarct artery to occur early, not necessarily with any myocardial salvage, in order to avoid the development of an arrhythmic substrate for ventricular tachyarrhythmias.

This research was supported by grants from the Finnish Foundation for Cardiovascular Research, Helsinki, and the Medical Council of the Academy of Finland, Helsinki, Finland.

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