ORIGINAL ARTICLES

Intravenous streptokinase for acute myocardial infarction reduces the occurrence of ventricular late potentials

Eng-Wooi Chew, Patricia Morton, J Gerard Murtagh, Michael E Scott, D Barry O'Keeffe

Abstract

The occurrence of ventricular late potentials in survivors of acute myocardial infarction treated with intravenous streptokinase was compared with that in a conservatively treated group and the relation between ventricular late potentials and patency of the infarct related artery was examined. Of 115 patients admitted with a first infarct, 55 were treated with intravenous streptokinase (streptokinase group) and 60 were treated conservatively (non-streptokinase group). A signal averaged electrocardiogram was recorded in all patients and coronary angiography was performed in 45 (81.8%) of the streptokinase group and in 21 (35%) of the non-streptokinase group. At a 40 Hz filter setting ventricular late potentials were significantly less common in patients treated with streptokinase (9 (16.4%) of 55) than in those who were not (26 (43.3%) of 60). A total of 66 patients underwent angiography. Of the 26 who had closed infarct-related arteries, 17 had ventricular late potentials at a 40 Hz filter setting (sensitivity 65.4%, specificity 95%) and 38 of the 40 patients with a patent infarct-related artery did not have ventricular late potentials (sensitivity 80.9%, specificity 89.5%).

Patients with acute myocardial infarction treated with intravenous streptokinase were significantly less likely to have ventricular late potentials than conservatively treated patients and the absence of ventricular late potentials at 40 Hz filter setting was a good non-invasive predictor that the infarct-related artery was patent.

Over the past 10 years, several groups using special non-invasive processing techniques have detected low amplitude, high frequency potentials late in the QRS complex and in the ST segment on the surface electrocardiogram.¹⁻³ In experimental and clinical studies these correlated well temporally with fractionated electrograms recorded from damaged cardiac tissue.⁴⁻⁶ Ventricular late potentials identify patients at risk of ventricular tachycardia after acute myocardial infarction and who are thus at increased risk of sudden cardiac death.⁷⁻⁹

Thrombolytic treatment reduces mortality after acute myocardial infarction¹⁰⁻¹² by limiting infarct size. Because thrombolysis also reduces the risk of ventricular arrhythmias we examined the proposition that ventricular late potentials were less common in patients with acute myocardial infarction who were treated with intravenous streptokinase than in those who were conservatively treated.

Some investigators have suggested that abrupt electrocardiographic repolarisation changes after thrombolytic treatment are predictive of (but with a low sensitivity (67%)) an open infarct-related artery.¹³ The second object of our study, therefore, was to examine the relation between ventricular late potentials and patency of the infarct-related artery.

Patients and methods

PATIENTS

A total of 123 consecutive patients admitted to our cardiac unit with a first acute myocardial infarction were enrolled into the study. In all patients the diagnosis of acute myocardial infarction was confirmed clinically, electrocardiographically, and by serum concentrations of total creatine kinase (CK) and creatine kinase MB. Eight patients whose electrocardiogram showed bundle branch block were excluded from the study.

Of the remaining 115 patients, 55 satisfied our criteria for treatment with intravenous streptokinase (the thrombolytic agent used in our cardiac unit), which was given as an intravenous infusion of 1.5 million IU over 20 minutes within six hours of onset of chest pain (streptokinase group). These patients had clear electrocardiographic evidence of evolving myocardial infarction and no contraindication to thrombolytic treatment. All these patients were subsequently managed identically with oral aspirin and intravenous heparin for five days. The rest were treated conservatively (non-streptokinase group). Patients in this group were admitted after the six hour "limit" or had a contraindication to thrombolysis.

SIGNAL AVERAGING TECHNIQUE

A signal averaged electrocardiogram was recorded at the end of the first week after acute myocardial infarction on a commercial Marquette-15 (Marquette Electronics, Mil-

Cardiac Unit,
Belfast City Hospital,
Belfast
E-W Chew
P Morton
J G Murtagh
M E Scott
D B O'Keeffe

Correspondence to
Dr Eng-Wooi Chew,
Cardiac Unit, Belfast City
Hospital, Lisburn Road,
Belfast BT9 7AB.

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waukee) machine that has a high resolution electrocardiogram option. The method is similar to that described by Simson³ and Denes *et al.*⁸ Other investigators have shown that the end of the first week is the best time to perform the recording.^{7,9,14} They noted a steady increase in the occurrence of late potentials throughout the hospital stay and that once late potentials had appeared they tended to remain. Late potentials recorded within the first 24 hours may not reflect future risk because the anatomical and electrophysiological alterations of ischaemic myocardium in this phase are unstable.

We used bipolar orthogonal X, Y, Z leads; and signals from 500 beats were amplified, digitised, averaged, and then filtered with bidirectional high band pass filters at 25 Hz and 40 Hz. We chose to analyse the results at two filter frequencies because there is controversy about which is the best band pass filter frequency for recording ventricular late potentials. Previous work from Denes *et al*, Verzone, *et al*, and Gomes *et al* suggests that the 40 Hz filter gives a better compromise between sensitivity and specificity.^{8,15,16}

Signals from the three leads were combined into a vector magnitude $V = \sqrt{(x^2 + y^2 + z^2)}$. Automated measurements were provided for the duration of the composite electrogram—that is “filtered QRS duration” (normal < 120 ms), the root-mean-square voltage of the last 40 ms of the filtered QRS complex (normal > 20 μ V), and the duration of the terminal low amplitude signals less than 40 μ V (normal < 38 ms). Ventricular late potentials were considered to be present if two or three of the above values were abnormal.

CORONARY ANGIOGRAPHY

Coronary angiography was performed in 45 (81.8%) of the streptokinase group and 21 (35%) of the non-streptokinase group. The decision to carry out coronary angiography was made by the attending cardiologist who was unaware of the results of the signal-averaged electrocardiogram. Often they were patients who had angina or inducible ischaemia on treadmill testing after infarction. The infarct-related artery was identified on the basis of electrocardiographic abnormalities in the acute phase. The degree of residual stenosis was graded according to the criteria of the TIMI (thrombolysis in myocardial infarction) trial investigators.¹⁷ Vessels in TIMI grades 2 or 3 were classified as “open”.

STATISTICAL ANALYSIS

We used the χ^2 test with Yates's correction for dichotomous variables and the two sample *t* test for continuous variables. We performed regression analysis using the presence or absence of ventricular late potentials as the dependent variable and the characteristics listed in the table as the independent variables. The level of statistical significance was set at 0.05 or 1 in 20.

Results

Figure 1 shows the signal averaged electrocardiogram of a patient treated with intravenous

streptokinase and fig 2 shows the signal averaged electrocardiogram of a patient treated by conventional means. The table shows the characteristics of patients in the two groups.

When analysed singly, three variables seemed to influence the presence of late potentials. These were the administration of streptokinase, patency of the infarct-related artery, and age. As the table shows, patients treated with intravenous streptokinase for acute myocardial infarction were less likely to have ventricular late potentials at the 40 Hz filter setting (9 of 55 (16.4%) in the streptokinase group compared with 26 of 60 (43.3%) in the

Figure 1 Signal averaged electrocardiogram from a patient with acute myocardial infarction treated with intravenous streptokinase. Shaded area represents last 40 ms of filtered QRS complex. Filtered QRS duration = 92 ms (normal); root-mean-square voltage of last 40 ms = 90 μ V (normal); duration of terminal signals less than 40 μ V = 16 ms (normal).

Figure 2 Signal averaged electrocardiogram from a patient with acute myocardial infarction treated conservatively. Shaded area represents last 40 ms of filtered QRS complex. Filtered QRS duration = 132 ms (abnormal); root-mean-square voltage of last 40 ms = 13 μ V (abnormal); duration of terminal signals less than 40 μ V = 40 ms (abnormal).

Characteristics (mean (SD)) of patients in streptokinase and non-streptokinase groups

Variable	Streptokinase (n = 55)	Non-streptokinase (n = 60)	p value
Age (mean (SD))	56.8 (12.4)	61.6 (10.5)	0.048
Number of men (%)	46 (84%)	41 (68%)	NS
Peak CK (U/l) (mean (SD))	1301 (1049)	1335 (806)	NS
Site of MI:			
Anterior	30 (54.5%)	39 (65%)	NS
Inferior	22 (40%)	18 (30%)	NS
Others	3 (5.5%)	3 (5%)	NS
Number with VLP at: 40 Hz	9 (16.4%)	26 (43.3%)	0.003
25 Hz	2 (3.6%)	6 (10%)	NS
Patent artery (%)	32 of 45 (71%)	8 of 21 (38%)	NS

CK, creatine kinase; MI, myocardial infarction; VLP, ventricular late potentials.

non-streptokinase group (p = 0.003)). The patency of the infarct-related artery also significantly influenced the presence of ventricular late potentials. Of the 26 patients with a closed infarct-related artery, 17 (65.4%) had late potentials compared with two (5%) of 40 patients with a patent infarct-related artery (p < 0.0001). Patients with ventricular late potentials also tended to be older (p = 0.048). The occurrence of ventricular late potentials did not seem to be influenced by the other variables such as sex, peak creatine kinase, and infarct site.

The occurrence of ventricular late potentials at 25 Hz in the two groups was not significantly different (although there was a trend towards a lower incidence in the streptokinase group—two (3.6%) of 55 in the streptokinase group compared with six (10%) of 60 in the non-streptokinase group (p = 0.33). At 25 Hz the patency of the infarct-related artery was not significantly associated with the occurrence of ventricular late potentials—three (11.5%) of 26 occluded arteries and two (5%) of 40 open arteries had late potentials (p = 0.57).

Of 66 patients who underwent angiography, 26 had closed infarct-related arteries. Of these, 17 had ventricular late potentials at 40 Hz (sensitivity 65.4%, specificity 95%) but only three had ventricular late potentials at 25 Hz (sensitivity 11.5%, specificity 95%). In 38 of the 40 patients with a patent infarct-related artery, there were no ventricular late potentials at a 40 Hz filter setting (sensitivity 80.9%, specificity 89.5%). At 25 Hz the corresponding sensitivity was 62.3% and the specificity was 60%.

When we used multifactorial analysis to examine the relation between the presence of late potentials and the other variables, the best predictor was the patency of the infarct-related artery followed by the administration of intravenous streptokinase and an inferior site of the infarct. The effect of the patency of the infarct-related artery was independent of that of streptokinase. The influence of age, apparent initially, became unimportant when these variables were taken into account.

Discussion

Most clinical studies of ventricular late potentials have examined their ability to identify patients at risk of ventricular arrhythmias after acute myocardial infarction. We showed that ventricular late potentials were less common in

patients with acute myocardial infarction treated with intravenous streptokinase than in those treated conservatively. Our study also showed that the absence of ventricular late potentials after acute myocardial infarction is a good, non-invasive predictor of the patency of the infarct-related artery. This may be valuable information because thrombolytic treatment is now widely used and the absence of ventricular late potentials may help to identify those patients who will benefit most from coronary arteriography and perhaps further invasive treatment.

Our study showed that the patency of the infarct-related artery exerts an independent effect on the presence of late potentials. Our data, in accord with those of others,^{9 18 19} do not suggest that the presence or absence of ventricular late potentials correlate with left ventricular ejection fraction. Successful thrombolytic treatment results in an electrically more stable myocardium²⁰⁻²² and Braunwald has suggested that a patent, blood-filled, infarct-related artery and vascular bed may provide a scaffolding that limits expansion of the necrotic myocardium.²³ We further propose that the lower incidence of ventricular late potentials in patients treated with intravenous streptokinase may be related to the reduction in mortality in this group compared with a conservatively treated group.

Gang *et al* found that the occurrence of ventricular late potentials in acute myocardial infarction was significantly less after successful thrombolytic treatment with tissue plasminogen activator (5%) than after conservative treatment (23%).¹⁹ Of the 157 patients studied by Eldar *et al*, 65 were treated with thrombolysis (24 with streptokinase and 41 with tissue plasminogen activator).²⁴ The frequency of late potentials in this group was 14%, compared with 22.5% in a conservatively treated group. Our results accord with these findings but we found that a higher percentage of patients in both groups (16.4% and 43.3% respectively) had ventricular late potentials. This may be explained by the different filter frequencies used and different definition of ventricular late potentials. The thrombolytic agent administered may be relevant because initial reports from the TIMI trial (phase 1) suggest that tissue plasminogen activator results in higher patency rates of the infarct-related artery than streptokinase.¹⁷ Our figure of 43.3% for late potentials in the conservatively treated group of patients is similar to that found by other investigators.^{25 26}

The problems remain of standardising the technique of surface signal averaging and of defining ventricular late potentials in order to compare results between centres. In most studies, the choice of filter setting has been arbitrary. Gomes *et al* showed that a 25 Hz filter setting gave a low sensitivity but the best specificity, whereas a 80 Hz filter provided best sensitivity but low specificity.¹⁶ A 40 Hz filter provides a sensitivity and a specificity intermediate between those at 25 Hz and 80 Hz. Furthermore, Denes *et al* showed that the 40 Hz filter gives better reproducibility of

measurements.⁸ For these reasons we used the 40 Hz filter in our analysis. Ventricular late potentials detected at 40 Hz filter setting were a more sensitive and specific method of predicting the patency of the infarct-related artery than the results at 25 Hz. We think that the 25 Hz filter underestimates the occurrence of ventricular late potentials. Gang *et al* used the 25 Hz filter in their study and found that patients with closed infarct-related arteries had a higher (but not statistically significant) incidence of ventricular late potentials than those with open arteries.¹⁹ Our study showed that the 40 Hz filter was better in predicting patency of the infarct-related artery. We are awaiting the results of a long term follow up in these patients, to compare the results with the 25 Hz filter with those with the 40 Hz filter. Preliminary results suggest that the 40 Hz filter may give the result that best predicts long term clinical outcome.

Our results showed a relation between late potentials and inferior infarcts. This was also noted by Kuchar *et al*⁷ but not by McGuire *et al*¹⁴ or Gang *et al*.¹⁹ The reason for this discrepancy may be related to the size of the study population and different definitions of late potentials used. It may be that because the inferior wall of the heart is one of the later parts to depolarise, low amplitude signals that originate there are more likely to become apparent.²⁷

This was not a randomised, placebo controlled study because early reperfusion is known to improve survival after acute myocardial infarction and we thought that a randomised trial would be unethical. Patients in the conventionally treated group presented after the six hour "limit" or had contraindications to treatment with streptokinase. Apart from this difference they are a group (table) that is comparable in age, sex, and site of infarct with the streptokinase group.

From this study, we conclude that intravenous streptokinase administered for acute myocardial infarction and the presence of an open infarct-related artery exert independent effects on the presence of late potentials. The absence of ventricular late potentials after acute myocardial infarction seems to be a good non-invasive predictor of the patency of the infarct-related artery. Detection of ventricular late potentials after thrombolytic treatment therefore is an additional non-invasive, simple means of predicting patency of the infarct-related artery and may help in selecting which patients require detailed invasive investigations.

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